

APASL 2024 Kyoto

The 33rd Annual Meeting the Asian Pacific Association for the Study of the Liver



Summary / Abstracts

Plenary Sessions

Young Investigator Workshop

Oral Free Papers / Poster Free Papers

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APASL
2024 Kyoto
-The Center of Hepatology

The 33rd Annual Meeting of
the Asian Pacific Association for the Study of the Liver



Chronic Hepatitis B Virus Infection

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Chronic hepatitis B virus (HBV) infection is a serious global health issue. Chronic HBV infection might lead to liver cirrhosis, hepatic decompensation, and hepatocellular carcinoma (HCC). Thus, the goal of treatment for chronic hepatitis B (CHB) is to improve survival and quality of life by preventing transmission, disease progression and HCC. Chronic HBV infection comprises four phases defined as immune tolerant phase, immune clearance phase (HBeAg-positive chronic hepatitis), inactive carrier phase, and reactivation phase (HBeAg-negative chronic hepatitis). Treating the patients with immune active chronic hepatitis B (both HBeAg-positive and negative) is recommended to decrease the risk of liver-related complications. Pegylated interferon and nucleos(t)ide analogues (NAs, including entecavir, tenofovir disoproxil fumarate and tenofovir alafenamide) are the preferred first line agents for CHB treatment. NAs are selected because of convenience, good tolerability, safety, high potency and minimal to no risk of resistance. However, NAs have no direct action on cccDNA, and long-term NAs therapy is required to maintain HBV suppression in HBeAg negative patients. There are several concerns, e.g. financial burden, adherence and willingness, for indefinite long-term NAs therapy. In addition, increase rates of HBsAg loss are observed after cessation of NAs treatment in HBeAg-negative patients. Finite NAs therapy in selected HBeAg-negative CHB becomes a recommendation. Discontinuation of NAs treatment in patients with cirrhosis is not recommended. For HBeAg-positive adults without cirrhosis who seroconvert to anti-HBe on NAs therapy, discontinue therapy after a period of consolidation treatment is suggested. NAs may be discontinued in HBeAg-negative patients without cirrhosis, who achieve long-term virological suppression. Decompensation and severe ALT flare may occur after cessation of NAs, especially in patients with liver cirrhosis. Close monitoring is warranted for the HBeAg-negative patients stopping NAs treatment. If hepatic decompensation developed, re-starting NA therapy should be given immediately. For patients with virological or clinical relapse, treatment indications for naïve CHB patients may be applied.

Epidemiology, Genotype Distribution, Prognosis and Treatment of Viral Hepatitis C and HCC in Mongolia

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In Mongolia, morbidity from liver cancer is 68.1 per 100 000 population, which is eight times higher than the global average. This is directly associated to the higher rate of morbidity of chronic hepatitis caused by HBV, HCV and HDV. Prevalence of HCV in Mongolia was high. The predominant genotype of HCV among general populations in Mongolia is 1b.

Between 2015 to 2019, 23 (0.5%) and 5,005 patients (99.5%) with genotype 1a and 1b HCV, respectively, were treated with a fixed-dose tablet containing 90 mg ledipasvir and 400 mg sofosbuvir for 12 weeks, and 81 patients (1.6%) with previous experience of interferon (IFN)-based treatment received additional 1,000 mg ribavirin. Most patients

(n=5,008; 99.6%) achieved ETR and SVR12 without virologic relapse. Patients with genotype 1a showed low rates of ETR and SVR12 in only 16 patients (69.6%). There was no significant difference in SVR12 rate between patients regardless of IFN experience (n=81; 1.6%), cirrhosis (n=1,151; 22.9%), HCV RNA >6×10⁶ IU/mL (n=866; 17.2%), or liver stiffness >9.6 kPa (n=1,721; 34.2%) (100.0%, 99.3%, 99.4%, and 99.4%, respectively). The most common AEs were headache (n=472; 9.4%), fatigue (n=306; 6.2%), abdominal discomfort (n=295; 5.9%), and skin rash (n=141; 2.8%).

Most patients had advanced HCC – 88 (45.1%) in stage III and 57 (29.2%) in stage IV. The risk factors associated with HCC development were history of acute hepatitis, chronic hepatitis, and the presence of liver cirrhosis. The most common etiology for HCC in our patients was HCV infection which is 46%, HBV infection -34%, co-infection B and C -14% and others which is 6.0%. According to the results of our study over 65% of patients had tumor size more than 5 cm. Single tumors was only found in 15%. The mean AFP level was 196 ng/ml. In 18.5% distant metastasis existed. Regarding tumor stage, there was no patient with stage 1. In addition, the most patients with HCC were diagnosed in advanced stage. In Mongolia HCC treatment modality is very limited. According to the results of our study, 14% of patients received surgical resection, and their survival was the best. 11.8% of patients received RFA and their survival was 11 months. About 55% of patients received TACE and their median survival was 17 months. The prognosis for patients with supportive care was very poor with a median survival of 5 months. Regarding cause of death, about 50% patients died of HCC progression and the others died of liver failure or GI bleeding. Regarding early detection of HCC in Mongolia, AFP is available in all hospitals except inter-soum and soum's hospitals.

HBV “Viral Elimination” in Asia-Pacific region-current status and challenges

Dr. George Lau

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In 2016, the World Health Assembly approved the World Health Organisation (WHO) Global Health Sector Strategy on HBV, with a goal of “elimination of HBV as a major health threat” by 2030, targeting a 90% reduction in new HBV infection and a 65% reduction in mortality due to HBV. However, recent data suggested deviation from these goals, with over 890,000 new HBV cases in 2019-2020 and a global HBV-related mortality rate exhibiting minimal change (annualized rate of change < 0.4% between 2015-2019). Two-thirds of the these HBV-related mortality occurred in Southeast Asia and Western Pacific regions. In real-world clinical practice, two major barriers hinder a significant reduction of disease burden due to HBV infection: lack of awareness (among public and policy makers) and under-treatment of those with a risk of developing complications related to HBV infection, with effective anti-viral therapy, namely high resistant barrier nucleos(t)ide analogues (NAs including tenofovir, entecavir, tenofovir alafenamide) or pegylated interferon or both, which have all been demonstrated to enable a drastic reduction in HBV-related morbidity and mortality with long-term follow-up. With the recent availability of low-cost rapid diagnostic tests for HBsAg with negligible false-negative results, which can be utilised for large-scale screening and diagnosis of HBV infection, only an estimated 15-30% of chronic HBV infection have been diagnosed. Hence, to further decrease global viral

and disease burden, it is of paramount importance to identify all patients with CHB infection and timely initiate effective antiviral therapy for them. In the meantime, increase public awareness to access hepatitis B test is essential. On the other hand, in accordance with the existing regional treatment guidelines, it was estimated that less than one-tenth of those CHB patients indicated for treatment received anti-HBV therapy. There is also a recent call to expand treatment criteria beyond existing guidelines to extend therapeutic benefits to more patients with CHB infection. Indeed, a cost-effectiveness analysis of expanded antiviral treatment for CHB infection, based on decision-tree Markov state-transition model, suggested expanding treatment to HBV-infected patients with ALT thresholds of 30 U/L and 19 U/L for males and females, with 80% treatment coverage for HBsAg-positive individuals aged 18–80 years. This expanded antiviral treatment with a modified ALT threshold, coupled with lower generic drug costs and a revised medical insurance subsidization policy, particularly in HBV-endemic countries like China, could reduce HBV-related complications and deaths to support the global target of 65% reduction in HBV-related death. With the recent surge of prevalence and emerging association of Metabolic dysfunction-associated fatty liver disease as a comorbidity factor for CHB patients, future treatment guidelines likely need to be modified accordingly. In future, we believe that a collaborative effort of all authoritative liver societies to revise and expand HBV treatment guidelines considering the drastically reduced cost of anti-viral therapy, along with universal screening for HBsAg positivity, will contribute to a meaningful reduction in disease burden due to HBV infection in Asia-Pacific region.

Post-Graduate Program (Hepatitis B)
PG1-4

Role of HBcrAg in Predicting Long-Term Outcomes for Patients with Chronic Hepatitis B

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Hepatitis B virus (HBV) infection poses a significant global health challenge. Individuals with chronic hepatitis B (CHB) infection face diverse adverse events, including the risk of severe hepatitis flare, potentially leading to acute-on-chronic liver failure (ACLF), cirrhosis, hepatocellular carcinoma (HCC), and other complications. Conversely, some individuals experience favorable outcomes, such as spontaneous clearance of hepatitis B surface antigen (HBsAg) or hepatitis B e antigen (HBeAg). Serum hepatitis B core-related antigen (HBcrAg) quantification is a valuable biomarker for covalently closed circular DNA (cccDNA) levels, providing crucial information for clinical management.

In the early phase of chronic HBV infection, HBeAg-positive patients are considered "immune-tolerant" due to active viral replication without significant liver damage. Our recent findings revealed that elevated HBcrAg levels (>100 million U/mL) correlate with a reduced likelihood of spontaneous HBeAg seroclearance in HBeAg-positive patients, particularly in the immune-tolerant subgroup. This insight aids physicians in deciding whether to initiate antiviral treatment or await spontaneous HBeAg seroclearance.

Functional cure, indicated by HBsAg seroclearance, is associated with lower HBcrAg levels, especially in those with HBsAg levels >1000 IU/mL. The reduction of HBcrAg precedes the decline of HBsAg, suggesting the need to target cccDNA for successful treatment. A delayed decline in HBsAg levels suggests additional agents targeting HBsAg derived from integrated HBV DNA may be necessary for achieving functional cure.

Current guidelines recommend antiviral therapy for immune-active CHB patients but not for inactive CHB patients due to their different HCC risk. However, more than half of the HBeAg-negative CHB patients find themselves in the "grey zone" (GZ). We developed a novel GZ-HCC risk score (EXPLORE) considering age, sex, platelet count, ALT levels, and hepatitis B core-related antigen. This is the first risk prediction model demonstrating that an HBcrAg-based HCC score outperforms HBV DNA-based HCC scores in HBeAg-negative GZ patients. The model has been validated in an independent Japanese cohort. Furthermore, we propose a GZ-HCC score of 8 to categorize GZ patients into high- and low-risk groups, aligning their HCC risk levels with those of immune-active CHB and inactive CHB patients, respectively.

In conclusion, HBcrAg is a valuable biomarker for predicting clinical outcomes, and its integration with various viral markers enables customized therapeutic approaches for CHB patients with distinct risk profiles.

Post-Graduate Program (Hepatitis C)
PG2-4

Dr. Yoshiyuki Ueno

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Viral hepatitis infection has been a great threat to human health globally. Although remarkable breakthrough has been made in the past several decades for prevention and treatment of viral hepatitis, still this infectious disease is increasing its risk. Actually, 905,700 people were diagnosed with and 830,200 people died from liver cancer in 2020. Moreover, the number of new cases and deaths from liver cancer could rise by >55% by 2040. Thus, HCC remains to be global risk for next decades. Of course, viral infection is a major cause of HCC in many countries. With this line, WHO aimed to set the global elimination of viral hepatitis by 2030. WHO's global hepatitis strategy, endorsed by all WHO Member States, aims to reduce new hepatitis infections by 90% and deaths by 65% between 2016 and 2030. However, except for few countries or regions, our actual achievement has been behind the track. In this session, our current status and future strategy will be summarized to keep our mission on the planned goals.

Post-Graduate Program (MAFLD)
PG3-2

Etiology and Usefulness of MAFLD in the Asian-Pacific region

Dr. Takumi Kawaguchi

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MAFLD is a major public health problem in the Asian-Pacific region. Excess energy intake and a sedentary lifestyle are major causes of hepatic steatosis. These unhealthy lifestyles also cause the accumulation of lipids in visceral adipose tissue, leading to adipose tissue inflammation. Adipose tissue produces proinflammatory cytokines including TNF- α , IL-1 β , and IL-6, which flow into the liver through the hepatic artery. These adipose tissue-derived factors promote the development of MAFLD.

Besides visceral adipose tissue, the gut is a major etiological organ of MAFLD. Dietary factors including excess fructose intake induce dysbiosis, leading to low-grade intestinal inflammation and an impairment of gut barrier function called leaky gut. A leaky gut facilitates the translocation of lipopolysaccharides and microbial metabolites to the

liver through the portal vein. This influx causes the production of pro-inflammatory cytokines and attracts immune cells through activation of Kupffer and liver sinusoidal endothelial cells in the liver.

Risk factors for MAFLD in Asians are like those in Westerners. In addition, a feature of Asians is non-obese MAFLD. In non-obese Asian individuals, possible etiologies of MAFLD are the following: visceral obesity, dysbiosis, sarcopenia, hypothyroidism, hypopituitarism, and hyperuricemia. Furthermore, another possible etiology is genetic predisposition including polymorphism in PNPLA3 (patatin-like phospholipase domain-containing protein 3), TM6SF2 (transmembrane 6 superfamily member 2), GSKR (glucokinase regulator), MBOAT7 (membrane bound O-acyltransferase domain containing 7), and HSD17B13 (hydroxysteroid 17-beta dehydrogenase-13).

MAFLD is a disease concept that actively encloses high-risk patients through inclusion criteria. In fact, various Asian-Pacific clinical studies demonstrated that MAFLD identifies patients with significant hepatic fibrosis and at high risk of HCC. In addition, MAFLD has been reported to identify patients at higher risk for atherosclerotic cardiovascular disease better than NAFLD. The superiority of MAFLD over NAFLD seems to be due to the presence of metabolic dysfunction rather than moderate alcohol consumption. Furthermore, MAFLD is more associated with various extrahepatic diseases including reflux esophagitis, colorectal adenoma, the recurrence of esophageal squamous cell carcinoma, chronic obstructive pulmonary disease (COPD), and psoriasis rather than NAFLD. Thus, MAFLD is useful to identify patients at risk of both liver-related events and extra-hepatic events.

In this session, I will introduce the etiology of Asian-Pacific MAFLD according to the APASL guidelines. I also mention the impact of MAFLD on the identification of patients at risk of hepatic events as well as extra-hepatic events in the Asia-Pacific region.

Post-Graduate Program (Fibrosis/Chirrosis)
PG4-3

Hepatocellular Carcinoma Risk prediction score (GES) in chronic hepatitis C patients with compensated advanced chronic liver disease (cACLD) after achieving SVR

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Introduction: We designed and validated a scoring system known as the General Evaluation Score (GES) for Hepatocellular Carcinoma (HCC) risk stratification. Our objective was to assess the efficacy of this score within a substantial prospective cohort comprising individuals with cured hepatitis C, with compensated advanced chronic liver disease, and achieved a sustained virological response following direct-acting antivirals.

Methods: This prospective study, conducted at the Egyptian Liver Research Institute and Hospital between January 2018 and October 2019, enrolled 463 consecutive patients with advanced fibrosis ($\geq F3$) who attained sustained virological response. Prior to antiviral therapy initiation, all patients underwent abdominal ultrasound and multislice computed tomography for HCC surveillance. Subsequent follow-ups occurred every 6 months post-treatment, utilizing ultrasonography, alpha-fetoprotein, and additional multislice computed tomography every 12 months.

Results: Of the 463 patients included, 197 (42.5%), 114 (24.6%), and 152 (32.8%) were stratified as having low, intermediate, and high-risk scores, respectively, before treatment initiation. The incidence rate of HCC was 2.61 per 100 person-years (95% CI = 1.73–3.80), with 25 cases developing HCC during the follow-up period. The respective HCC incidence rates in the low, intermediate, and high-risk groups

were 0.97% (95% CI: 0.31–2.34), 1.68% (95% CI: 0.53–4.05), and 5.57% (95% CI: 3.35–8.74). A significant positive correlation was observed between higher risk scores and increased HCC incidence ($p < 0.001$). Harrell's c-statistic for this model was 0.728.

Conclusion: This prospective study underscores the predictive capability of GES in anticipating HCC occurrence and effectively categorizing patients into low, intermediate, and high-risk groups

Post-Graduate Program (ACLF)
PG5-1

Prognostic predictors in patients with Acute-on-chronic liver failure (ACLF)

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Acute-on-chronic liver failure is a severe form of acutely decompensated cirrhosis with high mortality rate, 28-day mortality rate $>20\%$. Prognostic predictors can guide the optimal strategies for managing individual patient properly. The number of organ system failure is associated with severity and mortality of ACLF-patients. The ACLF grades, based on the number of organ failures (liver, kidney, brain, coagulation circulation, respiration) enable to categorize patients with a range of 28-day and 3-month mortality risks. There are currently a few scoring system for predicting mortality rate in patients with ACLF. The CLIF-C ACLF score was developed by combining the CLIF-C score with age and white cell count for predicting 28-day and 90-day mortality better than those of the MELD score, MELD-Na score and Child-Pugh score. The AARC score was developed for patients with ACLF diagnosed using the APASL for predicting short-term mortality. The NACSELD only based on failure of 4 organ systems (brain, kidney, circulation, reparation) defined by the physicians' response to the problem. The NACSELD may underestimates the risk of death in patients with ACLF. The COSHH Score was developed for patients with HBV-related ACLF. The newly proposed models and nomograms for predicting prognosis in patients with ACLF have shown some improvement on the CLIF-C ACLF score, but they require further validation. Inflammation severity has been shown as the most important predictor of ACLF.

Post-Graduate Program (PH)
PG6-1

Emerging non-invasive methods for evaluation of cirrhotic portal hypertension

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Clinically significant portal hypertension (CSPH) is associated with symptomatic gastro-oesophageal varices (GOV), the development of hyperdynamic circulation, and patients with compensated advanced chronic liver disease at risk of clinical decompensation. Hepatic venous pressure gradient (HVPG) measurement and esophagogastroduodenoscopy are the gold standard methods for assessing CSPH (HVPG ≥ 10 mm Hg) and GOV, respectively. However, they are limited by their invasiveness in clinical practice. In recently years, there are a lot of new technologies focuses on the development of non-invasive approaches to the diagnosis and serial monitoring of portal hypertension.

Imaging techniques used for portal hypertension include ultrasound, computed tomography (CT) and magnetic resonance (MR). Elastography techniques measure liver and spleen stiffness by quantifying the velocity of an induced shear wave, including transient elastography, point-shear wave elastography, and two-dimension shear wave elastography; and MR elastography. Liver stiffness measurement has been proved to be sufficiently accurate to identify CSPH and safe to screen high-risk varices combined with platelet count in clinical practice. Laboratory tests and serum markers need to be interpreted critically because some of their individual components can be affected by a variety of comorbidities. Artificial intelligence (AI) has made great strides in the field of medicine. Information of CT and MR imaging can be integrated and applied to detection of cirrhosis and portal hypertension by AI.

In summary, a wide spectrum of novel non-invasive tests have emerged and represent a major advantage in the assessment of portal hypertension. However, there are still many challenges to integrating non-invasive screening methods into clinical practice, and more data are needed to establish consensus on standard practice and implementation.

Post-Graduate Program (PH)

PG6-2

Current Endoscopic Gastrointestinal Interventions and Management

Dr. Hideki Kobara

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Endoscopic submucosal dissection (ESD) has been an attractive minimally invasive surgery during the past two decades. Currently, pure Endoscopic Full-Thickness Resection (EFTR) is focused as next-advanced technique. Meanwhile, post-ESD or EFTR defects, and iatrogenic perforation must be carefully managed to prevent and rescue adverse events.

Here, I would like to introduce these current gastrointestinal interventions and our ongoing research.

Post-Graduate Program (PH)

PG6-3

Role of HVPG in the management of portal hypertension

Dr. Hitoshi Maruyama

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Cirrhosis is the most advanced stage of chronic liver disease. It is accompanied with a risk of developing serious complications, including variceal bleeding, ascites, icterus, and hepatic encephalopathy. These events limit quality of life and long-term outcomes, therefore, patients with these conditions need to be properly monitored.

Hepatic venous catheterization is a safe and an established technique which enables measurement of hepatic venous pressure gradient (HVPG) by either jugular approach or femoral approach. Hepatic venogram is useful to demonstrate the typical appearance of cirrhosis and non-cirrhotic portal hypertension, which could be obtained by using either iodinated contrast material or carbon dioxide.

Portal hypertension is the principal pathophysiology of cirrhosis, and a HVPG is a representative marker for the severity of the condition. A HVPG of 10 to 12 mmHg is the threshold level for the development of esophageal varices, ascites, and the occurrence of variceal bleeding,

and a HVPG higher than 16 mmHg suggests an increased risk of death. Moreover, a HVPG higher than 20 mmHg is the best independent prognostic marker for acute variceal bleeding, and thus indicates the presence of much more severe status. In addition, a HVPG is an effective marker to offer the treatment direction of TIPS for variceal re-bleeding in cirrhosis, and to predict the prognosis after TIPS placement for refractory ascites. Thus, hepatic venous catheterization has a wide range of role in the management of portal hypertension. This presentation overviews recent studies regarding HVPG and summarizes the evidences.

Post-Graduate Program (HCC)

PG7-1

Discovery of therapeutic and biomarker for HCC through basic and translational research of tumor microenvironment

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HCC is a dismal disease with the third highest mortality rate among all cancer types. Its molecular entity is very complex and further clarification of its heterogeneous nature is required for prognostic improvement. With the progress of next-generation sequencers over the past decade, the genomic and epigenomic abnormalities in HCC have been well-documented with a large number of cases, and the whole picture has become clear. On the other hand, the recent development of innovative technologies such as single-cell analysis and spatial omics analysis has begun to open a new era in cancer research. In the tumor microenvironment, not only cancer cells but also various immune cells and stromal cells exist, and these form a complex network that leads to cancer formation and progression. In recent years, various drugs have been developed and made available for HCC. Importantly most of them, such as angiogenesis inhibitors and immune checkpoint inhibitors, target the tumor microenvironment rather than the cancer cells themselves, indicating the importance of understanding cancer as such an ecosystem to truly overcome cancer. One of the treatment goals of HCC therapy is personalized therapy with a variety of molecular-targeted drugs and their efficacy biomarkers. Recent advancement in HCC pharmacotherapy allows us to utilize 8 different therapeutic regimens but the efficacy of each drug is still limited. Further research efforts to discover novel drug targets and develop efficacy biomarkers are desired in the HCC field. In this presentation, I would like to share recent knowledge of the HCC tumor microenvironment and show our latest discoveries of therapeutics and biomarkers for HCC through basic and translational research. I also would like to discuss with the audience the future perspective of HCC research.

Post-Graduate Program (HCC)

PG7-3

Post-Graduate Program (HCC): Treatment guidelines update

Dr. Yi-Hsiang Huang

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HCC is prevalent in Asia Pacific countries and its incidence is expected to rise in the next decade. The treatment of HCC depends on tumor stage and liver function reserve. BCLC is widely adopted as the

staging system for HCC in most countries. The goal of treatment for early stage HCC is to curative resection or ablation for the tumor and avoid recurrence as possible. Several strategies have been established to be able to decrease the risk of recurrence, such as antiviral treatment for underlying chronic hepatitis B or C, and most recently adjuvant immunotherapy for high risk patients. For intermediate stage HCC, TACE is no longer the only option. Due to the heterogenous nature of BCLC B tumors, the outcome of TACE is varied depends on tumor burden and radiologic patterns. Due to the advance of systemic therapy, some patients with intermediate stage HCC have the potential to be curative conversion by atezolizumab/bevacizumab followed by locoregional treatment or surgical resection. TACE combined with immunotherapy, lenvatinib or sorafenib may also prolong the survival for BCLC B HCC. For advanced stage HCC, systemic therapy is the key treatment. Immunotherapy either by atezolizumab/bevacizumab, or tremelimumab/durvalumab is the standard of care if there is no contraindication for immunotherapy. Although there is no phase 3 clinical trial to support the optimal treatment as 2L after immunotherapy, different mechanism of action and tolerability of adverse event are the key considerations for the choice of subsequent treatment

Post-Graduate Program (HCC)
PG8-4

Post-Graduate Program (HCC) Systemic therapy

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Systemic therapy has become mainstream for hepatocellular carcinoma (HCC), with the development of molecular-targeted agents, such as sorafenib and lenvatinib as first-line treatment and regorafenib, ramucirumab and cabozantinib as second-line treatment, and of immunotherapies, such as atezolizumab plus bevacizumab, durvalumab plus tremelimumab and durvalumab monotherapy. In Japan, a total of 8 regimens are now available for unresectable HCC. Combined immunotherapies are firstly selected if patients have no contraindication for immunotherapies, such as autoimmune diseases. Molecular-targeted therapy is selected when immunotherapy is not indicated or proves ineffective. And, it is necessary to select the appropriate treatment taking into consideration the patients' clinical condition, expected treatment efficacy, and adverse effects of the treatment.

The indications for systemic therapy are currently expanding, although advanced-stage HCC was a good indication for systemic therapy previously. Systemic therapy is indicated for intermediate-stage HCC that is transarterial chemoembolization (TACE) refractory or TACE unsuitable. When performing non-curative-intent TACE, combination therapy of TACE and systemic therapy is expected to be a future treatment strategy, because phase III trial of TACE with durvalumab plus bevacizumab vs. TACE with durvalumab plus placebo vs. TACE with placebo (EMERALD-1) was press-released to meet the primary endpoint for progression-free survival. Furthermore, the indication might be expanding for early-stage HCC, because perioperative adjuvant therapy of atezolizumab plus bevacizumab demonstrated significantly better recurrent-free survival after curative surgical treatment or ablation (IMbrave050). Therefore, systemic therapy is now available for any stage of the disease. While previously, local therapies used to be the main treatment strategy for HCC, systemic therapy in combination with local therapies is being actively tried at present. Systemic therapy is currently promising topics of development of novel treatments for HCC.

APASL Targets for this Century
TC1-2

APASL clinical practice guideline on systemic therapy for hepatocellular carcinoma- 2024

Dr. George Lau

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Since the inception of the first Asian-Pacific Association for the study of liver (APASL) hepatocellular carcinoma (HCC) working party in 2007 and the publication of its first guideline published in 2010 and then revised in 2017, major advances in systemic therapy for hepatocellular carcinoma (HCC) have been made. Despite the availability of effective HCC surveillance and preventive measures, most of the HCC still present at advanced stage as reflected by the high mortality-incidence ratio across Asian-Pacific region. Most of these patients diagnosed with HCC are therefore beyond curative measures such as surgical resection, local ablation or liver transplantation. Even for those patients who are eligible to have curative measures in accordance to various HCC treatment guidelines, recurrence is still a very common clinical problem. The major etiology of the HCC in Asian-Pacific region are chronic hepatitis B and C infection, compounded by the recent rise of metabolic dysfunction-associated fatty liver diseases (MAFLD). In country like China, the incidence of HCC is not rising but account for close to half of the global annual cases. Most if not all are related to chronic hepatitis B infection.

In the recent few years, new targeted therapy and immune-checkpoint inhibitors have been registered as systemic therapy for hepatocellular carcinoma either as first-line or second-line therapy for unresectable or not eligible for locoregional therapy. The gravity of chronic hepatitis B and C as etiology of hepatocellular carcinoma in Asia-Pacific region, is of great relevance as the response to immune-checkpoint inhibitors are much higher, as compared to targeted therapy. Recently, new data is also emerging with the use of systemic therapy to prevent HCC after curative attempt with resection or local ablation therapy. The purpose of this clinical guideline is to provide an up-to-date recommendation based on clinical evidence and experience from regarded key opinion leaders in the field of hepatocellular carcinoma. Three key questions will be addressed, namely (1) which patients with HCC should be considered for systemic therapy? (2) which systemic therapy should be used? and (3) how should a patient planned for systemic therapy be managed and monitored?

APASL Targets for this Century
TC1-4

Looking ahead: MAFLD in the APASL region

Dr. George Jacob

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At its core, APASL's main objective is to advance the science and practice of Hepatology, particularly for patients in the Asia Pacific region. In 2024, the APASL pillars focussed on viral hepatitis elimination, liver cancer, acute on chronic liver failure through AARC, the APASL-ACLF Research Consortium (AARC), and MAFLD, through the APASL-MAIDEN (Metabolic fatty liver Disease consortium; maiden-apasl.com) consortium. While we have made tremendous progress over the past decades through vaccination against hepatitis B, curative treatments for hepatitis C and suppressive treatments for hepatitis B, the frontier that has now received the attention it deserves is MAFLD, projected to be the most common liver disease worldwide, with Asia

at its epicentre. The Asian Pacific region harbours a majority of the world's population, with just two countries, India and China the most populous. The region is witnessing an economic transformation becoming the engine for global growth, but at the same time, being home to a rising global burden of oversight/obesity and type 2 diabetes. These diseases drive a systemic physiological response driven by insulin resistance, which in the liver drives fat deposition (MAFLD) and in pre-disposed individuals, a low grade chronic inflammatory response that leads to hepatic inflammation (steatohepatitis), cirrhosis and its feared complications, liver failure and liver cancer (both hepatocellular and cholangiocarcinoma). However, MAFLD is more than a liver disease and is just one part of systemic metabolic dysfunction, the harbinger of cardio-reno-vascular disease, diabetes and extrahepatic cancer. Managing the consequences of these diseases, a very large proportion of health budgets in Asian Pacific countries will be consumed unless effective policy action and settings are undertaken. While effective pharmacotherapies for weight loss and type 2 diabetes are emerging or are clinically approved, at a population level, they are expensive. Hence, preventive frameworks focussing on food quality, food quantity and physical activity needs to be prioritised. For those with MAFLD, clinical pathways to identify those with significant liver disease, referral pathways to tertiary care and treatment is required. APASL as the peak body for Liver Disease in our region is well placed to lead these initiatives by developing pan-national educational toolkits that can subsequently be individualised to cater to local needs.

HBV Challenges for Elimination of CCC HBV DNA *HBV1-1*

Clinical utility of novel biomarkers for hepatitis B infection

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During the process of viral replication of hepatitis B virus (HBV) from the viral template, the covalently closed circular (ccc) DNA, there are production of viral nucleic acids, namely, HBV DNA and intermediate HBV RNA. Viral translation activities of different genomic regions of HBV also produce several mRNAs which would be transcribed into various viral antigens including HBsAg, HBcAg and HBeAg. Of note, HBsAg can also be generated from integrated HBV DNA. In the past, conventional measurements of serum viral biomarkers in patients with chronic hepatitis B (CHB) mainly include HBsAg, HBeAg and HBV DNA. It has been shown that measuring these conventional biomarkers have clinical significance for the disease monitoring and treatment. For example, serum HBsAg has predictive value for spontaneous and treatment-induced HBsAg seroclearance. However, existing nucleos(t)ide analog (NA) treatment has negligible effects on HBsAg level. Whereas baseline HBsAg levels before initiation of novel treatment predicts antiviral response including HBsAg seroclearance. Recently, a new entity of measuring several viral antigens, collectively named as hepatitis B core-related antigen (HBcrAg) which include HBcAg, HBeAg and p22cr becomes available. It was found that HBcrAg correlated well with cccDNA and other serum and intrahepatic viral markers. HBcrAg profile also relates to the development of CHB complications including hepatocellular carcinoma and cirrhosis, treatment outcome, disease relapse after treatment cessation and chance of HBV reactivation in occult HBV patients receiving immunosuppressive therapy. In addition, a certain proportion of occult HBV patients can be identified by the detectable HBcrAg levels in the blood where both HBsAg and HBV DNA remains undetectable. The detectability rate has been significantly increased by using the second version of the assay. Recently, there is another novel assay development measuring phosphorylated and non-phosphorylated forms of HBcAg in the serum. Clinical usage

of this new assay is being actively explored. HBV RNA is another novel HBV biomarker; its roles are overlapping with HBcrAg in some areas. HBV RNA measurement correlates with disease outcome, treatment response and HBV reactivation. HBV RNA seems to be prominently useful in patients who are on NA treatment. In conclusions, development of novel HBV biomarkers is able to provide additional and essential disease assessment and treatment guidance for CHB disease. Standardization and increased availability of these assays are highly encouraged.

HBV Challenges for Elimination of CCC HBV DNA *HBV1-2*

Identification of host factors that were essentially involved in hepatitis B virus persistence

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Background & aims: Hepatitis B virus (HBV) infection is difficult to cure owing to the persistence of covalently closed circular viral DNA (cccDNA). We performed single-cell transcriptome analysis of newly established HBV-positive and HBV-negative hepatocellular carcinoma cell lines and found host factors that were crucially involved in HBV persistence.

Methods: The cccDNA levels were measured by Southern blotting and real-time detection polymerase chain reaction in various hepatocytes including PXB cells by using an HBV-infected model. HBV capsid was investigated by super-resolution microscopy, proximity ligation assay, and time-lapse analysis. The binding partners of host factors were examined by liquid chromatography-tandem mass spectrometry, immunoblotting, and enzyme-linked immunosorbent assay.

Results: We found that four factors that were crucially involved in HBV persistence. One of the four host factors was dedicator of cytokinesis 11 (DOCK11), known as a guanine nucleotide exchange factor (GEF) for Cdc42. The cccDNA levels were strongly increased by DOCK11 overexpression and repressed by DOCK11 suppression. Interestingly, DOCK11 functionally associated with retrograde trafficking proteins in the trans-Golgi network (TGN), Arf-GAP with GTPase domain, ankyrin repeat, and pleckstrin homology domain-containing protein 2 (AGAP2), and ADP-ribosylation factor 1 (ARF1), together with HBV capsid, to open an alternative retrograde trafficking route for HBV from early endosomes (EEs) to the TGN and then to the endoplasmic reticulum (ER), thereby avoiding lysosomal degradation. Clinically, DOCK11 levels in liver biopsies from patients with chronic hepatitis B were significantly reduced by entecavir treatment, and this reduction correlated with HBV surface antigen levels.

Conclusions: HBV uses a retrograde trafficking route via EEs-TGN-ER for infection that is facilitated by DOCK11 and serves to maintain cccDNA. Therefore, DOCK11 is a potential therapeutic target to prevent persistent HBV infection.

HBV Challenges for Elimination of CCC HBV DNA *HBV1-3*

Analysis of HBsAg and cccDNA reduction by nucleotide analogue and pegylated interferon combination therapy

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Once HBV enters human hepatocytes, its genome is carried into the nucleus where it forms covalently closed circular DNA (cccDNA), similar to a minichromosome. This translocation of the HBV genome into the nucleus makes it difficult for either the host immune response or present antiviral therapies to eliminate the virus. Combined antiviral treatment using pegylated interferon (PEG-IFN) and nucleotide/nucleoside analogues (NAs) are currently used to suppress cccDNA levels in patients with chronic HBV infection. Although add-on therapy and sequential therapy using PEG-IFN have been attempted in chronic hepatitis B patients following long-term NA therapy, it has not been clarified which PEG-IFN therapy is most effective in reducing HBsAg levels. In this study, we investigated the change in HBsAg levels after PEG-IFN therapy (approval number: E-704) and conducted basic research on reduction of cccDNA in liver tissues by NA plus PEG-IFN combination therapy. The subjects included 21 HBeAg-negative chronic hepatitis B patients who had undergone NA therapy for more than one year at our hospital and related facilities. Sequential or add-on therapy using PEG-IFN was performed, and HBsAg levels were measured for up to 5 years after completion of PEG-IFN treatment. Furthermore, we performed add-on therapy on HBV-infected human hepatocyte chimeric mice and examined changes in intrahepatic HBV RNA and cccDNA levels. HBsAg level was reduced by a median of 0.48 LogIU/ml during PEG-IFN therapy. More than 1 Log HBsAg reduction was observed in 9 patients 5 years after the completion of PEG-IFN therapy. Five patients with sequential therapy and 2 patients with add-on therapy achieved HBsAg loss. ALT elevation during PEG-IFN therapy and lower serum IL-8 level at the end of PEG-IFN therapy contributed to HBsAg reduction at 1 year after completion of PEG-IFN therapy ($P=0.038$, $P=0.044$). ALT elevation during PEG-IFN therapy, platelet levels at the start of PEG-IFN therapy, and serum IL-8 levels at the end of PEG-IFN therapy were associated with HBsAg reduction at 5 years after PEG-IFN therapy ($P=0.034$, $P=0.049$, $P=0.041$). To confirm high HBsAg reduction by IFN treatment, we measured intrahepatic HBV markers using HBV-infected chimeric mice with add-on therapy. After add-on therapy, intrahepatic HBV RNA and cccDNA levels had decreased to less than 1/50 and 1/2 of that in untreated mice, respectively. Sequential therapy might be more effective in reducing HBsAg levels than add-on therapy, but add-on therapy has the potential to reduce intrahepatic cccDNA levels.

HBV Novel Detection Methods for HBV Markers
HBV2-1

Rethinking the disease status of chronic hepatitis B: The roles of novel detection methods for HBV markers

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Beyond widely available diagnostic tests used in the management of HBV, that includes quantitative (q) HBV DNA and qHBsAg, novel detection methods for HBV markers are scrutinized for their clinical utility in recent years, aiming to rigorous evaluation of functional cure (undetectable HBsAg and HBV DNA) and to appropriate risk stratification for hepatocellular carcinoma (HCC). Among them, ultrasensitive measurement of HBsAg or HBcrAg by iTACT (Immunoassay for Total Antigen including Complex via preTreatment) technology and specific detection of middle (M)- proteins in HBsAg of genotype C by the antibody against O-glycosylated residue (HBsAgGi) are promising candidates.

iTACT system have been applied to HBsAg or HBcrAg detection, the latter of which is a composite of HBcAg, HBeAg, and p22Cr. iTACT improves the detectability ten times more sensitive than the second-generation (standard) HBsAg and conventional HBcrAg assays, that is, the lower limit of quantification (LLOQ) of HBsAg and HBcrAg assays as 0.0005 IU/mL and 2.1 log U/mL, respectively. Consequently, even after HBsAg seroclearance (SC) in chronic hepatitis B (CHB) patients documented by standard assay, HBsAg and HBcrAg became detected in 36.8 % and 68.9% with iTACT, respectively¹⁾. Though chronological decline in the detectability of HBsAg and HBcrAg by iTACT after SC were also demonstrated, these results raise a number of important issues; the definition of functional cure should be reconsidered firstly, and more importantly, the clinical significance of low-level expression of HBV protein in patients with conventional SC deserves thorough investigation with regard to the persisting HCC risk²⁾ and HBV reactivation.

HBsAgGi measurement system detects HBsAg associated with infectious particles. In a cross-sectional analysis by the recent literature³⁾, low HBsAg (< 3 log IU/ml) and high HBsAgGi (> 3 log ng/ml) was associated with HCC development in genotype C chronic HBV patients. Moreover, HBsAgGi decreased significantly by 48-week NA therapy. Still preliminary, discrimination of infectious virions with M-HBsAg from non-infectious subviral particles is likely advantageous for the accurate evaluation of disease status in CHB.

Implementation of novel detection methods for HBV markers into clinics may not only add a new aspect in disease status, but also revolutionize the strategy of monitoring CHB patient by updating the concept of functional cure.

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HBV Novel Detection Methods for HBV Markers
HBV2-2

Novel biomarkers for the management of chronic hepatitis B

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The hepatitis B core-related antigen (HBcrAg) is a novel HBV serum biomarker that plays an essential role in reflecting intrahepatic covalently closed circular DNA (cccDNA) in chronic hepatitis B (CHB). We describe here the clinical application of highly sensitive HBcrAg and HBsAg assays in CHB patients, with a particular focus on current and novel therapies targeting intrahepatic HBV replication. (1) HBcrAg can be detected in clinical cases where serum HBV DNA is undetectable during anti-HBV therapy such as nucleos(t)ide analogues (NAs). (2) The combination of HBcrAg and HBsAg would be useful for the cessation of NA therapy. (3) Decreased HBcrAg levels have been significantly associated with promising outcomes in CHB patients, reducing the risk of progression or recurrence of hepatocellular carcinoma. (4) Recently, a fully automated, novel highly sensitive HBcrAg assay (iTACT-HBcrAg) has been developed (J Hepatol 2021). The sensitivity of iTACT-HBcrAg (2.1 Log U/mL) was approximately 10-fold greater than that of the conventional G-HBcrAg. The iTACT-HBcrAg as well as iTACT-HBsAg (cut-off value: 0.0005 IU/mL) should be of increased benefit for monitoring anti-HBV therapy in HBeAg-negative patients and early detection of HBV reactivation, as an alternative to HBV DNA. (5) Finally, we introduce a novel compound destabilizing HBV-RNA. In brief, drug screening from 30,000 library compounds using HepG2.2.15 cells and HBV-infected PXB cells was performed to optimize the hits that reduced the amount of

HBsAg in the culture supernatant, especially those with potent anti-HBV activity, to obtain SAG compounds (SAG-comp; IC₅₀=1.4 nM). The SAG-comp, a novel anti-HBV therapeutic agent, is an orally available and well-tolerated drug that potently suppresses HBsAg. It can destabilize HBV-RNA and may induce functional cure in combination therapy with NA. In such anti-HBV therapies aiming for functional cure, monitoring HBcrAg and HBsAg would be useful for determining the therapeutic efficacies of novel anti-HBV drugs targeting HBV-RNA and its related-proteins. In conclusion, HBcrAg and HBsAg, especially when measured by the recently developed iTACT assay, may be the most appropriate surrogate marker, over other HBV biomarkers, for the management of CHB patients.

HBV Novel Detection Methods for HBV Markers *HBV2-3*

HBV RNA – is it ready for clinical use?

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Pregenomic HBV RNA is a new diagnostic biomarker to monitor the disease of chronic hepatitis B. It reflects the transcriptional activity of intrahepatic cccDNA. In untreated patients, the level of HBV RNA correlates well with other HBV viral markers including HBV DNA and HBcrAg. The key clinical usage of HBV RNA is among patients under nucleos(t)ide analog treatment, as HBV DNA is often undetectable in these patients. The presence of HBV RNA indicates residual viral activity, which is associated with an increased risk of hepatocellular carcinoma. The value of HBV RNA to predict virological relapse after stopping nucleos(t)ide analog is controversial, but detectable HBV RNA is found to associate with an increased risk of hepatitis flare. With the development of new therapeutics for chronic hepatitis B, HBV RNA can be a biomarker for target engagement particularly for capsid assembly inhibitors.

HBV Functional Cure of CH-B in Real World *HBV3-1*

Advancing towards the functional cure of HBV

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As a therapeutic goal for the treatment of hepatitis B, the 'clearance of HBs antigen' is currently the goal. However, this achievement is challenging with the nucleoside analogs, which are widely used. Consequently, there is an active pursuit in the development of novel therapeutic agents. At present, the most promising approach is RNAi-based drugs, which can decrease the HBsAg levels. As an alternative approach, we focused on compounds that inhibit the degradation of the host factor Smc5/6 protein, which plays a role in suppressing the transcription of viral RNA from cccDNA. Through a screening of compounds, we identified two compounds that suppress the degradation of Smc5/6 protein complexes and show potential in suppressing the expression of viral RNA and viral proteins. Both compounds are utilized in the treatment of diseases other than HBV, raising expectations for their practical application through so called "drug repositioning". Simultaneously, this inhibition of Smc5/6 protein degradation suggests a potential link to the suppression of HBV-related oncogenesis. This

presentation will provide an overview of these mechanisms and discuss remaining challenges in HBV treatment after achieving a functional cure.

HBV Functional Cure of CH-B in Real World *HBV3-3*

Functional cure of CH-B in Real World

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Evidence from randomized controlled trials (RCT), e.g. OSST, Endeavor and Anchor study, as well as other relevant clinical studies has shown that sequential combination therapy with immunomodulators (e.g. peg-interferon) and NUC in virally-suppressed patients with chronic hepatitis B (CHB) can improve functional cure (HBsAg loss), as compared to NUC continuous monotherapy. Moreover, several strategies can be used to predict functional cure or identify patients likely to benefit from the sequential treatment with immunomodulators (e.g. peg-interferon), including baseline-guided therapy using pretreatment HBsAg level, response-guided therapy using early decline in HBsAg level, and HBVcrue crab model using end-of-therapy HBsAb level and HBcrAg level. We further have conducted two multicenter real-world studies---COST study and OCEAN study in China, aiming to investigate the efficacy and long-term outcome of sequential peg-interferon treatment in patients undergoing long-term NUC treatment who had HBV DNA undetectable and HBsAg level <3000IU/mL. The interim analysis of COST study demonstrated consistent results of the RCT studies. We are currently conducting a nationwide questionnaire survey on the application of functional cure strategies for patients with CHB.

MAFLD 1. Asian MAFLD: Clinical Features *MAFLD1-1*

MAFLD in Patients living with HIV; PLWH

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Metabolic syndrome and metabolic dysfunction-associated fatty liver disease (MAFLD) are emerging problems and play important role in the higher morbidities and mortality in patients living with HIV (PLWH). The high MAFLD burden among PLWH is one of a major concern issue according to the novel MAFLD criteria and it needs to identify those patients at risk for chronic liver disease. Generally, the prevalence of MAFLD varies from 10-36% depended on the criteria of diagnosis and investigating tools¹⁻⁵. Most of them are lean MAFLD with younger age in comparison to those MAFLD with diabetes or obesity. Current antiretroviral treatments for example tenofovir alafenamide fumarate (TAF) and particularly its combination with integrase inhibitors (INSTIs) appear to have the significant consequences on metabolic dysfunction by increasing insulin resistance^{3, 6, 7}. In addition, an unhealthy lifestyle, with a high calories dietary intake especially processed foods, high carbohydrates, saturated fatty acids, high fructose added beverages, as well as less physical inactivity, are key triggers for the progression of fatty liver to steatohepatitis, and

advanced liver fibrosis. Finally, we review the current recommendation of treatment in this special population at risk of MAFLD8-10.

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MAFLD 1. Asian MAFLD: Clinical Features
MAFLD1-2

How to follow up of patient with act Metabolic dysfunction-associated fatty liver disease (MAFLD)

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Metabolic dysfunction-associated fatty liver disease (MAFLD) is the most common cause of chronic liver disease worldwide. MAFLD includes a wide spectrum of liver injury including simple steatosis and non-alcoholic steatohepatitis (NASH) that may lead to serious complications such as liver cirrhosis and liver cancer.

The identification of Nonalcoholic steatohepatitis (NASH) or NAFLD is clinically important because NASH indicates an increased risk for fibrosis progression and the need for aggressive treatment and closer follow-up. Population based study suggests that NAFLD is becoming an important cause of HCC, and these rates are increasing by approximately 10% per year. So we need follow up guideline of patients with NAFLD but there is no accepted consensus on the optimal strategy for monitoring patients with NAFLD and their response to treatment.

According to The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease, patients with NAFLD may need a FibroScan yearly or once every three years. The frequency is dependent on your previous FibroScan results. It is important to distinguish mild (F1-F2) from advanced or severe (F3-F4) fibrosis, as patients with severe fibrosis have a greater risk of complications and need to undergo screening for hepatocellular carcinoma with NAFLD.

MAFLD 1. Asian MAFLD: Clinical Features
MAFLD1-4

Metabolic dysfunction-associated fatty liver disease: clinical features and implications

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In 2020, the term metabolic dysfunction-associated fatty liver disease (MAFLD) was introduced. This was followed by the term metabolic dysfunction-associated steatotic liver disease (MASLD) in June 2023, which effectively retired the old term non-alcoholic fatty liver disease (NAFLD). While both of the new terms are a clear step forward, there are nuances between them that deserve considerations. The criteria to define metabolic dysfunction for MASLD is present in a large proportion of the general population, even among those without hepatic steatosis. Among those with normal body weight, many would be considered as having metabolic dysfunction based on the criteria, although only a small proportion actually have insulin resistance. These suggest that the criteria to define metabolic dysfunction for MASLD may be too relaxed. Furthermore, patients diagnosed with MAFLD based on presence of type 2 diabetes have been shown to have more severe liver fibrosis and greater risk of cardiovascular, cancer and all-cause mortality compared with patients with MAFLD who are diagnosed based on the other two criteria. This is an important consideration in our strategy to tackle the disease of interest. Last but not least, the introduction of a new entity called MASLD and increased alcohol intake (MetALD) encroaches into the field of alcohol-related liver disease and may embroil the disease of interest with unresolved issues surrounding alcohol-related liver disease. Differences aside, the adoption of either term is a clear recognition that the disease of interest is part of the bigger problem related to excess adiposity, insulin resistance and low-grade meta-inflammation. A paradigm shift is needed, where primary prevention should be the prevention of the onset of metabolic dysfunction instead of the prevention of cardiovascular disease or advanced chronic liver disease. There must be an increasing focus on lifestyle habits for promoting and preserving metabolic health during the entire life course at the individual level and beyond.

MAFLD 2. Asian MAFLD: Basic Understanding (Molecular Pathogenesis)
MAFLD2-1

Metabolic Dysfunction-Associated Liver Cancer

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Metabolic dysfunction caused by abnormalities in hepatic lipid metabolism is associated with an increased risk of developing liver cancer. The molecular mechanisms underlying the progression of

MASLD/NAFLD-associated liver cancer (MALC) are not fully understood. Animal models are extensively used for examining the molecular events under the conditions that mimic human disease. Several mouse models for liver cancer associated with metabolic disease have been established by using specific diets, chemotoxic agents, genetic engineering, or combinations thereof. Mice fed methionine- and choline-deficient diets are conventional models of nonalcoholic steatohepatitis, but they undergo weight loss. Although high-fat diets (HFDs) promote hepatic lipid accumulation, long-term exposure is required for tumor development. Streptozotocin, a compound selectively eliminating β cells in the pancreas and resulting in type 1 diabetes, in combination with HFDs induces steatohepatitis and liver cancer without overweight or insulin resistance. Pten conditional knockout (KO) mice on HFDs also recapitulate MALC but not metabolic syndrome. Several congenital mutations are implicated in regulation of food intake and body weight in the hypothalamic nuclei, and these genetic mutations are the most common known monogenic causes of obesity in human. As reported in the previous studies, this regulator-KO mice exhibit obesity, insulin resistance, and dyslipidemia, and they develop steatohepatitis, liver fibrosis, and then well-differentiated liver cancer, suggesting this mouse model may be the best fit for reproducing the features of MALC. Cross-species comparison of gene expression signatures provides a powerful approach to evaluating the biological similarity between human patients and mouse models and to elucidating the molecular system in the common phenotype. Although there have been several comparative studies on human and mouse metabolic liver disease, the cross-species subtyping of liver cancer is focused in our studies. Here, we performed integrative transcriptome analysis of liver cancer resected from human patients and metabolic dysfunction-associated mice, and identified a subtype of liver cancer closely associated with metabolic syndrome, which was characterized by overexpression of several specific genes associated with metabolic dysfunction. We investigated the clinical significance of these metabolic molecules as a specific biomarker for this subtype and the correlation between the expression and metabolic dysfunction in our laboratory. Targeting these pathways may be a useful therapeutic strategy for the subtype-specific liver cancer.

MAFLD 2. Asian MAFLD: Basic Understanding (Molecular Pathogenesis)
MAFLD2-2

Roles of SGLT2 Inhibitor in MAFLD-related HCC

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MAFLD is becoming a leading cause of hepatocellular carcinoma (HCC) in the Asian-Pacific region. In the Japanese clinical practice guidelines for NAFLD/NASH, sodium-glucose co-transporter 2 inhibitor (SGLT2i) is recommended for patients with NAFLD and diabetes mellitus. However, the effects of SGLT2i on HCC remain unclear. First, we examined the expression of SGLT2 in human HCC cell lines and found that SGLT2 occurred and localized on mitochondria in Hep3B and Huh7 cells. Furthermore, SGLT2i significantly suppressed the proliferation of these HCC cell lines. To investigate the pathogenesis, we employed multi-omics analysis of metabolomics and absolute quantification proteomics (iMPAQT). This multi-omics analysis revealed that SGLT2i mainly altered the following metabolisms; 1) oxidative phosphorylation metabolism, 2) fatty acid metabolism, and 3) purine and pyrimidine metabolism. Moreover, SGLT2i altered the phosphorylation of AMP-activated protein kinase (AMPK) and acetyl-CoA carboxylase (ACC), which are sensors of intracellular ATP levels and regulators for beta-oxidation in mitochondria. Thus, We found that

SGLT2i may suppress the proliferation of HCC cell lines via the regulation of electron transport systems, beta-oxidation, and nucleic acid synthesis.

HCC is known to release various chemokines/cytokines to modulate the tumor microenvironment and regulate the proliferation and invasion of HCC cells. Next, we investigated the direct effects of SGLT2i on tumor-releasing chemokines/cytokines in human HCC cell lines. Hep3B and Huh7 cells were treated with SGLT2i or a control vehicle for 24 h. Then, the culture media were collected and subjected to 48 chemokine/cytokine assays using the human cytokine screening 48-plex panel (Bio-Plex Pro, Bio-Rad Laboratories, Inc., Hercules, CA). We first demonstrated that SGLT2i directly downregulated the three tumor-releasing chemokines such as C-X-C motif chemokine ligand (CXCL) 1, CXCL8, and CXCL10 in Hep3B and Huh7 cells. Based on the previous studies, these changes in chemokines may exert antitumor effects through alterations in tumor characters and tumor immunity. We also found that SGLT2i downregulated tumor-releasing macrophage colony-stimulating factor (M-CSF) in Hep3B and Huh7 cells. This downregulation of M-CSF may exert antitumor effects through the polarization of M1 macrophages.

In conclusion, SGLT2i directly suppressed the proliferation of HCC cells through alterations in mitochondrial oxidative phosphorylation metabolism, fatty acid metabolism, and purine and pyrimidine metabolism. SGLT2i also indirectly suppresses HCC by modulating the tumor microenvironment. I will introduce both direct and indirect molecular mechanisms for the effectiveness of SGLT2i on the suppression of HCC.

MAFLD 2. Asian MAFLD: Basic Understanding (Molecular Pathogenesis)
MAFLD2-3

The role of intestinal TM6SF2 in MAFLD

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Metabolic dysfunction-associated steatohepatitis (MASH) is associated with the loss-of-function variant of Transmembrane 6 superfamily member 2 (TM6SF2). While TM6SF2 is primarily expressed in the liver and small intestine, the role of intestinal TM6SF2 dysfunction in MASH development remains unclear. In this study, we utilized systemic, liver-specific, and intestine-specific Tm6sf2 knockout mouse models to investigate the impact of TM6SF2 deficiency on MASH progression. We subjected the knockout mice and wildtype littermates to high-fat high-cholesterol (HFHC) or choline-deficient high-fat diet (CD-HFD) for 2 months to induce MASH. Additionally, fecal microbiota transplantation was performed in germ-free mice, and the therapeutic potential of microbiota modulation was examined by co-housing intestine-specific Tm6sf2 knockout mice with wildtype controls. We characterized the gut microbiota using shot-gun metagenomic sequencing and performed untargeted/targeted metabolomics using liquid chromatography-mass spectrometry.

Our results showed that systemic Tm6sf2 knockout mice exhibited more severe steatohepatitis compared to liver-specific Tm6sf2 knockout mice, indicating the involvement of extra-hepatic TM6SF2 deficiency in MASH formation. Interestingly, intestine-specific Tm6sf2 knockout mice developed spontaneous MASH when fed a normal chow diet, which was further exacerbated by HFHC or CD-HFD supplementation. This MASH development in Tm6sf2 Δ IEC mice was accompanied by impaired gut barrier integrity and dysbiosis of the gut microbiome. We observed an enrichment of the metabolite lysophosphatidic acid (LPA) in the stool, portal vein, and liver tissues of Tm6sf2 Δ IEC mice, which in turn promoted hepatic lipid accumulation

and pro-inflammatory cytokine secretion. Moreover, intestinal cells of Tm6sf2ΔIEC mice secreted higher levels of arachidic acid, which induced intestinal barrier dysfunction, enrichment of pathogenic bacteria, and LPA secretion. Importantly, transplantation of stools from Tm6sf2ΔIEC mice into germ-free mice induced steatohepatitis, while co-housing Tm6sf2ΔIEC mice with wildtype controls ameliorated MASH development, resulting in reduced lipid accumulation and inflammation.

In conclusion, our findings demonstrate that intestinal TM6SF2 deficiency leads to gut dysbiosis and barrier dysfunction, thereby facilitating the translocation of LPA into the liver and promoting MASH. Manipulation of the gut microbiota represents a potential therapeutic strategy for preventing TM6SF2 deficiency-induced MASH.

MAFLD 2. Asian MAFLD: Basic Understanding (Molecular Pathogenesis)
MAFLD2-4

Therapeutic management of MAFLD/MASLD

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The global incidence and prevalence of non-alcoholic fatty liver disease (NAFLD) and its severe form non-alcoholic steatohepatitis (NASH) have been steadily increasing over the past 2 decades, with a huge disease and economic burden. Recently, NAFLD and NASH have been renamed and redefined as metabolic dysfunction associated fatty liver disease (MAFLD)/metabolic dysfunction associated steatotic liver disease (MASLD) and metabolic dysfunction associated steatohepatitis (MASH), which result from an imbalance between metabolic and inflammatory stress (mainly as a consequence of adipose tissue dysfunction and insulin resistance) and the defence and repair mechanisms of the steatotic liver. Once MAFLD/MASLD progresses to end-stage of liver disease, treatment efficacy becomes limited and may require liver transplantation. Early detection and intervention are crucial. Lifestyle modification is consequently the cornerstone of its management. Timely consideration of bariatric surgeries should be given to patients meeting specific criteria. A multidisciplinary approach is warranted, starting from the concept that steatotic liver and steatohepatitis are at the centre of the cardiovascular-liver-metabolic syndrome. In some cases, pharmacological treatment can complement lifestyle modification. Several drugs used to treat the cardiometabolic co-morbidities have some potential efficacy in resolution of MASH and slowing down progression of liver fibrosis, and some drugs have demonstrated efficacy on histological endpoints that are likely to translate into long-term clinical benefits. Optimising the use of these drugs within their licenced indications for type 2 diabetes and obesity is thus paramount for patients with MAFLD/MASLD. Several MASH-specific drugs are on the horizon and are likely to enrich our therapeutic armamentarium in the near future, particularly in non-cirrhotic MAFLD/MASLD. Much work still needs to be done to understand the specific features of MAFLD/MASLD-related cirrhosis and develop efficacious treatments for this disease stage. Future research should focus on optimising lifestyle intervention strategies, improving adherence and success rates, exploring the role of new weight-loss medications, and identifying effective weight loss surgical methods for MASH patients with obesity. Combination therapies targeting multiple pathways and the integration of digital health interventions hold potential for enhancing the efficacy and safety of MAFLD/MASLD treatments.

MAFLD 3. Diagnosis of MAFLD
MAFLD3-1

Pathological Diagnosis of NASH, Fibrosis and HCC

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Pathological diagnosis and interpretation of NASH is made based on the histopathological features of steatohepatitis, i.e. 'steatosis', 'lobular inflammation', hepatocyte 'ballooning', 'Mallory-Denk bodies' and 'fibrosis'. However, there are many borderline cases that are difficult to evaluate. Pathologically, degeneration refers to a continuous and reversible change of morphology commonly seen in injured cells, mild, and moderate to severe pathological changes can be observed contemporaneously. This characteristic may also cause inconsistency in recognizing and evaluating the presence of ballooning degeneration and Mallory-Denk bodies. The Japan Society of Hepatology published a clinical guidebook illustrating the typical histology of definitive hepatocyte ballooning and Mallory-Denk bodies. This guidebook may help to improve and unify the histological interpretations in diagnosing NASH. Despite these efforts, however, limitations of inter-observer variability will most likely remain. Therefore, quantitative assessment of these reversible and continuous degenerative changes is required.

It is widely recognized that accurate staging of liver fibrosis is crucial to guide therapeutic decisions and to predict prognosis for patients with NASH. Digital image analysis (computational pathology) has emerged as a promising tool for quantitative assessment of fibrosis in chronic liver diseases. We measured area ratios of collagen and elastin fibers in Elastica van Gieson-stained biopsy tissues. The combined fiber area ratios correlated strongly with Brunt's stage, but this relationship was nonlinear with striking differences between stage 4 and stages 0–3. The highest tertile of the combined fiber area ratios was associated with fibrosis-4 index and serum type IV collagen 7s domain.

Steatosis, is also a characteristic morphology of HCC. We previously reported that scirrhous HCC with steatosis has different clinicopathological significance than scirrhous HCC without steatosis. Furthermore, steatohepatic HCC, which is characterized by a steatohepatic morphology, has been reported as a subtype of HCC. We elucidated the features of macrovesicular steatosis (MaS) and microvesicular steatosis (MiS) in HCC. HCCs were classified as MaS-HCC, MiS-HCC, or conventional HCC (cHCC) according to the cutoff value of 30% MaS or MiS in tumor cells. MaS-HCC had less portal vein invasion, a higher proportion of HCC with intratumoral fibrosis, and a lower risk of recurrence than MiS-HCC or cHCC. Both MaS-HCC and MiS-HCC had lower incidences of hepatitis virus infection and higher levels of HbA1c than cHCC. These indicated that MaS-HCC and MiS-HCC were associated with metabolic dysfunction but exhibited different biologic behaviors.

In my lecture, these features of NASH/HCC will be discussed from pathological point of view.

MAFLD 3. Diagnosis of MAFLD
MAFLD3-3

Lean MAFLD

Dr. Mohammed Eslam

Storr liver center, Sydney University Australia

Excessive calorie consumption relative to expenditure, intake of unhealthy diets, and lack of physical activity are globally fuelling an increase in the prevalence of poor metabolic health, even in individuals

of normal weight. Consequently, this trend entails increased risk of various metabolic disorders, including metabolic associated fatty liver disease (MAFLD), which affects up to a third of the global population. MAFLD burden has grown in parallel with rising rates of type 2 diabetes and obesity and increases the risk of end-stage liver disease, hepatocellular carcinoma, death, and liver transplantation, and has extrahepatic consequences including cardiometabolic disease and cancers. Although classically is associated with obesity, there is accumulating evidence that not all overweight or obese develop fatty liver disease. On the other hand, a considerable proportion of patients with MAFLD are lean, indicating the importance of metabolic health in disease pathogenesis regardless of body mass index. A complex and dynamic interaction between a multitude of factors, including genetic, epigenetic, dietary, and lifestyle factors, enterohepatic circulation, and gut microbiota is likely to shape individual metabolic health status.

The clinical profile, natural history and pathophysiology of lean patients with MAFLD is not well characterised. In this talk, I am going to provide the recent epidemiological data on this group of patients. The talk will illustrate the novel concept considering the overall metabolic health and metabolic adaptation as a framework to best explain the pathogenesis of MAFLD and its heterogeneity, both in lean and non-lean individuals. This framework provides a conceptual schema for interrogating the MAFLD phenotype in lean individuals that can translate to novel approaches for diagnosis and patient care. I will also touch briefly on the current management of lean patients with MAFLD.

MAFLD 3. Diagnosis of MAFLD *MAFLD3-5*

Risk Stratification and Prediction of Hepatocellular Carcinoma in MAFLD

Dr. Takuma Nakatsuka

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Background: Metabolic dysfunction-associated fatty liver disease (MAFLD), which is strongly associated with systemic metabolic abnormalities, such as insulin resistance and glucose intolerance in the context of obesity, has become a leading cause of hepatocellular carcinoma (HCC) worldwide. Establishing an efficient surveillance strategy is urgently needed given the drastically increasing prevalence of MAFLD. However, optimal surveillance strategy remains unclear owing to the lack of evidence regarding risk stratification. Here we will show the utility of noninvasive tests for HCC risk stratification in patients with MAFLD.

Methods: Patients with MAFLD who underwent liver biopsy at our hospital were included. Liver stiffness measurement (LSM) using FibroScan was performed at the time of biopsy. FIB-4 index and Agile 3+ score (incorporating LSM, platelets, AST/ALT ratio, diabetes status, sex, age) were calculated. The performance of FIB-4 index, LSM, and Agile 3+ for diagnosing advanced fibrosis (AF: $\geq F3$) and predicting HCC was evaluated.

Results: Our cohort consisted of 300 patients with a median age of 55.0 years, median BMI of 27.8 kg/m², median FIB-4 of 1.45, and median LSM of 8.7 kPa; 62.3% were male and 30.3% had diabetes mellitus. AF diagnostic performance (AUROC) was 0.82, 0.84, and 0.90 for FIB-4, LSM, and Agile 3+, respectively, with the Agile3+ being the best (DeLong test, $P=0.001$). During a mean observation period of 38.0 months after liver biopsy, 7 patients developed HCC. Compared to non-HCC cases, HCC-developed cases had significantly higher age at biopsy (54 vs 63 years, $P=0.03$), diabetes complication rate (29% vs 71%), FIB-4 (1.44 vs 2.49, $P=0.03$) LSM (8.7 vs 20.0 kPa, $P<0.01$), and Agile 3+ (0.79 vs 0.98, $P=0.01$). The c-index for predictive ability of HCC were 0.78, 0.80, and 0.85, for FIB-4, LSM, and Agile 3+, respectively. LSM ≥ 10 kPa, recommended cut off value

of cACLD suspicion, could identify patients at high risk with an annual HCC incidence of 1.6%/PY, compared to 0.2%/PY in those with LSM <10 kPa (log-rank test, $P=0.02$). Furthermore, Agile 3+ >0.68 , recommended cutoff value for AF rule-in, could identify patients with at high risk with an annual HCC incidence of 1.2%/PY, compared to 0.0%/PY in those with Agile3+ ≤ 0.68 (log-rank test, $P=0.045$).

Conclusion: LSM and Agile 3+ allow efficient risk stratification of HCC in patients with MAFLD. Their utilization would optimize personalized HCC surveillance strategy in MAFLD. Further studies are warranted to validate the utility of these tests in diverse MAFLD populations.

MAFLD 4. Clinical Management of MAFLD (Lifestyle Change Nutrition and Need of Medications)

MAFLD4-2

Cancer Prevention in patients with chronic HCV Infections

Dr. Ming-Lung Yu

National Sun Yet-sen University and Kaohsiung Medical University Taiwan

Hepatitis C virus (HCV) infections are a significant global health concern, contributing substantially to hepatocellular carcinoma (HCC), the sixth most prevalent cancer and fourth-leading cause of cancer-related deaths worldwide. The progression from chronic HCV infection to HCC spans 20 to 40 years, influenced by factors such as age at infection, viral genotype and loads, alcohol consumption, comorbidities (diabetes and obesity), HIV coinfection, gender, liver fibrosis, and host genetics.

While primary prevention through vaccination is ideal, there is currently no HCV vaccine. Consequently, HCC prevention focuses on effective antiviral therapy as secondary prevention for de novo HCV-related HCC and tertiary prevention for HCC recurrence after curative therapy. Achieving sustained virological response (SVR) with interferon (IFN)-based or directly-acting antiviral (DAA) agents significantly reduces HCC incidence, liver-related mortality, and HCC recurrence post-curative therapy.

Despite SVR, the risk of HCC persists, with preexisting liver cirrhosis and age recognized as crucial risk factors. Understanding pathogenetic mechanisms and identifying risk surrogate biomarkers can enhance follow-up strategies post-HCV eradication. HCV infection induces epigenetic changes, including H3K27ac, associated with increased oncogene expression and decreased tumor suppression genes, persisting after SVR.

Several factors contribute to a higher post-SVR HCC risk, including advanced age, liver cirrhosis, diabetes, alcohol consumption, elevated baseline AFP (≥ 10 ng/mL), and specific genetic variations (MICA, PNPLA3, MBOAT7, TM6SF2, and GCKR). Notably, aspirin, metformin, and statin use have shown promising chemo-preventive effects, reducing HCC risk in large cohort studies among HCV-cured patients.

MAFLD 4. Clinical Management of MAFLD (Lifestyle Change Nutrition and Need of Medications)

MAFLD4-3

NAFLD/NASH and sarcopenia - usefulness of nutritional and exercise therapy -

Dr. Masahito Shimizu

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Sarcopenia is associated with poor prognosis and impaired quality of life in patients with chronic liver disease. Nonalcoholic fatty liver disease/nonalcoholic steatohepatitis (NAFLD/NASH) and its underlying obesity and diabetes are closely related to the development and progression of sarcopenia. Sarcopenia is also a risk factor for NAFLD/NASH and liver fibrosis. Thus, NAFLD/NASH and sarcopenia adversely affect each other and impair hepatic and skeletal muscle function. Particularly, increased ammonia and decreased branched-chain amino acids are closely associated with these pathologies. In the treatment of NAFLD/NASH complicated by sarcopenia, nutritional and exercise therapy that simultaneously improves liver and skeletal muscle function, i.e., “liver rehabilitation”, is important. Weight reduction with diet and exercise therapy improves liver function and liver histology in NAFLD/NASH. For NAFLD/NASH patients with obesity, a low-calorie diet that limits carbohydrates and fats should be taught to optimize energy intake. On the other hand, weight loss due to inappropriate nutritional therapy, such as excessive protein restriction, may contribute to increased skeletal muscle catabolism and sarcopenia. Combined diet and exercise can further improve hepatic function and liver steatosis, but these conditions in patients with NAFLD may be improved even when only exercise therapy is intervened without nutritional therapy. With regard to exercise intensity, moderate and higher levels are more useful, and when comparing aerobic and resistance exercise, resistance exercise similarly improves hepatic steatosis in NAFLD patients, even though energy expenditure is lower than that of aerobic exercise. Resistance exercise is also useful in the prevention of sarcopenia because it effectively improves muscle strength and muscle mass. BCAA supplementation improves the prognosis of cirrhotic patients with sarcopenia. In these patients, the combination of BCAA preparations and exercise therapy is also useful in the treatment of sarcopenia. On the other hand, abnormal BCAA metabolism and over-intake are associated with type 2 diabetes, insulin resistance, and obesity, and are thought to promote hepatic fat accumulation and the development and progression of NAFLD/NASH. In cirrhosis resulting from NASH, the progression of fibrosis and the dynamics of amino acids, including BCAA, should be evaluated and BCAA replacement therapy should be considered. In conclusion, it is critical to develop safe and appropriate liver rehabilitation to improve the prognosis and quality of life of NAFLD/NASH patients with sarcopenia.

MAFLD 5. The Prognostic Event for MAFLD: CVD or Extrahepatic Cancers?

MAFLD5-1

Treatment strategies of MASLD with a view to suppression of cardiovascular diseases and liver-related events

Dr. Norio Akuta

Department of Hepatology, Toranomon Hospital Japan

AASLD indicated that the most common cause of death in patients with MASLD is related to cardiovascular diseases (CVDs). Liver-related mortality was reported to be the second or third cause of death, and cancer-related mortality was among top three causes of death. In Asia, the incidence rates of these events still remain unclear. We retrospectively investigated the incidence of three complications (CVDs, malignancy except for liver cancer, and liver-related events) in 550 Japanese patients with biopsy-proven MASLD for median follow-up of 6.0 years. The yearly incidence rates of CVDs, malignancies, and liver-related events were found to be 1.04%, 0.83%, and 0.30%, respectively. Especially, in malignancy except for liver cancer, the incidence rates of colon cancer were 25.0%. The impacts of diet and exercise, and diabetes therapeutics with high evidence levels for suppression of CVDs should be evaluated in patients with MASLD. Regarding diet and exercise treatment, the subjects of retrospective cohort study

were 203 Japanese patients with SLD diagnosed by abdominal ultrasonography. All of them were introduced the personalized diet and exercise treatment. A diet of 25 to 30 kcal/kg multiplied by ideal body weight daily and aerobic and resistance exercise (exercise intensity of 4 to 5 metabolic equivalents daily, respectively) were performed for 6 days. Treatment efficacy was evaluated in terms of the rate of decrease of liver function tests, glycolipid metabolism markers, physical findings, image findings, and CVD risk score (Suita score) at 6 months compared to baseline, and these parameters improved significantly. Regarding diabetes therapeutics, histological impacts at 5 years after the start of SGLT2 inhibitors were investigated retrospectively in 6 Japanese patients with MASLD and T2DM, and liver biopsies were obtained at the points of pretreatment, 3 years, and 5 years after the start of treatment. The primary outcome was liver histopathological changes at 5 years (defined as decrease in MASLD activity score of one point or more without worsening in fibrosis stage, compared to the pretreatment). 2 patients were performed the additional treatment of GLP-1 receptor agonist after the point of 3 years, and evaluated as histological worsening. Histological improvement, no change, and worsening were 50, 17, and 33% at 5 years, respectively. None developed CVDs events. In conclusion, the most common event in Japanese patients with MASLD was CVDs. Personalized medicine with diet and exercise, and diabetes therapeutics are expected to improve the pathology of MASLD, including the suppression of CVDs and liver-related events.

MAFLD 5. The Prognostic Event for MAFLD: CVD or Extrahepatic Cancers?

MAFLD5-2

Prognostic event for MAFLD: CVD or Extrahepatic cancers

Dr. Yock Young Dan

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The diagnosis of Metabolic Associated Fatty Liver Disease (MAFLD) is based on the presence of hepatic steatosis associated with metabolic conditions such as type 2 diabetes mellitus (T2DM), obesity or metabolic dysregulation. The underlying metabolic disequilibrium, potentially manifesting as diabetes mellitus, hypertension, and hyperlipidaemia, is the same process that drives vascular atherosclerosis and increases the risk of carcinogenesis in multiple organs of the body. Hence it is no surprise that major adverse cardiovascular events (MACE) and extraintestinal cancers are the 2 commonest complications and causes of mortality in patients with MAFLD, constituting higher risks compared to liver complications such as cirrhosis and liver cancer.

We will review the risks for non-hepatic metabolic complications in patients at different stages of MAFLD and also the evidence for non-invasive tests (NIT) that can predict these life-threatening complications. Active management such as surveillance and aggressive management will be discussed.

MAFLD 5. The Prognostic Event for MAFLD: CVD or Extrahepatic Cancers?

MAFLD5-3

The Prognostic Event for MAFLD: CVD or Extrahepatic Cancers?

Dr. Rakhi Maiwall

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The metabolic dysfunction associated fatty liver disease (MAFLD) is a systemic disease that affects various extrahepatic organs. The prevalence varies from 30-40% and increases to 70% in patients who also have diabetes. Recent evidence has suggested an increase in the risk of chronic kidney disease as almost two-fold which is independent of the other cardiorenal risk factors. Apart from these, MAFLD is also associated with extrahepatic chronic complications. A very close association of MAFLD with diabetes, insulin resistance and obesity also confer a higher risk of hepatocellular carcinoma (HCC) including other extrahepatic malignancies. Mechanisms such as insulin resistance, metabolic stress causing disruption of the regulatory pathways for instance, nuclear factor-kappa B (NF- κ B), phosphatase and tensin homolog (PTEN), and microRNAs have been observed to be associated with the development of HCC. The role of lipopolysaccharide-mediated signalling of the toll-like receptor 4 (TLR-4) which further perpetuates the hepatic inflammation and gut dysbiosis causing disrupted metabolism of bile acids has also been causally linked to the development malignancies in patients with MAFLD. The microbiota cause conversion of primary to secondary bile acids such as deoxycholic acid. These secondary bile acids are hepato-toxic and cause worsening of inflammo-fibrosis in MAFLD patients. Dietary intake of high fat and fructose intakes along with genetic factors (e.g., PNPLA3 polymorphisms) have shown to cause progression of the disease increasing the hepatic lipid accumulation. This perpetuates hepatic fibrosis. Accumulation of fat at ectopic locations and adipose tissue dysfunction have also been implicated in the development of MAFLD. Secretion of various hepatokines such as retinol-binding protein-4, fetuin-A, fibroblast-growth factor 21 and inflammatory cytokines, tumor-necrosis-factor alpha, C-reactive protein and interleukin-6 cause hepatic gluconeogenesis, glycogen synthesis and insulin resistance which together drives complications in these patients.

HCV 1. DAA Treatment for CH-C in Asia Pacific Region
HCV1-1

Remaining issues in post-SVR era

Dr. Tetsuya Hosaka

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Current direct-acting antiviral agents (DAAs) regimens can achieve sustained viral response (SVR) of over 97% in patients with chronic hepatitis C infection (CHC). Therefore, we are less likely to struggle with antiviral treatment for CHC. Several reports showed the eradication of HCV infection by DAAs therapy reduce the risk of HCC development. However, there are some patients who develop hepatocellular carcinoma (HCC) after SVR. Older age and advanced fibrosis are known risk factors of HCC after SVR. It is important to evaluate other risk factors of HCC. Then, we are going to focus on some metabolic factors and their association with HCC incidences after SVR among patients treated with DAAs or interferon (IFN)-based regimens in this lecture.

HCV 1. DAA Treatment for CH-C in Asia Pacific Region
HCV1-4

Management of hepatitis C virus infection in Japan

Dr. Taro Yamashita

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Globally, about 58 million people are estimated to have chronic Hepatitis C virus (HCV) infection, and most affected areas are considered Eastern Mediterranean, Europe, Western Pacific, Africa, regions of Americas, and Southeast Asia. HCV infection has been the most common etiology of liver cirrhosis and hepatocellular carcinoma in Japan. Major genotype of HCV has been genotype 1b, which is resistant to interferon-based therapies, following 2a and 2b in Japan. Accordingly, sustained virological response (SVR) rates were less than 50% before direct-acting antivirals (DAAs) developed and became available in 2014 in Japan. Currently, pan genotype DAAs glecaprevir/pibrentasvir and sofosbuvir/velpatasvir regimens are recommended for the treatment of HCV by the Japan Society of Hepatology, with attention to the status of renal function, presence of decompensated cirrhosis, and viral mutations including p32 deletion. SVR rates of these DAA regimens exceed 95%, and now almost all HCV infection can be successfully eradicated. However, because HCV infection is generally asymptomatic until the development of liver cirrhosis and hepatocellular carcinoma, most of patients are unaware of their HCV infection without screening tests. Furthermore, although most of HCV infected patients could relatively easily reach HCV testing and receive DAAs in urban areas, numbers of HCV infected patients are still considered undiagnosed and therefore remained untreated especially in rural areas in Japan. We are currently making an effort to provide the opportunity to receive the diagnosis and treatment of HCV infection in these people by utilizing information and communication technology.

HCV 2. Treatment with Direct Acting Antivirals (DAAs) for Cirrhotic Patients with or Without HCC
HCV2-1

Treatment with Direct Acting Antivirals for Cirrhotic Patients with or without Hepatocellular Carcinoma

Dr. Wan-Long Chuang

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Hepatitis C virus (HCV) infection is a major health problem throughout the world. Patients with chronic hepatitis C (CHC) will lead to liver cirrhosis within 20 to 30 years. After the development of liver cirrhosis, the annual rates of hepatocellular carcinoma (HCC) occurrence are around 1 to 7%. The goal of antiviral treatment for HCV related cirrhosis is to suppress progression to liver failure and development of HCC and to prolong prognosis by reduction of liver inflammation and fibrosis, followed by HCV eradication. Simplified, treatment of chronic hepatitis C with pangenotypic drug regimens should be used in patients with compensated (Child-Pugh A) cirrhosis. However, protease inhibitor-containing regimens are contraindicated in patients with decompensated (Child-Pugh B or C) cirrhosis and patients with compensated cirrhosis with previous episodes of decompensation. Patients with decompensated cirrhosis not on the waiting list for liver transplantation and without severe concomitant comorbidities should be treated urgently. Patients with decompensated cirrhosis without HCC awaiting liver transplantation with a MELD score <18–20 should be treated prior to liver transplantation. Nonetheless, patients with decompensated cirrhosis without HCC awaiting liver transplantation with a MELD score > 18–20 should be transplanted first. If waiting time is greater than 6 months for MELD scores >18–20, patients should be treated before transplantation. Patients with compensated cirrhosis and HCC who are eligible for curative therapy should defer DAA therapy until HCC treatment is completed. In HCV-related HCC patients awaiting liver transplantation with a long waiting times, HCV treatment should be initiated before liver transplantation. Cirrhotic

patients with sustained virological response should undergo surveillance for HCC every 6 months by means of imaging and serum tumor markers.

HCV 2. Treatment with Direct Acting Antivirals (DAAs) for Cirrhotic Patients with or Without HCC
HCV2-2

Risk factors of treatment failure of DAAs in chronic hepatitis C

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In Japan, where the majority of patients are infected with Genotype 1 and 2, DAA treatment for chronic hepatitis C and compensated cirrhosis achieves SVR in nearly 100% of patients. In this study, we investigated the following two risk factors for the few cases of treatment failure among patients treated with DAA at Shinshu University Hospital and its affiliated hospitals in Japan: 1) DAA treatment for patients who had previously developed HCC and had been relapse-free for six months after radical treatment of HCC, and 2) serum chemokine levels measured before DAA treatment. 1) Of the 838 DAA-treated patients, 9.4% had prior HCC, and low pretreatment platelet counts and high AFP levels, advanced fibrosis (M2BPGi), and prior HCC were associated with treatment resistance, leaving prior HCC as the only risk factor in the multivariate analysis. 2) Nine chemokines were measured, and treatment resistance (56.3%; 9 of 16) was significantly observed in the group with low MIP-1 β and high RANTES before treatment. Future issues are to improve the prognosis of patients with uncompensated cirrhosis by DAA treatment and the indication of DAA treatment in patients with HCC.

HCV 2. Treatment with Direct Acting Antivirals (DAAs) for Cirrhotic Patients with or Without HCC
HCV2-4

Morphological changes in esophageal varices in cirrhotic patients who achieved sustained virological response by direct-acting antivirals

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Recently, DAAs have markedly improved treatment outcomes and have been approved for patients with liver cirrhosis including decompensated cirrhosis related with chronic HCV infection, which is frequently complicated by esophageal varices. Previously, some studies reported that achievement of SVR with DAAs decreased portal pressure to some extent. Recent studies reported post-SVR changes in the morphology of esophagogastric varices in patients with compensated cirrhosis. However, post-SVR esophageal variceal changes in patients with decompensated cirrhosis remain unclear. Therefore, this multicenter retrospective study aimed to clarify the morphological changes in esophageal varices after achieving SVR with DAAs treatment in patients with liver cirrhosis including decompensated cirrhosis. A total of 1,768 patients with chronic HCV infection achieved SVR with DAAs treatment at 26 participating institutions in Japan. Among them, 243 patients underwent esophagogastroduodenoscopy before DAAs treatment and after achieving SVR. Our study included 125 males and 118 females with compensated or decompensated cirrhosis with a median age of 68 (range, 44–91) years. Esophageal varices before DAAs

treatment were classified into no varix in 155, F1 in 59, F2 in 25 and F3 in 4 patients. The improvement, unchanged, and aggravation rates of esophageal varices after SVR were 11.9%, 73.3%, and 14.8%, respectively. Low platelet count was extracted as an independent factor associated with esophageal varices aggravation. Of the 155 patients without esophageal varices before DAAs treatment, 17 developed de novo post-SVR esophageal varices. High ALBI score was extracted as an independent factor associated with de novo post-SVR esophageal varices. The cumulative incidences of de novo esophageal varices were 0%, 6.7%, and 17.7% at 1, 3, and 5 years, respectively. In conclusions, patients with cirrhosis can experience esophageal varices aggravation despite achieving SVR. In particular, patients with low platelet count and high ALBI score such as decompensated cirrhosis had a high likelihood of developing esophageal varices aggravation and de novo esophageal varices, respectively, even for long periods after achieving SVR.

HCV 3. Prognosis Portal Hypertension HCC in Post SVR CH-C/cirrhosis
HCV3-1

Evaluation of the usefulness of liver stiffness in cancer development after DAA treatment for chronic liver disease type C

Dr. Koichi Takaguchi

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Purpose: DAA treatment eliminated Hepatitis C Virus (HCV) in most cases of type C chronic liver disease. However, some cases of SVR are also found to develop cancer. Here we report on whether subsequent carcinogenesis can be predicted in cases in which liver stiffness was measured at the start of treatment.

Method: Of the 751 patients who received DAA at our hospital by March 2023, 234 patients (115 men, 119 women, Average age: 64.6 years, Genotype 1: 144 cases, Genotype 2: 88 cases, Genotype 3: 1 case, Unknown: 1 case) with type C chronic liver disease were measured Liver stiffness (LS) before DAA treatment.

Results: The average observation period after completion of administration was 38.1 months. During this period, 7 cases developed cancer. The 5-year cancer incidence rates for all cases was 3.8%. The five-year cancer incidence rate for LS, platelets (PLT), Alb, AFP, ALBI score, hyaluronic acid, M2BPGi, FIB4 index, and FAST before administration was 1.0% for LS less than 14.8, 16.8% for 14.8 or more, and 9.0% for PLT less than 134,000/ μ L, 134,000/ μ L or more: 2.1%, AFP less than 7ng/mL: 2.5%, 7ng/mL or more: 7.4%, Hyaluronic acid less than 298ng/mL: 1.4%, 298ng/mL or more: 13.4%, M2BPGi less than 1.92: 1.9%, 1.92 or more: 6.2%, FIB4 index less than 3.20: 1.2%, 3.20 or more: 8.8%, significant differences were observed in all of the above items.

Conclusion: The liver stiffness measured before administration and the liver stiffness after administration were found to be predictive factors for subsequent carcinogenesis in patients with DAA treated chronic HCV infection.

HCV 3. Prognosis Portal Hypertension HCC in Post SVR CH-C/cirrhosis
HCV3-2

Prognosis, Portal Hypertension, HCC in Post SVR CH-C/Cirrhosis

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Globally, an estimated 58 million people have chronic hepatitis C virus (HCV) infection, with about 1.5 million new infections occurring per year. In 2019, an estimated 290,000 deaths were attributed to hepatitis C-related complications. The primary treatment goal for hepatitis C is the eradication of the HCV to prevent complications such as fibrosis, cirrhosis, portal hypertension, hepatocellular carcinoma (HCC), and extrahepatic manifestations, ultimately leading to a reduction in mortality. The clinical endpoint of antiviral therapy is achieving a sustained virologic response (SVR) at 12 weeks post-treatment, where no detectable HCV RNA is found in the bloodstream.

Recent advancements in interferon (IFN)-free direct-acting agents (DAAs) have dramatically improved SVR rates. Achieving SVR leads to improvements in fibrosis and portal hypertension. It is known that reaching SVR is associated with the regression of liver stiffness, which is linked to a decrease in liver-related complications and mortality. According to Lens et al.'s research, HCV-related cirrhotic patients who achieved SVR showed progressive reductions in hepatic venous pressure gradient (HVPG), and those with high baseline HVPG were more likely to experience decompensation events.

Achieving SVR significantly reduces the risk of hepatic decompensation. Meta-analyses show that SVR lowers this risk by 84% and 89% in the interferon and DAA eras, respectively. A Korean multicenter study found no significant difference in decompensation events between IFN-SVR and DAA-SVR patients.

Achieving SVR also reduces the risk of developing HCC. SVR results in an approximately 70% reduction in the risk of HCC development, with this effect becoming evident within 3–6 months and increasing over time. Some studies suggest that there may be differences in HCC risk reduction between cirrhotic and non-cirrhotic patients after SVR. And various prediction models for post-SVR HCC risk have been reported.

In conclusion, achieving SVR in hepatitis C patients is closely associated with favorable outcomes in terms of fibrosis regression, portal hypertension improvement, reduced HCC risk, and enhanced survival. However, it is important to note that certain high-risk groups may still require vigilant monitoring even after achieving SVR.

HCV 3. Prognosis Portal Hypertension HCC in Post SVR CH-C/cirrhosis
HCV3-3

Influence of HVPG in predicting outcomes in liver disease

Dr. Ankur Jindal

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Portal hypertension is a severe, almost unavoidable complication of chronic liver diseases and is responsible for the main clinical consequences of cirrhosis. Measurement of the hepatic venous pressure gradient (HVPG) is currently the best available method to evaluate the presence and severity of portal hypertension. Clinically significant portal hypertension is defined as an increase in HVPG to ≥ 10 mmHg; above this threshold, the complications of portal hypertension might begin to appear. Measurement of HVPG is increasingly used in clinical hepatology, and numerous studies have demonstrated that the parameter is a robust surrogate marker for hard clinical end points. The main clinical applications for HVPG include diagnosis, risk stratification, identification of patients with hepatocellular carcinoma who are candidates for liver resection, monitoring of the efficacy of medical

treatment, and assessment of progression of portal hypertension. Patients who experience a reduction in HVPG of $\geq 20\%$ or to < 12 mmHg in response to drug therapy are defined as 'responders'. Responders have a markedly decreased risk of bleeding (or rebleeding), ascites, and spontaneous bacterial peritonitis, which results in improved survival.

HCC Percutaneous Ablation for Liver Tumors
HCCI-2

Microwave Ablation for Hepatocellular Carcinoma

Dr. Shinichiro Nakamura

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Background and aim: The next-generation microwave ablation (MWA) has been developed as a new percutaneous thermal ablation therapy for hepatocellular carcinoma (HCC). Compared to radio-frequency ablation (RFA), MWA has the advantage of faster heating and less susceptibility to heat sink effects due to the higher temperature generated and can make predictable spherical ablation zones.

We describe our MWA procedure and the clinical outcomes of patients with HCC.

Methods: We treat Child A or B patients with tumors less than 4 cm in diameter and three or fewer tumors without vascular invasion. MWA-antenna puncture was performed under ultrasound guidance. When the tumor was difficult to visualize using B-mode ultrasound, contrast-enhanced US (CEUS) or fusion imaging with CECT or Gd-EOB-DTPA enhanced MRI was used as a complementary method for MWA. If needed, artificial pleural effusion or ascites were prepared using a 5% glucose solution.

Results: Between September 2019 and September 2023, 564 consecutive patients with 802 HCCs (maximum tumor diameter ≤ 40 mm) were included.

The median maximum tumor diameter was 13.0 (interquartile range, 10.0–18.0) mm. We use CEUS, pleural effusion, and artificial ascites during MWA in 326 (40.7%), 73 (9.1%), and 439 (54.7%) HCCs, respectively. The cumulative local tumor recurrence rates at 1, 2, and 3 years were 4.6%, 8.6%, and 9.8%, respectively. The cumulative local tumor recurrence rate differed significantly by tumor size group: ≤ 20 mm group ($n=651$), 20–30 mm group ($n=132$), and ≥ 30 mm group ($n=19$) ($p<0.0001$). In the multivariable analysis, tumor size (per 1 mm) (hazard ratio [HR], 1.07; 95% confidence interval [CI], 1.03–1.11; $p=0.0002$) and ablative margin (per 1 mm) (HR, 0.83; 95% CI, 0.74–0.93; $p=0.0019$) were significantly associated with local tumor recurrence. Complications after MWA were observed in 40 cases (5.0%), and the major cases were biloma, 10; portal vein thrombosis, 9; bile duct dilatation, 6; pleural effusion, 5. Only tumor size (per 1 mm) (odds ratio, 1.08; 95% CI, 1.04–1.13; $p=0.0002$) was significantly associated with complications. Tumors located at difficult-to-MWA ($n=135$, 16.8%): caudate lobe and areas near the primary and secondary branches of the intrahepatic portal vein, inferior vena cava, gallbladder, heart, duodenum, abdominal esophagus, collateral veins around the liver, and spleen, were not associated with the local tumor recurrence and complications.

Conclusions: MWA is a safe and effective local ablation therapy for HCC.

HCC Percutaneous Ablation for Liver Tumors
HCCI-4

Strategic Optimization of Percutaneous Liver Ablation: A Comprehensive Approach

Dr. Hyunchul Rhim

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Percutaneous liver ablation is pivotal in modern liver cancer management, necessitating a tailored strategy for heightened effectiveness. This overview explores the imperative of strategic optimization, highlighting key components contributing to enhanced patient outcomes. Strategic optimization involves a personalized methodology that extends beyond conventional practices. Incorporating advanced technologies and tailored patient care, practitioners can boost precision and procedural efficacy. Individualized treatment plans, guided by advanced imaging, enable accurate tumor delineation, minimizing collateral damage to healthy tissues.

Economic considerations are pivotal in the strategic optimization framework. Evaluating the cost-effectiveness of ablation techniques ensures judicious resource allocation without compromising patient care—a crucial aspect in the era of value-based healthcare.

Additionally, the overview emphasizes collaboration across medical disciplines. Integrating insights from radiology, oncology, and interventional medicine enriches research and facilitates the exchange of best practices.

In conclusion, strategic optimization in percutaneous liver ablation represents a paradigm shift. This overview outlines its key components, underlining its potential to redefine standards of care, improve outcomes, and shape the future of interventional oncology.

HCC Can Drug Therapy and Classical Local Treatment Coexist?
HCC2-3

TACE plus systemic therapy: How and Who

Dr. Stephen Lam Chan

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Conventionally, TACE is reserved for patients with intermediate disease of HCC while systemic therapy is indicated following TACE treatment or in the presence of advanced disease. However, this concept is being challenged by recent randomized data showing that the addition immunotherapy-based systemic therapy to TACE could improve outcomes. The lecture will review the latest efficacy and safety data on the combination. Patient selection for this treatment combination will also be discussed.

HCC Can Drug Therapy and Classical Local Treatment Coexist?
HCC2-4

Basis of combination therapy by radiofrequency thermal ablation and immune checkpoint blockade for unresectable hepatocellular carcinoma

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Introduction: Despite significant advancements in cancer treatment since the establishment of immune checkpoint blockade, a considerable number of patients do not benefit from the latest immunotherapies, often due to insufficient tumor-infiltrating lymphocytes or limited

antigen exposure. To address this, we propose leveraging the 'abscopal effect' through local ablation therapy before immunotherapy in patients with unresectable hepatocellular carcinoma.

Methods: We evaluated the antitumor effects of radiofrequency ablation (RFA) in BNL/MC38 tumor-bearing mice. RFA was applied to one of two bilateral tumors, with the untreated tumor monitored to assess antitumor responses. To explore the underlying mechanisms, we examined the roles of different immune cell subsets using nude mice, clodronate liposomes, and CD4/CD8 depletion antibodies. We also initiated a clinical study, "Randomized Phase II study of preceding radiofrequency ablation to atezolizumab plus bevacizumab combination therapy for patients with unresectable hepatocellular carcinoma (jRCT1041200075)." This study involves treating selected hepatic lesions with RFA before administering atezolizumab and bevacizumab to patients with unresectable hepatocellular carcinoma. The study includes a safety confirmation cohort (n=6) and a randomized cohort (n=60), focusing on progression-free survival as the primary endpoint and overall survival, objective responses, tumor control rates, and immunological responses as secondary endpoints.

Results: Animal studies demonstrated that RFA enhanced antitumor effects in residual tumors. Experiments in nude mice with BNL tumors confirmed that this enhancement was T-cell mediated. Macrophage ablation with clodronate liposome did not affect tumor growth in wild-type BNL mice. Tests using CD4 or CD8 depletion antibodies showed that T cells were responsible for the enhanced antitumor effects in MC38-bearing mice. Preliminary results from the clinical study's safety cohort indicate the combination therapy's safety and feasibility. Over a median observation period of 885 days, the best responses included one partial response and five stable diseases, with a median progression-free survival of 175 days.

Conclusions: The combination therapy involving RFA and cancer immunotherapy, with the aim of eliciting abscopal effects, presents a promising avenue in cancer immunotherapy. Preliminary results from the clinical trials support the safety and feasibility of this combination approach, encouraging further investigation.

HCC Will Adjuvant Chemotherapy Post-Curative Treatment for Hepatocellular Carcinoma Be a Paradigm Shift
HCC3-1

Will Adjuvant Chemotherapy Post-Curative Treatment for Hepatocellular Carcinoma Be a Paradigm Shift?

Dr. Masafumi Ikeda

Department of Hepatobiliary and Pancreatic Oncology at the National Cancer Center Hospital East Japan

According to the Barcelona Clinic Liver Cancer (BCLC) staging system, a single tumor or tumor size of ≤ 3 cm of hepatocellular carcinoma (HCC) are classified as early-stage, and liver resection, liver transplantation, or local ablative therapy is recommended. These treatments aim for complete cure, and systemic therapy was firstly developed as post-curative adjuvant therapy. Although no standard post-curative treatments have been established yet, the effectiveness of adjuvant atezolizumab plus bevacizumab (Atezo+Bev) therapy as compared to active surveillance (IMbrave050) was demonstrated in 2023. The primary endpoint of recurrence-free survival (RFS) demonstrated to be significantly better in Atezo+Bev than in active surveillance [12-month RFS: Atezo+Bev 79% vs. active surveillance 68%, hazard ratio 0.70 (95% confidence interval: 0.54-0.91, $p=0.007$)]. In the subgroup analysis of RFS, the benefits of Atezo+Bev were consistent across all subgroups. However, there was no difference in overall survival [hazard ratio 1.42 (95% confidence interval: 0.80-2.54)], and the Kaplan-Meier curves for RFS became close after 2 years, suggesting the suppressive effect for early recurrence and no suppressive effect after 2

years. As the follow-up period (median) is still short at 17.4 months, long-term follow-up results are warranted.

Currently, in the early-stage HCC, post-curative treatment of systemic therapies are underway as comparator of placebo: EMERALD-2 (NCT03847428) compared with durvalumab plus bevacizumab, CheckMate9DX (NCT03383458) compared with nivolumab, and KEYNOTE-937 (NCT03867084) compared with pembrolizumab. These phase III trials are focusing on combined therapy or monotherapy of immune checkpoint inhibitors. From these results, whether a single immune checkpoint inhibitor or a combination of an immune checkpoint inhibitor and a VEGF inhibitor is necessary for adjuvant therapy will be determined.

HCC Will Adjuvant Chemotherapy Post-Curative Treatment for Hepatocellular Carcinoma Be a Paradigm Shift

HCC3-3

The next step toward adjuvant therapy in patients with hepatocellular carcinoma

Dr. Kaoru Tsuchiya

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Adjuvant therapy for patients with hepatocellular carcinoma (HCC) after curative treatment, including resection and ablation, is still unestablished in clinical practice. There are some clinical studies that aim to prove prevention of HCC recurrence after curative treatment. The phase 3 clinical trial, atezolizumab plus bevacizumab versus active surveillance in patients with resected or ablated high-risk HCC (IMbrave050), already showed positive results. The recurrence-free survival (RFS) was significantly longer in the patients treated with atezolizumab plus bevacizumab compared to the patients with active surveillance. In this study, the majority (88%) of patients received resection, and 90% of the patients treated with resection had solitary tumors. Moreover, 82% of patients were recruited from Asia, and 62% had HBV infection. In Western countries and Japan, the percentage of HCC patients with HBV infection is about 10%, and the number of non-viral HCCs, including MASLD, has been increasing globally. Even though this study met the primary endpoint, the median duration of follow-up was only 17.4 months in the treatment group and 17.6 months in the active surveillance group. IMbrave050 trial was the first successful clinical study and the first step toward adjuvant therapy in HCC. However, there are many concerns about adjuvant settings. First, we have to identify the patients with high-risk populations of recurrence. In the IMbrave050 trial, only 7 patients in the treatment group and 3 patients in the active surveillance group had ≥ 3 tumours. Second, we should mention the etiologies of patients. Third, it is important to consider the toxicity of adjuvant therapy. In the IMbrave050 trial, grade 5 adverse events occurred in 6 patients (2 of which were treatment-related) in the treatment group and 1 patient in the active surveillance group. In real-world practice, several studies were performed by using transarterial chemoembolization (TACE) + portal vein chemotherapy (PVC) or internal radiotherapy (IRT) as adjuvant therapy after curative resection in HCC and showed positive results. Although atezolizumab plus bevacizumab has been recommended as first-line systemic therapy in most HCC guidelines, it should be evaluated by comparing other therapies as adjuvant therapy. The next step toward adjuvant therapy in HCC is to solve such clinical questions and establish the appropriate adjuvant therapy for each patient.

HCC Will Adjuvant Chemotherapy Post-Curative Treatment for Hepatocellular Carcinoma Be a Paradigm Shift

HCC3-4

Adjuvant Chemotherapy for HCC

Dr. Stephen Lam Chan

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Adjuvant treatment has been studied in HCC for long time with little success. At present, there remains no standard adjuvant therapy following patients with surgery or ablation. Immunosurveillance plays a key role in prevention of recurrence after treatment of curative intent. A number of adjuvant clinical trials on immune checkpoint inhibitors has been conducted. IMBRAVE050 showed that the use of atezolizumab and bevacizumab could improve the recurrence-free survival as compared to active surveillance amongst patients at high risk of recurrence following surgery or ablation. The readout of the IMBRAVE050 study has undoubtedly led to interest on immune based therapy in the adjuvant setting. The above will be covered by the lecture.

HCC Current Status and Future Perspective of Hepatic Resection

HCC4-1

ICG Fluorescence Imaging-Assisted Laparoscopic Anatomical Hepatectomy Using Inside-Out Transection

Dr. Osamu Itano

Department of Hepato-Biliary-Pancreatic & Gastrointestinal Surgery, International University of Health and Welfare School of Medicine Japan

Background: Anatomical liver resection should not require the dissection of Glissonean branches during the intersectional liver transection. However, the conventional transection method is to set the transection plane connected from the demarcation line on the surface to the root of the corresponding Glissonean pedicle, therefore, the vessels that appear on the transection plane are dissected, creating unnecessary ischemic or congestion areas which can lead to complications. In this paper, we will show how to correctly implement the concept of anatomical resection, which is called “inside-out transection by central approach”, and the synergistic effect of using ICG fluorescence imaging further increases accuracy.

Methods: The root of the corresponding Glissonean pedicle is identified visually at the hilum and liver dissection started on the assumed transection plane from the root. The intersectional transection is proceeded inside-out, towards the peripheral, recognizing the flow of the glissonean branches. The “chicken claw” shape of Glissonean branches is the end of the branch, and the line connecting these signs is used for dissection. As a result, the dissection of the Glissonean branch will not occur. The corresponding Glissonean pedicle is dissected intrahepatically when enough surgical space inside the parenchyma is made for safe procedures. The ICG fluorescence method is used at this time. The direction of hepatic resection becomes even easier to recognize. Liver parenchyma near the surface is dissected in the end.

Results: hemihepatectomy (L:8, R:5), Sectorectomy (A:4, P:5, AM:1, M:2) Median operation time was 349 min, Median blood loss was 176ml. There was no postoperative complications equal or more than CD3.

Conclusion: ICG fluorescence imaging-assisted inside-out transection enables us to perform precise intersegmental transection in laparoscopic anatomical liver resection.

HCC Current Status and Future Perspective of Transplantation *HCC5-4*

Liver-Resident Natural Killer Cells as Adjuvant Treatment for Hepatocellular Carcinoma Post-Liver Transplantation

Dr. Masahiro Ohira

Department of Gastroenterological and Transplant Surgery,
Hiroshima University Japan

Effective prevention or treatment strategies for hepatocellular carcinoma (HCC) recurrence following liver transplantation (LT) are currently lacking. Standard immunosuppressive protocols post-LT tend to preserve innate immune components while suppressing adaptive cellular immunity. Central to the innate immune response, Natural Killer (NK) cells are pivotal in defending against neoplastic cells, making their enhancement a viable immunotherapeutic strategy against HCC post-LT. We suggest that the adoptive transfer of liver-resident NK cells, harvested from the donor liver graft perfusate, could induce an anti-tumor response without harming the recipient's healthy tissues.

In our study, 99 patients who preoperatively met the Japan criteria were examined. Of these, 42 patients who postoperatively exceeded the Milan criteria demonstrated significantly lower recurrence-free survival rates compared to the 57 within the criteria ($p=0.022$). Remarkably, among patients beyond the Milan criteria, those treated with NK cell therapy ($n=17$) showed a marked improvement in recurrence-free survival rates. Following NK cell infusion, we observed a significant increase in NK cell cytotoxicity and the percentage of TRAIL+ NK cells in the patients' peripheral blood ($p<0.05$). The administered donor NK cells were detectable in the peripheral blood up to one month post-infusion.

Our collaborative research with the University of Miami, initiated in 2009, has extended this approach to deceased donor LT (DDLT) recipients. This phase I trial encompassed 17 subjects with a median follow-up of 96 months, recording no adverse events related to the study. The high-dose NK cell group exhibited a significantly superior overall survival rate compared to the low-dose group ($p=0.0064$). Among the DDLT series for HCC, 53% of patients meeting the Milan criteria preoperatively had pathological findings exceeding the criteria postoperatively, yet none have experienced HCC recurrence to date.

In conclusion, IL-2 stimulated NK cells from both living and deceased donor liver transplants have been safely administered, suggesting a promising adjuvant immune therapy for HCC patients post-LT. A multicenter phase II trial is now underway in Japan and the USA.

HCC Current Status of TACE and HAIC *HCC6-2*

New FP therapy for long-term prognosis in patients with advanced hepatocellular carcinoma

Dr. Hiroaki Nagamatsu

Department of Gastroenterology, Juntendo University Japan

Introduction: In Japan, hepatic arterial infusion chemotherapy (HAIC) is recommended as an optional treatment in the 2021 guidelines. In 2021, New FP therapy (NFP) was reported to have a longer prognostic effect than sorafenib in advanced hepatocellular carcinoma with intrahepatic lesions.

Objectives: I will show the performance of NFP in this study at our hospital.

Subjects: We perform 2 courses using the temporary indwelling catheter system via the left brachial artery, and then we remove the temporary reservoir during hospitalization. We repeat this treatment 3 to 5 times with an interval of about 2 months. We aim for cancer free by

performing conversion therapy when PR or CR is obtained by NFP. We performed NFP on 290 patients with advanced with vascular invasion.

Results: There is almost no deterioration liver function. A total of 200 patients (69%) responded to NFP therapy, of which 80 patients achieved cancer-free outcome. 32 patients became cancer-free outcome with only NFP. We were able to add hepatic resection to 33 patients. Median OS (MST) after HAIC in all patients was 18 months. MST in patients who responded was 29 months, and in patients who achieved cancer-free outcome, it was extended to 67 months. The 5-year survival rate of all patients was 22%, and 67% for patients who got cancer-free outcome.

Conclusions: NFP has a high response rate and contributes to improve or maintain liver function by controlling PVTT. In response cases, long-term survival can be obtained by adding conversion therapy.

HCC Current Status of TACE and HAIC *HCC6-3*

DEB-TACE combined with HAIC and iCIs could be an affordable treatment option for advanced stage of HCC

Dr. Yasuteru Kondo

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The treatment efficacy for patients with advanced-stage HCC has been improved by molecular-targeted agents (MTA), immune check point inhibitors (iCIs), and radiation therapy, in addition to TACE and/or hepatic arterial infusion chemotherapy (HAIC). However, the treatment efficacy for patients with advanced-stage HCC treated by a single agent has not been adequate. iCIs and/or MTA including sorafenib, lenvatinib, regorafenib and cabozantinib etc. are standard treatments according to current international guidelines. However, alternative treatment modalities are required because of the low response rates and unsuitability of MTA and iCIs in the real world. Combinations and/or sequential treatments with various agents have been carried out to improve the treatment efficacy for patients with advanced-stage HCC. We modified the treatment regimens to improve the efficacy of DEB-TACE and HAIC for intermediate and advanced HCC. I will present about the role of Ultra-FP therapy (DEB-TACE and HAIC) and iCI treatment for the HCC patients.

HCC Current Status of TACE and HAIC *HCC6-4*

Current indication of TACE and combination therapy with systemic agents for HCC

Dr. Toshihiro Tanaka

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Due to recent development of molecular targeted agents (MTA) and immune checkpoint inhibitors (ICI) for hepatocellular carcinoma (HCC), the role of transarterial chemoembolization (TACE) has been changing from palliative treatment to curative treatment. Previously it was reported that complete response (CR) obtained by TACE prolonged the overall survival. Therefore, the key is how to obtain CR in TACE. A randomized controlled trial (PRESIDENT study) conducted in Japan demonstrated the higher curability of selective conventional TACE (cTACE) compared with selective drug-eluting bead TACE (DEB-TACE). The CR rate at 3 months after TACE was 75.2 % in cTACE versus 27.6% in DEB-TACE. Recently, the result of primary

analysis of TACTICS-L trial was reported. The combination of TACE with Lenvatinib (LEN-TACE) achieved high CR ratio of 53.2 % at 4 weeks after first TACE and 67.7 % in the best response. These seem to be higher when compared to TACTICS trial with the CR rate of 28% in the TACE plus sorafenib group. Furthermore, LEN-TACE achieved high CR ratio in patients beyond Up-to-7 criteria. Currently, several clinical trials of TACE combined with systemic therapies are ongoing. Molecular biological and immunological effects of MTA and ICA could be expected in combination with TACE.

HCC Advancements in Radiation Therapy for Hepatocellular Carcinoma
HCC7-1

Carbon-ion radiotherapy for hepatocellular carcinoma

Dr. Masaru Wakatsuki

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Radical treatment options for bulky unresectable locally advanced hepatocellular carcinoma (HCC) are limited. Stereotactic Body Radio Therapy (SBRT) is becoming popular in many countries as an effective treatment option for relatively small hepatocellular carcinomas, there are problems in terms of its effects on the normal liver and its efficacy against large hepatocellular carcinomas. Carbon-ion radiotherapy (C-ion RT) has improved dose distribution properties owing to Bragg peak and less lateral scattering and enable to perform higher prescribed dose for HCC than that of photons. Take advantage of this feature, C-ion RT is becoming popular in Japan as a new curative treatment option. National Institute for Quantum Science and Technology (former the National Institute of Radiological Sciences) began treating patients with C-ion RT in 1994 and has treated approximately 1,000 cases of hepatocellular carcinoma to the present. Since April 2022. Its effectiveness was recognized and C-ion RT for hepatocellular carcinoma larger than 4 cm was approved by the Japanese National Health Insurance since. The number of patients treated is increasing. It has been shown to be a safe and effective treatment, especially for hepatocellular carcinoma with vascular invasion, patients with low liver function, and patients with bulky hepatocellular carcinoma.

In this presentation, I would like to show the results of treatment to date and introduce the challenges and future directions of C-ion RT for hepatocellular carcinoma.

HCC Advancements in Radiation Therapy for Hepatocellular Carcinoma
HCC7-2

The Role and Future of Stereotactic Body Radiotherapy for Hepatocellular Carcinoma

Dr. Yoshiko Doi

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With advancements in imaging diagnostics and radiation therapy techniques, the application of stereotactic body radiotherapy (SBRT), delivering high doses of radiation in a short time, has become more feasible. Numerous studies have reported the high therapeutic efficacy and safety of SBRT for hepatocellular carcinoma (HCC). A prospective, phase II multicenter study of SBRT in previously untreated solitary primary HCC (STRSPH study) was conducted in Japan and

reported a 90% local control rate and a 3-year overall survival (OS) rate of 78%. This study included many elderly patients and patients with comorbidities for whom standard treatments (radiofrequency ablation (RFA) and surgical resection) were not applicable, but the high local control rate and low toxicity of SBRT are thought to have led to the good results.

On the other hand, in the global treatment algorithm for HCC, decisions are guided by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system. Consequently, treatment options rich in evidence, such as liver resection, RFA, transcatheter arterial chemoembolization, liver transplantation, and chemotherapy, are considered in the selection of HCC treatment. Unfortunately, among studies evaluating SBRT outcomes, none have presented high-quality clinical evidence assessable by the GRADE system. So, SBRT is absent from the treatment algorithm.

Nevertheless, studies have shown positive results not only in SBRT outcomes, but also in studies comparing outcomes with other treatment modalities in retrospective study. A meta-analysis of tumor outcomes for HCC treated with RFA or SBRT, utilizing meticulously selected studies, reported no significant difference in the OS rate between the two modalities (1- and 2-year OS rates were 91.8% and 77.7% after RFA, and 89.0% and 76.0% after SBRT, respectively).

SBRT exhibits notably high local treatment efficacy, particularly acting as a breakthrough in challenging scenarios where RFA is difficult (such as lesions just below the diaphragm, on the liver surface, perivascular lesions, and conditions with a bleeding tendency, as well as cases with tumors not visible by ultrasonography) or in instances of recurrence post-TACE. This underscores its potential as a promising therapeutic approach contributing to overall prognosis improvement for HCC patients. It is imperative for radiation oncologists to communicate the heightened therapeutic efficacy and safety of SBRT to hepatologists and surgeons, making sustained efforts to broaden the applicability of SBRT implementation.

HCC Advancements in Radiation Therapy for Hepatocellular Carcinoma
HCC7-3

Experience in clinical trials combining immunotherapy and radiotherapy

Dr. Hee Chul Park

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While systemic therapy is recommended for HCC patients with MVI by many academic guidelines, various liver-directed therapies such as surgical resection, transarterial chemoembolization with or without radiotherapy, and radioembolization have demonstrated significant outcomes. There may be an unmet need for improved treatment strategies integrating systemic and liver-directed therapy in patients with HCC and MVI.

External beam radiation therapy (EBRT) can be applied to patients with HCC in various situations, including those with symptomatic primary liver or metastatic lesions. Recent advances in the EBRT techniques, such as with stereotactic body radiotherapy (SBRT), proton beam therapy (PBT), and carbon ion radiotherapy, have enabled the delivery of higher radiation doses to achieve excellent local control. Proton beam therapy (PBT), an EBRT, demonstrated non-inferiority for local progression-free survival to radiofrequency ablation for small residual or recurrent intrahepatic HCC as a curative option. The combination of EBRT and transarterial chemoembolization (TACE) showed tolerability and superior efficacy for HCC with MVI compared with sorafenib alone. Although little is known about the clinical outcomes of the concurrent use of radiotherapy and immunotherapy, it can

be expected to exert a synergistic effect in cancer treatment. Radiation therapy can have immunostimulatory effects. Substantial preclinical studies have shown that radiotherapy may synergize with immunotherapy. Preliminary clinical studies have recently been reported. A phase I trial of SBRT combined with immunotherapy (nivolumab with or without ipilimumab) exhibited favorable outcomes, and the combination therapy of EBRT and atezolizumab/bevacizumab demonstrated acceptable safety.

Based on the CheckMate-040 trial, which showed promising clinical activity and a favorable safety profile, nivolumab, a PD-1 inhibitor, obtained accelerated approval from regulatory agencies worldwide, including South Korea, as a second-line treatment, and a global first-line nivolumab trial could be initiated. Nivolumab monotherapy demonstrated a durable response in some patients; however, the response rate still remained at 20%. EBRT has shown good local control in HCC and may potentiate immunotherapy through immunomodulatory effects; therefore, we conducted a phase 2 study evaluating the efficacy and safety of concurrent therapy with nivolumab and EBRT in patients with advanced HCC and MVI.

HCC Bridging Clinical and Basic Research
HCC8-1

Molecular pathologic spectrum between HCC and cholangiocarcinoma and their relation to histopathologic subtypes

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Two main primary liver carcinomas are hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (iCCA). HCC is heterogeneous in moleculopathological features and biologic behavior. According to updated WHO Classification of Digestive System Tumors 5th edition, about 35 % of HCCs can be classified into distinct histopathological subtypes according to their molecular characteristics. Among the recently identified subtypes, macrotrabecular massive (MTM)-HCC, neutrophil-rich HCC, vessels encapsulating tumor clusters (VETC)-HCC, and progenitor phenotype HCC (HCC with CK19 expression) are associated with poor prognosis, and lymphocyte-rich HCC subtype is related to better prognosis.

iCCA is an aggressive primary liver malignancy with an increasing incidence worldwide. Recently, histopathologic classification of small duct type and large duct type iCCA has been introduced. Data from recent large-scale exome analysis have revealed the heterogeneity in the molecular profiles of iCCA, showing that small duct type iCCA exhibit frequent BAP1, IDH1/2 hotspot mutations and FGFR2 fusion, in contrast to frequent mutations in KRAS, TP53, and SMAD4 observed in large duct type iCCA.

Interestingly, an integrative analysis of transcriptome profiles of primary liver cancer revealed an iCCA-like HCC and HCC-like iCCA, suggesting a continuous molecular spectrum between HCC and iCCA. iCCA-like HCC is characterized by expression of the progenitor cell-like trait, TP53 mutations, and rim arterial-phase hyperenhancement in MRI and shows more aggressive behavior compared to typical HCC. HCC-like iCCA is mainly histopathological small duct type, associated with HCC-related etiologic factors and shows a better prognosis compared to typical iCCA. Diverse pathologic features of HCC and iCCA and their associated multi-omics characteristics are currently under active investigation, thereby providing insights into precision therapeutics for patients with HCC and iCCA. This lecture will provide the latest knowledge on the histopathologic classification of HCC and iCCA and their associated molecular features, ranging from tumor microenvironment to genomic and transcriptomic research.

HCC Bridging Clinical and Basic Research
HCC8-2

Establishment of Genome analysis center, From Genomic Analysis to Clinical Practice in Hepatocellular Carcinoma

Dr. Kenji Amemiya

Genome Analysis Center, Yamanashi Prefectural Central Hospital
Japan

In 2019, Comprehensive Genomic Profiling test became eligible for insurance coverage, marking the widespread adoption of cancer genomic medicine. Our institution established a Genomic Analysis Center in April 2013 and has been actively engaged in cancer genomic medicine.

Yamanashi Prefectural Central Hospital has accumulated cancer registration data since 2006, totaling 29,024 cases (including 1,163 with hepatocellular carcinoma, HCC), and has obtained genomic informed consent from 9,484 patients (including 313 with HCC). We developed an in-house panel targeting Significantly Mutated Genes for each cancer type. Using NGS platforms (Genexus, Proton, PGM), we performed sequencing on 15,213 samples (lung 2,758, biliary/pancreatic 1,839, gynecological 921, liver 906, stomach 572, urological 532, breast 304, and others), generating a total of 5.6 trillion bases. Additionally, we have published 112 peer-reviewed articles.

In HCC, registration using REDCap in the A-HOC (APASL Hepatology/Oncology Consortium) has reached 506 cases. Analysis using in-house HCC panels (72 SMGs: 59,016 amino acids) has been completed for 198 cases 355 nodules (solitary: 130 patients with 130 nodules, synchronous: 33 patients with 81 nodules, metachronous: 16 patients with 35 nodules, syn+meta: 19 patients with 75 nodules). Whole transcriptome data has been obtained for 300 of these samples. There are 689 cases of DAA (Direct-Acting Antiviral) treatment, and tumor marker data (AFP, AFP-L3, DCP) have also been collected for these cases. Considering these data, we aim to validate the clinical applications of HCC analysis from a multifaceted perspective, including ① post-DAA occurrence of HCC, ② dynamics of oncogenic driver in serially occurring HCC nodules ③ the correlation between tumor markers and clinical/genomic data.

HCC Bridging Clinical and Basic Research
HCC8-3

NAFLD becomes a promoter of hepatocellular and cholangiocellular tumors in mice

Dr. Shin Maeda

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Background: It is epidemiologically clear that NAFLD, which is an increasing trend in recent years, accelerates hepatic inflammation, fibrosis and liver cancer development. In contrast, it is unclear whether NAFLD affects the cholangitis or development of another liver cancer, cholangiocellular carcinoma (CCC). The aim of this study is to investigate whether high fat diet promotes cholangitis and development of cholangiocellular tumors in mice.

Methods: We use liver-specific E-cadherin gene (Cdh1) knockout mice, Cdh1ΔLi, which was generated by crossing Cdh1^{flox/flox} mice with Albumin-Cre transgenic mice, with spontaneous inflammation in the portal areas and periductal onion skin-like fibrosis, which resembles primary sclerosing cholangitis (PSC). High fat diet or normal diet

was fed into the Cdh1ΔLi mice for 7 months. In addition, Cdh1ΔLi mice was crossed with LSL-KrasG12D (active Kras) mice and also fed with high fat diet.

Results: Cdh1ΔLi mice that received a high-fat diet for 7 months increased in body weight similarly to control mice, and the degree of fat deposition in the liver was increased but not different from controls. On the other hand, the extent of cholangitis and fibrosis, and numbers of bile ductules significantly progressed as compared to normal diet-administered mice. CD44-positive stem cell-like cells were significantly increased and ALT and ALP levels were also increased in mice with high fat diet. Liver specific LSL-KrasG12D/ Cdh1ΔLi showed 2-10 macroscopically tumors with both hepatocellular and cholangiocellular components after 9 months of birth with normal diet, whereas high fat diet induced aggressive and numerous numbers of cholangiocellular tumors only after 3 months of high fat diet. Interestingly hepatocellular tumors were rarely found in these mice. In contrast, liver specific LSL-KrasG12D mice showed aggressive hepatocellular tumors by high fat diet.

Conclusion: NAFLD exacerbates cholangitis and becomes a strong promoter of not only hepatocellular tumors, but also cholangiocellular tumors. In addition, NAFLD may cause transdifferentiation from hepatocellular to cholangiocellular component.

HCC Bridging Clinical and Basic Research
HCC8-4

Development and Prospects of AI-aided Ultrasonography System -New Possibilities in Diagnosis of Liver Tumor-

Dr. Naoshi Nishida

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The integration of artificial intelligence (AI) has aimed to enhance operational efficiency and mitigate human errors in the medical field. Image diagnosis support, a pivotal area for AI development, has witnessed the initiation of large-scale database construction and the deployment of numerous models in society. Notably, liver malignancies stand as the fifth leading cause of cancer-related deaths in Japan, underscoring the urgency of early diagnosis through ultrasonography for improved prognosis and reduced medical costs. However, the variable quality of ultrasound (US) diagnosis, dependent on the skill of examiners, presents a challenge. Hence, achieving AI-assisted standardization in the quality of US examination becomes crucial for effective disease management of malignant liver tumor.

Within the framework of the Japan Agency for Medical Research and Development (AMED)-ICT Infrastructure Development and Artificial Intelligence Implementation Project, we established a system for collecting US images and ancillary information, and developed an AI capable of detecting and discriminating liver masses in abdominal US B-mode examinations utilizing a comprehensive database.

A 2-step method employing YOLOv5 as a mass detector, convolutional neural network (CNN-VGG19) as a tumor discriminator, and DeepSORT to prevent duplicate detection was implemented. The detector demonstrated exceptional performance in pre-clinical tests, surpassing 90% in recall, precision, and F1-score through a 10-fold cross-validation. The discriminator, designed for the differential diagnosis of hepatocellular carcinoma, metastatic hepatocellular carcinoma, hemangioma, and cysts, achieved high accuracy, sensitivity, and specificity in a four-class classification and benign-malignant discrimination in cross-validation.

In an exploratory clinical trial under the AMED-Practical Research for Innovative Cancer Control Project, the performance of prototype AI model integrating detectors and discriminators in series was evaluated to determine the impact of AI-assisted improvement in human US

diagnostic performance. The results revealed significant enhancements in liver mass detection indices (recall, precision, F1-score) and differentiation indices (accuracy, sensitivity, specificity, and Matthews correlation coefficient) particularly for non-expert, demonstrating the practical potential of the developed AI model to support human US diagnosis. Research projects are underway to refine and market the AI as Software as a Medical Device (SaMD). In addition, concurrently, efforts are also directed towards developing a model capable of differentiating intrahepatic cholangiocarcinoma.

The effectiveness of our AI in supporting US diagnostics has been recognized, especially among non-experts, where AI assistance has significantly improved all detection and differentiation indices. It can be described as a practical AI model that aids in the diagnosis of liver tumors in human US examinations.

HCC Optimal Treatment Selection in Hepatocellular Carcinoma
HCC10-3

A personalized approach for optimal treatment selection in HCC

Dr. Yi-Hsiang Huang

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The treatment of HCC is diverse depending on tumor stage and affordability of patients. A personalized approach remains an unmet medical need. Recently, the application of AI had introduced into the field of HCC management. In our recent study, the risk of recurrence after surgical resection of HCC could be predicted by an evolutionary learning-derived clinical-radiomic GARS models. This model can further discriminate the risk of recurrence either in high or low risk patients defined by IMbrave 050 study, indicating that the requirement of adjuvant immunotherapy after surgical resection of HCC can be determined by this AI model in our daily practice in near future. TACE unsuitability is an emerging issue for intermediate stage HCC. We have recently proposed a novel 7-11 criteria to divide BCLC B HCC into low-, intermediate-, and high tumor burden; and define the outcomes of TACE through different radiologic patterns, both can assist decision making before TACE. More studies support the concept that the dissimilarities in gut microbiome composition are associated with immune status and susceptibility to immunotherapy. Recently, we identify the associated of gut microbiota and metabolites with outcome of HCC undergoing immune checkpoint inhibitors treatment, supporting the potential role of gut microbiota in selection patients with HCC for immunotherapy.

HCC Optimal Treatment Selection in Hepatocellular Carcinoma
HCC10-4

Eliminating viral hepatitis C: Not to leave anyone behind from HCV cure

Dr. Masayuki Kurosaki

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Hepatitis C remain important background for liver-related mortality. HCV cure improve liver function and may reduce mortality in decompensated cirrhosis if treated before the point of no return. Identification of high-risk cases for HCC after HCV cure is important to personalize surveillance. Situation of DAA treatment for HCV patients

complicated with active HCC may differ between countries due to lack of evidence. These points will be discussed.

HCC Clinical Trials in Hepatocellular Carcinoma: Challenges of Multinational Multicenter Trials *HCC11-1*

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Hepatocellular carcinoma (HCC), the most common type of primary liver cancer, presents significant therapeutic challenges, particularly in the context of multinational, multicenter clinical trials. There are many challenges and propose strategies for effective management. The complexity of HCC, influenced by underlying liver disease, comorbidities, and diverse etiologies, necessitates a multifaceted approach in clinical research. Multinational, multicenter trials for HCC are pivotal in advancing global understanding and treatment strategies. However, these trials face unique challenges, including variability in clinical practices, regulatory differences, and heterogeneous patient populations. There is disparity in HCC epidemiology, risk factors, and standard care protocols across different countries. Variations in disease presentation and progression, influenced by geographic and genetic factors, further complicate trial design and outcomes analysis. Moreover, there are problems on patient recruitment, adherence to protocols, data collection consistency, and the impact of cultural and linguistic barriers. We underscore the importance of harmonizing regulatory requirements and clinical guidelines to facilitate smoother conduct of these trials. Clinical studies delve into the methodological challenges of ensuring statistical power and validity in such diverse settings. Strategies to overcome these include adaptive trial designs, robust statistical methods to handle heterogeneity, and the use of centralized data monitoring systems.

In conclusion, the complexities inherent in multinational, multicenter clinical trials for HCC are challenging. It advocates for international collaboration, standardization of practices, and innovative trial designs to enhance the efficacy and generalizability of clinical research in the realm of hepatocellular carcinoma.

HCC Clinical Trials in Hepatocellular Carcinoma: Challenges of Multinational Multicenter Trials *HCC11-2*

Utilizing Real-world Data for Systemic therapy in Hepatocellular Carcinoma.

Dr. Yoshinari Asaoka

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In the current landscape, the escalating costs of drug development not only pose challenges to the development process but also contribute to the rising prices of approved medications. Considering this situation, there is growing anticipation for new drug development utilizing real-world data (RWD). Developing a single novel drug using RWD is not necessarily straightforward. However, it seems possible to develop better treatment sequence by evaluating the effects of treatment sequencing, combination therapies, and their impact on therapeutic outcomes and adverse events.

Systemic therapy for advanced hepatocellular carcinoma (HCC) has made remarkable progress. In Japan, regimens including atezolizumab plus bevacizumab, sorafenib, and lenvatinib were available for first

line treatment, and regorafenib, ramucirumab, and cabozantinib for second line until the approval of tremelimumab plus durvalumab in 2022. In real-world clinical practice, treatment is being delivered in a variety of sequences. We launched the Hepatoma Registry of Integrating and Aggregating EHRs (electric health record): HERITAGE study to establish a registry of RWD in Japan. In this study, among the HCC cases registered in the nationwide follow-up survey of primary liver cancer conducted by Japan Liver Cancer Association, cases treated with systemic therapy between 2015 and 2022 were included. We will show the RWD of systemic therapy for HCC in Japan, including changing patient characteristics, treatment sequences, and treatment efficacy.

HCC Unraveling the Progression of Genomic Anomalies in Hepatocellular Carcinoma *HCC12-3*

Integrated Omics Analysis for the Progression of Hepatocellular Carcinoma

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University Japan

Recent advances in gene analysis technologies such as next-generation sequencing system have facilitated genome-wide investigation in various cancers including hepatocellular carcinoma (HCC). Comprehensive and un-supervised transcriptomic analysis has been conducted, revealing that HCC samples can be divided into several subtypes with distinct gene expression patterns. Additionally, genome and exome analysis through next-generation sequencing, as well as methylome, metabolome and proteome analysis using methylation array and mass spectrometry, have been conducted. During this period, the “two-class” model, categorizing HCC into proliferative and non-proliferative classes, was proposed. Publicly available data including mutation signatures and expression profiles of hundreds of HCC cases were generously provided by the Cancer Genome Atlas (TCGA) and International Cancer Genome Consortium (ICGC) Research Network, advancing the understanding of the relationship between the subtypes, clinicopathological factors, and tumor microenvironment including vascular endothelial cells and immune cells. On the other hand, since the approval of antiangiogenic agent sorafenib, treatment options have been lacking due to a series of clinical trial failures for nearly 10 years. However, other antiangiogenic inhibitors including regorafenib, lenvatinib, cabozantinib and antiangiogenic antibodies have emerged, followed by combination of immune checkpoint inhibitors, which can ameliorate progression-free and overall survival in HCC patients. Nevertheless, starting with the clinical report that HCC with CTNNB1 active mutations conferred potential resistance to immune checkpoint blockade, investigations on the link between the subtypes and drug response are ongoing by further use of single-cell gene analysis. In the same period as such development in genome-based medicine, it has coincided with the acceleration of remarkable innovations in genome-editing technology using the CRISPR/Cas9 system. The integration of comprehensive genome editing technologies, such as multiplex genome editing, which introduces multiple genomic aberrations simultaneously, with barcode sequencing technology has led to the development of in vivo screening methods, allowing preclinical models that mimic each subtype to be individually reproduced. Immunocompetent subtype models reflect the molecular characteristics of the subtype and the tumor immune microenvironment and can help evaluate the efficacy of single and combination therapies and understand the molecular and immunological mechanisms underlying vulnerability and resistance to them. Thus, consensus classifications and associated pre-clinical models are extremely promising for establishing predictive

biomarkers and escalating the clinical development of subtype-specific therapies.

HCC Unraveling the Progression of Genomic Anomalies in Hepatocellular Carcinoma *HCC12-4*

Unraveling the Progression of Genomic Abnormalities in Hepatocellular Carcinoma

Dr. Pei-Jer Chen

Hepatitis Research Center National Taiwan University & Hospital Taiwan

The natural history of hepatocellular carcinoma presumably evolves from initial chronic hepatitis, subsequent cirrhosis and eventually HCC. In analogous to most human cancers, genomic mutations gradually appear and accumulate during the process, and finally lead to HCC. However, so far we still cannot chronicle the time-sequences of the incriminated mutations in details.

Most of known common genetic mutations of human HCC, irrespective of etiology, such as TERT promoter mutations, p53 or beta-catenin, or ARID gene mutations, occur in the late stage, from dysplastic nodules to early HCC. In the non-dysplastic cirrhotic nodules, WGS failed to identify recurrent genetic mutations. Therefore, we still do not know what mutations drive the clonal expansion in the cirrhosis stage. One exception to this is noted in HBV-related HCC in which HBV DNA integration takes place in the very early stage of viral infection or hepatitis, probably 20-30 years before the development of HCC. Two HBV DNA integration hotspot genes have been identified in TERT promoters or Exon3-6 of MLL4 gene. HBV DNA integration into the two sites clearly grants advantages for subsequent evolution into HCC. This case may hint the early genomic abnormalities residing in these two pathways: TERT gene over-expression or truncated MLL4 mediated epigenetic mutations and warrant further investigation.

HCC Tumor Microenvironment in Hepatocellular Carcinoma *HCC13-3*

Understanding microenvironment of hepatocellular carcinoma for biomarkers and therapeutic discovery

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Despite recent success in cancer immunotherapies, the complex dynamics within tumor-immune microenvironment (TIME) remain elusive. With the multidimensional analysis pipeline, we have successfully identified and described key immunological factors in hepatocellular carcinoma (HCC) that contribute to disease progression and clinical response to therapy. Our team has identified peripheral immunological biomarkers associated to therapeutic response in HCC patients treated with radiotherapy and anti-PD-1 immunotherapy, shedding light on potential mechanism for treatment response and guiding the design of novel therapeutic strategies. More recently, we have explored the immune landscape of steatotic-related HCC to uncover potential mechanisms driving immunosuppression and to identify novel immunotherapeutic targets.

ACLF 1. Recent Changes of Incidence and Etiology of Acute Liver Failure in Asia Pacific Region *ACLF1-3*

Recent changes of incidence and epidemiology of acute liver failure in Asia-Pacific region

Dr. Nobuaki Nakayama

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There is no international registry of acute liver failure (ALF) in the Asia-Pacific region. Instead, data on the outcomes of ALF are available by referring to published studies on ALF evaluated in nationwide surveys and at individual centers. In Asia, viral hepatitis has been the main cause of ALF; however recent publications suggest that the incidence of ALF due to drugs and herbs is increasing in most countries (Jindal et al., 2022). Pan Zhao et al. reported in 2013 that traditional Chinese medicine was a major cause of ALF in China. In India, HEV was the etiology of ALF in 419 (28.7%) cases, whereas non-A non-E hepatitis, HBV, and antituberculosis therapy were the etiologies in 527 (36.0%), 128 (8.8%), and 103 (7.0%) cases, respectively (Shalimar et al., 2017). A large study by the Indian DILI Network disclosed that antituberculosis drugs (62.9%) were the most common types of drugs that had caused ALF (Devarbhavi et al., 2021). In South Korea, according to the prevalence of HAV infection, the number of HAV ALF cases requiring liver transplantation were increasing (Kim, 2010). In Australia, paracetamol was the most common etiology of ALF, accounting for 49.7% of cases (Hey et al., 2019).

The Intractable Hepato-Biliary Diseases Study Group of Japan conducted a nationwide survey on ALF and late-onset hepatic failure (LOHF) since 2011. Until 2011, they had performed such surveys on fulminant hepatitis and LOHF. A total of 2,368 patients with fulminant hepatitis and/or acute liver failure (acute and subacute) and 172 patients with LOHF were enrolled in nationwide surveys. In cases seen from 1998 to 2009, the viral etiology in the acute type of hepatitis accounted for 67.4%, whereas from 2010 to 2015, it decreased to 32.7% for overall cases of the acute type and 43.8% for hepatitis cases specifically. In the years 2016 to 2021, the respective percentages further declined to 26.9% and 39.1%, indicating a continued decrease in viral etiology rates. During that period, HBV was the etiology for 92 cases, representing 15.9% of the total cases of ALF (acute and subacute) and LOHF, and 20.2% of hepatitis cases. In cases of hepatitis, the ratios of autoimmune and drug-induced etiologies were 8.1% and 11.6%, respectively, for the period 1998 to 2009. However, in the years 2010 to 2015, these ratios increased to 14.4% and 11.0%, and further rose to 16.9% and 16.6% during the period from 2016 to 2021.

ACLF 1. Recent Changes of Incidence and Etiology of Acute Liver Failure in Asia Pacific Region *ACLF1-4*

Japanese style artificial liver support system

Dr. Kazuaki Inoue

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Japan is a country where blood purification therapy is most advanced than any other countries in the world. The reason for this is the development of Japanese industrial technology and the harsh environment surrounding transplant medicine. In Japan, blood purification therapy that can keep a patient awake and in a stable condition is essential. In the Japanese medical environment, a requirement for blood purification therapy is the ability to reliably awaken patients and maintain

them in a stable state. The method developed for this purpose is blood purification therapy that combines plasma exchange and hemodiafiltration. The characteristics of hemodiafiltration are that blood is purified using a large amount of replacement fluid and that blood purification takes a long time. Even though method of hemodiafiltration is the same, the conditions are very different from those used for renal replacement therapy. Since using this treatment, most patients have recovered from coma, and it is now possible to safely maintain them until their own livers regenerate or a suitable donor is found. Today, the number of elderly patients with comorbidities is increasing, and it is difficult to perform dialysis under strict dialysis conditions for such patients. Due to these circumstances, there are a certain number of patients with acute liver failure who do not undergo blood purification in recent years. In the future, it is necessary to improve vascular access and develop blood purification therapy that is easy to do.

ACLF 2. Treatments and Prognosis of ACLF in Asia Pacific Region *ACLF2-2*

Management of vascular disorders in patients with ACLF

Dr. Akash Shukla

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Vascular liver diseases like portal vein thrombosis (PVT) or Budd Chiari syndrome (BCS) may present with acute on chronic liver failure (ACLF). The possible associations of PVT with ACLF (PVT-ACLF) have been recently described and the principles of management of these patients proposed. The treatment options for PVT in this setting would include observation, anticoagulation and/or radiological interventions like thrombolysis and thrombectomy. The choice of therapy would depend upon the extent of thrombosis and the clinical consequences of PVT. The other vascular disease is BCS, where association with ACLF (BCS-ACLF) and its management is described. While we know that acute on chronic BCS is associated with poor outcomes, there is recent data on clinical features and management of BCS-ACLF. In patients with ACLF where the acute event is vascular thrombosis like PVT or hepatic vein thrombosis (HVT), there is a potential for reversibility of liver failure, especially in the 'golden window', similar to other ACLF, and all attempts need to be made towards urgent recanalization of these vein(s), while in patients with pre-existing BCS or cirrhosis with PVT who present with ACLF, liver transplant may be the best option.

ACLF 3. Liver Regeneration up to date *ACLF3-1*

Revolutionising Liver Health: The Science and Potential of Liver Regeneration

Dr. Kuo-Chao Yew

Gastroenterology and Hepatology Department Tan Tock Seng Hospital Singapore

The liver's extraordinary regenerative capability, coordinated by the intricate "Hepatostat" system, maintaining a consistent liver-to-body-weight ratio, sets it apart from other organs. Prominently demonstrated in partial hepatectomy, this regenerative capability offers profound insights into harnessing natural regenerative potential and serves as a tissue engineering model. However, chronic liver diseases disrupt this equilibrium, causing hepatocyte depletion, hepatic stellate cell

activation, and collagen buildup, while genotoxic environments can trigger liver oncogenesis through cellular diploidy induction.

In contemporary times, significant strides have been taken in comprehending cellular kinetics, histological transformations, and signalling pathways pivotal in liver regeneration. Moreover, understanding zone-specific initiation unravels the precise orchestration of diverse soluble factors governing liver zonation. The identification of progenitor cells opens doors to innovative therapies involving cellular, drug, and gene manipulation. Excitingly, the past decade has witnessed breakthroughs such as bioengineered livers for disease modelling, 3D printing in liver transplantation, and integration of artificial intelligence, signifying newfound enthusiasm in the field.

This lecture delves into the potential of liver regeneration, providing a glimpse into the promising future of Hepatology.

ACLF 3. Liver Regeneration up to date *ACLF3-3*

Development of Regenerative Therapy for Liver Cirrhosis - Mesenchymal stem cells, HMGB1 peptide, extracellular vesicles-

Dr. Shuji Terai

Division of Gastroenterology & Hepatology, Graduate School of Medical and Dental Sciences, Niigata University Japan

We have been developing regenerative therapies for liver cirrhosis. The liver is a regenerative organ, but fibrosis reduces its regenerative capacity, and a clinical study in 2003 and a subsequent multicenter clinical study (Autologous bone marrow cell infusion therapy) showed that improvement of fibrosis induces regeneration in patients with non-compensated liver cirrhosis. Subsequently, since 2015, conducted a clinical trial for cirrhosis using allogeneic mesenchymal stem cells. From a series of basic studies. The mechanism was clarified that mesenchymal stem cells administered from peripheral blood vessels repopulated mainly to the lungs, where they emit extracellular vesicles, making macrophages anti-inflammatory, improving fibrosis, and inducing regeneration. Furthermore, extracellular vesicles obtained by induction of mesenchymal stem cells with IFN γ were found to be useful for improving fibrosis and inducing regeneration. On the other hand, the optimization of the liver fibrosis evaluation method in clinical trials for liver cirrhosis has also been clarified by conducting clinical trials of mesenchymal stem cells and HMGB1 peptide as a corporate clinical trial and an investigator-initiated clinical trial. In the future, we are preparing to establish an international standard for how extracellular vesicles can be used as a treatment that maintains clear quality in terms of Mode of Action.

In this presentation, we will present the future perspective of a new regenerative therapy for liver cirrhosis.

ACLF 3. Liver Regeneration up to date *ACLF3-4*

Next-Generation Stem Cell Therapeutics for the Treatment of Liver Cirrhosis: from bench to bedside based on Functional Enhancement System

Dr. Si Hyun Bae

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Liver cirrhosis are common clinical manifestations of advanced liver diseases. Currently, liver allograft transplantation is the gold standard

for the treatment of end-stage liver disease. A shortage of suitable organs, high costs and surgical complications limit the application of liver transplantation. Nowadays, stem cell therapy gained more and more attention due to its attractive efficacy in treating liver disease especially in cirrhosis during the clinical trials. Due to the regenerative properties of the liver, various kinds of cell therapies using hepatocytes, hematopoietic stem cells, bone marrow mononuclear cells, and mesenchymal stem cells (MSCs) are being investigated as alternative treatments to liver transplantation.

Among them, Mesenchymal stem cell therapy has been considered as a promising alternative approach for end-stage liver disease, because they show potential to regenerate injured tissues or organs, such as homing, transdifferentiation, immunosuppression, and cellular protective capacity.

Some clinical trials have confirmed the effectiveness of MSC therapy for liver disease, but currently, there is no approved MSC therapy for the treatment of liver disease, because the types of liver disease that are most suitable for MSC application should be determined, and the preparation and engraftment of MSCs should be standardized. These may be bottlenecks that limit the use of MSCs.

More robust preclinical and clinical studies will be needed for the key strategies to enhance the functionality of MSC which include priming factors such as cytokines, genetic modification, and tissue engineering treatments for liver diseases. In the future, each method has its advantages and challenges, and researchers continue to explore the most effective and safe approaches for liver regeneration using MSCs.

ACLF 4. Drug Induced Liver Injury in Asia Pacific Region
(Including Herbs)

ACLF4-2

Unraveling the Pathophysiology of ICI-Induced Immune-Mediated Hepatotoxicity through a Comparison with Autoimmune Hepatitis

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Japan

Autoimmune hepatitis (AIH), although a well-known disease, still lacks sufficient understanding of its pathogenesis. Additionally, there is a need for the development of biomarkers, especially for cases resistant to steroids or experiencing relapse. On the other hand, advancements in cancer immunotherapy have brought forth a new concern—immune-mediated hepatotoxicity induced by immune checkpoint inhibitors (ICI), known as ICI-induced immune-mediated hepatotoxicity (IMH). Given its recent emergence, the pathophysiology of IMH remains unclear, and established treatment methods are yet to be defined. While steroids are the primary choice for IMH treatment, resistance cases are frequent compared to AIH. In such instances, empirical recommendations include agents like mycophenolate mofetil, but definitive evidence is lacking.

The anticipation of the growing importance of immunotherapy in the future underscores the urgency for understanding the pathophysiology of these conditions. As part of our efforts in what we term "next-generation precision medicine," we have conducted multi-omics analyses using liver tissues from AIH patients for pathophysiological insights and biomarker development. Currently, we are integrating multi-omics data, including liver biopsy samples from IMH, which shares commonalities with immune-related liver disorders. Through this comprehensive analysis, incorporating the transcriptome data from AIH alongside IMH samples, we aim to elucidate the pathophysiology of both conditions and identify biomarkers. In this session, I will present a portion of this data.

PH Elastography: Current Strategy for Practical Care
PHI-1

Role of Elastography in Hepatitis Elimination

Dr. Grace Lai-Hung Wong

Medical Data Analytics Centre (MDAC), Center for Liver Health,
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Elastography is one the most popular noninvasive assessments of liver fibrosis in patients with chronic viral hepatitis. Specifically, Vibration controlled transient elastography (VCTE) is now an integral part of the clinical care pathway of chronic viral hepatitis in order to determine the prognosis, the need of treatment, as well as monitor disease progression and response to treatment. As alanine aminotransferase (ALT) is one of the major confounding factors of liver stiffness in chronic hepatitis B, an ALT-based algorithm has been developed and higher liver stiffness measurements (LSM) cutoff values for different stages of liver fibrosis should be used in patients with elevated ALT levels up to 5 times of the upper limit of normal. Otherwise falsely-high LSM results up to cirrhotic range may occur during ALT flare. VCTE is also useful in predicting patient prognosis such as development of hepatocellular carcinoma (HCC), portal hypertension, post-operative complications in HCC patients, and also survival. Failed acquisition of VCTE may happen up to 25% in obese patients. Furthermore, obese patients may have higher LSM results even in the same stage of liver fibrosis. The XL probe, a larger probe with lower ultrasound frequency and deeper penetration, increases the success rate of VCTE in obese patients. The median LSM value with XL probe was found to be lower than that by the conventional M probe, hence cutoff values approximately 1.2 to 1.3 kPa lower than those of M probe should be adopted. Recent studies revealed a novel ultrasonic controlled attenuation parameter (CAP) of the machine is a useful parameter to detect even low-grade steatosis noninvasively. CAP may also be used to quantify liver steatosis by applying different cutoff values. As both LSM and CAP results are instantly available at same measurement, this makes VCTE a very convenient tool to assess any patients who are at risk or confirmed to suffer from chronic liver diseases.

PH Elastography: Current Strategy for Practical Care
PHI-3

Clinical utility of the liver and spleen stiffness measurement in the patients with portal hypertension

Dr. Masashi Hirooka

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Portal hypertension is a critical condition often associated with complications such as varices and ascites, making measurement of the hepatic venous pressure gradient (HVPG) a well-established surrogate marker. HVPG measurement allows prediction of complications associated with cirrhosis, including varices and ascites. According to the Baveno VII criteria, liver stiffness measurement (LSM) plays a crucial role in the diagnosis of clinically significant portal hypertension (CSPH). LSM values below 10 kPa effectively rule out compensated advanced chronic liver disease (cACLD), while LSM values between 15 kPa and a platelet count of 150,000 or greater may rule out CSPH. LSM values above 25 kPa suggest the presence of CSPH. However, the challenge lies in the "gray zone" cases that cannot be definitively categorized using these criteria.

To overcome this limitation and reduce the gray area, markers that correlate better with HVPg than LSM are needed. The spleen, which is emerging as a potential marker, shows a promising role in the assessment of HVPg. Spleen stiffness measurement (SSM) has been reported to correlate better with HVPg than liver stiffness and various fibrosis markers, with a high predictive ability for high-risk esophageal varices.

Our research group, the Spleen Stiffness-IPD-MA Study Group, conducted a systematic review and meta-analysis of individual patient data and reported the favorable diagnostic performance of the Baveno VII SSM criteria. Despite the promising results, accurate measurement of SSM poses challenges compared to LSM. Proper measurement techniques, including the use of new devices and accurate assessment of low controlled attenuation parameter (CAP) values, can improve the reliability of SSM measurements.

In conclusion, our findings suggest the potential of SSM as a valuable marker in the prediction of portal hypertension complications when added to LSM.

PH Management of Portal Hypertension: Standard and Beyond
PH2-1

Innovation Management in Portal Hypertension: Standard and Beyond

Dr. Cosmas Rinaldi Adithya Lesmana

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Portal hypertension (PH) is still a challenging condition in daily practice as it carries a lot of complications, such as the presence of vascular complication (esophageal varices/EV, gastric varices/GV, gastric antral vascular ectasia/GAVE, gastropathy, colopathy, rectal varices), ascites, hepatic encephalopathy, hepatorenal syndrome, and hepatopulmonary syndrome. The diagnosis of PH is confirmed when the portal pressure reaches 5 mmHg and above. Clinically significant portal hypertension (CSPH) is the most important condition in liver cirrhosis (LC) patients, as it can predict the possible complications arise, and to decide further management including porto-systemic shunting procedure and liver transplantation. However, the gold standard for PH is the indirect measurement, hepatic vein pressure gradient (HVPg) measurement. Even though this procedure is considered as a safe and minimally invasive, but possible adverse events, such as bleeding, pain, infection, and perforation could still happen. It is not always accurate in the setting of non-cirrhotic portal hypertension condition. This procedure is also cannot be performed concomitantly with esophagogastroduodenoscopy (EGD) procedure.

Recently, endoscopic ultrasound (EUS) has been developed for managing liver disease condition. There have been innovations in measuring portal pressure using a novel manometer as well as standard manometer. EUS can be used for portal pressure gradient measurement, where it is a direct measurement, and it can be done with other innovation procedures, such as EUS-guided liver biopsy, EUS-guided vascular injection, and EUS-guided radiofrequency ablation (RFA) for liver tumor. It would need a special training and further validation before it can be recommended as the first-line approach in the future.

PH Management of Portal Hypertension: Standard and Beyond
PH2-3

Interventional Radiology for Portosystemic Shunt Related Disease

Dr. Akira Yamamoto

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Interventional radiology for portosystemic shunt related diseases addresses embolization of portosystemic shunts (PSS) causing varices and hepatic encephalopathy. Balloon occluded retrograde transvenous venography (BROTO) for a treatment for gastric varices, a form of PSS, has been reported to improve liver function. In recent years, studies have suggested that the more liver function is preserved prior to treatment, the better liver function improves. This presentation will discuss embolization of large PSS and its results, as well as our approach in cases of encephalopathy with PSS with poor liver function.

PH Cross Talk with Multiple Organs in Cirrhosis
PH3-1

Impact of 2022 ESC/ERS diagnostic criteria for pulmonary hypertension in cirrhotic patients with portal hypertension in Japan

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Portopulmonary hypertension (PoPH) is defined as PAH associated with portal hypertension. So far, conventional PoPH was defined as a mean pulmonary artery pressure (mPAP) ≥ 25 mmHg, pulmonary vascular resistance (PVR) > 3 Wood units (WU), and pulmonary arterial wedge pressure (PAWP) ≤ 15 mmHg according to the previous diagnostic criteria, whereas in 2022, the European guideline for pulmonary hypertension revised the hemodynamic definition of pulmonary hypertension in pre-capillary PH by lowering the mPAP to > 20 mmHg and the PVR to > 2 WU. From now on, prevalence of patients with PoPH according to the new guideline may change among cirrhotic patients with portal hypertension. At Nippon Medical School, 186 patients with liver cirrhosis and portal hypertension were subjected and underwent right heart catheterization in this analysis. The median mPAP, PVR and PAWP were 12.9 mmHg (range, 6.6–40.8), 0.8 WU (range, 0.1–4.5) and 7.5 mmHg (range, 2.2–15.4) respectively. For both diagnostic criteria, many of the 186 patients were below the cut-off values for both mPAP and PVR, respectively (conventional, $n = 184$; new, $n = 182$). Two (1.1%) patients had conventional PoPH. In addition, two patients that were not diagnosed as PoPH by the conventional diagnostic criteria were included in the PoPH range by the new diagnostic criteria. For each diagnostic criteria, there were no patients that met only one criterion of mPAP and PVR, and were divided into two groups. mPAP and PVR were significantly but weakly correlated ($p = 7.44 \times 10^{-5}$, $r = 0.286$). With the new diagnostic criteria of PoPH, there were patients that were not diagnosed with PoPH by conventional diagnostic criteria, resulting in an increase in the number of patients diagnosed with PoPH from 1.1% to 2.2% in this cohort. In particular, it is possible that the change in the cut-off value of PVR was particularly important, since patients with a PVR of 2 to 3 WU were newly diagnosed. As new diagnostic criteria are likely to be adopted in Japan in the future, the number of patients diagnosed with PoPH is expected to increase.

PH Noncirrhotic Portal Hypertension: Current Status and Problem
PH4-1

Non cirrhotic portal hypertension: Current status and problem

Dr. Sudhamshu K C

Department of Hepatology, National Academy of Medical Sciences Nepal

First described by Banti in 1889, non-cirrhotic portal hypertension (NCPH) refers to a heterogeneous group of liver disorders characterized by portal hypertension, splenomegaly, hypersplenism, and cytopenia in absence of liver cirrhosis. It has been referred to by different names over time such as non-cirrhotic portal fibrosis (Indian subcontinent), hepatoportal sclerosis (West), and idiopathic portal hypertension (Japan). NCPH is diagnosed after excluding other causes of portal vein or hepatic venous outflow tract obstruction. The disease progresses through different phases with symptoms ranging from splenomegaly and anemia to complications of portal hypertension such as gastrointestinal bleeding, ascites.

Later, the term idiopathic non-cirrhotic portal hypertension (INCPH) was proposed by a consensus of experts who introduced a common nomenclature and diagnostic criteria: essentially, the presence of an unexplained portal hypertension and the absence of cirrhosis in liver histology.

Recently, in order to overcome those difficulties and to reach a uniformity in the nomenclature, the term Porto-Sinusoidal Vascular Disease (PSVD) has been proposed by the European Association for the Vascular Liver Disease. Now it is not limited to the exclusion criteria but provides positive diagnostic criteria. The new diagnostic criteria define the diagnosis of PSVD in presence of one of the three following features:

1. At least one specific sign of portal hypertension (gastroesophageal or ectopic varices, porto-systemic collaterals, bleeding due to portal hypertension) in the absence of cirrhosis at a liver biopsy
 2. At least one specific histological sign of PSVD (obliterative portal venopathy, nodular regenerative hyperplasia, incomplete septal fibrosis or cirrhosis) and absence of cirrhosis at liver biopsy. As per this criteria there may be absence of signs of portal hypertension;
 3. At least one non-specific sign of portal hypertension (ascites, low platelets, splenomegaly) at an adequate liver biopsy and in addition to at least one non-specific histological sign of PSVD (portal tract abnormalities: multiplication, dilation of arteries, periportal vascular channels, and aberrant vessels; architectural disturbance: irregular distribution of the portal tracts and central veins; non-zonal sinusoidal dilation; mild perisinusoidal fibrosis) and to the absence of cirrhosis
- The exact cause of INCPH or PSVD remains a mystery, prompting ongoing research. There are no specific tests. Instead, accurate diagnosis relies on a high-quality liver biopsy, and the skilled interpretation of a pathologist. Notably, no treatments specifically aimed at controlling the disease progression have been explored. Currently, the treatment relies on the prevention of complications related to portal hypertension, following current guidelines of cirrhotic portal hypertension.

PH Noncirrhotic Portal Hypertension: Current Status and Problem
PH4-2

Non-cirrhotic Portal Hypertension: Problem and Current Status

Dr. Ashish Kumar

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Non-cirrhotic portal hypertension (NCPH) is a significant medical condition characterized by increased pressure in the portal vein system, which is not caused by cirrhosis of the liver. This condition is relatively rare compared to cirrhotic portal hypertension but carries substantial clinical implications. My presentation will explore the etiology, pathophysiology, clinical manifestations, diagnosis, and management strategies for NCPH.

Etiology and Pathophysiology

NCPH can arise from a variety of causes, including vascular disorders like portal vein thrombosis, splenic vein thrombosis, or Budd-Chiari syndrome; structural abnormalities like schistosomiasis; and systemic diseases such as sarcoidosis and autoimmune hepatitis. Unlike cirrhotic portal hypertension, where the primary issue is increased resistance to blood flow within the liver, in NCPH, the resistance may occur pre-hepatically (before the liver), intrahepatically (within the liver but not due to cirrhosis), or post-hepatically (after the liver).

The pathophysiology of NCPH involves the disruption of normal portal venous flow due to these varied causes, leading to increased portal pressure. This increase in pressure can lead to the development of collateral vessels and splenomegaly, among other complications.

Clinical Manifestations

Patients with NCPH may present with a range of symptoms. The most common manifestation is gastrointestinal bleeding, typically from esophageal or gastric varices, similar to what is seen in cirrhotic patients. However, patients with NCPH often have preserved liver function. Other presentations can include splenomegaly, ascites (less common than in cirrhosis), and features of hypersplenism like pancytopenia.

Diagnosis

Diagnosis of NCPH requires a combination of clinical, laboratory, and imaging findings. Liver function tests are typically normal or show only mild abnormalities. Imaging studies, such as Doppler ultrasound, CT scan, or MRI, are critical for identifying the site and cause of the increased portal pressure. In some cases, a liver biopsy may be necessary to exclude cirrhosis and to identify intrahepatic causes of NCPH.

Management

Management of NCPH focuses on treating the underlying cause, if identified, and managing complications. Primary prevention of variceal bleeding is essential and can be achieved through pharmacotherapy (e.g., beta-blockers) or endoscopic interventions. In cases of variceal bleeding, endoscopic therapy is the mainstay of treatment. Additionally, management of hypersplenism and its hematologic complications may be necessary.

In cases where medical management is inadequate, surgical options such as shunt surgeries or even liver transplantation may be considered, depending on the underlying pathology and patient's overall condition.

Conclusion

Non-cirrhotic portal hypertension is a complex condition with diverse etiologies and manifestations. Its management requires a thorough understanding of its pathophysiology and a multidisciplinary approach. Early recognition and appropriate intervention are key to improving outcomes in patients with NCPH. Further research is needed to better understand this condition and to develop more effective management strategies.

PH Cirrhosis Care Emerging Changes
PH5-1

Effects of Exercise on Physical Function and Prognosis of Patients with Liver Cirrhosis and HCC

Dr. Takumi Kawaguchi

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Sarcopenia and frailty are highly prevalent in patients with liver cirrhosis and hepatocellular carcinoma (HCC). Generally, the beneficial effects of exercise on sarcopenia and frailty have been established. However, opposing results have been reported regarding the effects of exercise on serious events in patients with liver cirrhosis. Due to the lack of scientific evidence, exercise therapy remains weakly recommended in the Japanese clinical practice guidelines for liver cirrhosis.

First, we performed a meta-analysis of randomized controlled trials (RCTs) to examine the effects of exercise on physical function and serious events in patients with liver cirrhosis. A literature search was conducted in 2022. Eleven RCTs were selected for the meta-analysis (exercise group, n=232; control group, n=193). A meta-analysis was performed using a random-effects model. In the eleven RCTs, a meta-analysis demonstrated the 6-minute walking distance significantly improved in the exercise group compared with the control group. Moreover, in a stratification analysis based on a combination of aerobic and resistance exercise, the incidence of serious events was 6.25% and 24.7% in the combination exercise and control groups, respectively. A meta-analysis demonstrated a significant reduction in the incidence of serious events in the combination exercise group compared with the control group.

Next, we investigate the effects of exercise on the prognosis of patients with HCC. We performed a prospective observational study, which analyzed 152 patients with HCC who underwent transcatheter arterial chemoembolization (TACE). Patients were classified into the exercise (n=85) and control (n=67) groups. Independent factors associated with survival were evaluated by Cox regression analysis. There were no exercise-related severe adverse events throughout the study periods. Along with Child-Pugh class A, "exercise" was identified as an independent factor associated with survival in Cox regression analysis. The survival rate was significantly higher in the exercise group than in the control group.

In conclusion, we demonstrated that exercise improved physical function in patients with liver cirrhosis. We further demonstrated that resistance exercise in combination with aerobic exercise reduces serious events in patients with liver cirrhosis by a meta-analysis of RCTs. Moreover, in patients with HCC, exercise had beneficial effects on the prognosis with no worsening of liver function. These findings suggest that exercise therapy should be considered a fundamental therapy for patients with both liver cirrhosis and HCC.

PH Cirrhosis Care Emerging Changes *PH5-2*

Cirrhosis Care: Emerging Changes

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Cirrhosis is characterized by degeneration, regeneration and fibrosis because of the common end stage in a number of chronic progressive liver diseases. It is an important health and economic problem in the world. Five and a half million patients are affected at a cost of more than \$1.5 billion annually in the United States. There is a significant difference in terms of prognosis between compensated and decompensated stages. Acute decompensation- of liver cirrhosis should be prevented. Etiologic factor(s) such as viral, autoimmune, metabolic, alcoholic and toxic should be treated according to guidelines. Smoking, toxic drugs for liver and alcohol should be stopped. Infections should be treated adequately. Vaccinations for HAV, HBV, Influenza, Pneumococcus, Herpes zoster are strictly recommended. Mortal complications like bleeding, ascites, encephalopathy, spontaneous bacterial peritonitis (SBP), acute on chronic liver disease may occur after decompensation of the cirrhosis.

The patients with cirrhosis who have no documented history of previous GI bleeding, and have medium/large varices on endoscopy, should receive either non-selective beta blocker or endoscopic variceal ligation (EVL) within one month of varices diagnosis. If the patients are found to have bleeding esophageal varices, they should receive EVL at the time of index endoscopy. They should receive EVL every 1-2 weeks until obliteration, non-selective beta blockers, or a combination

of EVL and non-selective beta blockers to prevent recurrence of variceal hemorrhage.

Ascites is treated with both sodium restriction and diuretics with furosemide (40-160 mg /day) and spironolactone (100-400 mg/day). Patients undergoing large volume paracentesis (>5 liters removed) should receive intravenous albumin, 6-8 grams per liter removed. TIPS can be applied as a vital salvage therapy. SBP, hepatorenal syndrome and hepatic encephalopathy should be managed according to guidelines. Screening for HCC should be performed by ultrasound examinations and AFP in every 6 months. Sarcopenia and nutritional screening should be performed, and nutritional support focusing on late-night snacks, avoiding fasting, high (1 g/kg/day) protein and calorie. (~30 kcal/kg/day) consumption, increasing physical activity should be recommended. Bone diseases should be screened and managed accordingly. The management of common non-pain symptoms such as pruritus, muscle cramps, sleep disturbances, sexual dysfunction and fatigue should be managed adequately. The patients with cirrhosis and MELD score ≥ 15 should be evaluated for liver transplantation.

PH Liver fibrosis: from Bench to Bedside *PH6-1*

Liver Fibrosis & Portal Hypertension: Molecular Mechanisms and Therapeutic Opportunities

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Portal hypertension represents one of the major clinical consequences of chronic liver disease, having a deep impact in patients' prognosis and survival. Its pathophysiology defines a pathological increase in the intrahepatic vascular resistance as the primary factor in its development, being subsequently aggravated by a paradoxical increase in portal blood inflow. Elevation in vascular resistance derives from derregulations in hepatic cells function, which leads to the development of intrahepatic vascular dysfunction and fibrosis. Additionally, now we know that hepatic mechanobiological cues actively contribute to aggravate and perpetuate portal hypertension.

Hepatic microvascular dysfunction occurs early in the course of chronic liver disease as a consequence of inflammation and oxidative stress and determines loss of the normal phenotype of liver sinusoidal endothelial cells (LSEC) that become proliferative, pro-thrombotic, pro-inflammatory and vasoconstrictor. The cross-talk between LSEC and hepatic stellate cells (HSC) induces activation of the later, which in turn proliferate, migrate and increase collagen deposition around the sinusoids, contributing to fibrogenesis, architectural disruption and angiogenesis, which further increase the hepatic vascular resistance and worsen liver failure by interfering with the blood perfusion of the liver parenchyma. Moreover, recent data suggest that the phenotype of liver cells could be further impaired due to the altered mechanical properties of the cirrhotic liver itself, therefore creating a deleterious vicious cycle that would further worsen portal hypertension in advanced stages of the disease.

This lecture will critically summarize the current knowledge in portal hypertension pathophysiology, focusing on the intrahepatic mechanisms leading to fibrosis and vascular dysfunction development.

PH Liver fibrosis: from Bench to Bedside *PH7-1*

How to follow up of patient with act Metabolic dysfunction – associated fatty liver disease (MAFLD)

Dr. Hong Soo Kim

Soon Chun Hyang University Hospital, Internal medicine Korea

Metabolic dysfunction-associated fatty liver disease (MAFLD) is the most common cause of chronic liver disease worldwide. MAFLD includes a wide spectrum of liver injury including simple steatosis and non-alcoholic steatohepatitis (NASH) that may lead to serious complications such as liver cirrhosis and liver cancer

The identification of Nonalcoholic steatohepatitis (NASH) or NAFLD is clinically important because NASH indicates an increased risk for fibrosis progression and the need for aggressive treatment and closer follow-up. Population based study suggests that NAFLD is becoming an important cause of HCC, and these rates are increasing by approximately 10% per year. So we need follow up guideline of patients with NAFLD but there is no accepted consensus on the optimal strategy for monitoring patients with NAFLD and their response to treatment.

According to The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease, patients with NAFLD may need a FibroScan yearly or once every three years. The frequency is dependent on your previous FibroScan results. It is important to distinguish mild (F1-F2) from advanced or severe (F3-F4) fibrosis, as patients with severe fibrosis have a greater risk of complications and need to undergo screening for hepatocellular carcinoma with NAFLD.

PH Liver fibrosis: from Bench to Bedside

PH7-2

Endoscopic Treatment for Esophageal and Gastric Varices in Japan

Dr. Takuto Hikichi

Department of Endoscopy, Fukushima Medical University Hospital Japan

Esophageal varices (EVs) and gastric varices (GVs) are treated with drug therapy, interventional radiology, and surgical operation, but endoscopic treatment is the mainstay of treatment for patients with bleeding or high risk of bleeding.

Endoscopic treatment for EVs is widespread worldwide, and endoscopic variceal ligation (EVL) is widely used not only for bleeding cases but also for prophylactic cases. In Japan, endoscopic injection sclerotherapy (EIS) using intravariceal injection with ethanolamine oleate (EO) as a sclerosant agent has long been used for prevention of EV rupture. EIS is a treatment to embolize the inflow from portal vein that forms EVs, and theoretically has a low recurrence rate. However, due to the complexity and difficulty of the procedure, an increasing number of centers in Japan are using EVL as the main EV treatment, and EIS is now limited to high-volume centers. To reduce the EV recurrence rate by intravariceal EIS alone, extravariceal EIS with polidocanol has been used after intravariceal EIS. In addition, argon plasma coagulation (APC) after intravariceal EIS or extravariceal EIS is also used in Japan. At our institution, we are trying ablation using high-frequency hemostats as an alternative to APC. As a device for endoscopic treatment of EVs, EIS with ligation, in which the variceal puncture site is ligated during EIS, and EIS with ligation of the perforating vein that causes an extraesophageal shunt have also been performed. Recently, Furuichi et al. reported a technique for reliable intravariceal EIS using red dichromatic imaging, a kind of image enhanced endoscopy (IEE), to estimate the wall thickness and depth of EVs. Moreover, we have been using a technique to improve the success rate of variceal puncture by injecting gel into the esophageal lumen and using texture and color enhancement imaging, which is a kind of IEE.

The Sarin classification is a well-known endoscopic classification of gastric varices (GVs), based on the continuity with EVs and the location of GV, and is divided into four categories: GOV (gastroesophageal varices)-1, GOV-2, IG (isolated gastric varices)-1, IG-2. Among them, GOV-1 is a varix flowing from the gastric cardia to the esophagus, and is defined as EVs in Japan. On the other hand, the Japan Society for Portal Hypertension classifies GV into Lg-c, Lg-cf, Lg-f, Lg-a, and Lg-b. Lg-c is a varix localized at the gastric cardia, Lg-cf is a varix extending from the cardia to the fornix, and Lg-f is a varix localized at the gastric fornix. Lg-c, Lg-cf, and Lg-f correspond to IG-1, and Lg-a and Lg-b correspond to IG-2. In the following, EVs are defined as those corresponding to IG-1. Endoscopic treatment for GV is mainly endoscopic cyanoacrylate injection with N-butyl-2-cyanoacrylate (NBCA). In cases of GV hemorrhage, endoscopic cyanoacrylate injection with NBCA is preferred over EVL because of the rapid blood flow. In addition, we have been using endoscopic cyanoacrylate injection combined with intravariceal EIS with EO for prevention of GV rupture. The GV is occluded by NBCA and the inflow is embolized by EO. Furthermore, Irisawa et al. reported the combination of endoscopic-guided coil deployment and intravariceal EIS for prevention of GV rupture.

I will give a presentation on the current status of endoscopic treatment of EVs and GV in Japan.

PH Liver fibrosis: from Bench to Bedside

PH7-4

Portal Hypertension in unusual condition

Dr. Sudhamshu K C

Department of Hepatology, National Academy of Medical Sciences Nepal

Portal hypertension (PH) is defined as increased blood pressure in the portal venous system above 5 mg. Portal hypertension is classified as prehepatic, intrahepatic, and posthepatic. While cirrhosis dominates as the leading cause of PH in routine practice, NCPH and even rarer conditions can also appear in clinical settings. This presentation delves into PH seen in these less common scenarios. Following are the conditions where we can encounter PH

1. Arteriovenous malformations (AVMs)
2. Nodular regenerative hyperplasia (NRH)
3. Pseudocirrhosis
4. Hepatic fibrosis
5. Hepatic amyloidosis

First described in 1886 by Weigert, AVMs are generally uncommon, certain types can indeed contribute to PH. AVMs can be intrahepatic or extrahepatic. Extrahepatic can be of two main types namely mesenteric AVMs and splenic AVMs. Hepatic arterioportal fistulas (HAPFs) are intrahepatic causes of AVMs. It is usually categorized into three classes, as follows: Type 1: small peripheral intrahepatic; Type 2: large central HAPF; and Type 3: diffuse congenital intrahepatic.

NRH is a rare liver disease characterized by the abnormal growth of small, regenerative nodules throughout the liver. Unlike cirrhosis, which features scarring and fibrosis, NRH lacks fibrous septa between the nodules, making it a form of non-cirrhotic portal hypertension. NRH can be seen in autoimmune disorders like systemic lupus erythematosus, vascular diseases such as cystic fibrosis, viral infections and medications like azathioprine or methotrexate.

Pseudocirrhosis is a radiologic term to describe the development of diffuse hepatic nodularity caused by chemotherapy for hepatic metastasis, especially from breast cancer, pancreatic neuroendocrine, colorectal cancer. Portal hypertension can be observed in about 80% of patients with pseudocirrhosis. It is characterized by morphologic changes mimicking liver cirrhosis following chronic liver diseases. Increase in

portal flow resistance at any site within the portal venous system due to mechanical obstruction is the plausible mechanism of PH.

Congenital hepatic fibrosis is a rare condition that manifests as intra-hepatic bands of fibrous tissue originating in the portal tracts and surrounding multiple bile ductules and this can lead to the development of PH. This pathological finding often co-occurs with a spectrum of inherited renal disorders.

Lastly PH is a rare complication of hepatic amyloidosis and seems to be related to reduced sinusoidal lumen and increased resistance to blood flow due to massive perisinusoidal amyloid deposits.

Biliary 1. Current Surgical Management of Hilar Cholangiocarcinoma (Including Transplantation) *Biliary1-1*

Aggressive surgery for advanced perihilar cholangiocarcinoma under careful preoperative preparation ~ a Japanese single-center experience in the past 15 years ~

Dr. Yu Takahashi

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Perihilar cholangiocarcinoma (PHCC) is a devastating disease, and the required operative resection is technically demanding and remains to be the most difficult challenge for HPB surgeons. Major hepatectomy and extrahepatic bile duct resection has been accepted as the standard procedure. A recent systematic review showed that the mortality rate was approximately 10% and liver failure was the most common reported cause of death. In some Japanese high-volume centers, trisectionectomy of the liver, combined pancreatoduodenectomy or combined vascular resection have been aggressively performed to achieve curative resection. Various preoperative preparations have been made to reduce postoperative mortality. We report here on the preoperative management and surgical outcomes of PHCC over the past 15 years, focusing on the following points:

- Preoperative Management: Biliary drainage (inside-stent) and portal vein embolization
- Hapatopancreatoduodecetomy
- Combined vascular resection
- Left trisectionectomy of the liver

Biliary 1. Current Surgical Management of Hilar Cholangiocarcinoma (Including Transplantation) *Biliary1-2*

Pre- & Post Operative Management of Perihilar Cholangiocarcinoma

Dr. Kei Nakagawa

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Treatment of biliary tract cancer (BTC) begins with a determination of whether the cancer is resectable or not. In resectable cases, radical surgery followed by adjuvant therapy is the standard treatment. Perihilar Cholangiocarcinoma (PHC) is the most invasive surgery among BTC. The results of basic-level resection of PHC at 24 high-volume centers in three countries are reported. Serious complications occurred in more than half of the cases, and a median mortality rate of 7% at 3 months postoperatively was reported.

Safety considerations must be taken into account for surgical indications for PHC.

In preparation for surgical treatment, it is necessary to determine the side to be resected and the surgical procedure to be used. It is important to determine where to resect the bile duct, artery, and portal vein respectively. It is also necessary to properly set the predicted liver dissection plane. MDCT before biliary drainage is permissive for these decisions. This process determines the postoperative course. Identifying the number of bile ducts to be transected is also useful information during anastomosis.

After this decision is made, biliary drainage are often required. In cases requiring massive hepatectomy, preoperative portal vein embolization (PE) is attempted to increase the residual liver volume. PE is expected to increase the volume of the remaining liver by about 20%. (ex. L234, 280 ml → 340 ml) The residual liver volume and the results of the ICG study are combined to avoid postoperative liver failure.

Postoperatively, Ultrasonographic confirmation of hepatic arterial, portal, and venous blood flow is useful. Obstruction of hepatic arteries and impaired hepatic venous return cause rapid liver failure. Increased ascites and coagulation disorder are signs of portal vein thrombosis or infection. Continued surveillance cultures from drain effluent and bile should be performed. When bile leaks occur during hepatic resection with choledochal-jejunostomy, infection and abscesses occur very efficiently. Recovery is difficult if postoperative liver failure or DIC develops. Adequate drainage position is important to maintain leakage of choledochal-jejunostomy and bile leakage from the plane of liver dissection. Endoscopic anastomotic dilation and drainage may be beneficial.

The most important aspect of radical surgery of PHC is the process leading up to resection. Compared to hepatic resection without biliary reconstruction, careful postoperative management is required due to bile leakage and liver positional instability.

Prompt judgment and treatment of any abnormalities is necessary until 2-3 weeks postoperatively, when the liver regenerates and liver function is restored.

Biliary 2. Liver transplantation of biliary diseases *Biliary2-3*

Endoscopic Management of Biliary Complications after Living doner Liver Transplantation

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Living donor liver transplantation (LDLT) has emerged as a crucial option for patients with end-stage liver disease. The key advantage of LDLT lies in its ability to ensure timely transplantation, resulting in a significant reduction in waiting list mortality, especially in the situation where the number of deceased donors is limited. Notable advances in surgical techniques and perioperative management have contributed to improved outcomes in LDLT, however, biliary complications remain a major unresolved issue to be addressed.

Currently, endoscopic management is a mainstay for post-LDLT biliary complications. Specifically, in cases complicated by bile leakage, endoscopic nasobiliary drainage is the preferred intervention. As for cases with anastomotic stricture, the standard strategy is balloon dilation followed by plastic stent placement, with repeat stent exchange until stricture resolution. The use of inside stents may prevent duodenobiliary reflux, and thus extending stent patency and minimizing the need for multiple stent exchange. Alternatively, recently developed covered self-expandable metallic stents with a lasso, enabling removal even after placed into the bile duct, provide an option to the multiple plastic stents placement. Furthermore, with the advent of balloon-assisted enteroscopy, it is now possible to endoscopically manage biliary complications in LDLT patients with Roux-en-Y hepaticojejunostomy.

However, these procedures are highly challenging due to the intricate nature of the biliary system in LDLT. Therefore, a comprehensive approach that integrates percutaneous and surgical interventions may be required as a salvage option when endoscopic management fails. In this study, we comprehensively investigated clinical outcomes of endoscopic management for post-LDLT biliary complications. Additionally, we discuss recent advances as well as future perspectives in this field.

Biliary 3. Management of post operative biliary complications *Biliary3-2*

EUS Management of Bilio-Enteric Anastomotic Stricture

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Benign biliary stricture may be a problem as a postoperative complication in surgically alter anatomy cases. In many cases, it is treated with balloon enterocopy assisted ERCP (BE-ERCP), but the endoscope may not be able to reach the anastomosis or find the bilo-enteric anastomosis. The long scopes may also limit the devices and may not provide adequate treatment. The longer treatment time of BE-ERCP is also a problem, which raises health issues not only for the patient but also for the doctor due to prolonged exposure to radiation. If stent exchange is performed frequently, radiation exposure becomes an unacceptable health problem. Percutaneous transhepatic bile duct drainage is also useful, but cosmetic problems and reduced quality of life are major problems. In addition, the long period of drainage tube placement can cause a variety of problems such as skin trouble, infection, and migration of drainage tube. In recent years, endoscopic ultrasound biliary drainage has come to be used not only for malignant biliary stricture but also for benign biliary stricture. However, the evidence for interventional EUS in benign disease is still insufficient, and there are many issues such as its indications, strategies for stenosis dilatation and treatment of concomitant bile duct stones. In this session, I will discuss bilio-enteric anastomotic stricture using endoscopic ultrasound biliary drainage, including our own approach.

Biliary 3. Management of post operative biliary complications *Biliary3-3*

Endoscopic treatment of hepaticojejunostomy anastomotic strictures with a double-balloon endoscope

Dr. Naminatsu Takahara

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Hepaticojejunostomy anastomotic stricture (HJAS) is a major complication of surgical biliary reconstruction, leading to a deterioration of quality of life as well as high morbidity and mortality. The surgically altered anatomy complicates the endoscopic approach to the hepaticojejunostomy anastomosis, making percutaneous transhepatic biliary drainage or surgical re-anastomosis the standard of care. However, with the emergence of the double-balloon endoscope (DBE), HJASs are increasingly managed endoscopically.

Several clinical studies have suggested that endoscopic treatment of HJAS is technically feasible, providing a reasonably high stricture resolution rate ranging 70–100%. However, there is a paucity of data on long-term outcomes in a large-scale cohort, and predictive factors for successful endoscopic management remain unclear. Furthermore, an

optimal treatment strategy for refractory cases has not yet been determined.

In this study, we aimed to evaluate clinical outcomes of DBE-assisted ERCP for HJASs and identify predictive factors for long-term treatment success.

Biliary 3. Management of post operative biliary complications *Biliary3-4*

Short- and Long-term Outcomes for Secondary hepatolithiasis: Analysis from a Nationwide Cohort Study

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Background: Hepatolithiasis is characterized by its intractable nature and frequent recurrence. Furthermore, cholangitis, sepsis, liver abscess, and cholangiocarcinoma frequently occur. The secondary hepatolithiasis following biliary reconstruction has been increased. In the eighth nationwide multicenter survey, 48% was secondary hepatolithiasis. Additionally, there is a noticeable rise in non-surgical treatments, particularly endoscopic interventions. The outcomes of secondary intrahepatic stone treatment, especially long-term results, remain unclear. This study evaluates secondary hepatolithiasis treatment modalities' short- and long-term outcomes to consider appropriate management strategies.

Methods: The study included 128 cases of secondary hepatolithiasis registered in a nationwide cross-sectional survey conducted by the Ministry of Health, Labour and Welfare in 2017. Based on medical records, this retrospective cohort study analyzed disease backgrounds, short-term outcomes of each treatment modality, and complications, including stone recurrences, cholangitis, and cholangiocarcinoma.

Results: The cause of choledoch-enterostomy was congenital biliary dilatation in 34 cases (27%), followed by anomalies of the pancreaticobiliary junction in 29 cases (23%). Treatment was administered in 110 cases (86%), with 94 cases undergoing non-surgical treatment, 13 cases undergoing exclusive surgical treatment, and 3 cases receiving both non-surgical and surgical treatments. Endoscopic retrograde cholangiography by balloon endoscopy (ERC) was the most frequently performed in 77 cases. In surgical treatment, systematic hepatectomy was the most common surgical treatment in 12 cases. The residual stone rate between hepatectomy and balloon ERC showed no significant difference in residual stones (0% vs. 16%, $p=0.344$). There was no significant difference in stone recurrence between the two groups (5-year incidence: liver resection 28.6% vs. balloon ERC 42.3%, $p=0.400$). During post-treatment follow-up, bile duct strictures were observed in 47 cases (37%), and bile duct dilation was observed in 72 cases (56%). Stricture was a significant risk factor for stone recurrence (5-year incidence: 67.3% vs. 17.8%, $p<0.001$) and cholangitis (5-year incidence: 56.1% vs. 10.1%, $p<0.001$). The bile duct dilation was a risk factor for stone recurrence (4-year incidence: 55.7% vs. 33.3%, $p=0.006$) but not for cholangitis.

Conclusion: Minimally invasive treatment, such as endoscopy, is recommended as a first choice treatment, but a combination with other treatment modalities, including surgery, should be considered in cases where its effectiveness is insufficient. Treatment for hepatolithiasis should address complete stone removal and the management of bile duct strictures and dilation.

Biliary 3. Management of post operative biliary complications *Biliary3-5*

Novel choledochojejunostomy technique “T-shaped anastomosis” for preventing the development of postoperative cholangitis in pancreatoduodenectomy: A propensity score matching analysis

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Background: Cholangitis after pancreaticoduodenectomy (PD) is a serious complication that impairs quality of life including from repeated rehospitalization. However, there have been few studies of countermeasures to prevent this.

Objective: We developed a novel method of choledochojejunostomy with a larger anastomotic diameter, the “T-shaped anastomosis,” whose effectiveness we examine in this study.

Methods: The study included 261 cases of PD. The T-shaped choledochojejunostomy was performed with an additional incision for a distance greater than half the diameter of the bile duct at the anterior wall of the bile duct and the anterior wall of the elevated jejunum. To compensate for potential confounding biases between the standard anastomosis group (n=206) and the T-shaped anastomosis group (n=55), we performed propensity score (PS) matching. The primary endpoint was the incidence of medium-term postoperative cholangitis (within 18 months after surgery) adjusted for PS.

Results:

1) In the PS matching analysis, 54 patients in each group were matched, and the median bile duct diameter measured by preoperative CT was 8.8 mm vs. 9.3 mm, the rate of preoperative biliary drainage was 31% vs. 37%, the incidence of cholangitis within 1 month before surgery was 9% vs. 13%, and the incidence of postoperative bile leakage was 2% vs. 2%, with no significant differences.

2) The incidence of medium-term postoperative cholangitis was 14.8% vs. 3.7%, and logistic regression with PSs showed that the incidence of postoperative cholangitis was significantly lower in the T-shaped anastomosis group (odds ratio, 0.221, 95% CI 0.032-0.937; $P=0.039$). Multivariate analysis revealed that the T-shaped choledochojejunostomy was an independent predictor of reduced incidence of cholangitis (odds ratio, 0.17, 95% CI 0.02-0.81; $P=0.024$).

3) In addition to 1:1 matching, a 2:1-matching, inverse-probability-of-treatment-weighting analytical method was performed as a sensitivity analysis. All analyses showed that the incidence of medium-term postoperative cholangitis was significantly lower in the T-shaped anastomosis group.

Conclusions: The T-shaped choledochojejunostomy was shown to be effective with a significant reduction in the incidence of medium-term postoperative cholangitis.

Biliary 4. Tips and tricks in Endo-Hepatology with EUS
Biliary4-1

Current Status of Endo-hepatology

Dr. Yosuke Nakai

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Traditionally, the role of gastrointestinal endoscopy was limited to management of esophageal/gastric varices and portal hypertensive gastropathy. However, since the introduction of the concept of endo-hepatology in 2012, several procedures have been developed for endoscopic management of liver diseases. These include endoscopic ultrasound (EUS)-guided liver biopsy, liver stiffness measurement, portal pressure gradient measurement, ablation of liver tumors, and vascular interventions for conditions like gastric varices. In this presentation,

the current status and a future direction of “Endo-hepatology” for liver diseases and their complications will be discussed.

Biliary 4. Tips and tricks in Endo-Hepatology with EUS
Biliary4-2

Current Status of EUS-BD

Dr. Kazuo Hara

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EUS-BD (Endoscopic Ultrasound-Guided Biliary Drainage) is rapidly becoming popular worldwide due to its usefulness. Especially notable is the advancement in endoscopic instruments, where the development and improvement of these instruments have led to increased success rates and enhanced safety of the procedure.

The indications for EUS-BD have also evolved over time. Previously, EUS-BD was indicated only for cases where ERCP (Endoscopic Retrograde Cholangiopancreatography) was unsuccessful or not feasible. However, recently, in cases where ERCP is anticipated to be challenging, Primary EUS-BD is performed without attempting ERCP. Moreover, the indications have expanded from malignant to benign conditions. In this presentation, I would like to explain, using video, the changes in indications for EUS-BD, the development of instruments, and the advancements in techniques.

Biliary 4. Tips and tricks in Endo-Hepatology with EUS
Biliary4-3

Tips & Tricks in Endo-hepatology with EUS

Dr. Sundeep Lakhtakia

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Endohepatology is an emerging subspecialty dealing with endoscopic diagnosis and management of liver diseases. It includes both - diagnostic endoscopic ultrasound (EUS) guided elastography, and interventional EUS guided therapy for gastric varices, EUS-guided liver biopsy and direct portal pressure measurement.

EUS guided Elastography is an exploratory diagnostic technique that evaluates tissue stiffness. Liver fibrosis alters the liver's stiffness, making it an ideal target for elastography. EUS ‘shear wave elastography’ plays a significant role in evaluating liver fibrosis. By quantifying the stiffness, EUS elastography can help in staging the degree of fibrosis. Its comparison with transcutaneous liver stiffness measurement (VCTE) using liver biopsy as gold standard showed good correlation and thus a safe and reliable alternative to VCTE. It offers advantage in obese patients, where ‘percutaneous transient elastography’ might be less effective due to the increased distance between the probe and the liver.

EUS guided Liver Biopsy (EUS-LB) has emerged as viable alternative for acquiring liver tissue compared to traditional percutaneous and trans-jugular routes. EUS-LB is particularly useful in cases where other methods are contraindicated, such as in patients with ascites, coagulopathy, or obesity. EUS-LB offers several advantages, including decreased patient anxiety, increased satisfaction due to sedation, shorter post-procedural monitoring time, less post-procedure pain, and lower complication rates.

EUS guided Portal Pressure gradient (EUS-PPG) measurement a newer technique, is gaining attention as a potential alternative to conventional HVP. Direct EUS-PPG involves sequential trans-gastric puncture of hepatic vein and portal vein under EUS guidance using a

fine-needle aspiration (FNA) needle which is connected to a digital pressure transducer. By subtracting hepatic venous pressure from portal pressure, the EUS-PPG measurement is determined.

EUS guided management of Gastric Varices using coil and/or glue injection is an evolving technique in managing gastric varices. This method utilizes the advanced imaging resolution of EUS to precisely identify and target gastric varices. The standard protocol involves placing coils within the varices, followed by the injection of cyanoacrylate glue under direct visualization. These coils act as a scaffold, enhancing the glue's efficacy in variceal obliteration, promoting thrombosis, and thus reducing the bleeding risk. This targeted approach reduces the required volume of glue, diminishing the likelihood of systemic embolic events, a notable concern in glue-based therapies. The combination of coil and glue results in superior variceal obliteration, reduced rebleeding rate.

Biliary 4. Tips and tricks in Endo-Hepatology with EUS *Biliary4-5*

Tips and Tricks in Endo-Hepatology with EUS: Challenge and Limitations

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Esophageal varices (EV) is one of the most common complications in patients with liver cirrhosis (LC). Bleeding esophageal varices (BEV) is one of the challenging conditions in clinical practice due to its high mortality rate. Esophagogastroduodenoscopy (EGD) is the standard tool for screening the presence of EV as well as managing the high-risk stigmata EV. However, the portal pressure itself, and the possible of extra-luminal EV (deep EV) has become a new challenge in patients with recurrent bleeding. Recently, endoscopic ultrasound (EUS) has been investigated to be the most promising tool not only for portal pressure evaluation, but also for a better prevention of variceal bleeding. In the need of liver disease progression evaluation, EUS has been showed to be an important tool to get liver biopsy specimen. EUS is a one stop comprehensive modality for diagnosis, treatment, and make a prognosis especially in LC patients. In patients with liver mass or small nodules which might be difficult to be detected through imaging evaluation, EUS would become a better alternative as the need of liver biopsy as well as possible local treatment, such as radiofrequency ablation (RFA) for malignant liver tumor can be performed in the same session. The limitations are to get adequate tissue sample due to its hard liver parenchyma in advance LC patients, narrowed and irregular hepatic vein for hepatic vein pressure measurement, and the tumor mass location at the right lobe of the liver which is more difficult to approach for EUS-guided RFA. Pre-procedural comprehensive evaluation is still the most important thing to do, such as coagulation issue, the presence of massive ascites, and the target location of the liver mass. Other factors such as the needle type, additional liver elastogram software, and the scope position would give a better result.

In the biliary cases, EUS has been showed to have high sensitivity for gallstones, and possible malignant condition, especially for distal malignant biliary obstruction. The only limitation is to evaluate the possible hilar malignancy (intraductal cholangiocarcinoma). In this situation, intraductal ultrasound (IDUS) might be a better option for hilar or mid common bile duct lesions assessment.

Biliary 5. Immune and target therapy for cholangiocarcinoma *Biliary5-2*

Real world data of gemcitabine, cisplatin, and durvalumab combination therapy for advanced biliary tract cancer.

Dr. Takashi Sasaki

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Background: Drug therapy for advanced biliary tract cancer has made steady progress. In recent years, in addition to conventional chemotherapy using cytotoxic agents, molecular targeted drugs and immunotherapy have been introduced into treatment. In particular, first-line treatment with immune checkpoint inhibitors is expected to be a promising approach. Currently, the combination of gemcitabine (GEM) + cisplatin (CDDP) with durvalumab or pembrolizumab have been reported to be effective for advanced biliary tract cancer. In Japan, GEM + CDDP + durvalumab combination therapy has been in clinical use for more than a year.

Patients and methods: We retrospectively analyzed consecutive patients with advanced biliary tract cancer who were treated with GEM + CDDP + durvalumab combination therapy as 1st line therapy between March 2023 and October 2023 at our institution.

Results: A total of 42 patients were included. Median age was 67 and 25 patients (60%) were performance status 0. The primary sites were: intrahepatic cholangiocarcinoma 15, extrahepatic cholangiocarcinoma 15, gallbladder cancer 11, and ampullary carcinoma 1). Seventeen patients (40%) were recurrent case. Response rate and disease control rate were 19.0% and 81.0%, respectively. The median progression-free survival was 5.6 months. The median overall survival was not reached. Two patients were converted to surgical resection. Major grade 3/4 adverse events were neutropenia. Skin rash occurred in 8 patients (19%) and one patient experienced immune-related adverse event of adrenal insufficiency.

Conclusions: GEM + CDDP + durvalumab combination therapy has shown the efficacy and safety for the treatment of advanced biliary tract cancer in clinical practice.

Biliary 5. Immune and target therapy for cholangiocarcinoma *Biliary5-3*

Unveiling the Cellular Origins and Therapeutic Targets in Extrahepatic Cholangiocarcinoma: Insights from Mouse Models and Genetic Markers

Dr. Hayato Nakagawa

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The cellular origin of cholangiocarcinoma is a fascinating subject. Regarding extrahepatic cholangiocarcinoma (ECC), there has been a focus on peribiliary glands (PBGs) as a potential stem cell niche for biliary epithelial cells (BECs), raising interest in PBGs as the cellular origin of ECC. We recently developed a new mouse model of ECC by activating Kras specifically in CK19-positive duct cells and deleting TGFβR2 and E-cadherin. In this model, BECs undergo detachment and apoptosis due to the loss of E-cadherin, leading to chronic inflammation in the bile duct. Detailed histological analysis revealed the gradual dysplasia of PBGs during inflammation, eventually progressing to cholangiocarcinoma.

To definitively establish PBG as the cellular origin of biliary tract cancer, we needed animal experiments utilizing a PBG-specific gene recombination system. Consequently, we aimed to identify PBG-specific markers and discovered that Axin2, a target gene of the Wnt/β-catenin pathway, is specifically expressed in PBGs of the periampullary region. Genetic lineage-tracing demonstrated that Axin2+ periampullary PBG

cells function as biliary epithelial stem cells. Notably, the deletion of PTEN in periampullary PBG cells resulted in ampullary carcinoma, which was suppressed by a Wnt inhibitor. Therefore, Wnt signaling emerges as a potential therapeutic target for ampullary carcinoma. Moreover, we have established additional mouse models of extrahepatic cholangiocarcinoma by combining different genetic abnormalities and have identified lipid metabolic reprogramming as a potential therapeutic target. In this session, I will present a portion of this data.

Biliary 5. Immune and target therapy for cholangiocarcinoma *Biliary5-5*

Liquid biopsy of tumor-derived DNA in pancreaticobiliary malignancies in bile and plasma

Dr. Hiroshi Ohyama

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BACKGROUND: Pancreaticobiliary cancer (PBCA) is a highly progressive disease with a poor prognosis. Obtaining sufficient pancreaticobiliary tumor tissue for genomic profiling has limitations because many PBCAs are unresectable, and only a small amount of tissue is obtained via biopsy. Liquid biopsies using plasma do not provide sufficient sensitivity. Thus, this study aimed to determine the effectiveness of liquid biopsy between bile and plasma for identifying oncogenic and drug-matched mutations.

METHODS: A panel of 60 significantly mutated genes specific to PBCA was generated in-house and it was used for genomic analysis of 212 deoxyribonucleic acid (DNA) samples (87 bile supernatant, 87 bile precipitate, and 38 plasma) from 87 patients with PBCA. Of the 87 patients with PBCA, 33 (38%) were in early (stages I or II), and 54 (62%) were in advanced stages (stages III or IV). A total of 87 bile cytological specimens were collected from 87 patients, of which 32 (36%) were Class V, and 4 (5%) were Class IV. The quantity of extracted DNA from bile and plasma was compared, as were genomic profiles of 38 pairs of bile and plasma from 38 patients with PBCA. Finally, we investigated 87 bile and 38 plasma for the ability to detect druggable mutations.

RESULTS: The amount of DNA was significantly lower in plasma than in bile ($P < 0.001$). Oncogenic mutations were identified in 21 of 38 (55%) patients in bile and 9 (24%) in plasma samples ($P = 0.005$). Bile was significantly more sensitive than plasma in identifying drug-gable mutations ($P = 0.032$). Oncogenic mutations were detected in 0/3 (0%), 5/11 (45%), 7/17 (41%), 9/20 (45%), 4/4 (100%), and 24/32 (75%) in unsuitable and classes I to V, respectively, with differences between classes ($P = 0.012$). We detected 23 drug-matched mutations in combined bile and plasma, including 5 ERBB2, 4 ATM, 3 BRAF, 3 BRCA2, 3 NF1, 2 PIK3CA, 1 BRCA1, 1 IDH1, and 1 PALB2.

CONCLUSIONS: Bile is an ideal clinical specimen in PBCA because it contains a large amount of tumor-derived DNA. Liquid biopsy using bile may be useful in searching for therapeutic agents, and the utilization of the obtained genomic information may improve the prognosis of patients with PBCA.

Biliary 6. Interventional EUS for biliary diseases *Biliary6-1*

Terminology and Classification in Interventional-EUS

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Development of Interventional EUS (I-EUS) is rapidly, and new procedure, indications and devices are reported day by day. There are no standard rules in the words which used in published numerous reports, and confusions are arising. The authors had published "Clinical practice guidelines for safe performance of endoscopic ultrasound/ultrasonography-guided biliary drainage: 2018" in 2019, and confused in terminology of I-EUS. Then, Japan Gastroenterological Endoscopy Society (JGES) decided to make "Subcommittees for Terminology of Interventional EUS" (Chair: Isayama H). In this lecture, the progress of this activity and decided terminology and classifications of I-EUS will be told. From our discussion, I-EUS are classified into 5 categories; 1) EUS-sampling, 2) EUS-guided through-the-needle examination (EUS-TTNE), 3) EUS-guided drainage/anastomosis (EUS-D/A), 4) Trans-endosonographically/guided created route (Tran-ESCR) procedure, 5) EUS-guided delivery. 1) EUS-sampling is including tissue acquisition (EUS-TA) and fluid sampling, and can use EUS-FNA as well. 2) EUS-TTNE is the diagnostic procedures through the punctured needle; imaging, measurement and biopsy (TTNB) using miniature devices can through the needle cavity. 3) EUS-D/A is drainage procedures for organs and fluid collections. EUS-D/A for the organs (bile duct, pancreatic duct, gallbladder, digestive tract, etc.) is drainage procedure but anastomosis simultaneously, then use "stomy" (EUS-guided hepaticogastroenterology, EUS-guided pancreatogastrostomy). However, fluid collection is disappeared after drainage, then only words of drainage is available (transgastric EUS-PFD for WON). 4) ESCR is proposed new word represents a general term of EUS-guided/endosonographically created route. Endoscopic necrosectomy is performed through the matured route after EUS-guided drainage of walled off necrosis. Other trans ESCR procedures are antegrade stenting or stone management through the anastomosis. 5) EUS-guided delivery is the procedure to deliver the liquid, drug, equipment, energy, etc. after the puncture. Tumor ablation therapy, neurolysis implantation of fiducial markers are included. In this proposal, there were some newly created words. T-DAS is "transluminal drainage/anastomosis stent" including plastic and metallic stent, and lumen apposing metal stent is representative. The aim of T-DAS is keeping the ESCR differ from the conventional stent which keep the luminal patency at the stricture. Many doctors are using "fistula" for created route in EUS-D/A, however, "Fistula" is originally means accidentally created unusual route which are harmful, inconvenient and should be closed. Then, we proposed "anastomosis" and "route" in EUS-D/A and "ESCR" as a general term. We believed newly proposed terminology and classifications are useful to categorize various and brand-new procedures.

Biliary 6. Interventional EUS for biliary diseases *Biliary6-3*

Tips and Tricks of Interventional EUS for Liver

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The intervention for the liver using Liner EUS includes liver biopsy, liver tumor biopsy, and liver abscess drainage. Recently, EUS-FNB (Fine Needle Biopsy) from liver tumors has been increasingly performed to collect tumor specimens for cancer genomic medicine. In particular, tumors in the liver S1 region, located deep in the body, are difficult to access percutaneously, making EUS-FNB useful. The use of EUS enables simultaneous liver tumor biopsy, biopsy of enlarged lymph nodes, and ascites collection, offering greater utility than percutaneous biopsy. Understanding the EUS anatomy of the liver is necessary to visualize the targeted liver area. The trick to visualize the liver area is to focus on the vessel. In my presentation, a video will be used to explain the visualization of the liver segment, EUS-FNA, and liver abscess drainage.

Biliary 6. Interventional EUS for biliary diseases *Biliary6-4*

Interventional EUS for Biliary Diseases

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The integration of interventional Endoscopic Ultrasound (iEUS) into routine clinical practice has significantly bridged a critical gap in managing biliary diseases, notably aiding patients with complex anatomical challenges or those at high risk from conventional surgical or endoscopic procedures. Its minimally invasive nature, coupled with the capability for direct visualization and intervention, has established iEUS as a vital tool in pancreatobiliary disease management. EUS-guided biliary drainage (EUS-BD) offers a straightforward technique for bile duct drainage, whereas EUS-guided gallbladder drainage (EUS-GBD) provides a minimally invasive solution for high-risk surgical patients with acute cholecystitis, achieving high success rates with minimal adverse events.

Regarding the long-term outcomes of EUS-BD, a Korean retrospective study analyzed the clinical outcomes of EUS-guided choledochoduodenostomy (EUS-CDS) and hepaticogastrostomy (EUS-HGS) for treating distal malignant biliary obstruction (MBO). The study included 116 patients, divided into EUS-CDS (n=56) and EUS-HGS (n=60) groups. Both groups exhibited high technical success rates—98.2% for EUS-CDS and 96.7% for EUS-HGS. Clinical success was also significant, at 96.4% for EUS-CDS and 88.3% for EUS-HGS. The EUS-CDS group showed a significantly longer average stent patency of 770.3 days compared to 165.5 days for the EUS-HGS group. The only independent risk factor for stent dysfunction identified was systemic treatment following EUS-guided biliary drainage. The incidence of stent dysfunction was higher in the EUS-HGS group compared to the EUS-CDS group, with no significant differences in late adverse events. This study highlights the efficacy and safety of interventional EUS techniques in managing distal MBO, particularly emphasizing the superior stent patency associated with EUS-CDS.

In addition, a recent meta-analysis compared the efficacy and safety of EUS-GBD with percutaneous gallbladder drainage (PTGBD) in patients with acute cholecystitis. The analysis included four studies with a total of 535 patients. Although PTGBD showed a slightly higher technical success, EUS-GBD was associated with fewer adverse events, reduced unplanned readmissions, and a lower need for reinterventions, indicating its potential as a safer and more effective alternative to PTGBD, especially for patients at high surgical risk.

The adoption of iEUS has not only enhanced the safety and efficacy of treating pancreatobiliary diseases but also significantly improved patient comfort and recovery times. As technology and expertise in this field continue to evolve, iEUS is poised to play an increasingly central role in a multidisciplinary approach, promising even better patient outcomes and broader applications in gastroenterology.

Biliary 6. Interventional EUS for biliary diseases *Biliary6-5*

Biliary access in interventional EUS

Dr. Saburo Matsubara

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Endoscopic retrograde cholangiopancreatography (ERCP) is the gold standard method for biliary drainage worldwide. However, the biliary access is sometimes impossible due to the failed biliary cannulation, the duodenal invasion of the tumor, or the surgically altered anatomy. Endoscopic ultrasound-guided biliary drainage (EUS-BD) has recently emerged including transmural drainage, antegrade stenting and rendezvous with ERCP; transmural drainage includes EUS-guided choledochoduodenostomy (EUS-CDS), EUS-guided hepaticogastrostomy (EUS-HGS), EUS-guided hepaticojejunostomy (EUS-HJS), and EUS-guided hepaticoduodenostomy (EUS-HDS). In unresectable malignant biliary obstruction, transmural drainage and antegrade stenting can be a good alternative for failed ERCP. On the other hand, transpapillary approach using EUS-guided rendezvous (EUS-RV) is desirable for benign biliary diseases such as benign biliary strictures or choledocholithiasis.

EUS-RV is a rescue technique for the failed biliary cannulation in ERCP, which was firstly reported by Mallery et al. in 2004. After the puncture of the bile duct, a guidewire is inserted into the bile duct and subsequently manipulated to pass the stricture and the sphincter of Oddi. After the placement of the guidewire in the duodenum, an echendoscope is exchanged to a duodenoscope keeping the guidewire left in place. Finally, the transpapillary biliary cannulation is attempted with the help of the EUS-placed guidewire.

In EUS-RV, there are four approach routes: the puncture of the distal extrahepatic bile duct (EHBD) from the duodenal second part with a stretched (short) scope position, the puncture of the proximal EHBD from the duodenal bulb with a pushed (long) scope position, the puncture of the left intrahepatic bile duct (IHBD) from the stomach with a short scope position, and the puncture of the right IHBD from the duodenal bulb with a long scope position. The puncture of the distal EHBD from the duodenal second part is likely to be the best approach route, because the maneuverability of the guidewire is favorable due to the short distance between the puncture site and the papilla, and the favorable direction of the needle. Rates of technical success and adverse events of EUS-RV were reported as 82% and 13%, respectively.

Biliary 7. Hot topics in PSC *Biliary7-1*

Diagnostic criteria for primary sclerosing cholangitis

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Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease of unknown cause that is characterized pathologically by an inflammatory and fibrotic process centered on the epithelium, leading to diffuse biliary stenosis and increased wall thickness throughout the intra- and extra-hepatic biliary trees. The diagnostic criteria for PSC proposed by the Mayo Clinic have been used internationally in the diagnosis of PSC for a long time.

Japanese nationwide survey in 2015 revealed that several clinical aspects of PSC differed between Japan and Western countries. The Intractable Hepato-Biliary Diseases Study Group in Japan proposed Japanese diagnostic criteria in 2016 (PSC2016). The PSC2016 consisted of the major and minor items. Major items are directly related to bile duct changes based on biliary tract imaging and an increased alkaline phosphatase (ALP) level. Minor items consist of an association with inflammatory bowel disease and liver histology. It is necessary to exclude IgG4-related sclerosing cholangitis (IgG4-SC), secondary sclerosing cholangitis caused by diseases with an obvious pathogenesis, and malignant diseases such as biliary cancer.

Several years have passed since PSC2016 was published, and several limitations were found in PSC2016. Firstly, it is difficult to diagnose

pediatric patients because only ALP is incorporated in the evaluation of increased biliary enzyme. Secondly, small duct PSC cannot be diagnosed. Thirdly, PSC recurrence following liver transplantation cannot also be diagnosed. New findings and knowledge have accumulated after the proposal of PSC2016.

The Intractable Hepato-Biliary Diseases Study Group of the Committee of Research on Measures for Intractable Diseases in Japan established a working group consisting of researchers specializing in PSC. The working group develops tentative revised diagnostic criteria for PSC to overcome these limitations of PSC2016. Revised criteria also consist of four items. They are 1) biliary finding, 2) association with inflammatory bowel disease, 3) increased biliary enzyme, and 4) liver histology. Revisions are as follows; 1) Cholangiographic finding is revised to biliary finding to use other modalities (EUS, IDUS, POCS) in addition to ERC/MRCP. 2) Gamma-glutamyl transpeptidase is incorporated in addition to ALP for the evaluation of elevated biliary enzyme. 3) Diagnostic criteria for PSC recurrence following liver transplantation are added. The working group is going to propose the revised diagnostic criteria for PSC after the discussion and public hearing.

Biliary 7. Hot topics in PSC *Biliary7-2*

Anti-Integrin $\alpha\beta6$ Autoantibodies in Patients with Primary Sclerosing Cholangitis

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Patients with primary sclerosing cholangitis (PSC) possess autoantibodies against biliary epithelial cells. However, the target molecules remain unknown. In addition, although diffuse biliary stricture is the most important finding for diagnosing with primary sclerosing cholangitis (PSC), some cases have potential to be misdiagnosed with other biliary diseases. Therefore, the development of specific diagnostic markers for PSC is needed.

We recently found that PSC patients possessed anti-integrin $\alpha\beta6$ autoantibodies. By enzyme-linked immunosorbent assays (ELISA), anti-integrin $\alpha\beta6$ antibodies were detected in 49/55 (89.1%) patients with PSC and 5/150 (3.3%) controls ($P < 0.001$), with a sensitivity and specificity of 89.1% and 96.7%, respectively, for PSC diagnosis. When focusing on the presence or absence of IBD, the proportion of the positive antibodies in PSC with IBD was 97.2% (35/36) and that in PSC alone was 73.7% (14/19) ($P = 0.008$). Integrin $\alpha\beta6$ was expressed in bile duct epithelial cells. Immunoglobulin (Ig)G from 15/33 patients with PSC blocked integrin $\alpha\beta6$ -fibronectin binding through an RGD (Arg-Gly-Asp) tripeptide motif.

In conclusion, autoantibodies against integrin $\alpha\beta6$ were detected in most patients with PSC; anti-integrin $\alpha\beta6$ antibody may serve as a potential diagnostic biomarker for PSC.

We proceeded studies further. Our study above was conducted on patients from only two institutions. Therefore, a validation research in multi-centers is needed to eliminate selection bias. In addition, the study was examined using our conventional in-house enzyme-linked immuno-sorbent assay (ELISA) method. To compare the data from different facilities, development of a universal kit for the antibody measurement is needed.

The Intractable Hepato-Biliary Diseases Study Group in Japan has conducted the nation-wide PSC registry study "Establishment of disease registry of primary sclerosing cholangitis for investigation of clinical features, natural history, and prognostic factors" to prospectively register clinical information and sera of patients with PSC in Japan. Using these serum samples and clinical information, we examined

diagnostic value of anti-integrin $\alpha\beta6$ autoantibody for PSC as a Japanese nation-wide validation study.

In addition, we collaborated with Medical and Biological Laboratories CO., LTD. to establish Anti-Integrin $\alpha\beta6$ ELISA Kit which enables easier detection of the anti-integrin $\alpha\beta6$ antibodies. The use of monoclonal antibody for integrin $\alpha\beta6$ with known concentration facilitated the standardization of anti-integrin $\alpha\beta6$ autoantibody titers.

I will show these results in this section.

Biliary 7. Hot topics in PSC *Biliary7-3*

Endoscopic Treatment in PSC

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Primary sclerosing cholangitis (PSC) is a challenging clinical condition which is required a good and proper diagnosis before deciding the best strategy approach as it can lead to malignancy condition. Liver transplantation is still the best treatment for PSC; however, regular endoscopic approach is the most routine procedure in daily practice. Despite the imaging innovation, such as magnetic resonance cholangiopancreatography (MRCP), other innovations in endoscopy, such as transpapillary biopsy, fluorescence in-situ hybridization (FISH) method from the brush material, intraductal biopsy using innovation and dedicated cholangioscope have increased the diagnostic value, especially for cholangiocarcinoma (CCA) early detection. Biliary stenting through endoscopic retrograde cholangiopancreatography (ERCP) procedure is the main procedure in daily practice for PSC management. Endoscopic luminal radiofrequency ablation (ELRA) is one of innovative treatment for biliary stricture, especially to maintain biliary stent patency in intraductal CCA.

Biliary 7. Hot topics in PSC *Biliary7-4*

Dr. Toshio Fujisawa

Biliary 7. Hot topics in PSC *Biliary7-5*

Recent advances in medical treatment for PSC

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Primary sclerosing cholangitis (PSC) is a disease characterized by fibrotic strictures of intra- and extrahepatic bile ducts, leading to liver cirrhosis due to bile stasis. While its pathogenesis involves presumed autoimmune mechanisms, it remains incompletely understood. At present, liver transplantation stands as the sole definitive treatment, but opportunities for deceased donor liver transplantation are limited, and living donor liver transplantation pose significant challenges. Additionally, graft failure due to a high recurrence rate after transplantation remains a concern. Though no established pharmacological treatment exists, various studies are underway with promising outcomes expected.

Ursodeoxycholic acid (UDCA) represents the most extensively studied pharmacotherapy, demonstrating reduction in hepatic and biliary enzymes in numerous randomized controlled trials. However, due to reported increased mortality and liver transplantation at high doses, it is not considered standard therapy in various national guidelines. Nonetheless, recent reports associating decreased serum ALP levels with prognosis have renewed interest in the potential of UDCA to improve outcomes. Retrospective analyses using nationwide surveys in Japan have reported improved transplantation-free survival rates associated with UDCA therapy.

Bezafibrate, a medication for dyslipidemia, acts as an agonist for Peroxisome Proliferator-Activated Receptor alpha (PPAR α) and has been reported to decrease hepatic and biliary enzymes in PSC. However, its evidence remains limited to a few cases, lacking established confirmation.

Other pharmacotherapies include a Phase II randomized trial showcasing improvement in hepatic and biliary enzymes with cilofexor, a farnesoid X (FXR) receptor ligand, followed by an ongoing Phase III trial. Recent advances reveal the involvement of the gut microbiota in PSC pathogenesis, driving research toward pathophysiology-based treatments. Reduced diversity in the gut microbiota of PSC patients has been reported, with expectations that restoring diversity through fecal microbiota transplantation may lead to therapeutic benefits. Moreover, *Klebsiella pneumoniae* is frequently detected in the intestines of PSC patients, prompting investigations into its role in causing liver inflammation via bacterial translocation. Studies on bacteriophage therapy targeting *K. pneumoniae* are also underway.

Progress in understanding PSC's pathophysiology fuels optimism for further advancements in treatment-related research in the foreseeable future.

Biliary 8. Endoscopic management of hilar obstruction *Biliary8-1*

The revised TOKYO criteria for hilar biliary obstruction

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The consensus-based TOKYO criteria were introduced as a standardized reporting system to address the inconsistent documentation of outcomes of endoscopic transpapillary biliary drainage. The main aim was to solve issues arising from heterogeneous reporting practices across different studies, which hindered the comparability and interpretation of stent outcomes. However, the original TOKYO criteria were less applicable to recent endoscopic biliary drainage modalities such as those based on endoscopic ultrasound or balloon endoscopy. As opportunities for managing hilar biliary obstruction and benign biliary strictures through endoscopic drainage have expanded, and biliary ablation has been introduced for both benign and malignant strictures, there is a growing need to revise the criteria. Additionally, with cancer patients experiencing prolonged survival times, there is an increased focus on evaluating overall outcomes throughout the period of endoscopic biliary drainage rather than solely concentrating on the initial stent patency.

Acknowledging these gaps, a committee within the Japan Gastroenterological Endoscopy Society has been formed to revise the TOKYO criteria to align with current clinical practices in endoscopic biliary drainage. The revised criteria propose standardized reporting items applicable to endoscopic biliary drainage as a whole, along with specific items tailored to different conditions and interventions. The term "stent-demanding time" has been introduced to encompass the entire duration of endoscopic biliary drainage, providing a comprehensive evaluation of overall stent-related outcomes. The adoption of these

revised TOKYO criteria is expected to facilitate the design and reporting of clinical studies, offering a goal-oriented approach to assessing endoscopic biliary drainage.

The revised TOKYO criteria aim to evaluate the following conditions and interventions: distal biliary obstruction, hilar biliary obstruction, EUS-guided biliary drainage, biliary drainage via balloon-assisted endoscopy, benign biliary stricture, scheduled exchange of a plastic stent, biliary ablation. In this presentation, I will focus on the part of assessing endoscopic biliary drainage for hilar biliary obstruction.

Biliary 8. Endoscopic management of hilar obstruction *Biliary8-3*

Endoscopic Management of Hilar Obstruction

Dr. Jae Hee Cho

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Hilar cholangiocarcinoma (hilar CC), a rare but prevalent form of bile duct cancer, poses significant treatment challenges due to its advanced stage at diagnosis and the historical lack of effective treatments, resulting in poor survival rates. The primary treatment approach involves surgical resection, targeting both intra- and extrahepatic bile ducts and the affected liver lobe.

Preoperative biliary decompression is crucial for patients presenting with obstructive jaundice, a common symptom of hilar CC, and scheduled for major liver surgery. Traditionally, percutaneous transhepatic biliary drainage (PTBD) has been preferred, especially in cases with additional complications such as cholangitis, malnutrition, or liver dysfunction. More recently, endoscopic methods like endoscopic nasobiliary drainage (ENBD) have become popular due to their diagnostic benefits in evaluating bile volume and characteristics. Despite its advantages, ENBD can cause bile loss and patient's discomfort, leading some clinicians to opt for endoscopic biliary stenting (EBS). However, EBS may carry a higher risk of obstructive cholangitis and post-operative issues, making ENBD the recommended first-line treatment, although EBS may still be used if it provides sufficient drainage.

In cases of inoperable hilar CC, the optimal method for liver drainage is still debated. Generally, draining more than 50% of the liver volume is advised, but the choice between plastic stents (PS) and uncovered self-expandable metal stents (uSEMS) is controversial. PS are often selected for their ease of replacement and removal, while uSEMS are preferred for their durability and longer patency. The decision between unilateral and bilateral stenting also varies, with some evidence suggesting that bilateral stenting might offer longer stent patency.

Another therapeutic consideration is intraductal radiofrequency ablation (ID-RFA), which shows promise for treating unresectable malignant biliary obstructions. However, due to the perihilar bile duct's proximity to critical vascular structures, the risk of ID-RFA-related complications may be elevated. Our research suggests using the shortest available ID-RFA probe to minimize these risks, based on findings from animal studies that showed increased bile duct perforation risk with standard ID-RFA settings.

In summary, the management of hilar CC, including preoperative and palliative biliary decompression, requires a tailored approach that considers the complexities of each case. A multidisciplinary team's expertise is crucial in determining the most appropriate treatment strategy, whether it involves surgical resection, biliary decompression, or advanced therapies like ID-RFA. Despite the advancements, a consensus on the best practices for hilar CC is still needed, underscoring the importance of individualized treatment plans supported by collaborative decision-making.

Biliary 8. Endoscopic management of hilar obstruction *Biliary8-4*

Suprapapillary placement of plastic stents for unresectable malignant biliary hilar obstructions

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Unresectable malignant obstructions of the biliary hilum represent a significant challenge in the field of palliative pancreatobiliary endoscopy. Prior meta-analyses have favored uncovered metal stents due to their prolonged patency compared to plastic stents placed across the papilla. However, advancements in cancer treatment have rendered the uncovered design problematic because it cannot be removed. Once the metal stent becomes occluded, it induces idiopathic cholangitis which interrupts cancer therapies, reduces quality of life, and requires extremely complicated treatments since it cannot be removed.

Plastic stents, alternatively, offer reversibility, simplifying re-interventions, despite their shorter function periods when placed across the papilla. Recently, the focus has shifted to suprapapillary placement, which has been proven to be feasible in recent studies. Retrospective or single-arm studies have reported median patency periods of suprapapillary plastic stents from 99 to 190 days, making this approach a viable option.

In our multicenter, randomized control trial comparing suprapapillary placed plastic and metal stents, we found no significant differences in the technical success, clinical success and adverse events between the groups. While plastic stents exhibited a tendency for shorter function periods compared to metal stents without statistical significance (250 vs. 361 days, $p = 0.34$), both are potential initial permanent drainage techniques, considering the removability of plastic stents.

Other 1. Recent Advances for Hepatitis A and E
Other1-2

Hepatitis A and E viruses: recent advances in research and clinical practice recommendations

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In 2018, there was an outbreak of hepatitis A virus (HAV) infection in Japan, and hepatitis A is also considered a sexually transmitted disease. Patients with hepatitis A should be receiving attention, and this disease needs to be prevented more than ever. Despite the development of an effective vaccine against hepatitis A, universal vaccination has not yet been performed in Japan.

In Japan, until the early 2000s, acute hepatitis E virus (HEV) infection was considered rare until reports emerged confirming the existence of HEV genotype 3 and 4 infections. Until now, vaccines against hepatitis E have not yet become available in Japan. The Japanese National Health Insurance System does not approve anti-HAV and anti-HEV drugs.

Recently, we discovered several effective drugs against HAV infection and their mechanism by drug repositioning, in silico screening (Sasaki-Tanaka R, et al. J Virol. 2022 Sep 28; Sasaki-Tanaka R, et al. J Virol. 2023 Feb 28; Sasaki-Tanaka R, et al. Int J Mol Sci. 2023 Jun 3; Int J Mol Sci. 2022 May), etc. Although the use of off-label ribavirin for HEV infection was shown to be effective, the development of antivirals against HAV and HEV infection is urgently required.

The Japan Agency for Medical Research and Development (AMED) Hepatitis A and E viruses (HAV and HEV) Study Group has recently

published the recent advances in research and clinical practice recommendations for hepatitis A. Here, the recent advances in research and clinical practice recommendations for HAV and HEV infections in Japan will be presented.

Other 1. Recent Advances for Hepatitis A and E
Other1-3

Management of Hepatic Encephalopathy with Special Reference to Combination Therapy

Dr. Barjesh Chander Sharma

Gastroenterology, GIPMER India

Hepatic encephalopathy (HE) is characterized by wide spectrum of neurological and psychiatric alterations resulting due to advanced liver malfunction. It is a neurological ailment related to hepatic insufficiency and/or portosystemic shunts. Its clinical features include neuropsychiatric dysfunction, ranges from subclinical changes to coma. Overt HE is found in 30–45% of patients with cirrhosis and 10–50% of patients with a transjugular intrahepatic portosystemic shunt (TIPS). Recurrence of HE is seen in 47–57% of patients by the end of one year despite being on treatment. Occurrence of each bout of HE results in increased morbidity, hospitalization, health care burden, poor prognosis and increased mortality. Combination of rifaximin with lactulose has favourable effect on patients with recurrent HE who have recurrent bouts of HE despite on lactulose. Thus, rifaximin along with lactulose should be considered for preventing the recurrent episodes of HE. With use of rifaximin as addition to lactulose for the prophylaxis of third and further episodes of HE, cost can be saved both from a hospital and healthcare payer's perspective. From healthcare payer's view, costs raise by adding rifaximin to lactulose is reduced due to improved survival with rifaximin causing relatively low drug and liver transplant related costs. Combination of lactulose plus albumin is also more effective than lactulose alone in the management of overt HE with more decrease in the levels of arterial ammonia, interleukin-6, interleukin-18, tumor necrosis factor-alpha, and endotoxins. Triple combination of L-ornithine L aspartate (LOLA) with lactulose and rifaximin is more efficacious than only lactulose and rifaximin in improving grades of HE, recovery time from HE and with reduced 28-days mortality. In cirrhotic patients with advanced HE adjuvant treatment with LOLA along with lactulose and metronidazole is safe and associated with fast improvement and reduced hospital stay. In conclusion combination therapy including lactulose, rifaximin, albumin and LOLA is effective in the management and prevention of recurrent HE.

Others 2. New Paradigm of Delta Infection
Other2-3

New Paradigm of Delta Infection

Dr. Robert Gareth Gish

Hepatitis B Foundation USA

Hepatitis D virus (HDV) is an RNA "sub-virus" that infects patients with co-existing hepatitis B virus (HBV) infections. HDV burden is estimated to be approximately 15–20 million people worldwide. Despite HDV severity, screening for the HDV remains inadequate. HDV screening would benefit from a revamped approach that automatically reflexes testing when individuals are diagnosed with HBV if HBsAg+, to anti-HDV total and then to quantitative HDV-RNA polymerase chain reaction (PCR) rather than only testing those at high risk sequentially. There are no current treatments in the United States (US) that

are Food and Drug Administration (FDA)-approved for the treatment of HDV; and one approved therapy in the EU by the EMEA with conditional approval; however, bulevirtide and is under review with the US FDA. Current treatment strategies in many countries are centered on the use of pegylated interferon alfa-2a (PEG-IFNa-2a). There are other therapies in development globally that have shown promise, including lonafarnib (LNF) and the NAP: REP 2139. LNF has shown substantial response in the LOWR trials, but trials halted due to some liver toxicity risk. BLV is a well-tolerated drug, but it is not finite therapy and has shown significant on-treatment HDV RNA responses in the multiple MYR clinical trials, and the FDA cited concerns with the manufacturing and patient preparation of the drug that have delayed approval. The PDUFA date for BLV in the US is mid-2024. Current studies with both BLV and LNF are limited in providing sustained virological response (SVR); future trials will need to demonstrate more substantial SVR with possible triple combination trials as options. REP 2139 is in compassionate use trials in the EU region. In summary, HDV/HBV is a very high-risk viral infection and justifies a test all approach and a treat all approach who are HDV RNA+. Interferon remains a global tool for HDV treatment with response rates in the 20% range with newer therapies in evolution.

Others 3. Coinfection of Viral Hepatitis and HIV
Other3-2

Clinical features and vaccine efficacy of hepatitis A virus infection in HIV infection

Dr. Takeya Tsutsumi

Department of Infection Control and Prevention, Department of Infectious Diseases, Faculty of Medicine The University of Tokyo Japan

In 2018, there was an outbreak of hepatitis A virus (HAV) infection in Japan, following outbreaks in foreign countries such as European countries, United States, and Taiwan. Most of infected patients were men who have sex with men (MSM) including human immunodeficiency virus (HIV)-infected patients. HAV is usually transmitted through fecal-oral infection, and the outbreak was probably spread by unique sexual activities of MSM. A similar HAV outbreak was observed among MSM in Japan around 2000. About 20 years passed, and the treatment strategy for HIV infection has been developed, leading to better immunological condition of people living with HIV (PLWH). Accordingly, the clinical presentation of HAV infection in PLWH was different from the previous outbreak.

To prevent HAV infection, HAV vaccine is generally useful. Centers for Disease Control and Prevention (CDC) recommends HAV vaccine for MSM as well as people traveling to endemic countries. However, the efficacy of HAV vaccine to obtain enough anti-HA IgG antibody (anti-HA-IgG) has been shown to be lower among PLWH compared to non-HIV-infected people. It is known that even PLWH who have a good HIV control sometimes cannot respond to other vaccines. Furthermore, compared to healthy people, PLWH have difficulty maintaining sufficient titers of anti-HA-IgG to prevent HAV infection. As mentioned above, the clinical characteristics of HAV infection in PLWH, including my own experience, will be introduced

Global Steatotic Liver Disease Symposium
APASL/AASLD/EASL/ALEH
GS1-2

Role of Alcohol in Steatotic Liver Disease

Dr. Aleksander Krag

Department of Gastroenterology and Hepatology University of Southern Denmark & Odense University Hospital Denmark

Steatotic Liver Disease (SLD), former known as fatty liver disease, encompasses a range of liver conditions with fat accumulation in the liver. However, the role of alcohol in the progression and exacerbation of SLD is significant and multi-faceted. Alcohol consumption, particularly chronic and heavy use, directly contributes to the development of Alcohol-Related Liver Disease (ArLD), a subset of SLD. ArLD progresses from simple steatosis (fatty liver) to more severe forms like alcoholic hepatitis, fibrosis, and cirrhosis. The liver, responsible for metabolizing alcohol, undergoes oxidative stress and inflammation due to the toxic metabolites produced during this process. This stress damages liver cells, leading to fat accumulation, inflammation, and eventually scarring. The interplay between alcohol and other risk factors for SLD, such as obesity, metabolic syndrome, and diabetes, can accelerate liver damage. These risk factors are synergistic. Alcohol exacerbates insulin resistance, a key component of metabolic syndrome, which in turn contributes to the progression of Metabolic dysfunction Associated Steatotic Liver Disease (MASLD), another form of SLD. Furthermore, alcohol can influence gut microbiota, affecting metabolic functions and promoting liver inflammation.

The threshold of alcohol consumption that leads to ArLD varies among individuals, influenced by genetic factors, gender, overall health, and concurrent metabolic conditions. This variability complicates the management and prevention strategies for SLD. Biomarkers play a crucial role in diagnosing and managing Alcohol-Related Liver Disease (ArLD). They enable early detection of liver damage, monitor disease progression, and assess the response to treatment.

Management of SLD, particularly ArLD, involves lifestyle interventions with a focus on reducing alcohol intake. Complete abstinence is often recommended for individuals with ArLD, as even moderate alcohol consumption can aggravate liver damage. Moreover, addressing other metabolic risk factors, such as obesity and diabetes, is crucial in managing SLD.

State-of-the-Art Lecture

SAL2-1

Can Blood-Based Biomarker HCC Surveillance Replace Ultrasound?

Dr. Tawesak Tanwandee

Department of Medicine Faculty of Medicine Siriraj Hospital, Mahidol University Thailand

Hepatocellular carcinoma (HCC), a leading cause of cancer mortality globally, especially in Asia, often presents at advanced stages with limited therapeutic options. Current surveillance standards recommend ultrasound in conjunction with alpha-fetoprotein, yet the effectiveness of ultrasound is notably reduced in patients with advanced cirrhosis or obesity, and is subject to radiologist interpretative variability. Advances in HCC screening, such as short protocol CT or MRI, demand complex equipment and experienced radiologists.

Recent studies have explored multi-biomarker blood tests (mt-HBT) for HCC surveillance, especially in compensated cirrhosis patients. These include biomarkers like AFP-L3, PIVKAI, and algorithms such as GALAD, GAAD, and ASAP score. Risk-based surveillance approaches have also been investigated for enhanced cost-effectiveness. Additionally, emerging research on cell-free DNA-based tests shows higher specificity for HCC. This body of evidence suggests that mt-HBT significantly outperforms ultrasound in early-stage HCC detection. Hypothetical models indicating improved adherence to blood-based biomarkers further underscore their potential advantages.

These findings could revolutionize HCC surveillance protocols, enhancing detection efficiency and potentially improving long-term patient outcomes. However, current studies have not extensively examined implementation in real-world settings, leaving questions about potential false positives and negatives unaddressed.

In conclusion, while blood-based HCC surveillance appears promising, offering increased sensitivity and reduced interpretative bias, its efficacy in replacing ultrasound as the standard practice requires further validation in real-world applications.

State-of-the Art Lecture
SAL8-1

APASL initiative to reshape the discipline of Hepatology in Asian-Pacific region beyond 2024

Dr. George Lau

Humanity and Health Clinical Trial Center, Humanity and Health Medical Group, Hong Kong SAR, China

Till 2023, liver diseases remain a major health threat in Asian-Pacific region,

accounting for two-third of the global deaths due to acute-on-chronic liver failure, end-staged liver cirrhosis and hepatocellular carcinoma. The major aetiology of liver diseases are chronic hepatitis B and C, metabolic dysfunction-associated (MAFLD) and alcoholic fatty liver disease (AFLD). Asian-Pacific Association for the Study of Liver (APASL) is the premier Asian-Pacific liver society set up in 1978 aiming to create and to disseminate the best evidence-based clinical knowledge to relieve patients' suffering from liver diseases. Sharing the same vision, APASL is in alliance with European Association for the Study of the Liver (EASL), American Association for the Study of Liver Diseases (AASLD) and Latin American Association for the study of the liver (ALEH). In the past few decades, there have been rapid advancement and availability of laboratory, imaging diagnostic and endoscopic technology, more stringent and transparent conduct of clinical trials, development of sophisticated computation and big data collection (with artificial intelligence-AI) and change in social-economic environment. Very importantly, machine learning (ML) and AI algorithms can help to address data integrity by ensuring consistency and reliability across various data sources and over time. In the age of AI, where machine learning models continuously learn and evolve, maintaining data integrity is not just a one-time effort; it's an ongoing discipline that requires robust strategies and advanced technological support. New drug development is anticipated to be supercharged with AI. With the digitalisation of medical data, more personalised medical care can be provided to our patients, especially those living in resource-limited areas. With AI-assisted robotics, medical procedures can also be more effectively and safely performed. Skills and knowledge are also necessary to perform ultrasound-based examination for liver and how to read CT-based or MRI-based imaging data. Basic sciences related to laboratory techniques used to provide clinical data should be understood. The application of AI to guide screening, diagnosis and treatment of patients with liver diseases should be enhanced. Therefore, it is now time to reshape the discipline of hepatology to update knowledge and skills which will allow us to advance our clinical management to our patients. Finally, it is of great importance to integrate the art of humanities into medical practise to reshape and modernise professional hepatology discipline with emphasize on empathy, communication, and teamwork.

State-of-the Art Lecture
SAL9-1

AI research for clinical application: from research planning to regulatory approval

Dr. Ryuji Hamamoto

National Cancer Center Research Institute Japan

Expectations for artificial intelligence (AI) have been rising in recent years due to advances in machine learning technology, particularly deep learning, the emergence of inexpensive, high-performance GPUs (Graphics Processing Units), and the expansion of public databases as the Big Data era begins, making it easier to utilize large data sets. In the long history of AI research, however, it has not been smooth sailing. There have been periods of high expectations for AI, known as the "AI boom," and then a period of "AI winter," when AI failed to technologically meet those high expectations, leading to widespread disappointment in AI. On the other hand, an important aspect of the third AI boom, which began with the advent of deep learning, is that social implementation is progressing. AI is now being utilized in a wide range of fields, such as face recognition for airport security, automatic translation, automatic voice recognition, and home appliances. The medical field is no exception, and the development of SaMDs (software as medical devices) utilizing AI is underway around the world, and many products have been approved as medical devices and are being used in clinical practice. In 2016, we launched the project "Development of an Integrated Cancer Medical System Using Artificial Intelligence" as a JST CREST research project, and have been working on various medical AI research and development projects. As a result, our AI-based endoscopy diagnosis support software was approved as a medical device in Japan in 2020, and later conformed to the CE Mark in Europe, and is already in clinical use in Japan and Europe. In addition to AI-based endoscopy-assistive software, the company has also published a variety of other medical AI-related results that have led to clinical applications. In this presentation, I will introduce the current status and future possibilities of medical AI based on our experience in promoting the entire process from research planning to actual clinical application.

State-of-the Art Lecture
SAL14-1

Role of liver resection in the era of advanced systemic therapy for hepatocellular carcinoma

Dr. Norihiro Kokudo

National Center for Global Health and Medicine Japan

The recent dramatic progress in systemic therapy for hepatocellular carcinoma (HCC) provides the possibility of a combination of surgery and systemic therapy including adjuvant, neoadjuvant, or conversion settings. After the turn of the century, there have been at least three negative studies testing adjuvant therapies after curative resection or ablation, including Uracil-Tegafur an oral chemotherapeutic drug, sorafenib, and peretinoin, a synthetic retinoid that may induce apoptosis and differentiation of liver cancer cells. Using more potent immun-checkpoint inhibitors (ICIs), there are at least 4 phase-III trials ongoing for adjuvant immunotherapy: Nivolumab, Durvalumab/Bevacizumab, Pembrolizumab, and Atezolizumab+Bevacizumab. Very recently, the last one showed significantly better RFS for adjuvant Atezolizumab+Bevacizumab. Another promising combination of surgery and systemic therapy is neoadjuvant therapy for potentially resectable cases or conversion strategy for oncologically unresectable cases. There have been 2 neoadjuvant trials for technically or oncologically unresectable HCCs ongoing in Japan: LENS-HCC trial using Lenvatinib and RACB study using Atezolizumab+Bevacizumab. Although we may need longer follow-up, OS in resected cases seems

much higher than that for unresectable cases. Recently, Japan Liver Cancer Association (JLCA) and the Japanese Society of HPB Surgery (JSHPBS) created a joint working group on "so-called borderline resectable HCC." They compiled a Japanese consensus on this issue and it has been published on the websites of JLCA and JSHPBS. The definition of resectability or borderline resectability provides the common language on advanced HCC for investigators and it is a useful tool for future clinical trials.

Basic and Clinical Research of Cholangiocellular Carcinoma *BCRI-1*

Role of pathology in terms of Basic and Clinical Research of Cholangiocellular Carcinoma

Dr. Mina Komuta

Pathology department, International University of Health and Welfare, School of Medicine, Narita Hospital Japan

Cholangiocarcinoma (CCA) harbours actionable mutations in 50% of cases, offering promising treatment options. However, CCA is a heterogeneous tumour driven by the diversity of cholangiocytes, primarily dictated by the size of the bile duct (BD), complicating tumour characterization. Cholangiocytes, lining the epithelia of the biliary tree, exhibit distinct phenotypes based on BD size: cuboidal-shaped cholangiocytes line the small BD without apparent mucin production, while cylindrical cholangiocytes with mucin production cover the large BD. Intrahepatic CCA (iCCA) is categorized into two subgroups: the large and small BD types. As cancer maintains the phenotype of its cell of origin, both iCCA subtypes display disparate features in terms of clinical, pathological, and genetic characteristics. Accounting for these differences is crucial in research endeavours. Additionally, the large duct type of iCCA shares clinical, pathological, and molecular features with extrahepatic CCA (eCCA). This is because both CCAs originate from the similar cell of origin which are mucin-producing cylindrical cholangiocytes in the intra-, and the extrahepatic BD. In contrast, the small duct type of iCCA exhibits tumour heterogeneity, posing challenges in distinguishing it from other primary liver cancers such as hepatocellular carcinoma (HCC) and combined HCC-CCA, particularly in certain circumstances. This heterogeneity is particularly relevant for characterizing perihilar CCA and understanding its origin. Furthermore, it should be noted that CCA is an adenocarcinoma, a frequent histological subtype of metastatic liver cancer. Distinguishing between primary and metastatic lesions is crucial. Based on these different characteristics, it is essential to be aware of this point to avoid inaccurate data assessment. In my presentation, I will clarify the phenotypes of primary liver cancers (HCC, cHCC-CCA, and iCCA) and subsequently focus on iCCA phenotypes to highlight their distinctions. This analysis will be linked to treatment selection, including the identification of actionable mutations before genetic investigation.

Basic and Clinical Research of Cholangiocellular Carcinoma *BCRI-2*

Current diagnosis of intrahepatic cholangiocarcinoma -From tumor localization to genetic abnormalities-

Dr. Tatsuya Kakegawa

Gastroenterology & Hepatology, Tokyo medical university Japan

The incidence of intrahepatic cholangiocarcinoma (ICC) is increasing, with the highest rates seen in Eastern Asia when compared with

Western countries. It is asymptomatic in the early stages, and about 20% of ICC are diagnosed incidentally, and no effective screening method has been established yet. It is important to know risk factors including primary sclerosing cholangitis and non-bile duct specific diseases as chronic hepatitis C virus and hepatitis B virus infection, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, alcoholic liver disease, and autoimmune hepatitis. Screening these populations by clinical examination, tumor markers, and abdominal ultrasound may aid in early diagnosis. On clinical examination, persistently elevated bilirubin levels, hepatobiliary enzymes, and the tumor markers CA19-9 and CEA are useful for auxiliary diagnosis. Contrast-enhanced CT (CECT) is widely used for differential diagnosis and localization evaluation of ICC from the viewpoints of simplicity, dissemination, and cost. Also Gd-EOB-DTPA contrast-enhanced MRI is useful for localization diagnosis because it shows the tumor as a clear low-signal area in the hepatocellular phase. The Kupffer phase of contrast-enhanced US (CEUS) depicts the tumor as a clear defect image, and its detection sensitivity is reported to be high. However, CEUS is only an adjunct to CECT and MRI due to the presence of blind spots and reproducibility problems. The most common extra-hepatic metastases of ICC are lung, bone, and distant lymph node metastases. The advantage of FDG-PET/CT is that it allows systemic search for these metastases in a single examination. Meta-analysis shows that "vascular invasion" is one of the prognostic factors, and it is important to accurately determine the presence or absence of vascular invasion. EUS is excellent for the diagnosis of hilar cholangiocarcinoma and is particularly useful in predicting the extent of bile duct invasion in cases of specific resection. Cholangiography has good spatial resolution and is useful in diagnosing the extent of cancer invasion. In ICCs near the porta hepatis, mapping biopsy under direct view with cholangioscopy can diagnose the extent of bile duct invasion and reduce the number of positive cases of surgical resection margins. Liver tumor biopsy is also an option for atypical cases on imaging and for non-resected cases that require systemic therapy. Biopsy can help identify ICC-specific driver gene abnormalities, such as FGFR2 fusion gene and IDH1/2 mutations, and aid in the selection of therapeutic agents.

Basic and Clinical Research of Cholangiocellular Carcinoma *BCRI-3*

The Progress of Internal Medicine for Intrahepatic Cholangiocarcinoma

Dr. Shun Kaneko

Department of Gastroenterology and Hepatology, Tokyo Medical and Dental University (TMDU) Japan

Cholangiocarcinoma (CCA) is the second most common liver cancer after hepatocellular carcinoma. CCAs are a group of heterogeneous tumors classified as either intrahepatic or extrahepatic (perihilar and distal) based on its location in the biliary tract. Globally, the incidence of intrahepatic CCA (ICC) is increasing. ICC is a highly aggressive malignancy that arises within the liver and presents with features of biliary differentiation. The sole potentially curative treatment is surgical resection. However, due to the late manifestation of clinical symptoms, fewer than one-third of patients are eligible for surgery. Unfortunately, ICC is inherently highly resistant to chemotherapy, with a median overall survival below one year under palliative chemotherapy (gemcitabine + cisplatin). Though unresectable ICC exhibits very poor prognosis, the development of novel therapeutic agents is emerging, as the genomic profile of ICC comes to light. Second-line therapies are available to target pathways associated with specific gene mutations (e.g., FGFR2, IDH1, NTRK). Notably, the combination of durvalumab with chemotherapy (gemcitabine + cisplatin) has shown significant improvements in overall survival, progression-free survival, and

objective response rate compared to a placebo in conjunction with chemotherapy, as first-line therapy. In addition to these advancements in systemic therapy, the background liver disease and liver function are focused on prognosis associated with liver function in the context of ICC, including our data. This presentation provides an overview of internal medicine treatment in relation to ICC.

Comprehension of Asian HCC by A-HOC Study and APASL HCC Guideline
HOC1-4

Evaluation of data from the A-HOC (APASL Hepatology/Oncology Consortium) study of patients with hepatocellular cancer in Turkey

Dr. Muhsin Murat Muhip Harputluoglu

University Medical Faculty Liver Transplant Institute, Transplant Hepatology and Gastroenterology Dept Turkey

A-HOC (APASL Hepatology/ Oncology Consortium) study is the abbreviated name of study of 'Survey on Current Status and Treatment of Hepatitis and Liver Cancer in the Asia-Pacific Region'. This international multicenter study examines the actual incidence and treatment of hepatocellular cancer in Asia Pacific countries, the background of viral and non-viral hepatitis, the actual situation of health and medical problems, and the development of new treatment methods in each country.

Aim of this presentation is to evaluate Turkey data in the A-HOC study. Basic patient data, physical examination findings at the time of carcinogenesis, blood and biochemical tests at the time of carcinogenesis, tumor characteristics, treatment methods and dates and prognostic informations of the patients entered into the A-HOC REDCap system from centers in Turkey were analyzed.

Comprehension of Asian HCC by A-HOC Study and APASL HCC Guideline
HOC1-5

Innovation on Clinical Management of Hepatocellular Carcinoma in the era of Systemic Therapy

Dr. Cosmas Rinaldi Adithya Lesmana

Department of Internal Medicine, Hepatobiliary Division, Dr. Cipto Mangunkusumo National General Hospital, Medical Faculty Universitas Indonesia, Indonesia

Hepatocellular carcinoma (HCC) is still becoming a major burden all over the world due to increase of metabolic liver disease despite hepatitis virus B and C infection. Metabolic dysfunction associated fatty liver disease (MAFLD) is an emerging disease, where it can lead to portal hypertension, liver cirrhosis, as well as liver cancer development. Most of the patients have come in the late stage of the disease. Therefore, early detection is still the main key for a success disease control and prolong patient's survival, however, in the case of MAFLD, it is not always easy to find early cancer development due to standard screening methods limitations. Innovation in endoscopic ultrasound (EUS) can be a promising secondary tool not only for confirming diagnosis, but also in the advance management.

Surgical approach is still the best treatment for managing liver cancer, however, the post-surgical recurrence rate is still high. In the intermediate stage of HCC, the combination of loco-regional therapy with immunotherapy as well as oral systemic therapy have shown a satisfaction result when compared to loco-regional therapy alone.

The new concept of neo-adjuvant therapy after resection has opened the new horizon in the liver cancer management. Recently, adjuvant therapy has been proposed to prevent tumor recurrency after surgery. This might be a promising concept for the future beyond the guidelines. It would still need further and larger study to conclude that this concept would be incorporated in the clinical practice guideline.

Advances in Hepatobiliary Imaging
AHII-2

Applications of artificial intelligence for hepatobiliary MR imaging

Dr. Keitaro Sofue

Department of Radiology Kobe University Graduate School of Medicine Japan

Global interest in artificial intelligence (AI) applications for MR imaging is growing rapidly, fueled by significant advances in computing power and new deep learning algorithms. Recently, deep learning reconstruction (DLR) algorithms have been developed for MRI that are trained to improve image quality, and the combination of DLR with various sequences has produced favorable results in hepatobiliary MR imaging. DLR has been proven successful in reconstructing MR images with a high signal-to-noise ratio from undersampled k-space data to reduce acquisition times while maintaining high image quality. Additionally, a newly developed deep learning reconstruction method for upscaling resolution of low-resolution (superresolution) has been implemented into the MR machine. These DLR algorithms may help to improve visualization and characterization of hepatobiliary diseases. In this presentation, I would like to present our attempts to apply AI to improve image quality for hepatobiliary MR imaging.

Big Data and AI for Hepatology
BDI-1

The usefulness of AI for tumor microenvironment analysis in HCC.

Dr. Hitoshi Mochizuki

Genome Analysis Center / Department of Gastroenterology, Yamanashi Central Hospital Japan

Introduction: The tumor mass consists not only of a heterogeneous population of cancer cells but also a variety of resident and infiltrating host cells, secreted factors, and extracellular matrix proteins, collectively known as the TME(tumor microenvironment).

The recent advances in machine learning are essential to elucidate what cells make up a TME and how these cells change and organize into different cellular communities in response to the signaling environment.

Aims: In this study, we will evaluate TME based on DNA and RNA analysis and compare HCC with other cancer types, predict the efficacy of immune checkpoint inhibitors, and discuss issues in evaluating TME.

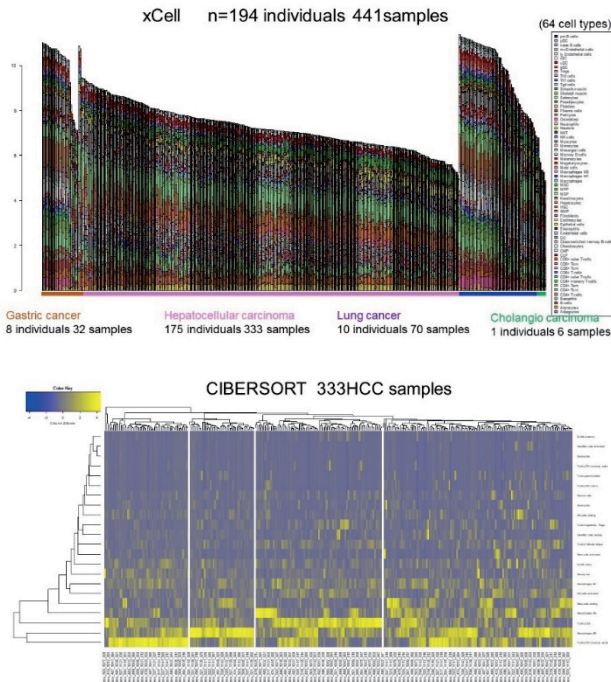
Methods: DNA and RNA were extracted from 441 surgical samples of Tumor (including 333 HCCs) during treatment.

T cell prevalence can be estimated (General Additive Model) by sequencing the rearranged T cell receptor- α gene (T Cell ExTRECT). Transcriptome analysis makes it possible to estimate the abundance of cells with well-known mRNA expression profiles, such as immune cells, from bulk RNAseq data (CIBERSORT: 22 cell types, xCell: 64 cell types).

Moreover, we analyzed using EcoTyper, a machine-learning framework for large-scale identification and validation of cell states and multicellular communities from bulk, single-cell, and spatially resolved gene expression data.

Results: The use of AI in TME Analysis of Tumors elucidates fundamental units of cellular organization in HCC and provides a framework for large-scale profiling of cellular ecosystems in any tissue.

From a real-world clinical perspective, it was also shown that irAE caused by ICI(Immune Checkpoint Inhibitors) is caused in specific clusters.



Big Data and AI for Hepatology
BDI-4

Application of Machine Learning in the Diagnosis and Management of Liver Disease

Dr. Masaya Sato

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While there has been significant progress in developing therapies for liver diseases, the prognosis for hepatocellular carcinoma (HCC), especially in advanced-stage patients, remains very poor. Artificial intelligence (AI), which combines computer science and mathematics, involves creating computer algorithms to improve the performance of computer programs. It does this by using various data sources and employing analytical or probabilistic models. The intersection of machine learning (ML) and the medical field has great potential to revolutionize diagnostic methods, particularly in laboratory medicine. Because liver diseases are complex and multifaceted, an ML approach that integrates multiple factors seems promising. This approach aims not only to improve diagnostic accuracy but also to predict how patients will respond to treatment and their future prognosis. Electronic medical records contain a wealth of data crucial for advancing medical research. By using AI and ML techniques and incorporating various factors into the analysis, we can enhance the precision of decision-making processes. This not only refines diagnostic accuracy but also helps predict

outcomes in the intricate network of factors associated with liver diseases. In this presentation, we will explore the potential use of AI and laboratory medicine in the field of liver disease.

Gilead
I-2

Secondary Prevention of HBV-Related HCC

Dr. Young-Suk Lim

Department of Gastroenterology Asan Medical Center, University of Ulsan College of Medicine Korea

Recently we analyzed the association between a broad range of serum HBV DNA levels and long-term HCC risk in a total of 6949 HBeAg-positive and HBeAg-negative, non-cirrhotic, treatment-naïve CHB patients who are not generally indicated for antiviral therapy by current practice guidelines because of no significant ALT level elevation.¹ We found that the association between HBV DNA levels and HCC risk is not linear but parabolic in these patients. The HCC risk was highest at moderate HBV DNA levels around 6 log₁₀ IU/mL, with decreasing HCC risk at higher and lower HBV DNA levels. Very high HBV DNA levels (>8 log₁₀ IU/mL) showed the lowest HCC risk which was not significantly different from that of very low HBV DNA levels (≤4 log₁₀ IU/mL).

Our additional studies have demonstrated that the level of serum HBV DNA at baseline impacts the on-treatment risk of HCC in non-cirrhotic patients with CHB.^{2, 3} We found that patients with moderate baseline viral load, particularly around 6 log₁₀ IU/mL, demonstrated the highest on-treatment HCC risk, despite long-term antiviral treatment. Compared with the matched untreated patients, the treated patients in the high and moderate viral load groups had a significantly lower risk of HCC. Nonetheless, the reduced risk of the treated patients in the moderate viral load group was significantly higher than that of the treated patients in the high viral load group. Initiating antiviral treatment at either high (≥8.00 log₁₀ IU/mL) or low (3.30–4.99 log₁₀ IU/mL) viral loads was associated with a significantly lower on-treatment risk of HCC compared to starting the treatment at a moderate baseline viral load (5.00–7.99 log₁₀ IU/mL).

Therefore, early initiation of antiviral treatment with a high viral load (≥8.00 log₁₀ IU/mL) may maintain the lowest risk of HCC in those patients.

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Abstracts

Young Investigator Workshop

Abstract Submission No. 101132
WS-001

Safety and Efficacy of Microwave ablation to HCC

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Background: We started using microwave ablation (MWA) in December 2019 and its use is increasing (43.3% of all ablation treatments in 2023). We reviewed the safety and efficacy of 47 nodules in 43 patients who underwent MWA in our department.

Methods: We assessed 1) frequency of sedation and complications, 2) complications from MWA treatment, and efficacy by 3) effectiveness determination after treatment, 4) local recurrence, and 5) comparison with RFA during the same period (n=76).

Results: Patients (n=43) had a median age of 75 (58-88) years, 60% male, background liver HBV/HCV/alcohol/other 7/23/7/6, first/recurrent 10/33. Nodules (n=47) had a mean diameter of 18.9±6.6 mm, left lobe/right lobe 8/39, internal/surface 26/21, with/without artificial ascites during MWA treatment 22/25. 1) Sedation was used in 21 patients (48.8%), with a mean dose of midazolam 1.9 mg. There were no complications due to sedation. 2) After MWA treatment, one patient developed an abscess in the treated area. 3) We had two residual cases (4.2%). 4) Local recurrence occurred in eight patients, with a local recurrence rate of 10.9% at 1 year and 31.3% at 2 years (mean follow-up: 406 days). 5) The median nodule diameter was 18 (7-33) mm in the MWA group and 15 (6-29) mm in the RFA group, which was significantly larger in the MWA group (p<0.001), but there was no difference in the local recurrence rate.

Conclusion: MWA is a safe and effective treatment method. Factors related to local recurrence could not be identified, so further follow-up are needed.

Abstract Submission No. 101623

WS-002

A prospective study of cardiohemodynamic profile changes in acutely decompensated cirrhosis and ACLF

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Background: Cardiohemodynamic changes in early ACLF are incompletely known but may significantly influence multi-organ dysfunction and short-term prognosis.

Methods: This is a prospective, observational, follow-up study including patients admitted for acutely decompensated (AD) cirrhosis in a tertiary referral center. We performed ECG, echocardiographic assessment of cardiac function, and serum biomarker analysis (proBNP, TNF- α , Growth Arrested Specific-6, IL-6) at 3 time points: admission, 5-7 days later, and at one month. The main outcomes were mortality at one and 3-months. We explored serological and echocardiographic biomarkers of cardiac dysfunction to establish a cardiohemodynamic risk profile.

Results: We analyzed 66 patients (59±10 years, 20/46 women/men) with a median MELD-Na score of 19 (IQR 8), mostly with alcohol-related cirrhosis (79%) admitted for AD (86% with ascites, 18% with infection, 9/66 with ACLF). 12% of patients died before one month (24% before 3 months). Lower median blood pressure (75 vs 89 mmHg, p=0.002; AUROC=0.840), higher proBNP (587 vs 178 pg/mL, p=0.03), and echocardiographic parameters of left ventricular diastolic

dysfunction (septal e', lateral e', E/e', A wave) predicted death at one and 3 months. Median blood pressure on admission correlated with proBNP levels (-.488, p<0.001) and MELD-Na score (r=-.306, p=0.01). Patients with ACLF had lower levels of GAS-6 (p=0.04) but did not otherwise differ from patients with AD according to serological or cardiohemodynamic profile.

Conclusions: Comprehensive clinical-biological work-up of cardiohemodynamic status in acute decompensation of cirrhosis helps predict outcome. Median blood pressure is a simple indicator of increased risk for early death.

Funding: This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CNCS – UEFISCDI project number PN-III-P.1-1.1-PD-2021-0180, within PNCDI III.

Abstract Submission No. 101109

WS-003

Prevalence and clinical profiles of primary sclerosing cholangitis in China

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Background: Epidemiology of primary sclerosing cholangitis (PSC) is completely lacking in China. We aimed to investigate the prevalence by sex, time period, geographic distribution, and to depict the clinical features of PSC in China.

Methods: PSC cases reported during 2000 to 2023 in China were identified and included from two data sources: electronic medical records and systematical literature retrieval. The period prevalence of PSC in the general population was indirectly estimated using the multiplier method based on hospital-specific and nationwide clinic volumes.

Results: A total of 1358 PSC cases reported from 299 hospitals were included. The period prevalence of PSC from 2000 to 2023 was estimated to be 2.36 (95% CI: 1.82, 3.34) per 100,000. Males bore a relatively higher PSC prevalence than females (2.56 vs. 2.14 per 100,000). The prevalence of PSC more than doubled after 2010 than that before 2010 (1.68 vs 0.67 per 100,000). Geographic distribution revealed the highest prevalence of PSC was in East China and the lowest in South China. GDP per capita (RR 1.65, [1.03, 2.65]) and healthcare expenditure (RR 1.94, [1.13, 3.38]) were identified to be associated with PSC prevalence. Males accounted for 55.7% of the PSC cases and 25.7% presented concomitant inflammatory bowel disease (IBD).

Conclusion: Our data quantify for the first time a lower prevalence of PSC in China than in Western countries, with relatively higher prevalence reported in males, after 2010, and in more developed geographic

areas. PSC patients in China exhibit a diminished male-predominance and reduced IBD concomitance.

Abstract Submission No. 102001
WS-004

Preoperative Inflammatory Biomarker Analysis as a Predictor toward Hepatocellular Carcinoma Survival

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Background: An elevated systemic inflammatory response (SIR) is associated with reduced survival in patients with operable cancer like hepatocellular-carcinoma (HCC). This study aimed to determine whether SIR biomarker analysis obtained from routine preoperative blood tests can be used to predict overall-survival in HCC patients who undergo surgery.

Methods: This comprehensive study was conducted according to the Preferred Reporting Items for Systematic-Reviews and Meta-Analysis (PRISMA) guidelines. We systematically searched ScienceDirect, Pubmed, Cochrane Library, ProQuest, and Google Scholar databases until the end of October 2023. We collected articles on real-world studies comparing systemic inflammatory response syndrome (SIRS) events after surgical treatment for predicting the overall-survival rate in patients with HCC. Pooled mean differences (MD) and 95% confidence Interval (CI) were used to determine overall events.

Results: Of 61 articles were included for this meta-analysis, there was a significant relationship between elevated C-reactive protein (CRP) ($p<0,00001$), C-reactive-protein-to-albumin ratio (CAR) ($p<0,00001$), Glasgow Prognostic Score/Modified Glasgow Prognostic Score (GPS/mGPS) ($p<0,00001$), Lymphocyte-to-CRP ratio (LCR) ($p<0,005$), Lymphocyte-to-monocyte ratio (LMR) ($p<0,00001$), Neutrophil-to-lymphocyte ratio (NLR) ($p<0,00001$) in a HCC patient who had bad overall-survival. We also conducted subgroup analysis by country associated with inflammatory markers and their correlation to mortality rate. Subgroup analysis was performed to eliminate any potential factors that might be caused by different heterogeneity levels.

Conclusions: These results consolidate the prognostic value of the CRP, CAR, GPS/mGPS, LCR, LMR, and NLR in patients with HCC. This is particularly true for the SIR biomarker analysis should form part of the routine preoperative and postoperative workup.

Abstract Submission No. 101167
WS-005

Deficient Hepatic Canalicular Exporter Proteins Associated with Chronic Drug-Induced Liver Injury

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Introduction: Inhibitory effects of various drugs on canalicular exporters can cause severe drug-induced liver injury (DILI). This study aimed to assess the canalicular exporters in liver biopsies of DILI and its association with chronic DILI.

Patients and Methods: Cases with the clinicopathological diagnosis of DILI with liver biopsies from January 2016- Dec 2020 were included in this study. Clinical and laboratory information were recorded. Immunohistochemically, BSEP, MDR3, and MRP2 were assessed. Chronic DILI was considered as biochemical nonresolution after six months of discontinuation of the drugs.

Results: 379 of 405 cases were analyzed (26 excluded due to incomplete data). Chronic DILI was noted in 41 patients (10.8%), and commonly implied drugs were complementary and alternative medicine (66%), antimycobacterial (6%), and antibiotics (5%). At least one transporter loss of expression (51 patients) was more in cases that had chronic DILI {27/41 (52.9%) vs 24/338 (7.1%), $p<0.001$ }. More than one deficient transporter in zone 2 and 3 (23 patients) was more pronounced in chronic DILI {19/41 (44 %) vs. 4/338 (1.1%), $p<0.001$ }. Bile acids levels were higher in cases with deficient transporter expression {273, (IQR: 219-369) vs 98 (IQR: 72-183) micromol/L, $P<0.001$ } and more prominently in those developed chronicity {354, (IQR: 305-439) vs 126 (IQR: 73-193) micromol/L, $P<0.001$ }. In the liver biopsies at baseline, mixed and cholestatic pattern ($p=0.015$), ductular, and canalicular cholestasis ($p=0.001$) were prominent, whereas fewer eosinophils ($p=0.02$) in those who developed chronic DILI.

Conclusions: Deficient expressed canalicular exporters and elevated bile acids were noted in DILI cases that progressed to chronic DILI

Abstract Submission No. 100489
WS-006

Prevalence, Risk Factors, and Clinical Outcomes of Infections in Acute Decompensation of Cirrhosis

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Background: This study delved into cirrhosis-related infections to unveil their epidemiology, risk factors, and implications for antimicrobial decisions.

Methods: We analyzed acutely decompensated cirrhosis patients ($n=971$) from 2013-2023 at a tertiary center. Microbiological and clinical features based on infection sites (EASL criteria) and patient outcomes were assessed.

Results: Median age was 45 years; 87% were males with 47% having alcoholic hepatitis. Of these, 675 (69.5%) had infections; 305 (45%) were culture-confirmed. Notably, 71% of confirmed cases were MDRO-related, chiefly carbapenem-resistant (48%). MDRO prevalence was highest in pulmonary (80.5%) and skin-soft-tissue infections (76.5%). Site-specific distribution and antimicrobials were suggested. Predictive models identified hospitalization (OR:2.23), norfloxacin prophylaxis (OR:2.26), prior broad-spectrum antibiotic (BSAbx) exposure (OR:1.61), SIRS (OR:1.75), procalcitonin (OR:4.64), and HE-grade (OR:1.41), with an AUC of 0.891 for infection prediction. For MDRO infection prediction, second infection (OR:7.19), norfloxacin prophylaxis (OR:2.76), prior BSAbx (OR:1.66), rifaximin (OR:0.44), CLIF-C-OF (OR:1.10), multi-site (OR:3.67), and polymicrobial infections (OR:4.55) yielded an AUC of 0.779 and 93% specificity. Norfloxacin prophylaxis, multisite infection, mechanical ventilation, prior BSAbx exposure, and infection as acute precipitant predicted carbapenem-resistant infection (AUC: 0.821).

Infections (culture-proven or probable), MDROs, carbapenem/pan-drug resistance, and second infections independently linked with mortality ($p<0.001$), adjusted for age, leucocytosis, and organ failures. A model incorporating age (HR:1.02), infection (HR:1.52), prior hospitalization (HR:5.33), norfloxacin (HR:1.29), multisite infection (HR:1.47), and CLIF-C OF (HR:1.17) predicted mortality with C-statistics of 0.782 ($p<0.05$).

Conclusion: High MDRO burden, especially carbapenem-resistant, necessitates urgent control measures in cirrhosis. Site-specific epidemiology and risk models can guide empirical antimicrobial choices in cirrhosis management.

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Conclusion: High MDRO burden, especially carbapenem-resistant, necessitates urgent control measures in cirrhosis. Site-specific epidemiology and risk models can guide empirical antimicrobial choices in cirrhosis management.

Abstract Submission No. 100833

WS-007

Exploring Trends in Liver Cancer Causes in China: A Focus on Hepatitis B and Emerging Factor

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Background: The burden of liver cancer is still on the rise. Although NASH has become an important component of the etiology of liver cancer worldwide, viral hepatitis, particularly hepatitis B virus (HBV), remains the dominant cause of liver cancer in China.

Methods: We collected the data from the 2019 Global Burden of Disease (GBD) study, which includes mainland of China and Taiwan Province, prevalence and incidence rate per 100,000 person-years were calculated.

Results: Data from China and Taiwan (1990-2019) reveal that HBV remains the leading cause of liver cancer. Despite a decline in hepatitis B incidence (2000-2019), likely linked to hepatitis B vaccine adoption in 1992, liver cancer rates have raised since 2010. The dominance of HBV in liver cancer cases contrasts with relatively stable HCV, NASH, and alcohol-related cases. Notably, Chinese young population shows low HBV-related liver cancer (<20 years) while cases surge in those aged over 20. This rise is attributed to a large population of existing hepatitis B patients, and limited standardized management in China. Taiwan, with higher diagnosis and treatment rates, demonstrates decreasing liver cancer cases. Further analysis reveals a sharp increase in HBV-related liver cancer cases since 2010, surpassing HCV, alcohol, and NASH cases.

Conclusion: HBV-related liver cancer among adults in mainland of China continued to rise, our findings emphasize the need for increased hepatitis B screening, standardized treatment, and public awareness for liver cancer prevention among high-risk populations.

Abstract Submission No. 101913

WS-008

Bacterial Vesicle Cargos induces Systemic Inflammation and hepatic Injury in Autoimmune Hepatitis

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Background: In autoimmune hepatitis (AIH), there is a growing emphasis on the pivotal role of the gut-liver axis, as attention turns toward microbial dysbiosis as a driving force in AIH pathogenesis. It is understood that the bacterial microbiota promotes local and systemic inflammation, which can promote inflammation in AIH. We propose that Bacterial vesicles(BV) as mediator of AIH, due to their potent immune stimulatory composition and capability to influence inflammation.

Method: BVs isolated from AIH plasma [$n=61$, biopsy-proven,(HAI) score >2] and healthy control plasma (HC) $n=30$ was characterized by TEM, NTA, western blot and proteomics. Further, AIH and HC BV were adoptively infused intravenously in C57BL/6J female mice to determine if BVs contribute to the acceleration and exacerbation of inflammation and hepatic injury.

Result: BVs were significantly higher in AIH patients than HC [10.5 vs 3.7; $p=0.003$, 87.7 vs 10.3; $p=0.015$].the AIH BVs progressively increase with increasing HAI score[$r=0.62$; $p=0.001$], transaminases{ALT, AST[$r=0.59$; $p=0.001$, $r=0.57$; $p=0.001$]} and IgG antibodies[$r=0.37$; $p=0.018$].The proteomics of AIH BV revealed >10-fold increase in immunoglobins and complement-associated proteins including complement C3,GAPDH, Transmembrane glycoprotein with 5 virulence factors having epitope mimicry helping in immune modulation and Adherence. miPrebase mapping identified an experimentally verified peptide sequence IYQIDNHQQARKPIAD of methyltransferase family mimicking component of pyruvate dehydrogenase complex of the host mitochondria.Upon,AIH-BV administration in mice within 12h,the liver enzymes and liver weight index were elevated [AST($p=0.0286$);ALT($p=0.0452$); LI($p=0.008$)] than HC-BV. The liver histology showed raised focal acute inflammation in AIH-BV than HC-BV($p<0.001$) with significantly high infiltration of F4/80⁺ macrophages and Ly6G⁺ neutrophils in the liver ($p<0.001$).

Conclusion: The data suggests that BVs cargoes potentiates in promoting systemic inflammation which could contribute to the development and severity of AIH condition. These findings offer new insights into the role of BVs in microbiota-host interactions in AIH.

Abstract Submission No. 100462
WS-009

The impact of metabolic dysfunction on mortality in chronic hepatitis B with steatotic liver disease

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Background: Steatotic liver disease (SLD), including metabolic dysfunction-associated steatotic liver disease (MASLD), is prevalent in the chronic hepatitis B (CHB) population. However, the impact of SLD subtypes on all-cause/cause-specific mortality among these patients remains unknown.

Methods: CHB patients with concurrent SLD were consecutively recruited at the National Taiwan University Hospital. MASLD, alcohol-associated liver disease (ALD), and cryptogenic SLD were defined by the newly-proposed criteria. Cumulative incidences of all-cause and cause-specific mortality were compared after accounting for competing risks.

Results: From 2006 to 2021, 8,773 CHB patients with SLD were included. At baseline, CHB patients with concurrent MASLD (n=6,562) or ALD (n=55) were older, had a lower proportion of HBeAg positivity and lower levels of HBV DNA than cryptogenic SLD patients (n=2,156). After a median follow-up of 9.1 years, ALD (adjusted HR [aHR]: 11.80, 95% CI: 5.89-23.60, $p < 0.001$) and MASLD patients (aHR: 1.79, 95% CI: 1.24-2.58, $p = 0.002$) had higher all-cause mortality risks than those with cryptogenic SLD after adjustment for clinical and viral factors. Furthermore, cumulative metabolic dysfunctions, defined by the cardiometabolic criteria of MASLD, increased the risks of all-cause, liver-related, non-liver cancer, and cardiovascular mortality with a dose-dependent effect, contributing to the higher risks in MASLD than cryptogenic SLD patients.

Conclusions: Among CHB patients with hepatic steatosis, concurrent ALD and MASLD increase the risk of all-cause mortality, and cumulative systemic metabolic dysfunctions dose-dependently increase all-cause and various cause-specific mortality. Refraining from alcohol intake and managing these metabolic risk factors are crucial for better survival in CHB patients.

Abstract Submission No. 100617
WS-010

HBV DNA integration profiles in the natural history of chronic hepatitis B

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INTRODUCTION: HBV integration in the natural history of chronic hepatitis B (CHB) is not well-defined. We utilized next-generation sequencing (NGS) to delineate integration profiles across CHB disease phases.

METHODS: Liver biopsies were obtained from 55 patients (3 HBeAg-positive/HBeAg-positive infection; 13 HBeAg-positive/HBeAg-positive hepatitis; 7 HBeAg-positive/HBeAg-negative infection; 12 HBeAg-positive/HBeAg-negative hepatitis; 10 HBeAg-seroclearance; 10 occult-HBV). Target-capture NGS followed by sequencing was performed (NovaSeq-6000). The Virus-Clip platform was used to characterize integrations using soft-clipped sequencing reads, with integrations defined as chimeric fusions in ≥ 1 soft-clipped reads and ≥ 2 total-reads.

RESULTS: HBV integrations were detected in all 35 HBeAg-positive patients (100%), and was detectable in 8 (80%) HBeAg-seroclearance patients and 7 (70%) occult-HBV patients respectively. Integration events showed a stepwise decrease when comparing the HBeAg-positive/HBeAg-positive (9.6 log integrations per-patient), HBeAg-positive/HBeAg-negative (8.7 log) and HBeAg-negative groups (7.3 log) ($p < 0.001$). Infection (ALT < upper limit of normal [ULN]) or hepatitis (ALT $\geq$ ULN) status had no impact on integration frequencies in both HBeAg-positive or -negative patients. HBeAg-seroclearance or occult-HBV also had no impact on integration frequencies in HBeAg-negative patients (all $p > 0.05$). HBV genome-breakpoints clustered around nucleotide-1800 in all disease phases (associated with C-terminal truncated HBx-protein in HBV-hepatocarcinogenesis). Human genome-breakpoints were frequently detectable in HCC-associated genes. LINC00486, a known passenger mutation in HBV-related HCC, was the most frequently involved gene in all disease phases.

CONCLUSION: HBV integration frequency changes dynamically during the progression of CHB. Deleterious integrations associated with HCC are present in all phases, challenging the notion of quiescent disease phases and supporting the need for early treatment.

Abstract Submission No. 100996
WS-011

Interferon reduce hepatocellular carcinoma risk in high-risk Asian patients with chronic hepatitis B

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Objective: To demonstrate the efficacy of pegylated interferon- α (PegIFN α)-based therapy and nucleoside analog (Nuc) in reducing hepatocellular carcinoma (HCC) risk in High-risk Asian patients with chronic hepatitis B.

Methods: The analysis was conducted in the data from a multi-center, prospective real-world study (OASIS Project) from China which started recruiting from October, 2020. Data on those who have completed 48 weeks of treatment and uploaded complete laboratory testing data were analyzed. Each patient was evaluated by algorithms that have been proven of good performance in Asian patients, including aMAP score, modified PAGE-B score and Toronto HCC Risk Index (THRI) if there was cirrhosis simultaneously, and the highest risk level was taken.

Results: A total of 8364 patients with PegIFN α -based therapy and 3422 with Nuc treatment were analyzed. At baseline, 52.60%, 39.90%

and 7.50% of patients in IFN group were stratified into low-risk, intermediate-risk and high-risk for HCC, respectively. And in Nuc group, the ratio was 43.40%, 37.80% and 18.80%, respectively. After 48-week treatment, 21.3% of high-risk patients in IFN group changed into intermediate-risk, and 14.9% in Nuc group (Figure 1) changed. In Nuc group, the 1-year HCC incidence was higher in high-risk population (0%, 0.2%, 0.9% in low, intermediate and high risk, respectively, $P=0.001$). While in IFN group, the 1-year HCC incidence was similarly low in high-risk and other population (0.1%, 0.1% and 0.3%, $P=0.194$).

Conclusions: Anti-viral treatments reduce the HCC risk in HCC patients, and IFN-based therapy seems superior.

Abstract Submission No. 100380

WS-012

Optimizing a hepatitis C screening model for general population using easily accessible data

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Background: Globally, an estimated 58 million chronic hepatitis C virus(HCV) infections. Direct-acting antiviral medicines(DAAs) can cure more than 95% of persons with HCV infection, but access to diagnosis(20%) and treatment(15%) was low. We aimed to develop screening algorithms that accurately identifies HCV infection using easily accessible demographic parameters.

Methods: We obtained data from population-based cohorts National Health and Nutrition Examination Survey(NHANES 1990-2020), and divided them into training(6-cycles; $n=46243$) and testing(5-cycles; $n=37060$) cohort. Then, we applied logistic regression to calculate the odds ratio(OR) of 4 demographic factors(sex, ethnicity, blood transfusion history, birth year) for diagnosing HCV infection. Next, we developed and compared 9 machine learning(ML) algorithms to diagnose HCV infection in training cohort. Finally, we adopted the selected algorithm to establish the diagnostic model and test the performances.

Results: The overall cohort($n=83303$) was 49.0% male; 37.9% White, 23.2% Black, 29.0% Hispanic, and 10.0% other; 8.8% of participants had a history of blood transfusion; with a mean birth year of 1972 ± 23 . The positive rates of anti-HCV and HCV RNA among studied population were 1.3% and 0.8%(unweighted). In multivariate analysis, all four parameters were significantly correlated with HCV infection: male sex(OR 2.01; $P<0.001$); Black versus White(OR 1.96; $P=0.008$); blood transfusion history(OR 2.14; $P<0.001$); born 1970 and before(OR 8.98; $P<0.001$). Comparing the AUC values of 9 ML algorithms in the training cohort, XGBoost was selected as the best prediction model. The AUC of the XGBoost model for diagnosing HCV infection was 0.891(95%CI 0.880-0.903) for the training set. In the testing set, the AUC was 0.843(0.827-0.858), and the sensitivity, specificity, PPV and NPV were 0.78, 0.78, 0.288 and 0.967, respectively.

Conclusions: To predict HCV infection in general population, only 4 easily obtained demographic features are needed using our ML model.

Abstract Submission No. 100506

WS-013

Durvalumab + Tremelimumab (STRIDE) vs Durvalumab Alone for Unresectable HCC Patients: A MetaAnalysis

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Background: Hepatocellular carcinoma (HCC) is the leading cause of mortality in cirrhotic patients, with an annual incidence of 1-6%. Most HCC patients usually require systemic therapy, being unresectable at the time of diagnosis. Durvalumab has gained popularity for patients with unresectable HCC versus sorafenib and atezolizumab + bevacizumab due to its safety profile, and the combination of Durvalumab (PD-L1 inhibitor) and Tremelimumab (CTLA-4 inhibitor) have shown additive antitumor activity and immunostimulatory effects. This study aims to compare the efficacy of STRIDE (Single Tremelimumab Regular Interval Durvalumab) compared to Durvalumab alone in unresectable HCC patients.

Methods: Major electronic databases and grey literature sources were searched up to June 2022 for randomized controlled trials assessing the effectiveness of STRIDE versus durvalumab monotherapy in unresectable HCC patients.

Results: The mortality rates between STRIDE and Durvalumab monotherapy were compared. Resulting I2 of 0% ($p=0.72$) implies that heterogeneity does not exist, hence a fixed effects model is preferred. Resulting pooled odds ratio 1.079 (95% CI 0.59 to 1.06) is not significant ($Z=1.57$, $p=.12$), implying no significant difference between the two groups. The forest plot also shows that the diamond market intersects the 1 axis, suggesting that the odds ratio is not significant.

Conclusion: The addition of Tremelimumab in STRIDE (Single Tremelimumab Regular Interval Durvalumab) has no significant difference in the mortality rates among unresectable HCC patients versus Durvalumab alone. Hence, the additional costs and risks of STRIDE is upon the discretion of the patient and physician.

Abstract Submission No. 100555

WS-014

RISK FACTORS AND PROGNOSIS AFTER PRIMARY CURATIVE HEPATECTOMY IN HEPATOCELLULAR CARCINOMA PATIENTS

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Background: We do this research at Cho Ray Hospital, Vietnam in order to evaluate some prognostic factors for recurrence, mortality, disease-free survival time (DFS) and overall survival time (OS) of HCC patients.

Method: retrospective cohort study

Result: From January 2015 to December 2019, there are 1704 patients whom received primary curative hepatectomy were enrolled in this study. All patients were followed up until June 2023. We recorded overall recurrent rate is 61.56% with 1-, 2- and 3-year recurrent rate are 56.69%, 74.24%, 84.04%, respectively. The overall survival rates at 3 and 5 years are 47.54% and 18.43%. Mean and median disease-free survival time are 16.8 and 9.5 months while mean and median overall survival time are 37.9 and 34.7 months. Univariate analysis showed that AFP level, vascular invasion, tumor number, tumor size, histological pattern, Edmonson-Steiner staging, tumor necrosis, accompanying resectable metastatic tumors, resection level are related to recurrence and DFS and OS, while underlying liver disease is only related to DFS. Logistic regression model showed that AFP level, vascular invasion, tumor number, tumor size, accompanying resectable metastatic tumors are independent prognostic factors for recurrence and mortality. Multivariate analysis using the Cox proportional-hazards regression

showed that tumor number was independent prognostic factors for DFS and OS.

Conclusion: tumor number is the independent prognostic factor for HCC recurrence and mortality.

Abstract Submission No. 101293

WS-015

Nonselective β blocker use does not impact on mortality in patients with hepatocellular carcinoma

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Background: Hepatocellular carcinoma (HCC) contributes to a substantial burden of mortality across the globe. Increasing evidence supports the role of non-selective beta-blockers (NSBB) in reducing liver decompensation and prolonging survival in cirrhotic patients. However, the effect of NSBB on liver-related mortality in HCC patients remains unestablished.

Materials and methods: All patients with HCC and esophageal and/or gastric varices from January 2000 to December 2020 were identified from a territory-wide database in Hong Kong. Participants were classified into three groups using a time-dependent covariate (i) propranolol users (ii) carvedilol users (iii) NSBB non-users. The primary endpoint was liver-related mortality in 5 years. Cause-specific hazard model was used for competing risk analysis. Liver transplantation and non-liver-related mortality were considered as competing events.

Results: A total of 5,454 patients with 4119 propranolol users, 86 carvedilol users, 1249 non-users (mean age 60.4 $\pm$ 11 years, male 82.0%) were included in the analysis. Most patients had viral cirrhosis (78.3%). The use of propranolol and carvedilol did not have a significant impact on liver-related mortality (adjusted cause-specific hazard ratio [aC-SHR] 1.03, 95% CI 0.97-1.12, p=0.42; aC-SHR 0.90, 95% CI 0.57-1.43, p=0.67) and non-liver-related mortality (aC-SHR 0.99, 95% CI 0.86-1.15, p=0.94; aC-SHR 1.40, CI 0.75-2.65, p=0.293).

Conclusion: In this territory-wide retrospective study, use of NSBB did not impact on liver-related and non-liver-related mortality in HCC patients over a follow-up period of 5 years.

Abstract Submission No. 100237

WS-016

Comparative Role of Tenofovir and Entecavir in Patients with HBV Decompensated Cirrhosis of Liver

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Background: Decompensated cirrhosis is cirrhosis as an acute deterioration of liver function and characterized for jaundice, ascites, hepatic encephalopathy, hepatorenal syndrome and varices.

Objective: To compare of Treatment of HBV decompensated Cirrhosis of Liver Patients by Tenofovir and Entecavir.

Methods: The study was carried out at Department of Hepatology, Bangabandhu Sheikh Mujib Medical University and Kurmitola General Hospital, Bangladesh. The study enrolled 100 treatment-naïve patients with HBV decompensated cirrhosis of liver on entecavir (1 mg) or tenofovir (300 mg) from January 2013 to December 2018.

Result: There are three follow up taken, three-month, sixth month and twelve months after medication. In 3rd follow up (after one year), 100% patients were found undetected HBV DNA in tenofovir group and 97.56% in entecavir group. The difference was not statistically significant (p>0.05) between two groups. At 1 year total death was 9 patients, out of them 03 were tenofovir group and 06 were entecavir group. In tenofovir patients, Mean Child Pugh score was 12.1 $\pm$ 1.3 in pretreatment and 5.8 $\pm$ 1.3 at 1 year. Mean MELD score was 25.0 $\pm$ 3.1 in pretreatment and 9.3 $\pm$ 3.2 at 1 year. In entecavir patients, Mean Child Pugh score was 12.0 $\pm$ 1.5 in pretreatment and 9.3 $\pm$ 0.9 at 1 year. Mean MELD score was 26.5 $\pm$ 2.0 in pretreatment and 17.0 $\pm$ 2.1 at 1 year. The difference of MELD and CTP score improvement was statistically significant (p<0.05) between two groups.

Conclusion: In treatment of decompensated cirrhosis of liver, entecavir and tenofovir both are significantly improved liver function, HBV DNA undetection and patient's survival. But Tenofovir shown more improvement.

Abstract Submission No. 100663

WS-017

Sarcopenia is Associated with the Risk of Minimal Hepatic Encephalopathy in Patients with Cirrhosis

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Background: Sarcopenia has gained significance in the evaluation of cirrhosis patients, and this nutritional status can have a detrimental impact on clinical outcomes, including minimal hepatic encephalopathy (MHE). This prospective study aimed to assess the association between sarcopenia and MHE in cirrhotic patients.

Methods: We enrolled outpatients with cirrhosis to evaluate the presence and severity of sarcopenia according to the 2019 criteria by the Asian Working Group for Sarcopenia. MHE was diagnosed using the paper-based Psychometric Hepatic Encephalopathy Score.

Results: Among the 210 patients (57.1% male, mean age 62.7 $\pm$ 9.6 years) with cirrhosis, 54 (25.7%) exhibited sarcopenia, with 26 (12.3%) classified as having severe sarcopenia. Additionally, 37 (17.6%) were diagnosed with MHE. The prevalence of sarcopenia was significantly higher in cirrhotic patients with MHE compared to those without MHE (45.9% vs. 21.4%, p=0.002). MHE was notably associated with education level, Mini-Mental State Examination score, and a history of hepatic decompensation. Conversely, no significant associations were observed regarding gender, BMI, comorbidities, sleep quality, etiology and severity of liver disease assessed by MELD score and transient elastography. In a multivariable logistic model, MHE was significantly associated with age (adjusted odds ratio [aOR] 1.08, 95% CI 1.02-1.13), sarcopenia (aOR 3.29, 95% CI 1.44-7.50), and a history of overt hepatic encephalopathy (aOR 7.40, 95% CI 1.20-45.56) and variceal bleeding (aOR 3.13, 95% CI 1.38-7.10). Furthermore, severe sarcopenia was independently associated with MHE (aOR 3.64, 95% CI 1.32-10.05).

Conclusions: Sarcopenia is not uncommon among outpatients and is an independent risk factor for MHE in cirrhotic patients.

Abstract Submission No. 101626

WS-018

Early Clinical Features of Peritoneovenous Shunt in Patients with Decompensated Liver Cirrhosis

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Background and Aims: Refractory ascites affects the prognosis of liver cirrhosis. Peritoneovenous shunt (PVS) placement is a palliative treatment for refractory ascites that is expected to improve the patient's quality of life; however, it is associated with serious complications, such as heart failure. Thus, understanding the clinical course and risks of complications after PVS placement is important. We aimed to evaluate the early clinical features after PVS placement for refractory ascites associated with liver cirrhosis.

Methods: This was a retrospective study of 14 patients with refractory ascites with decompensated cirrhosis who underwent PVS placement between June 2011 and June 2023. The clinical characteristics, changes in cardiothoracic ratio (CTR), and laboratory data were evaluated.

Results: No serious complication associated with the procedure occurred in all cases. Ten and four patients had Child-Pugh classes B and C, respectively. Increased brain natriuretic peptide (BNP) and D-dimer levels, decreased platelet count, and slightly worsening of CTR were observed two days after PVS placement; however, all cases tended to improve after seven days. The mean PVS patency was 345.4 days, and the median survival after PVS placement was 474.4 days. Although patients with class B cirrhosis tended to have longer PVS patency, there was no significant difference in patency between patients with class B and C cirrhosis.

Conclusions: PVS placement for refractory ascites is a technically feasible palliative therapy. Evaluating changes in CTR, platelet count, and BNP and D-dimer levels may be useful for early prediction of the efficacy of PVS placement.

Abstract Submission No. 102079

WS-019

Morphofunctional restoration of the hepatopulmonary axis in the early stages of liver cirrhosis

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One of the peculiarities of the liver is that it is connected to the portal system and the lungs in a sequential manner. Pulmonary complications during cirrhosis play an important part in the manifestations of the disease and the quality of life of patients with this disease can contain a significant signal in the chain of the hepato-Reasonable early differential diagnosis of complications of the disease will make it possible to prevent serious consequences and irreversible damages. It was the basis to set a goal to study the spectrum of hepatopulmonary complications in the early stages of liver cirrhosis development with personalized analysis.

In this study the patterns of serum protein electrophoresis results were evaluated against histopathological abnormalities in the liver and lungs, with the application of Hematoxylin and eosin (H&E) and

When pre-symptoms of liver cirrhosis are clearly observed in the anatomical and histological features during the initial stage of cirrhosis, lung lesions are quite severe, according to the developed histopathological scale. There is a decrease in the tendency to pulmonary lesions over the two-week post-poisoning after period, and in males.

Thus, in the acute and/or subacute stages of cirrhosis development, hormonal features play a crucial role in determining the hepatopulmonary axis differential diagnosis along with behavioral and emotional characteristics. We are sure that at some point in time there comes a moment of harmony (like in life, between males and females) when pathological processes manifest in the same way in both sexes.

Abstract Submission No. 100909

WS-020

Performance of aMAP, FIB-4, and APRI for Predicting F2 Fibrosis in Chronic Hepatitis B Patients

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Background: In line with WHO's 2030 hepatitis elimination target, effective chronic hepatitis B (CHB) strategies are vital. For those with HBV DNA >2000 IU/mL and persistently normal ALT, fibrosis assessment via transient elastography (TE) is advised. The aMAP score, recently introduced for fibrosis staging in CHB patients, has yet to be validated for assessing significant fibrosis.

Method: In this cross-sectional study, CHB patients with concurrent laboratory data and TE results within three months were evaluated. A TE value of at least 7 kPa indicated significant fibrosis. The aMAP score's efficacy was compared to the Fibrosis-4 index (FIB-4) and the aspartate aminotransferase to platelet index (APRI) in predicting F2 fibrosis. Metrics such as sensitivity, specificity, NPV, and PPV were assessed.

Results: Among the 628 analyzed CHB patients (mean age 48.6 years; 51% male; 79.8% HBeAg-negative; median HBV DNA 2042.5 IU/mL), the areas under the receiver operating curves for F2 fibrosis prediction were 0.693, 0.7061, and 0.7254 for aMAP, FIB-4, and APRI scores respectively. Statistical comparisons with aMAP showed no significant difference (p-values: 0.398 for FIB-4 and 0.137 for APRI). Optimal aMAP score thresholds were determined at 93% sensitivity (cutoff: 40) and 89% specificity (cutoff: 55).

Conclusions: The aMAP score emerges as a potential non-invasive metric for predicting significant fibrosis in CHB patients, with a 40 cutoff optimal for ruling out significant fibrosis. However, its performance mirrors existing scores. A more accessible, simplified score for predicting F2 fibrosis, preferable to TE, is desired, especially when TE is unavailable in resource-limited settings.

Abstract Submission No. 101348

WS-021

GENETIC FEATURES OF PATIENTS WITH WILSON'S DISEASE IN REPUBLIC OF MOLDOVA: A PILOT STUDY

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INTRODUCTION: Wilson disease (WD), a rare metabolic disease, is an autosomal recessive disorder associated with phenomenal mutational polymorphism and high clinical variety.

OBJECTIVE: To assess epidemiological characteristics and genetic features of Moldovan patients with WD.

METHODS: It was conducted a retrospective study on 108 patients suspected of WD, between 2006 and 2023. The Leipzig Scoring System was used to specify the diagnosis.

RESULTS: Of 108 persons, 57.4% (62/108) were male. The mean age was 16 years (range 3-63 years). All persons were of Caucasian origin, and 79% were of Moldovan ethnicity. No consanguineous relationships have been described. Patients mostly come from the center (59.4%) and south (15.94%) of the country. Hepatic onset was more frequent in women (45.8%, $p < 0.01$) and neurological in men (61.5%, $p < 0.05$). In 61.35% of the performed genetic tests, mutations were detected, of which 70.2% are pathogenic variants. The most frequent mutation identified is p.H1069Q (62.1%), of which 36.1% are in homozygous recessive state and 41.7% - associations with other variants (pathogenic, benign, or uncertain), and the second mutation is unknown in 22.2%. In 52.8% of cases, this mutation is associated with liver damage, which was diagnosed at the onset or during the natural evolution of WD.

CONCLUSIONS: p.H1069Q represents the most frequent pathogenic variant identified in the Republic of Moldova. Patients with hepatic presentation are diagnosed at younger ages, while those with neuropsychiatric type are diagnosed at older ages and with longer diagnosis delays.

Abstract Submission No. 100177

WS-022

Investigating unique clinical, pathological traits, and genetic variations in MAFLD among Indians.

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Background and aims: Fatty liver disease (FLD) is characterized by excessive fat accumulation in the liver and is closely linked to metabolic syndrome (MetS). However, the unique features and genetic factors influencing FLD in the presence or absence of MetS remain poorly understood. We aimed to investigate the clinical and genetic aspects of fatty liver disease (FLD) in individuals with and without metabolic syndrome (MetS).

Methods: A cohort of 551 individuals, with and without fatty liver, was categorized into four groups based on metabolic dysregulation: MAFLD, NAFLD, MetS, and healthy controls. Our study analysed clinicopathological attributes and associations of SNPs with MAFLD.

Results: The results showed that nearly half of the participants had FLD (47.2%), and the majority had MetS (71.87%). MAFLD individuals exhibited significantly higher age, increased adiposity, more severe diabetes, abnormal lipid profiles, elevated liver damage markers,

CRP levels, decreased bone mineral content, and more extensive liver damage. Notably, both obese and non-obese individuals in this group displayed these adverse characteristics. Furthermore, the study identified 21 genetic variants associated with the increased risk of MAFLD, mapped in *SAMM50*, *PNPLA3*, *TM6SF2*, *CECR5*, *TTC39B*, *SLC9A9*, and *PDXDC1*. Additionally, rs7200543-AA carriers among MAFLD patients showed poorer skeletal health.

Conclusion: Our study demonstrated that FLD in combination with MetS results in the most severe disease phenotype. It highlighted the importance of considering both clinical and genetic factors when studying FLD and provided insights into the complex interplay between genetics and metabolic disorders in liver disease.

Abstract Submission No. 100323

WS-023

Hepatic lobular inflammation is the most impacted prognostic factor in MAFLD: A Multi-Center study

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Background and Aims: Metabolic dysfunction-associated fatty liver disease (MAFLD) captures patients with fatty liver at high risk. However, limited information is available on the prognosis of MAFLD and prognostic liver histology. We aimed to investigate the prognosis of patients with biopsy-proven MAFLD and the most important histological finding associated with the prognosis using a multi-center longitudinal cohort.

Methods: We enrolled 1,444 patients with fatty liver who underwent liver biopsy (age 57, BMI 27.4). Patients were classified into the following groups: the MAFLD group, non-MAFLD group (steatosis without metabolic dysfunctions), or Burnt-out group (no steatosis on biopsy). Kaplan-Meier analysis and decision-tree analysis were performed to investigate the difference in mortality in these subgroups and the most impacted histological finding related to the prognosis of each group, respectively.

Results: During the 9,083 person-years of observation, 4.3 person-years of deaths occurred, and 84.2% (32/38) of these were patients in the MAFLD group. Significant differences were seen in prognosis among the three groups (log-rank $p = 0.0009$). Ten-year survival rate was 65.6% in the MAFLD group, while no patient died in the non-MAFLD group. The MAFLD group showed the highest proportion of high NAFLD activity scores. Although hepatic fibrosis was the histological finding most impacted on mortality in the Burnt-out group, hepatic inflammation was identified as the most impacted prognostic finding in the MAFLD group.

Conclusions: We demonstrated that patients with MAFLD have a worse prognosis than patients with non-MAFLD. Hepatic inflammation rather than fibrosis was the most impacted prognostic histology in patients with MAFLD.

Abstract Submission No. 100517

WS-024

Long-term Risks for Cirrhosis and Hepatocellular Carcinoma Across Steatotic Liver Disease Subtypes

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Aim: The prospective study aimed to investigate the long-term associated risks of cirrhosis and hepatocellular carcinoma (HCC) across various subtypes of steatotic liver disease (SLD).

Method: We enrolled 332,175 adults who participated in a health screening program between 1997 and 2013. Participants were categorized into various subtypes, including metabolic dysfunction-associated steatotic liver disease (MASLD), MASLD with excessive alcohol consumption (MetALD), and alcohol-related liver disease (ALD), based on ultrasonography findings, alcohol consumption patterns, and cardiometabolic risk factors. We utilized computerized data linkage with nationwide registries from 1997 to 2019 to ascertain the incidence of cirrhosis and HCC.

Result: After a median follow-up of 16 years, 4,458 cases of cirrhosis and 1,392 cases of HCC occurred in the entire cohort, resulting in an incidence rate of 86.1 and 26.8 per 100,000 person-years, respectively. The ALD exhibited the highest incidence rate for cirrhosis and HCC, followed by MetALD, MASLD, and non-SLD group. The multivariate-adjusted hazard ratios for HCC were 1.92 (95% CI: 1.51-2.44), 2.91 (95% CI: 2.11-4.03), and 2.59 (95% CI: 1.93-3.48) for MASLD, MetALD, and ALD, respectively, when compared to non-SLD without cardiometabolic risk factors. The pattern of the associated risk of cirrhosis was similar to that of HCC (all p value < 0.001). The associated risk of cirrhosis for ALD increased to 4.74 (95% CI: 4.08-5.52) when using non-SLD without cardiometabolic risk factors as a reference.

Conclusion: This study highlights elevated risks of cirrhosis and HCC across various subtypes of SLD compared to non-SLD, emphasizing the importance of behavioral modifications for early prevention.

Abstract Submission No. 100821

WS-025

Risk factors of liver-related events in patients with T2DM

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Background: Data on the prognostic risk factors of liver-related complications among patients with type 2 diabetes mellitus (T2DM) remains limited.

Methods: This territory-wide retrospective study identified 718,974 adult patients with the diagnosis of T2DM between January 2007 and December 2021 in Hong Kong. The exclusion criteria include presence of chronic viral hepatitis, excessive alcohol use, other metabolic and autoimmune liver diseases, malignancies, and liver-related events (LRE) before T2DM diagnosis. The primary endpoint was LRE, defined as hepatic decompensation or the development of hepatocellular carcinoma. Uni- and multi-variable Fine-Gray regression model was estimated.

Results: 575,000 patients with T2DM were included (mean age 61.9 years; 52.3% males); the incidence rate of LRE was 1.279 (95% CI 1.243-1.315) cases per 1000 person-years at risk. Older age, male gender, presence of compensated cirrhosis, hypertension, underweight, baseline use of sulphonylureas and insulin were associated with an increased risk of LRE. By multivariable analysis, higher body mass index was associated with a higher risk of LRE, whereas aspirin and insulin use at baseline was associated with a lower risk. Among all covariates, older age explained the most about the incidence of LRE (36.7%) and non-liver-related mortality (44.3%), followed by compensated cirrhosis for LRE (17.7%) but not for non-liver-related mortality (5.3%) (Figure).

Conclusions: Advanced age, male gender, high BMI, and cirrhosis were risk factors for LRE in patients with T2DM. Advanced age was the most important risk factor for LRE and non-liver-related mortality. Cirrhosis significantly contributes to LRE but to a less extent to non-liver-related mortality.

Abstract Submission No. 100932

WS-026

Prevalence and risk factors for metabolic associated fatty liver disease in South Indian population

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BACKGROUND: Metabolic associated fatty liver disease (MAFLD) is the latest entrant in hepatology. There is paucity of data regarding MAFLD in the general population so this study aims to identify the prevalence and risk factors for MAFLD among the ethnic South Indian population.

METHODS: Demographic details, lifestyle habits, anthropometric details, biochemical tests and ultrasound findings of the subjects were recorded. A diagnosis of MAFLD was made with evidence of fatty liver along with one criteria for metabolic dysfunction. Statistical analysis was done using SPSS version 23, Chi Square test and Independent t test.

RESULTS: 2290 subjects were included in this study with mean age as 43.83 with SD of 13.601, age range from 19 to 78 and majority were in 41 to 50 age group (27.95%). Males were more common (58.95%). 27.95% of study population have MAFLD (640 subjects). Alcohol consumption was more commonly seen compared to other risk factors (33.62%) and hypertension was less commonly seen (23.58%) for developing MAFLD. Risk is more in smokers, alcohol consumption, diabetics, hypertensives, those with age more than 40 and females. On applying Chi square test significant association for getting MAFLD was found in diabetics, hypertensives and those with age more than 40. On applying Independent t test there was significant difference between MAFLD and Non MAFLD with p value < 0.05 in all parameters except uric acid.

CONCLUSION: Our study highlights the increasing burden of MAFLD in the community and to address the growing issue with targeted therapy for comprehensive patient care.

Abstract Submission No. 101219
WS-027

GENDER RELATED ASSOCIATION OF BMI AND AGE WITH MAFLD / SLD IN PAKISTANI POPULATION: CROSS SECTIONAL

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Background: When there is excessive fat in liver, condition is called (MAFLD). MAFLD most commonly occurs in patients having certain underlying conditions such as hyperlipidemia, metabolic syndrome, central obesity, hypothyroidism, polycystic ovarian syndrome, and type 2 diabetes mellitus. This study is designed to determine the link of MAFLD with age, gender, and body mass index.

METHODS: It is the cross-sectional, retrospective, single center study that was conducted in the Department of Gastroenterology & Hepatology, Jinnah Postgraduate Medical Center (JPMC), Karachi for a period of January 2020 to September 2023. All the adult males and females admitted and/or presented in the out-patient-department (OPD) with clinical signs & symptoms suggesting fatty liver disease were included for this study. Baseline and clinical data were collected by association of age, gender, and BMI with MAFLD was analysed using SPSS version 26.0.

RESULTS: Total 1140 participants were included for final analysis, the overall prevalence of MAFLD was 72.5% (n = 827). Patients with MAFLD were older (42.1±10.2) years as compared to controlled group (42.5±11.2) years and female patients were more prevalent than males, 78.6% vs. 21.4%, but they are insignificantly associated with MAFLD. Overweight patients were more likely to have MAFLD as compare to MAFLD with controlled and Obese.

CONCLUSION: A multitude of factors showed significant association with MAFLD and need to be researched in-depth to better understand the mechanisms behind them and the therapeutic measures that can be taken. Surprisingly, age and gender did not showed significant association with MAFLD but BMI did.

Abstract Submission No. 101764
WS-028

RCT evaluating efficacy of Saroglitazar vs OCA in pateints of MAFLD/MASH

CTRI/2023/03/050213

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Aim: NAFLD/NASH is a burgeoning cause for cirrhosis worldwide, but pharmacotherapy for the same remains elusive. Only Saroglitazar so far has received acceptance from DCGI. This study explores the potential efficacy of Obeticholic acid in patients of NAFLD/NASH.

Methods: This prospective, comparative study evaluated efficacy of Obeticholic acid 10 mg (n =50) and Saroglitazar 4mg (n =50) in patients of NAFLD/NASH. All patients were analyzed for change in primary outcomes i.e., Fibrosis (LSM) and steatosis (CAP) at baseline

and at 24 weeks measured through fibroscan and secondary outcomes including, ALT, AST, Lipid profile and non invasive scores of fibrosis .

Results: In Obeticholic acid group LSM reduced by 20.9%, p value <0.001 while in Saroglitazar limb it reduced by 23.20% p value <0.001 at 24 weeks, however there was no difference between 2 groups p value < 0.26. CAP in Obeticholic acid group reduced by 21% p value <0.001 while in Saroglitazar limb it reduced by 10.70 % P value, 0.001. CAP value reduced more significantly in Obeticholic acid group p value 0.01. Secondary endpoints , also improved significantly in both the groups post 24 weeks of treatment .

Conclusion: Obeticholic acid has a comparable effect with Saroglitazar in reducing Fibrosis (LSM), ALT, AST and serum Triglyceride, while it has an edge over the Saroglitazar in reducing Steatosis (CAP) .

Abstract Submission No. 101906
WS-029

Clinical features of MetALD and ALD in patients with hepatocellular carcinoma

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Aim: A subgroup of individuals with intermediate alcohol consumption among steatotic liver diseases has been classified as metabolic dysfunction-associated steatotic liver disease (MetALD). Therefore, we compared the clinical features of MetALD and alcohol-associated liver disease (ALD) in patients with hepatocellular carcinoma (HCC).

Method: The study included: 1) Cross-sectional comparison of 64 cases of MetALD-HCC and 207 cases of ALD-HCC diagnosed at our institution from 1989 to 2021, and 2) Retrospective cohort analysis of 271 cases post HCC diagnosis, including mortality rate, causes of death, and analysis of mortality risk factors.

Results: The median age of was 66/52 years, with a male ratio of 92.2/93.7%. The average daily ethanol intake was 32/108g. HCC stage IV was 9.4/6.3%. Significant differences (p<0.05) between the two groups were observed in age, prevalence of hypertension (67.2/51.7%), dyslipidemia (37.5/16.9%) and cirrhosis (65.6/77.8%), albumin (Alb) 4.4/3.7 mg/dL, total bilirubin (T-Bil) levels 0.5/0.9 mg/dL, and platelet count 25/10 × 10⁴/μL. 2) The 5-year survival rates were 69.6/49.5%, significantly lower in the ALD-HCC group (p<0.01). Mortality due to infections (20.8/5.8%) was significantly higher in the MetALD-HCC group (p<0.02). Risk factors for death included Child-Pugh classification at diagnosis, HCC stage, and curative treatment feasibility. Additionally, non-complication of dyslipidemia in the MetALD-HCC group and old age and low Alb levels in the ALD-HCC group were extracted.

Conclusion: The MetALD-HCC group showed a better prognosis compared to the ALD-HCC group. However, attention is needed for non-liver-related deaths in the MetALD-HCC group.

Abstract Submission No. 100722
WS-030

Daily nucleotide analogues reduces the severity of COVID-19 in patients with chronic liver disease

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Background: The effect of nucleotide analogues (NAs) against severe acute respiratory coronavirus 2 (SARS-CoV-2) infection and associated clinical outcomes among patients with chronic liver disease (CLD) remain unclear.

Methods: 579 CLD patients with available data of SARS-CoV-2 infection were included in this study during Omicron subvariants BA.5 wave. Demographic and clinical data were collected by standardized questionnaires and electronic medical records. Multivariate logistic regression models were used to assess the association between NAs and coronavirus disease 2019 (COVID-19) outcomes.

Results: CLD patients with daily NAs therapy had significant lower proportions of SARS-CoV-2 infection (72.8% vs. 84.3%, $p=0.001$), severe COVID-19 (2.3% vs. 7.8%, $p=0.003$) and COVID-19-related death (1.7% vs. 5.3%, $p=0.016$) than those without NAs therapy. Similar trends were also shown in other severe outcomes including intensive care unit (ICU) admission, mechanical ventilation and overall death although there was no significant difference. Multivariable logistic regression analysis further demonstrated the negative associations between daily NAs therapy and SARS-CoV-2 infection (adjusted odd ratio [aOR], 0.61; 95% confidence interval [CI], 0.36-1.02; $p=0.059$), severe COVID-19 (aOR, 0.26; 95% CI, 0.09-0.77, $p=0.015$) and COVID-19 related death (aOR, 0.23; 95% CI, 0.06-0.91, $p=0.036$).

Conclusions: Daily NAs therapy reduces the severity of COVID-19 among CLD patients and has potential protective effect against Omicron infection. This finding suggests that NAs might be used as pre-exposure prophylaxis or early treatment of COVID-19, especially for immunocompromised patients including decompensated cirrhosis with suboptimal vaccine responses and those CLD patients for which hepatic safety concerns arise with other antiviral drugs.

Abstract Submission No. 101025

WS-031

Pattern of Liver Injury and its Outcome in Covid-19 Patients

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Objective: COVID-19 is a highly contagious respiratory disease caused by the SARS-CoV-2 virus. Evidence suggests that it can cause liver damage through various mechanisms, but the prevalence and clinical significance of abnormal liver function tests (LFTs) in patients with COVID-19 is relatively unexplored.

Method and Material: Descriptive cross-sectional study was conducted at the Aga Khan University Hospital, Karachi from 26th 61 February 2020 till June 2020. All patients above 18 years of age, admitted with confirmed COVID-19 infection were included. Data on patient demographics, clinical symptoms, laboratory test results, length of hospital stay, and clinical outcomes was collected. Statistical analysis of the variables was conducted using SPSS.

Results: A total of 533 hospitalized patients were included in this study, with a mean age of 53 $\pm$ 16 67 years, of which 61.5% were male. The most prevalent comorbidities were hypertension 68 (42%) and diabetes mellitus (36%). LFTs were found to be deranged in 92% of the total 69 patients, with Aspartate aminotransferase (81%), Gamma-glutamyl transferase (69.4%), and Alanine transaminase (66.8%) being the most commonly affected liver enzymes. On comparative analysis, deranged LFTs showed significant correlations with the male gender (p -value 0.012), age group >60 years (p -value 0.001), fever (p -value <0.001), cough (p -value 73 0.028), shortness of breath (p -value 0.021), hemoglobin levels (p -value 0.003), serum 74 sodium (p -value 0.006), serum C-Reactive Protein (p -value <0.001) serum ferritin (p -value

<0.001), serum Lactate Dehydrogenase (p -value <0.001), and length of hospital stay (p value <0.001)

Conclusion: The study showed a high prevalence of abnormal liver enzymes in mild-moderate COVID-19 cases. Our findings suggest a correlation between abnormal liver function tests and various demographic and clinical factors, but further investigation is needed to determine the clinical significance of liver injury in COVID-19 patients. These findings have important implications for patient management and outcomes.

Keywords: Covid-19, Deranged LFTs, Gastrointestinal Manifestations

Abstract Submission No. 101052

WS-032

RCT: Reduction of Bilirubin after Steroids for Biliary Atresia

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Background: Biliary atresia remains a global public health problem. Although Kasai therapy has been established for a long time, the need for liver transplantation is still high. Liver transplantation is not available in all countries. Pathogenesis of autoimmunity in development of biliary atresia obliterative fibrosis is currently widely discussed. This study analyzes the effect of methylprednisolone on bilirubin levels in biliary atresia infants.

Methods: This study is a RCT on infants aged 2 week - 3 months with biliary atresia at Dr Soetomo General Academic Hospital, Surabaya. Subjects were grouped into methylprednisolone vs placebo group. Methylprednisolone was given at a dose of 2 mg/kg/day for 14 days and bilirubin levels were assessed before and after treatment. Data analysis was performed with SPSS.

Results: The study included 40 infants, 20 in the methylprednisolone group and 20 in the placebo group. Pre-treatment bilirubin levels were not significantly different between the methylprednisolone and placebo groups (direct bilirubin 9.87 (6.11-14.20) mg/dL vs 6.68 $\pm$ 2.44 mg/dL; total bilirubin 9.87 (6.11-14.20) mg/dL vs 9.44 $\pm$ 3.91 mg/dL; $p>0.05$). Bilirubin reduction was significantly greater with methylprednisolone than with placebo (direct bilirubin 3.88 $\pm$ 2.58 mg/dl vs 1.40 $\pm$ 2.22 mg/dl; $p=0.002$; total bilirubin 4.45 (3.17-7.65) mg/dl vs 2.39 $\pm$ 2.30 mg/dl; $p=0.03$).

Conclusions: Methylprednisolone reduced bilirubin levels at 2 weeks of therapy. Bilirubin improvement with steroids supports the evidence of immunity in the pathogenesis of biliary atresia.

Key word: Biliary atresia, Bilirubin level, Methylprednisolone

Abstract Submission No. 100419

WS-033

Modified ALBI grade and platelet count to predict high-risk varices in hepatocellular carcinoma

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Background: Baveno VII employs non-invasive tests to rule out high-risk varices (HRV) in cirrhosis; however, this approach doesn't extend to HCC. We aim to validate and refine the previously studied Albumin-bilirubin and platelet (ALBI-PLT) score for predicting HRV in HCC.

Methods: Our retrospective study included HCC patients with EGD reports and no prior upper GI bleeding at King Chulalongkorn Memorial Hospital from 2019 to 2023. F2 or F3 esophageal varices (EV) were defined as HRV. ALBI-PLT was computed following Chen et al. Modified ALBI-PLT (mALBI-PLT) calculated by combining mALBI grading (1 point for grade 1 or 2a; 2 points for grade 2b or 3) and platelet (1 point for $> 150,000/\mu\text{L}$; 2 points for $\leq 150,000/\mu\text{L}$).

Results: 277 HCC patients were enrolled. Of these, 22, 56, 147, and 52 fell into mALBI grades 1, 2a, 2b, and 3, while 131, 85, and 60 had HCC BCLC A, B, and C. 38 (15.6%) participants had HRV. The AUROC of the ALBI score and platelet for predicting HRV were 0.755 and 0.738. On multivariate analysis, platelet $\leq 150,000/\mu\text{L}$ and mALBI grade 2b and 3 were significantly associated with HRV with adjusted odd ratio of 4.29 (1.79-10.27) and 3.72 (1.08-12.81). ALBI-PLT and mALBI-PLT > 2 demonstrated excellent sensitivity of 100% and 97.37%, with a negative predictive value of 100% and 98.18% in predicting HRV.

Conclusion: mALBI grade and platelet at $150,000/\mu\text{L}$ showed significant association with HRV in HCC. Moreover, HCC patients with mALBI grade 1 or 2a and platelet $> 150,000/\mu\text{L}$ may avoid EV surveillance.

Abstract Submission No. 100221

WS-034

Depression Level Among Elderly with Liver Function Decrease and Hypertension Status

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Indonesia is entering an aging society with the elderly population reaching 29.3 million (10.8%). In Indonesia, liver disease is the highest comorbid factor in increasing the risk of death by 19.5 times in the elderly and complications make it even worse. Using the 2014 Indonesia Family Life Survey (IFLS), this study aims to analyze mental health problems in older adults (60+) with liver cancer and Hypertension status. The analysis shows that the Elderly with hypertension reach 42% (male: 60.7%), Elderly with liver cancer reach 6.1% (male: 70.6%). The elderly with both problems reaches 0.7% dan 55% of them experienced mental health problems and the percentage is higher in women. Based on 10 depression assessment questionnaires, the symptoms are: (1) I was bothered by things that usually don't bother me; (2) had trouble concentrating on what I was doing; and (3) I felt everything I did was an effort. However, the percentage of elderly with liver and hypertension experiencing mental health problems will decrease by 6.78% when they have a cell phone. Nearly half of older people's educational attainment is in elementary school, which reaches 46.05%. The elderly with higher digital literacy prefer to seek treatment at a community health center or Puskesmas (44.11%), specialist (29.41%), and private hospital (11.76%). Increasing digital aging encourages elderly health literacy, as well as decreasing mental health problems.

Abstract Submission No. 100470

WS-035

What percentage of the Japanese population has already been tested for HBV and HCV?

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Background: Japan has actively promoted the discovery of HBV or HCV infections by implementing nationwide hepatitis virus testing for all residents aged over 40 in 2002. This study reveals the testing coverage rate among the general population in Japan.

Methods: Nationwide surveys were conducted in 2011, 2017, and 2020, with 74,000, 30,000, and 20,000 residents selected through a two-stage random sampling method. We employed self-administered anonymous questionnaires. Those with blood donation, childbirth, or surgery history but no self-awareness of hepatitis virus testing was labeled as 'unrecognized testing'. We also conducted a pilot survey with 1,916 individuals who had testing experience at health checkups to adjust the 'unrecognized testing' rate based on the proportion who had forgotten their history of testing.

Results: In the three nationwide surveys (with responses from 23,720, 10,203, and 8,810 individuals), HBV and HCV recognized testing rates remained steady (17-20% for HBV, 15-18% for HCV). However, the testing rates including unrecognized testing increased by more than 10% from 2011 to 2017 (HBV: 58.4%, 71.0%, 71.1%; HCV: 48.0%, 61.6%, 59.8%). A pilot survey with 993 respondents found that 52.7% of those who had hepatitis virus testing during health check-ups had forgotten their testing history. Adjusting the nationwide survey based on this proportion, testing rate at 2020 reached 85.5% for HBV and 76.4% for HCV.

Conclusions: In Japan, 76.4-85.5% of the general population has already undergone hepatitis virus testing. The WHO's elimination goal of over 90% of infected individuals getting tested is likely almost achieved.

Abstract Submission No. 101529

WS-036

The Present and Future Hopes for Laparoscopic Hepatectomy Education Using a Visual Assistance AI

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Background: Laparoscopic hepatectomy (LH) requires accurate recognition and proper handling of hepatic veins and Glissonean pedicles that suddenly appear on the liver transection plane. We have developed a novel artificial intelligence (AI) system to assist in the visual

recognition and color display of tubular structures in order to correct the surgeon's recognition and for medical education.

Methods: Annotations were performed on 400 video frames capturing LH, after which a deep learning model was developed. The effectiveness of AI in medical education of surgery was qualitatively evaluated by 10 residents. 70 medical students were divided into two groups, one with and the other without AI analysis videos, to evaluate qualitatively the educational effect of intrahepatic tubular structure based on a questionnaire.

Results: The AI model was able to individually recognize and colorize hepatic veins and the Glissonean pedicle in real time. The IoU and Dice coefficients were over 0.42 and 0.53, respectively. The residents assessed the AI to be very effective (mean score, 1.86 ± 0.35 ; from 0 to 2; Excellent). There was a significant difference in medical students' anatomical recognition between the AI and non-AI groups (0.71 vs. 0.57 $p=0.027$; from 0 to 1; Excellent).

Conclusions: It was suggested that this AI could contribute to improving the visual recognition of residents and medical students in LH. We expect that residents and medical students might develop an interest in and understanding of surgery and local anatomy by viewing surgeries in which the AI colorizes and displays structures in real time.

Abstracts

Oral Free Papers

Abstract Submission No. 100999

O-0001

Nogo-B Deletion Alleviates Alcohol-Induced Liver Injury by Anti-inflammatory Macrophage Polarization

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Background: Nogo-B plays a crucial for maintaining ER tubular structure. Macrophage Nogo-B has been implicated in the severity of liver injury in alcohol-associated liver disease(ALT) patients. We hypothesized that deletion of Nogo-B in macrophages can ameliorate ALT by reducing macrophage-mediated inflammation.

Method: Macrophage-specific Nogo-B knockout(NGB-MΦKO) mice and their littermate wild-type(WT) controls(Nogo-B^{fl/fl}) were fed a high-fat diet(HFD, 60% kcal% fat) for three months, followed by maltose or ethanol gavage(5g/kg weight).

Results: NGB-MΦKO mice(n=10) exhibited a 40% reduction in ALT levels($p<0.01$), decreased neutrophil infiltration(30%, $p<0.01$), and decreased TNF- α (75%, $p<0.05$), IL-1 β (85%, $p<0.01$), and IL-6 (80%, $p<0.01$) expression, compared to WT mice(n=9) when subjected to HFD with alcohol. Structural analysis of macrophage ER using fluorescent microscopy and transmission electron microscopy(TEM) revealed that Nogo-B KO increased sheet ER structure while decreasing tubular ER(1.12-fold, $p<0.05$). REEP5 (another ER tubular protein) knockdown produced similar effects; increasing sheet ER and diminishing tubular ER (1.2-fold, $p<0.01$) in BMDM. Furthermore, REEP5 suppression inhibited pro-inflammatory polarization by reducing IL-6(44%, $p<0.001$), IL-1 β (15%, $p<0.05$), and TNF- α (45%, $p<0.001$) in BMDM, similar to NGB KO. TEM analysis showed that NGB KO

reduced tubular ER-mitochondria contacts (45%, $p<0.001$) and restored mitochondrial size(1.7-fold, $p<0.001$) in LPS-treated BMDM. Moreover, Seahorse analysis indicated decreased ER-mitochondria contact protected mitochondrial function (respiration rate)(1.9-fold increase, $p<0.01$) compared to WT macrophages, suggesting a mechanistic link between ER-mitochondrial contact, metabolic alteration, and macrophage polarization.

Conclusion: Nogo-B deletion modulates ER structure and metabolic function to promote an anti-inflammatory macrophage phenotype, thereby protecting against ALT. Nogo-B may represent a promising therapeutic target for the ALT treatment.

Abstract Submission No. 101014

O-0002

AKR1B8 deficiency prevents the progression of alcoholic liver disease in mouse model

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Alcoholic liver disease (ALD) is a major cause of chronic liver disease, which causes an extremely severe healthcare burden worldwide. Alcoholic fatty liver (AFL), an early stage of ALD progression, is a clinically important spectrum of alcohol-related fatty liver disease (ALD). Presently, there is no approved drug for ALD. To explore the potential therapeutic target of AFL, we constructed a Lieber Decarli diet-induced AFL mouse model and analyzed the RNA transcriptomic of liver tissues. We found that Aldo-keto reductase family 1 member B8 (Akr1b8), the NAD(P)H-dependent oxidoreduction of various carbonyl compounds, was significantly downregulated in the liver of AFL group mice. Furthermore, we found that there were fewer lipids in the liver of *Akr1b8* knockout AFL group by oil red O staining, and it was not due to the hepatocyte injury identified by Ki67 levels in different groups. Further liver tissue RNA transcriptomic of two groups revealed that there were several differently expressed genes enriched in alcohol metabolism-related pathways and lipid metabolism-related pathways. To verify these results, western blot was employed and the expression levels of lipid catabolism enzymes, including PPAR- γ and SCD1, were down-regulated in the KO-AFL group, suggesting that there were fewer lipids needed to be catabolized. Taken together, these results indicate that AKR1B8 is a potential therapeutic target of ALD.

Abstract Submission No. 101221

O-0003

ALDH2 rs671 polymorphism predicts clinical prognosis of alcohol related HCC after hepatectomy

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Background: The impact of ALDH2 rs671 polymorphism as predictors of clinical prognosis in alcohol-related hepatocellular carcinoma (HCC) after hepatectomy remains largely unknown.

Methods: This prospective cohort study enrolled 238 alcohol-related HCC patients who underwent hepatectomy from 2011 to 2022 at the E-Da Hospital, I-Shou University, Kaohsiung, Taiwan. Data analyses were finalized on October, 2023. Alcohol intake was defined as consuming over 20 g of ethanol each day for at least 5 years. ALDH2 rs671 polymorphism was analyzed. The primary endpoint was HCC recurrence and overall mortality.

Results: 196 (82.4%) were men and the mean (SD) age was 62.3 (10.2) years. HCC recurrence occurred in 70 patients, and 64 patients died. The cumulative incidences of HCC recurrence and mortality after resection in all patients were 40.6% and 37.7%, respectively. The ALDH2 rs671 polymorphism is significantly associated with HCC recurrence and mortality. The cumulative incidences of HCC recurrence and mortality were significantly higher in patients with the ALDH2 rs671 genotype GA/AA than in those with the ALDH2 rs671 genotype GG. In Cox proportional analyses, the ALDH2 rs671 genotype GA/AA and AST ≥ 40 IU/L were significantly associated with increased HCC recurrence (HR: 2.66, 95% CI: 1.59-4.43, $P < 0.001$; and HR: 1.93, 95% CI: 1.18-3.17, $P = 0.009$). Furthermore, the ALDH2 rs671 genotype GA/AA (HR: 2.02, 95% CI: 1.17-3.49, $P = 0.012$) and age ≥ 65 years-old (HR: 1.67, 95% CI: 1.01-2.78, $P = 0.048$) were significantly associated with increased mortality.

Conclusion: ALDH2 rs671 genotype GA/AA is significantly associated with worse clinical prognosis in alcohol-related HCC patients who underwent hepatectomy.

Abstract Submission No. 101276

O-0004

JPHX formula treated acute ALD in mice by regulating the metabolism of bile acids via gut-liver axis

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Background: Effective pharmacotherapies of alcohol-related liver disease (ALD) are still lacking. JianPiHuoXue formula (JPHX), as a traditional Chinese medicine, has shown a therapeutic effect to ALD in clinical practice. Here, we aimed to reveal the mechanism of JPHX in the treatment of ALD.

Method: The mice acute ALD model was established by a persistent alcohol diet, and JPHX was given by intragastric administration. The detection of serological indicators and histopathological examination of liver and intestine tissues were performed. Meanwhile, non-target metabolomics (NTM) of liver tissues, and 16S ribosomal DNA sequencing (16S seq) of gut microbiota were used to investigate the mechanism of JPHX on ALD.

Results: Compared with the model, the intervention of JPHX significantly reduced serum levels of ALT and AST, alleviated hepatic steatosis, and restored the integrity of the intestinal structure. In non-target metabolomics, the Kyoto Encyclopedia of Genes and Genomes pathway enrichment analyses of differentially expressed metabolites between groups showed that JPHX may affect Primary bile acid biosynthesis and Glutathione metabolism pathways. In the gut microbiota analyses, the results of 16S seq showed that at the genus level, the

JPHX treatment mainly increased the content of norank_f_Muribaculaceae, unclassified_f_Lachnospiraceae and so on, mainly decreased the content of Monoglobus and Escherichia- Shigella.

Conclusion: JPHX could effectively restore the liver and intestine injury caused by alcohol in acute ALD mice. And these effects may be achieved by regulating the gut-liver axis, mainly in the metabolism of bile acids.

Abstract Submission No. 101383

O-0005

TFR2 p.A75V mutation aggravates liver iron overload in alcoholic liver disease via ERK pathway

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Background: Liver iron overload is commonly observed in individuals with advanced alcoholic liver disease (ALD). Genetic factors may play a role in the progression of ALD. We aimed to investigate the involvement of hemochromatosis-related genes in liver iron deposition among ALD patients.

Methods: We analyzed clinical data from 97 ALD patients and sequenced exons of HFE, HJV, HAMP, TFR2 and SLC40A1 in 43 patients. We evaluated the severity of iron overload in ALD mice by measuring serum iron metabolism indices, liver iron quantification, and liver iron staining. We examined the effects of TFR2 p.A75V on HAMP induction and its underlying mechanism *in vivo* and *in vitro*.

Results: ALD patients with liver iron overload had worse liver function and prognosis scores compared to those without iron overload. We identified a potential functional mutation, TFR2 p.A75V, in ALD patients with iron overload. We established a new mouse model of ALD with liver iron overload. After administering recombinant AAV carrying the wild-type TFR2 gene, we observed a significant reduction in iron deposition in hepatocytes. However, the TFR2 p.A75V mutation did not alleviate iron overload in hepatocytes as the wild-type TFR2 did. The TFR2 p.A75V mutation may affect HAMP induction of iron by disrupting the ERK pathway, partially due to abnormal localization of the TFR2 protein in the cytoplasm.

Conclusion: TFR2 p.A75V mutation in ALD may reduce the sensitivity of hepatocytes to iron stimulation *in vivo* and *in vitro* by inhibiting the expression of HAMP through the ERK pathway, thereby aggravating iron overload.

Abstract Submission No. 101874

O-0006

Impact of alcoholic cirrhosis on development of renal insufficiency post-liver transplantation

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Objectives: Renal insufficiency is a common complication of liver transplantation (LT) and a risk factor for transplant related mortality. We aim to explore the impact of pre-LT alcoholic cirrhosis on development of post-LT renal insufficiency.

Methods: This retrospective study enrolled adult patients who had LT from January 2015 to January 2019 at a referral hospital. Patients were categorized into alcoholic cirrhosis and non-alcoholic liver disease groups. The incidence of chronic renal insufficiency, defined as creatinine $> 97 \mu\text{mol/L}$ / $> 115 \mu\text{mol/L}$ for female / male, persisting for > 3 months post-transplant, was compared between two groups. Multivariate logistic regression was performed to explore the risk factors for renal insufficiency.

Results: A total of 139 consecutive patients who had LT were recruited (78.3% male, median age 47.46 years), among which 38 had alcoholic cirrhosis and 101 had non-alcoholic liver disease. Renal insufficiency prevalence was 20.14% overall, higher in alcoholic cirrhosis (34.2%) than non-alcoholic disease (14.9%) patients ($P = 0.027$), with a relative risk of 2.30 (95%CI 1.21-4.38). After adjustment for confounding factors, alcoholic cirrhosis (OR=4.03, 95%CI 1.07, 15.19, $P=0.040$), male sex (OR=0.13, 95%CI 0.04, 0.51, $p=0.003$), and low tacrolimus trough concentration (reduced dosage due to renal insufficiency, cutoff values 4.75 ng/mL) (OR=0.68, 95%CI 0.51, 0.89, $p=0.001$) were the independent factors associated with renal insufficiency.

Conclusion: Alcoholic cirrhosis independently increases the risk of chronic renal insufficiency after liver transplantation. Close monitoring of tacrolimus concentration is crucial for individuals with alcoholic cirrhosis post-LT.

Abstract Submission No. 100327

O-0007

Alcohol consumption patterns among various presentations of alcoholic liver disease in South Asians

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Background and Aim: Alcohol consumption patterns vary between spectrum of alcoholic liver disease (ALD). Few studies compare drinking patterns with varied presentations of ALD among South Asians. We compared patterns of alcohol consumption among ALD with acute on chronic liver failure (ACLF), decompensated cirrhosis (D-CLD) and alcoholic steatohepatitis (ASH)

Methods: Patients presenting with ALD from August to November 2022 included. Data regarding patterns of alcohol consumption collected using patient filled questionnaires filled in presence of family members and treating physician. Comparison of various parameters related to alcohol consumption between D-CLD, AH/ACLF and ASH done using SPSS

Results: 30 ALD patients included. Median age 48(31-63) with 89.7% males with no significant difference in demographic features. Dose consumed during single binge measured in units (1 unit = 30 ml of whisky) was significantly higher in AIH/ACLF group in comparison to other groups, 15(2-36) vs 7(3-15) and 10(5-10). Median duration of consumption in months 154(2-360), 90 (3-480), 192(72-360) among AIH/ACLF, D-CLD and ASH and difference was not significant. Frequency of binges, snacking, make and type of liquor did not show difference between the 3 groups

Conclusion: Though duration of alcohol intake was similar, AIH/ACLF was associated with a higher dose of alcohol intake each time within same duration of drinking. Patients with intake of cirrhotogenic doses of alcohol, albeit in lower amount each time over a similar period of time presented with a D-CLD or alcoholic

steatohepatitis. Observation of such patterns in larger cohorts may help identify those patients with alcoholism likely to present with AIH/ACLF

Abstract Submission No. 100490

O-0008

Addressing ARLD and AUD with an innovative hepatology nurse-led alcohol reduction program

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Background: Alcohol-related liver disease (ARLD) is a major underfunded and often neglected area of healthcare. Liver clinics with an integrated focus on addiction have improved outcomes. However, currently, Alcohol Use Disorder medications and psychological services are underutilised by Hepatologists. By establishing a pilot hepatology nurse-led alcohol reduction program, this study aims to address gaps in the current care model for patients with ARLD.

Methods: Patients were enrolled through the liver clinic at Sunshine Coast University Hospital, a tertiary Australian hospital. Seventeen patients were referred to the Pilot Hepatology Alcohol Reduction Program, for which ten patients elected to proceed with the program. Patients completed a 3-month program with two weekly follow-ups with an individualised patient-centred approach to address AUD, with titration and adherence to medications, psychological support including motivational counselling with the option of concurrent psychology assessments.

Results: All patients had ARLD, with 80% diagnosed with cirrhosis. At four weeks, the standard drinks per week reduced from 91.35 [CI 67.72-114.98] to 20.3 [CI 10.15-30.45] p -value < 0.01 . 70% of patients utilised AUD medications through this clinic, and 50% underwent formal psychology reviews.

Conclusion: Through a nurse-led clinic, patients achieve a significant reduction in alcohol intake and improvement in the utilisation of medications and psychological services.

Abstract Submission No. 100710

O-0009

Alcohol consumption and the risk of liver disease: a nationwide, population-based study

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Introduction: Although most patients with alcohol-related liver disease (ALD) have a history of prolonged and heavy drinking, there is no clear threshold defining the level of alcohol consumption that leads to ALD. We aimed to evaluate the correlation between average alcohol consumption and the risk of liver disease.

Materials and methods: Using the Korean National Health Insurance database, we identified participants who underwent a health-screening program. The primary outcome was to determine the incidence of newly diagnosed liver-related diseases during the observation period and compare the incidence of liver-related diseases among non-drinkers and drinkers based on the amount of alcohol consumption.

Results: A total of 53,006 patients were enrolled. The participants were divided into five groups: no alcohol, 1st quartile, 2nd quartile, 3rd quartile, and 4th quartile. The corresponding number of glasses of alcohol consumed per week for each quantile (Q1, Q2, Q3, and Q4) was labeled 2.5 ± 1.1 standard units, 5.4 ± 1.9 standard units, 11.5 ± 3.3 standard units, and 27.9 ± 18.2 standard units, respectively. Compared with non-drinkers, the risk of liver-related disease was found to be higher in Q1 drinkers (adjusted hazard ratio [aHR], 1.09; 95% CI, 0.90-1.33), Q2 drinkers (aHR, 1.10; 95% CI, 0.91-1.32), Q3 drinkers (aHR, 1.33; 95% CI, 1.11-1.59), and Q4 drinkers (aHR, 1.47; 95% CI, 1.24-1.75).

Conclusions: We report that our study has shown that drinking more than 11.5 ± 3.3 standard units/week (92 ± 26.4 g/week) significantly increases the risk of developing liver-related diseases.

Abstract Submission No. 100869

O-0010

Secular trend of disease burden of alcoholic hepatitis in region endemic with chronic viral hepatitis

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Objective: Alcoholic hepatitis is a relatively uncommon in Hong Kong, a city endemic with viral hepatitis. With many bars and restaurants shut down during COVID-19 restrictions in 2020 to 2022, off-premise sales of alcohol soared and may lead to increase burden of alcoholic hepatitis. We aimed to evaluate the secular trend of the disease burden of alcoholic hepatitis over the last decade in Hong Kong.

Methods: This was a territory-wide cohort study of consecutive patients with alcoholic hepatitis from January 2010 to June 2023. Alcoholic hepatitis was defined with at least one of the relevant diagnosis codes (ICD-9 571.1 or ICD-10 K70.10, K70.11) together with at least three of the following laboratory criteria: 1) ALT or AST > 50 IU/L; 2) AST:ALT ratio > 2; 3) INR > 2; and/or 4) bilirubin > 3.0 mg/dL.

Results: 943 patients were diagnosed with alcoholic hepatitis; their mean age was 51.1 ± 12.7 years; 89.5% were male. The incidence rates of alcoholic hepatitis fluctuated over the last decade, with a clear increasing trend in the first two years of COVID-19 pandemic in 2020-2021 (2.72-2.83 per 100,000 population), then dropped in 2022-2023 in men. The incidence rates remained steadily low (below 0.5 per 100,000 population) in women (Figure).

Conclusion: Alcoholic hepatitis is uncommon in Hong Kong where chronic viral hepatitis is endemic. There was a transient increase in incidence rates of alcoholic hepatitis during the first two years of COVID-19 pandemic. Fortunately, this trend did not last while the pandemic has gone.

Abstract Submission No. 101541

O-0011

Incidence, and outcomes of alcohol related liver diseases in Korea: nationwide analysis

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Background: The purpose of this study is to address the critical public health issue of alcoholic liver disease, focusing on its trends, incidence and outcomes.

Methods: National Health Insurance Service claims data and health check-up information from 2011 to 2017 was utilized. Population's overall drinking amount and the incidence of alcoholic liver disease was calculated based on ICD-10 diagnosis codes.

Results: There has been an overall increase in the rates of regular drinking (49.3% to 51.1%), moderate drinking (15.4% to 16.4%), and stable proportion of high-risk drinking (14.9% to 14.7%) between 2011 and 2017. The incidence rate of alcoholic liver disease increased in proportion to the amount of alcohol (moderate drinker 0.15%, high risk drinker 0.93%) and relatively higher in men than women. There is a decreasing trend in alcoholic fatty liver disease (26% to 22%) but an increase in alcoholic cirrhosis (16% to 26%). Both men and women show an increasing trend in the progression from alcoholic liver disease to cirrhosis over a 3-year follow-up period, with a higher increase rate observed in women. Additionally, medical costs for patients are rising annually, and patients with alcoholic liver disease require more hospitalization and outpatient care compared to the control. However, there was a decreasing trend in the co-diagnosis of alcohol use disorders since 2016 (9.43% to 7.98%).

Conclusion: This study underscores the growing health and social challenges posed by alcoholic liver disease. The rising rates of severe liver disease forms and associated costs indicate an ongoing public health concern.

Abstract Submission No. 101542

O-0012

Impact of Smoking on Alcoholic Liver Disease and Mortality: Compounding Hazards

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Background: This study aimed to reveal the additional risk of smoking on the incidence and outcome including mortality of alcoholic liver disease in chronic drinkers.

Methods: National Health Insurance Service claims data and health check-up information from 2011 to 2017 was utilized. High-risk drinking was defined as drinking 7 or more drinks for men or 5 or more drinks for women twice a week.

Results: The smoking rate was higher in the high-risk drinking group compared to the social drinker group for both men (53.49% vs. 31.56%) and women (19.56% vs. 2.56%). The smoking rate gradually decreased among men from 2011 to 2017, but there was no significant change among women. The 3-year incidence rate of alcoholic liver disease was significantly higher in the high-risk drinker with smoking group compared to the high-risk drinker only group (2.24% vs. 1.90%). In particular, the risk of smoking increased more among women than among men. In men, the relative risk (RR) of developing alcoholic liver disease increased from 4.62 to 4.83 when smoking, while in women, it increased significantly from 6.34 to 13.47 when smoking.

Additionally, smoking significantly increased the 3-year mortality rate in the high-risk drinker group (0.64% vs. 0.49%), and the risk increased significantly in women (RR men 1.18, women 1.95).

Conclusion: Smoking worsens the incidence and mortality of alcoholic liver disease in high-risk drinkers. In particular, because the risk increases more for women than for men, smoking cessation education for female drinkers is important.

Abstract Submission No. 101576
O-0013

Neutrophil-to-Lymphocyte Ratio and Infection in Patients with Severe Alcoholic Hepatitis

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Background & aims: Severe alcoholic hepatitis (SAH) may appear liver failure or decompensation, with infection and high short-term mortality. We assessed the predictive value of blood neutrophil/lymphocyte ratio (NLR) for infection in patients with SAH.

Methods: The patients with SAH were divided into infected group and non-infected group. The indexes in the two groups were compared, and the relationship between NLR and infection was clarified by the generalized additive model. If the curve fitting result between the two groups was non-linear. We analyzed the threshold effect by the piecewise regression model.

Results: The clinical data of 143 patients with SAH were collected. According to the presence or absence of infection, we divided the patients into the non-infected group (n = 69) and the infected group (n = 74). When $NLR < 13.37$, the risk of infection increased by 15% for each 1.00 increase in NLR, OR = 1.15, 95% CI (1.04, 1.27), P = 0.0065. NLR was positively correlated with the risk of infection in a certain range. **Conclusions:** NLR was an indicator to predict infection in patients with SAH.

Keywords: alcoholic hepatitis; neutrophil to lymphocyte ratio; prognosis; infection

Abstract Submission No. 101962
O-0014

Genetic Analysis Of The Composition Of Fatty Acid In Diagnosis and Therapy of Alcoholic Liver Disease

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Introduction: The large number of microbiota that inhabit the human digestive system have an important role with the immune system. Microbiota produce a wide variety of metabolites, including short chain fatty acids. Alcohol-related liver disease is liver damage due to excessive and long-term alcohol consumption. This study aims evaluate the compositions of short chain fatty acid producing gut microbiota in diagnosis and therapy of alcoholic liver disease.

Method: Data obtained from 29 sequences of the compositions of short chain fatty acid producing gut microbiota of alcoholic liver disease on secondary data form on <https://www.ncbi.nlm.nih.gov/>. The phylogeny analysis was constructed with UPGMA method using MEGA7.0 software.

Result: The optimal tree with the sum of branch length = 28.01713153 is shown. The tree is drawn to scale, with branch lengths in the same

units as those of the evolutionary distances used to infer the phylogenetic tree. Genetic variation comes from mutations in genetic material, migration (gene flow), and changes in gene composition through sexual reproduction. Variations also come from the exchange of specific genes. Genetic diversity is the key in character improvement programs for specific genes. This is due to the maximization of genetic acquisition of certain traits. High genetic variation will produce adaptive traits. **Conclusion:** Genetic Variation of The compositions of short chain fatty acid producing gut microbiota in diagnosis and therapy of alcoholic liver disease have high degree of genetic variability. This information is important for future genetic improvement.

Keyword: Genetic Variation, Short Chain Fatty Acid, Gut Microbiota, Alcoholic Liver Disease

Abstract Submission No. 102012
O-0015

Hyperimmune bovine colostrum is safe and effective in steroid ineligible severe ACLF- AH patients

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Background: Hyperimmune Bovine colostrum(HIBC) with its rich content of immunoglobulins has shown to be immunomodulatory and decrease the effects of leaky mucosal barrier. We aimed to study the effects of hyperimmune bovine colostrum on outcomes in steroid ineligible alcoholic hepatitis patients.

Methods: In this retrospective analysis conducted at a tertiary hospital at Hyderabad, India, 66 patients with ACLF-AH (Steroid ineligible with mDF scores 32-90) were screened and 40 patients were analysed. HIBC was given at a dose of 15g/day (4 weeks) along with SMT. Aim of study was to study 90 days transplant free survival and incidence of infections, changes in mDF & MELD and improvement in grade of ascites.

Results: Mean age of 38 ± 4.5 years with baseline mean MELD 21.7 ± 4.7 ; mDF of 68.9 ± 17.8 . 30 day and 90-day transplant free survival was seen in 87.5 % (35/40) and 77.5% (31/40) patients respectively. Infections during 90-days were seen in 27.5% (11/40) patients. On Multivariate analysis on predictors of 90 day transplant free survival, baseline MELD score {HR(95% CI) 1.95, (0.920-4.78), P=0.01}; mDF {HR(95% CI), 2.57(1.32-7.11), P=0.01}, baseline albumin {HR(95% CI), 1.217 (0.788-4.589), p=0.04} were significant. mDF cutoff of 52.5 had AUC of 0.54 with sensitivity & specificity 73.8 % and 71% in predicting 90-day transplant free survival. Δ mDF { 15.2 ± 4.52 vs 6.27 ± 1.89 , P<0.05} and MELD scores { 5.21 ± 1.12 vs 2.12 ± 0.26 , P<0.05} was higher among survivors.

Conclusion: HIBC in combination with standard medical treatment is effective in improving 90-day transplant free survival in ACLF -AH.

Abstract Submission No. 200077
O-0016

Effect of leucogen in treating alcoholic liver cirrhosis with thrombocytopenia or leukopenia

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Background: Thrombocytopenia and leukopenia are common complications of alcoholic liver cirrhosis (ALC) and are associated with an increased risk of bleeding, infection and mortality. We aimed to evaluate the therapeutic effect of leucogen, a cysteine derivative that increases platelet and white blood cell (WBC) counts in patients with ALC.

Methods: A total of 413 patients with ALC who had thrombocytopenia (platelet < 100×10⁹/L) and/or leukopenia (WBC < 4.0×10⁹/L) were enrolled in this retrospective study, the patients were treated with leucogen (20mg, 3 times per day) or not. The primary endpoint was an increase in platelet or WBC count of ≥5% from baseline. Propensity score matching (PSM) was utilized to minimize the impact of selection bias.

Results: Among the 320 patients included in the final analysis after PSM, patients receiving leucogen had significantly higher proportions of platelet increase (46.9% vs. 32.5%, *p* = 0.012), WBC increase (50.0% vs. 36.2%, *p* = 0.018) and both PLT and WBC increase (28.1% vs. 15.6%, *p* = 0.010). The leucogen group exhibited superior fold increases in platelet count (OR 1.833; 95% CI 1.164-2.885; *p* = 0.009) and WBC count (OR 1.759; 95% CI 1.125-2.750; *p* = 0.013) compared to the non-leucogen group. Subgroup analysis revealed that patients with baseline factors such as age <60 years, ALT <40 U/L, and AST <40 U/L showed favorable treatment outcomes.

Conclusions: Leucogen is an effective treatment for thrombocytopenia and leukopenia in patients with alcoholic liver cirrhosis.

Abstract Submission No. 100040

O-0017

Metabolic reprogramming of CD4⁺ T cells by MSC-EVs attenuates AIH through mitochondrial transfer

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Background: Autoimmune hepatitis (AIH) is a serious liver disease characterized by immune disorders (e.g., abnormal T cell activation), and more efficient therapies for treating AIH are urgently required. However, the metabolic features of CD4⁺ T cells in AIH and the corresponding targeted therapies have not been well-explored.

Methods: CD4⁺ T cells of AIH patients were isolated from peripheral blood by immunomagnetic cell sorting, and the levels of key enzymes related to glycolysis were measured. Liver biopsy specimens from AIH patients were stained with CD4 and GLUT1 (carrier protein responsible for glucose transport). 2-DG (a glycolysis inhibitor) or mesenchymal stem cell-derived extracellular vesicles (MSC-EVs) were injected into AIH mice to evaluate their therapeutic effects. RNA-sequencing was used to identify the gene profile changes in CD4⁺ T cells subjected to MSC-EVs.

Results: Enhanced glycolysis of CD4⁺ T cells was verified as a key factor in AIH in patient samples and mouse models. More importantly, MSC-EV treatment reduced CD4⁺ T cell activation by inducing a metabolic switch from enhanced glycolysis to mitochondrial oxidative phosphorylation (OXPHOS), ameliorating liver damage in AIH mice. Mechanistically, MSC-EVs contained abundant mitochondrial contents (e.g., electron transport chain proteins) and thus transferred such contents to metabolically reprogram CD4⁺ T cells, while disrupting mitochondrial transfer attenuated the therapeutic potency of MSC-EVs in activated CD4⁺ T cells.

Conclusion: This study highlights that MSC-EVs can metabolic reprogram T cell phenotype by transferring mitochondrial components,

which may offer a new avenue for treating autoimmune disease, such as AIH.

Abstract Submission No. 100367

O-0018

MSC-derived exosomes attenuate hepatic fibrosis in PSC through inhibition of Th17 differentiation

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Primary sclerosing cholangitis (PSC) is an autoimmune cholangiopathy characterized by chronic inflammation of the biliary epithelium and periductal fibrosis, with no curative treatment available and liver transplantation is inevitable for end-stage patients. Human placental mesenchymal stem cell (hpMSC)-derived exosomes (Exo^{MSC}) have demonstrated the ability to anti-fibrosis, inhibit collagen production in autoimmune liver disease and possess immunomodulatory properties. Here, we prepared hpMSC-derived exosomes (Exo^{MSC}) and further investigated the anti-fibrotic effects and detailed mechanism on PSC. Results show that Exo^{MSC} ameliorated liver fibrosis in PSC mice (Mdr2^{-/-}) with significant collagen reduction in the preductal area where Th17 differentiation was inhibited as demonstrated by RNAseq analysis, and the percentage of CD4⁺ IL-17A⁺ T cells was reduced both in Exo^{MSC}-treated Mdr2^{-/-} mice (Mdr2^{-/-}-Exo) *in vivo* and Exo^{MSC}-treated Th17 differentiation progressed *in vitro*. Furthermore, Exo^{MSC} improved the hypersecretory phenotype and intercellular interactions in the hepatic Th17 microenvironment by regulating Perk/Chop signaling as supported by multicellular organoids. Thus, our data provide mechanistic and therapeutic insights into the role of Exo^{MSC} in liver fibrosis of PSC or Th17-related diseases.

Abstract Submission No. 100368

O-0019

ROS-responsive nanoparticle delivery of OCA mitigate mitochondrial biogenesis and cholestasis in PSC

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Primary sclerosing cholangitis (PSC) is a rare, cholestatic liver disease characterized by inflammation and fibrosis of intrahepatic and extrahepatic bile ducts without approved treatment. Obeticholic acid (OCA) is a potent farnesoid X receptor (FXR) agonist approved for the treatment of cholestatic liver disease. However, OCA-induced liver injury in PSC patients puts them at risk of acute chronic liver failure, thus

limiting the clinical application of OCA. Here we developed a reactive oxygen species (ROS) responsive biodegradable polymer-conjugated OCA encapsulated in the cytomembrane of human placental derived mesenchymal stem cells (hP-MSCs). In H₂O₂-stimulated PSC derived organoid, OCA-loaded ROS-responsive polymer nanoparticles cloaking hP-MSCs membrane (named MPPFTU@OCA), can increase cellular uptake, attenuate expression of bile acid related genes and inhibit mitochondrial ROS activation mediated apoptosis. Besides, in DDC and Mdr2^{-/-} preclinical PSC models, intravenous MPPFTU@OCA can not only improve cholestasis but also alleviate mitochondrial metabolism, without causing systematic toxicity. Taken together, these results demonstrate that this combination of ROS responsive and self-positioning biomimetic platform with OCA reveals a synergetic effect of rewiring mitochondrial metabolism and relieving cholestasis, and thus has essential application prospects in PSC treatment.

Abstract Submission No. 100407
O-0020

Cellular senescence-triggered dysfunction of hepatocyte aggravates autoimmune liver injury

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Background: Autoimmune hepatitis (AIH) is an inflammatory liver disease characterized by immune cell-mediated autoimmune response against liver autoantigens. However, little is known about the role of hepatocyte senescence in AIH pathogenesis.

Methods: A novel murine AIH model was established by inhibiting hepatocyte cytokinesis. Cellular senescence was assessed through SA- β -Gal staining and senescent associated secretory phenotype assay. Biochemical and histopathological experiments were performed to detect the hepatic function and liver injury in AIH model. scRNA sequencing was carried out to explore the cellular transition and transcriptomic profile of hepatocyte in AIH. Therapeutically, the efficacy of senolytic treatment (dasatinib plus quercetin) was also investigated in murine AIH model.

Results: Inhibition of cytokinesis induced senescent phenotype in hepatocyte, demonstrating as cell cycle arrest, morphological changes as well as senescent associated secretory phenotype. The liver with senescent hepatocytes exhibited AIH features, including increased ALT and AST levels, presence of autoantibodies and severe interface hepatitis and fibrosis on liver histology. scRNA sequencing analysis revealed a unique hepatocyte cluster with senescent characteristic in AIH liver, which strongly communicated with CD4⁺ T cell and CD8⁺ T cell. Unexpectedly, when the AIH mice were treated with senolytic drugs, the liver injury was dramatically alleviated. The increased hepatocyte senescence was also found in AIH patients compared with healthy persons and the senescence proportion was correlated with clinicopathological features.

Conclusions: This study established a novel murine AIH model and revealed the critical role of hepatocyte senescence in AIH pathogenesis. The senolytic treatment is highlighted as a promising therapeutic strategy for AIH.

Abstract Submission No. 100679
O-0021

Immunoregulatory myeloid cells counter T cell activation in AIH by exosome-mediated metabolic shift

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Background: Autoimmune Hepatitis (AIH) poses a complex challenge with an elusive pathogenesis. In this study, we probed purine metabolism changes in AIH patients and murine models, seeking to unravel its potential implications in disease development.

Methods: Plasma samples from 48 AIH patients and 36 healthy controls were collected to scrutinize metabolite profiles. Parallel investigations were carried out using a murine model. RNA-seq analysis illuminated the gene regulation linked to these changes. Employing single-cell sequencing and flow cytometry, we unearthed these primary alterations predominantly within immunoregulatory myeloid cells. To delve deeper into the mechanisms of action of these cells, we isolated and extracted extracellular vesicles they secreted, identified purine metabolism-associated proteins, and explored metabolic shifts when cocultured with CD4⁺ T cells, shedding light on their precise modes of regulation.

Results: Our inquiry uncovers significant shifts in purine metabolism in both AIH patients and the ConA-induced mouse model, underlining the pivotal role of the CD39-CD73-ADA purinergic axis in the disease's pathogenesis. Immunoregulatory myeloid cells migrating to the liver emerge as crucial orchestrators of CD4⁺ T cell activation through the release of extracellular vesicles bearing purine metabolic enzymes, thereby generating immunosuppressive purine metabolites, primarily adenosine and inosine.

Conclusion: These findings furnish valuable insights into AIH's pathophysiology, underscoring the potential therapeutic implications of targeting the CD39-CD73-ADA axis and purine metabolism in disease management. This research opens a promising avenue for further investigation and intervention in AIH and related autoimmune disorders.

Abstract Submission No. 100947
O-0022

MSC-EV protects against immunological liver injury by suppressing ferroptosis via Nrf2/GPX4 axis

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Ferroptosis plays an important role in the pathogenesis of various liver diseases, yet it has rarely been investigated in human autoimmune hepatitis (AIH). This study is meant to explore the protective effect and mechanism of extracellular vesicles of mesenchymal stem cells (MSC-EVs) on ferroptosis and excessive inflammation of immunological liver injury (ILI). We found that inflammation associated hepatocytes ferroptosis occurred in ILI mice, whereas deferoxamine attenuated liver injury. In ILI mice, MSC-EVs might reduce hepatocytes ferroptosis and subsequently improve liver injury, while KEGG pathways enrichment analysis also validated that ferroptosis inhibition was involved in the underlining therapeutic mechanisms. Besides, further GPX4 inhibition experiments revealed that MSC-EVs alleviated inflammatory response induced ferroptosis via upregulating GPX4 in vitro. Meanwhile, MSC-EVs could increase the expression of Nrf2 and Nrf2 inhibition alleviated the effects of MSC-EVs. Transwell assay revealed that MSC-EVs could prevent the recruitment and chemotaxis of macrophages induced by ferroptotic hepatocytes. Moreover, we found that there was a significant correlation between levels of circulating 4-HNE and transaminases and treatment response, while over-activation of ferroptosis was revealed in hepatocytes in AIH patients. In conclusion, MSC-EVs could ameliorate inflammatory injury in ILI by suppressing hepatocytes ferroptosis via the Nrf2/GPX4 signaling pathway.

Abstract Submission No. 100954
O-0023

Targeting monocytes via CCL2/CCR2 axis in autoimmune hepatitis by macrophage-derived exosomes

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Background: Autoimmune hepatitis is a serious chronic liver disease with immune disorders, histological lesions and liver dysfunction, with a gradually increasing prevalence. Yet the cellular and molecular mechanisms of immune dysregulation in AIH are poorly understood.

Methods: Using proteomic analysis, we comprehensively profiled the differentially expressed proteins and signaling pathways of liver during human AIH. Then, monocytes and macrophage from blood and livers of AIH patients and controls were analyzed. The recruitment and polarization of monocyte-derived macrophages in AIH and the mechanism of CCL2/CCR2 axis activation were investigated by Concanavalin induced experimental AIH (EAH). The CCL2/CCR2 axis was blocked by CCL2 neutralizing antibody and CCR2 antagonist to determine its effect on AIH mice. Finally, M2 macrophage-derived extracellular vesicles (M2-EVs) were isolated and extracted as drug delivery tool of CCR2 antagonist, and its therapeutic effect on AIH mice was determined.

Results: Proteomic analysis took expression ratio (FC) > 1.5 times and P<0.05 as screening criteria, and a total of 1028 proteins were identified as increased or decreased. KEGG analysis suggested that differential expressed proteins were mainly associated with metabolic processes. The expression of mononuclear macrophage system marker proteins CD14, S100A9, CD163, CD68 and CD11b increased in the liver tissue of AIH patients as revealed by proteomic analysis and immunohistochemistry. The proportion of classical monocytes in peripheral blood of AIH was increased, which was positively correlated with the levels of ALT and AST of AIH patients. The co-localization analysis of liver tissue suggested that CCL2 originated from Kupffer cells (KC), and the expression of CCR2 increased after circulating monocytes infiltrated liver. The expression of M1 marker in AIH liver tissue increased. AIH mouse models suggest mobilization of inflammatory monocytes on the bone marrow-liver axis and spleen-liver axis. Blocking-up of CCL2/CCR2 axis with CCL2 neutralizing antibody or CCR2 antagonist, respectively, alleviated liver injury in AIH mice, while recombinant CCL2 injection increased recruitment of inflammatory monocytes with bone marrow-liver axis and spleen-liver axis to liver, aggravating liver injury. CCR2 antagonist-M2-EV can target circulating mononuclear cells and activated mononuclear macrophages in the liver, respectively, to reduce liver injury in AIH mice.

Conclusion: AIH mediates the recruitment of inflammatory monocytes from bone marrow and spleen to liver through the CCL2/CCR2 axis, which can be inhibited by different methods to reduce liver inflammatory injury in AIH mice. M2- EVs delivers CCR2 antagonists targeting activated pro-inflammatory monocytes and hepato-splenic mononuclear macrophage system in the circulating pool, indicating that CCR2 antagonists-EVs could be a potential agent for liver and monocyte targeted therapy for AIH.

Abstract Submission No. 101938
O-0024

Bile multi omics provide molecular insight and classify signatures of carcinoma of gall bladder

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Carcinoma of the gall bladder (CAGB) has poor prognosis. Molecular analysis (proteome/metabolome) of bile could recapitulate changes associated with CAGB development and help in characterization of putative indicators for early CAGB diagnosis. Bile samples screened for proteomics-metabolomics signatures capable of early detection of cancer in GB anomalies. Analysis of training cohort (n=87) showed that bile of CAGB patients has distinct proteomic (217up- and 258 down-regulated; FC>1.5) and metabolomic (111 up- and 505 downregulated; FC>1.5) phenotype as compared to Gallstone or HC (p<0.05, FDR<0.01). Partial least square discriminant analysis and unsupervised hierarchical-clustering segregated CAGB patients. CAGB bile was significantly enriched for proteins/metabolites linked to inflammation, and alternate energy pathways (pentose phosphate pathway, amino acid metabolism, lipid metabolism, and others). CAGB bile showed reduction of Proteins/metabolites associated to glycolysis, cholesterol metabolism, PPAR, RAS, and RAP1 signaling glutathione, histidine, purine metabolism, oxidative phosphorylation, and others (p<0.05). Integration analysis revealed strong correlation (r²>0.5, p<0.05) between significant proteins/metabolites and clinical parameters and showed alteration of pathways linked to lipid metabolism, platelet activation, amino acid metabolism, and others (p<0.05). Metabolite/protein signature-based probability of detection for CAGB was >90% (p<0.05) with AUC>0.94. Validation of top four metabolites panel: Toluene, 5,6-DHET, Creatine, and Phenyl acetaldehyde using five machine-learning algorithms in two separate cohorts (n=40; bile [test cohort 1] and paired plasma [test cohort 2]) showed accuracy (99%) and sensitivity/specificity (>98%) for CAGB detection. **Conclusion:** Bile proteome and metabolome alteration provides critical molecular understanding and outlines metabolomics panel which may offer universal utility for early detection of CAGB.

Abstract Submission No. 102064
O-0025

The analysis of risk factors for hepatocellular carcinoma in patients with autoimmune liver disease

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Aim: Autoimmune liver disease including primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH) is rare as the cause of hepatocellular carcinoma (HCC) in Japan. However, the hepatocarcinogenesis in autoimmune liver disease is still unclear. Metabolic syndrome such as obesity or type 2 diabetes mellitus (DM) has been reported to increase the risk of HCC. Thus, we have conducted a study to clarify the clinical risk factors for developing HCC in patients with autoimmune liver disease.

Patients and Methods: We investigated 608 PBC patients (females; 86%, median age; 59 (21-85) and 314 AIH patient diagnosed (females 84% age 52 (19-86) as Japanese Criteria. We observed all 922 patients without HCC at the time of the initial diagnosis with PBC or AIH for a median of 9.4 years (0.3-35) to evaluate risk factors for the development of HCC.

Results: HCC newly developed in 57 patients. The cumulative appearance rate of HCC was 0.5% and 1.2% at the end of the fifth and tenth years by Kaplan-Meier analysis. Independent risk factors for HCC by Cox model were cirrhosis [hazard ratio (HR) 4.459, $p = 0.005$], higher age (HR 1.077, $p = 0.014$), male gender (HR 2.884, $p = 0.027$), and complicated DM (HR 1.538, $p = 0.031$).

Conclusions: The independent risk factors for HCC in patients with autoimmune liver disease were cirrhosis, age, male, and DM. Careful observation of patients with a high risk of HCC will improve the prognosis of patients with PBC or AIH.

Abstract Submission No. 100049
O-0026

Low serum complement is common in autoimmune hepatitis and is related to high serum immunoglobulin G

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Objective: Complement could mediate immune response and inflammation in systematic immune diseases, but its role in autoimmune hepatitis (AIH) has not been clearly clarified.

Methods: We retrospectively collected 146 patients with diagnosis of AIH, systemic lupus erythematosus and other liver diseases were excluded. Biochemical tests were performed before treatment. In our hospital, normal range of complement 3 (C3) is 0.785-1.520 g/L, and C4 is 0.145-0.360 g/L. So, we defined C3 <0.785g/L as low-C3 and C3 >1.520g/L as high-C3, C4 <0.145g/L as low-C4 and C4 >0.360g/L as high-C4. The G grade (Scheuer score system) of inflammation of liver biopsy tissues were evaluated. Firstly, we analyzed the correlations between complement and transaminase (ALT and AST). Then, because guidelines recommended that immunoglobulin G (IgG) > 2x upper limit of normal (ULN) is an indicator of immunosuppressive therapy, so we divided patients into two groups according to IgG ($\leq 2x$ ULN and $> 2x$ ULN) for further analysis. Also, we performed comparison between patients with different G grade (G1-G2 and G3-G4). Finally, because cirrhosis could lead to elevated serum IgG and low complement, we excluded patients with cirrhosis for further analysis.

Results: Eighty-three (56.8%) patients with low-C3 and 71 (48.6%) patients with low-C4. No patients had high-C3 and only one patient had high-C4. There were no significant correlations of C3 and ALT/AST ($P=0.766$, $r=0.025$; $P=0.256$, $r=-0.094$, respectively). For C4, the correlations between it and ALT/AST were weak ($P=0.001$, $r=0.264$; $P=0.005$, $r=0.229$). And we found that patients in IgG $>2x$ ULN group had lower serum complement than that in IgG $\leq 2x$ ULN group [C3: 0.588 ± 0.288 g/L, 0.770 ± 0.25 g/L, $P<0.001$; C4: 0.116 (0.102, 0.129) g/L, 0.155 (0.122, 0.203) g/L, $P<0.001$]. In addition, 139 patients performed liver biopsy, patients in G3-G4 group had lower serum complement than that in G1-G2 group [C3: 0.712 ± 0.265 g/L, 0.813 ± 0.234 g/L, $P=0.026$; C4: 0.135 (0.106, 0.181) g/L, 0.167 (0.136, 0.216) g/L, $P=0.003$]. Sixty-seven patients were excluded because cirrhosis. Then, further comparisons indicated that patients with low serum complement had higher IgG [low C3 vs non-low C3: 26.7 (20.0, 32.4) g/L, 17.8 (16.3, 23.3) g/L, $P=0.003$; low C4 vs non-low C4: 26.6 (20.0, 33.5), 18.6 (16.0, 24.9), $P=0.002$]. But no matter for C3 or C4, percentages of G3-4 were not significantly different between two groups [low C3 vs non-low C3: 15 (51.7%), 24 (51.1%), $P=0.955$; low C4 vs non-low C4: 13 (65.0%), 26 (46.4%), $P=0.154$].

Conclusion: Low serum C3/C4 was very common in AIH patients, and it was related to high serum IgG.

Abstract Submission No. 100057
O-0027

Glucose Metabolism Reprogramming of Neutrophils in Autoimmune Hepatitis

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Background: Autoimmune hepatitis (AIH) is an inflammatory liver disease caused by immune homeostasis imbalance. Neutrophils contributes to several autoimmune disorders. However, there are limited studies reporting the function of neutrophils and the effect of neutrophil metabolic reprogramming in AIH. We aim to examine alterations in neutrophil numbers and functions in AIH while exploring associations between dysregulated neutrophils and glucose metabolism.

Methods: Neutrophil frequency and functions were detected in AIH patients and healthy controls (HCs). In Con A-induced immune hepatitis, a Ly6G neutralizing antibody was administered to deplete neutrophils. Circulating neutrophils from AIH patients and HCs were collected for RNA sequencing. In addition, the parameters related to glucose metabolism were assessed in PMA-treated neutrophils and the effect of the glycolytic inhibitor 2-DG on neutrophils was investigated in vitro.

Results: The hepatic frequency of neutrophils was increased in AIH patients. Circulating neutrophils of AIH patients were activated and released more NETs and MPO than those of HCs. Notably, neutrophil depletion alleviated liver apoptosis and necrosis in Con A-induced immune hepatitis, suggesting a pathogenic role of neutrophils in AIH. Moreover, RNA sequencing indicated downregulation of the oxidative phosphorylation pathway in circulating neutrophils of AIH patients. After PMA stimulation, glucose uptake and lactic acid production were enhanced in neutrophils. Also, the expression of key glycolytic genes was increased in PMA-induced neutrophils. 2-DG reduced PMA-induced NETs in vitro.

Conclusion: This study revealed abnormal neutrophil infiltration and functions in AIH. Glucose metabolism reprogramming may promote neutrophil activation, leading to immune disorders in AIH. Inhibiting glycolysis may reverse neutrophil dysfunction in AIH patients.

Abstract Submission No. 100139
O-0028

Multi-omics reveal underlying mechanisms of drug-response in PBC/AIH variant syndrome

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Background: Primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH) variant syndrome (VS) present a complex overlap of AIH features with PBC, creating challenges for clinical management. This study aims to elucidate the mechanisms underlying drug response in PBC/AIH VS by integrating whole-transcriptomics and metabolomics, complemented by cytokinomic analysis.

Methods: We performed whole-transcriptome sequencing on liver tissues from 10 PBC/AIH VS patients, categorizing them into good responders (GR) and poor responders (PR). Additionally, we conducted plasma metabolomics on 50 PBC/AIH VS patients, further divided

into GR (n=20) and PR (n=30). A wide range of cytokines was quantified in the same plasma using bead-based immunoassay technology. **Findings:** Analysis identified 224 differentially expressed (DE) mRNAs, 189 DE long non-coding RNAs, 39 DE circular RNAs, and 63 DE microRNAs. Functional pathway analysis enriched in immune response and metabolic pathways. We constructed 256 lncRNA-miRNA-mRNA networks and 19 circRNA-miRNA-mRNA networks, offering insights into regulatory interactions. Furthermore, we detected 71 metabolites exhibiting significant differences between GR and PR. Joint pathways analysis highlighted primary bile acid biosynthesis, and taurine and hypotaurine metabolism. Additionally, we identified eight cytokines significantly differing between the two groups, indicating correlations between the balance of Th1 and Th2, as well as Th17 and Treg subsets, and drug response.

Conclusion: This exploratory study enhances our understanding of drug response mechanisms in PBC/AIH VS through comprehensive whole-transcriptome analysis. It also unveils distinctions in metabolic and immune profiles between patient subgroups by integrating metabolomics and cytokinomics. These findings offer new perspectives for treatment of these patients.

Abstract Submission No. 100239
O-0029

Identification of High-Risk Group for Relapse in Autoimmune Hepatitis Patients

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Background and Aim: Autoimmune Hepatitis (AIH) is a relatively rare disease caused by autoimmune disorder. While steroid therapy is effective in many cases, some cases have relapses during steroid tapering. In this study, we investigated the risk factors for relapse during steroid therapy in AIH patients.

Methods: We retrospectively analyzed 31 cases of AIH patients who started steroid therapy at our institution from October 2010 to April 2023. We defined the patients who had relapse before tapering prednisolone to a dosage of 5mg/day as Relapse group, while others as Remission group. Risk factors for relapse were analyzed by using logistic regression model.

Results: Among 31 cases, 26 kept being remission, while five had relapse. All cases of Relapse group were brought under control by the addition of azathioprine. Multivariate analysis showed only age was an independent risk factor for relapse (odds ratio = 0.85, 95% confidence interval (CI) = 0.728-0.992, p-value = 0.04). Relapses were observed only in younger group (< 66 years, n = 15). In that group, high International AIH Group (IAIHG) scores at pretreatment showed a significant trend as a risk factor in univariate analysis (odds ratio = 1.53, 95% CI = 0.943-2.490, p-value = 0.085). We defined high-risk group as the patients who were young (< 66 years) and had high IAIHG scores (>15 points), and the relapse rate of that group was 66.7% (4/6 cases).

Conclusions: AIH patients with both younger age and high IAIHG scores have a higher risk of relapse during steroid tapering.

Abstract Submission No. 100387
O-0030

Azathioprine on Risk of Extrahepatic Malignancy with Autoimmune Hepatitis: A Nationwide Claims Study

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Background and aims: Long-term immunosuppressive therapy in patients with autoimmune hepatitis (AIH) increases the risk of extrahepatic malignancy in addition to hepatocellular carcinoma. However, the risk of extrahepatic malignancy is unknown in Korean AIH patients. We aimed to evaluate the impact of azathioprine (AZT) treatment on extrahepatic malignancy risks.

Methods: We identified all persons diagnosed with AIH between 2008 and 2020. We included 8,280 patients with AIH, using the national claims data of the Health Insurance Review and Assessment Service (HIRA). The numbers of patients treated with and without AZT were 3,059 and 5,221, respectively. We estimated the cumulative risks of extrahepatic malignancy and hazard ratios (HRs) between patients treated with and without AZT.

Results: Among 8,280 patients, the mean age was 56.7±13.5 years, 84.3% were women, and the follow-up period was 49.8±43.1 months. The mean age and sex are not different between patients treated with and without AZT. However, the number of patients with diabetes was higher in patients treated with AZT (31.3% vs. 28.0%). The number of patients with liver cirrhosis was higher in patients treated without AZT (36.0% vs. 38.9%). At the time of diagnosis, 85.5% of patients with AZT and 30.0% of patients without AZT were treated with steroids for more than 90 days (P<0.001). The incidence of extrahepatic malignancy was 1.36 and 1.23 per 100 person-years in the patients treated with AZT and without AZT, respectively (P=0.685). After we adjusted for confounding by age, sex, diabetes, and liver cirrhosis, the HR was 1.09 (95% confidence interval 0.79-1.51, P=0.600).

Conclusion: The national claims data of HIRA did not show that AZT significantly increases the risk of extrahepatic malignancy among AIH patients.

Abstract Submission No. 100549
O-0031

Association of sarcopenia with treatment response and outcomes in non-cirrhotic PBC patients

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Background: The prevalence of sarcopenia and its effects on the treatment outcomes of ursodeoxycholic acid (UDCA) in patients with non-cirrhotic primary biliary cholangitis (PBC) remains uncertain.

Aims: To investigate the prevalence of sarcopenia and its association with biochemical responses and clinical outcomes in non-cirrhotic PBC patients.

Methods: Between January 2009 and July 2022, consecutive PBC patients were retrospectively enrolled. Sarcopenia was assessed via pre-treatment CT or MRI scans at the L3 level. Baseline characteristics, response rate of UDCA treatment, liver-related adverse events, as well as the gene expression and protein level of C-reactive protein (CRP) and interleukin-6 (IL-6) were compared in patients with and without sarcopenia.

Results: 142 non-cirrhotic PBC patients were included with sarcopenia identified in 58 (40.8%) cases. Levels of liver enzyme ($P<0.05$) and AST-to-PLT ratio index (APRI) (0.48 (0.26,0.75) vs. 0.27 (0.18, 0.46), $P=0.001$) at baseline were higher in the sarcopenia group than the non-sarcopenia group. Furthermore, the sarcopenia group demonstrated a lower biochemical response rate (44.9% vs. 64.8%; $P=0.031$) after 12 months of UDCA treatment and higher incidence of new onset ascites (28.1% vs. 13.1%, $P=0.027$). Elevated levels of serum CRP and IL-6, as well as increased gene expression of CRP in liver tissue, were also observed in the sarcopenia group ($P<0.05$).

Conclusions: Sarcopenia was highly prevalent in non-cirrhotic PBC patients. Concomitant sarcopenia may adversely affect the biochemical responses to UDCA treatment of PBC patients without cirrhosis. However, the exact role of sarcopenia in the progression and outcomes of PBC requires further investigation.

Abstract Submission No. 100766
O-0032

A Rare Case of Autoimmune Hepatitis-Primary Biliary Cholangitis Overlap Syndrome in a Filipino Adult

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Autoimmune hepatitis - primary biliary cholangitis overlap syndrome (AIH-PBC OS) is a rare disease with non-specific signs and symptoms. We report a case of a Filipino adult female presenting with one week history of abdominal pain, accompanied by malaise and jaundice. Laboratory tests revealed gamma glutamyl transferase (GGT) ≥ 5 times upper limit of normal (ULN) and presence of anti-mitochondrial antibodies (AMA); alanine aminotransferase (ALT) activity ≥ 5 times ULN and liver biopsy with moderate interface hepatitis. These parameters fulfilled two out of the three criteria each for the diagnosis of PBC and AIH, respectively, hence the diagnosis of AIH-PBC OS - AIH predominant was made. She was started on prednisone and ursodeoxycholic acid (UDCA). However, on dual energy X-ray absorptiometry (DEXA) scan, she was noted to have osteoporosis, hence prednisone was continued to be tapered and discontinued. Azathioprine was added to the treatment, with note of progressive decrease in liver enzymes, ALP, and bilirubin. This case emphasizes that AIH-PBC OS may be missed if thorough evaluation of possible etiologies of liver disease is not done. The treatment of choice is still controversial, due to its rarity and lack of clinical trials. This case also aims to add knowledge as it is essential to pursue further studies, because prognosis seems to be worse compared to either AIH or PBC alone.

Abstract Submission No. 100871
O-0033

Analysis of diagnostic predictors in patients with PBC-AIH overlap syndrome from AIH

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Background: Autoimmune hepatitis (AIH) is one of the main categories of autoimmune liver disease (AILDs). Approximately 10% of AIH patients displayed overlapping features of both AIH and PBC, referred

as PBC-AIH overlap syndrome (PBC-AIH OS). This study aimed to explore the indicators for early diagnosis of PBC-AIH OS from AIH.

Methods: By retrospective analysis, the general characteristics, clinical manifestations, biochemical tests, immunological tests, and liver histological examinations in patients with PBC-AIH OS and AIH at the time of initial diagnosis were analyzed. Univariate logistic regression analysis and multiple-factors analysis via multivariate logistical regression were used to predict the diagnosis of PBC-AIH OS based on the hematological indicators.

Results: A total of 105 AILDs patients were included in this retrospective study who underwent liver biopsy. There were no statistically significant differences in mean age, sex, or symptoms between PBC-AIH OS and AIH patients. Compared to AIH patients, PBC-AIH OS patients showed significantly high levels of serum globulin, ALP, GGT, PTA, AMA-M2, IgM and significantly low levels of ALT, AST and INR. The expression of ANA, ASMA, AMA and RO52 were significant differences in these two groups. Univariate logistic regression analysis and multiple-factors analysis via multivariate logistical regression showed that GGT and AMA-M2 were significant predictors of PBC-AIH OS.

Conclusion: The degrees of cholestasis and dysimmunity in PBC-AIH OS patients were significantly higher than that in AIH patients. However, hepatocyte inflammation is more severe in patients with AIH. GGT and AMA-M2 can be used as noninvasive diagnostic indicators to predict PBC-AIH OS.

Abstract Submission No. 101086
O-0034

Clinical characteristic and prognosis of premature ductopenic variant of primary biliary cholangitis

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Objective: Some primary biliary cholangitis (PBC) patients present with prolonged cholestasis and extensive bile duct loss (ductopenia) but no significant fibrosis or cirrhosis. We aimed to clarify the clinical and pathological features and prognosis of PBC patients with premature ductopenia.

Methods: This retrospective study recruited patients with early-stage PBC (Ludwig stage I or II). Demographic, laboratory, and pathological data were recorded, and clinical outcomes, including decompensated cirrhosis, liver transplantation or death, were followed up by interview. Logistic regression was conducted to identify the baseline features associated with ductopenia.

Results: A total of 141 patients with early-stage PBC were ultimately included, of which 34 had ductopenia and 107 did not have ductopenia. Early-stage PBC patients with ductopenia had higher levels of ALT, AST, ALP, GGT, TBIL, TBA, CHOL, and TG but lower levels of IgG and IgM at baseline than those without ductopenia (all $P<0.05$). Importantly, early-stage PBC with ductopenia had a lower response rate according to the Paris II, Barcelona and Rotterdam criteria. However, during a median follow-up period of 4.5 years, there was no significant difference in clinical outcome between early-stage PBC with vs. without ductopenia. Logistic regression analysis showed that baseline total CHOL levels were independent predictors for ductopenia.

Conclusion: Ductopenia was a significant risk factor for worse biochemical profiles and poor treatment response but not for a short-term prognosis in early-stage PBC patients. High levels of CHOL at baseline may be associated with ductopenia in early-stage PBC patients.

Abstract Submission No. 101092
O-0035

Clinical, serological and histological features of autoimmune liver diseases.

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Autoimmune liver disease (ALD) is a rare spectrum of disease comprising of autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC) and overlap syndrome. There is no population based data on the incidence or prevalence of AIH in Pakistan.

To evaluate the clinical, serological and histological features in patients presenting with autoimmune liver diseases in a tertiary care hospital in Karachi, Pakistan.

A cross-sectional case series of 31 patients which were enrolled in study from January 2017 till date presenting at Jinnah Postgraduate Medical Center, Karachi. Demographic and clinical data including liver function tests, clotting profile, gamma globulin levels, autoimmune serology and liver histology were recorded on designed proforma.

Mean age of patients was 28.19±8.6 years. Females 23 (74.2%) and males 8 (25.8%). Most common symptom was fatigue (96.8%), followed by arthralgia (77.4%), anorexia and jaundice (61.3%). Type I AIH was present in 19 (61.3%), Type II AIH in 11 (35.5%) and AIH/PBC overlap in 1 (3.2%) patient respectively, however, no discrete case of PSC and PBC was reported. Immunoglobulin G level was raised in all patients with mean of 1672±530. Liver histology showed lymphoplasmacytic interface hepatitis in 19 (61.3%) patients and lobular hepatitis with centrilobular necrosis in 11 (35.5%) patients respectively.

Autoimmune liver disease can occur at any age, in both sexes with favorable results on immunosuppression. It can progress to several complications like decompensated liver disease, hepatocellular carcinoma, osteoporosis and dyslipidemia.

Abstract Submission No. 101120
O-0036

A worse subgroup of PBC: jaundice in patients with ductopenia

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Objective: Hyperbilirubinemia associated with poor prognosis of PBC, while not all PBC patients with ductopenia (bile duct loss greater than 50%) present prolonged jaundice. We aimed to clarify the clinicopathological features, prognosis and underlying mechanism of these subgroup icteric PBC patients with ductopenia.

Methods: This retrospective study recruited PBC patients with ductopenia diagnosed by liver biopsy. Demographic, clinicopathological data, treatment response and long-term prognosis of these patients were followed and recorded. Immunohistochemical stain of BSEP and MRP2 were conducted in these ductopenic patients with or without jaundice.

Results: A total of 265 patients with liver biopsy were included, of which 77 had ductopenia (18 accompany with jaundice and 59 did not). We found ductopenic patients with jaundice had higher levels of TBIL, TBA, CHOL, and TG but a similar level of ALT, AST, ALP, GGT than those without jaundice (all $P < 0.05$). Additionally, ductopenic PBC patients with jaundice had a lower survival rate when compared to those without jaundice ($P < 0.05$). There was no significant difference in

UDCA response between ductopenic PBC with or without jaundice (Paris II, Barcelona and Rotterdam criteria: $P > 0.05$). The expression of BSEP and MRP2 was higher in patients without jaundice but significant lower in those with jaundice ($P < 0.05$).

Conclusion: Jaundice does not seem to follow the same course as ductopenia in PBC. Ductopenic PBC patients with jaundice showed a similar worse treatment response but a poorer prognosis and uncompensated bile salt transporter helps to explain.

Abstract Submission No. 101179
O-0037

Developing a Baseline Data-Driven Prognostic Index for Primary Biliary Cholangitis

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Background/Aims: This study aimed to develop a prognostic index based on data at initial presentation for primary biliary cholangitis (PBC) to predict transplant-free survival (TFS). This index offers a practical alternative to internationally recognized indices that only depend on one-year follow-up data.

Methods: We performed Cox regression analysis to investigate the associations between various factors including PBC patient's demographics, laboratory values, autoantibody levels, symptoms, and comorbidities upon admission, and their impact on TFS. To validate the prognostic index's performance in predicting TFS over 5-, 10, and 15-year, we employed a ROC analysis and compared its accuracy to other well-established indices including the UK-PBC and GLOBE scores.

Results: Out of the initial 425 registered patients with PBC, 256 met the specified inclusion and exclusion criteria. The resulting cohort exhibited a mean age of 53.3±12.2 years, with a majority of 91.4% being female. During a mean follow-up period of 10.9 years, 2.3% of the patients underwent liver transplantation, while 18.8% died on the waiting list. The TFS rates at 5-, 10-, and 15-year were 90%, 82%, and 75%, respectively. Albumin, AST, MCV and age at presentation were significantly negatively correlated with TFS. The prognostic index derived from these findings demonstrated remarkable accuracy in predicting 15-year survival, resulting in a sensitivity of 100% and specificity of 80.5%, as indicated by an important AUC of 0.951 ($p < 0.0001$). This performance was superior to the UK-PBC and GLOBE scores, although the difference was not statistically significant. Additionally, within the first year of treatment, MCV also emerged as a significant predictor.

Conclusion: AST, albumin, age, and MCV at baseline are reliable predictors of TFS in PBC patients. The developed prognostic index demonstrates nearly perfect sensitivity and substantial specificity for up to 15 years of TFS prediction. MCV has emerged as a novel and significant predictive biomarker.

Abstract Submission No. 101223
O-0038

Late UDCA response is associated with worse prognosis of PBC patients compared to early response

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Introduction: Our aim was to describe parameters after 6 months of UDCA treatment that are associated with poor prognosis in UDCA responders after 12 months of treatment.

Cohort of the patients: We analyzed 249 patients treated with UDCA for PBC at Slovak and Croatian centers; Patients were followed for a mean of 5.0 years. Therapeutic response after 12 months of treatment was defined according to Toronto criteria.

Results: 146 patients who achieved a response at 12 months using the modified Toronto criteria were included in the final analysis. 115 of these patients met the modified US criteria after 6 months of treatment - early responders; 31 patients did not meet these criteria after 6 months - late responders. Complete response was defined as normalization of total bilirubin and ALP at the last visit; optimal complete response was defined as bilirubin < 0.6 ULN and normalized ALP at the last visit. Early responders achieved complete response and optimal complete response at the last visit more frequently compared to late responders (59.1% v.s.38.7% p 0.043), (47.8% v.s. 29% p 0.061). The risk of death and liver transplantation during the follow up was significantly lower in early responders compared to late responders (0% v.s..4% p 0.041).

Conclusions: Late UDCA response is associated with increased mortality and less frequent complete therapeutic response to UDCA compared to early UDCA response. For PBC patients with inadequate UDCA response, second-line treatment should be considered after 6months of treatment.

Abstract Submission No. 101308

O-0039

Building hepatic MRI models predict histopathological severity and insufficient response in AIH

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Abstract

Background: The correlation between hepatic magnetic resonance imaging (MRI) and liver histopathology has rarely been reported in autoimmune hepatitis (AIH). We built models using hepatic MRI features to predict histopathological severity/treatment response in AIH patients.

Methods: AIH patients with abdominal contrast MRI and liver biopsy were retrospectively retrieved from our AIH database (n=329, 2002-2023). Laboratory tests, hepatic MRI features and treatment response were collected. The liver volume was measured, and liver histopathological severity was evaluated according to the Ishak system. Models for predicting histopathological severity and response were constructed by logistic regression.

Results: Ninety-two AIH patients (median age: 56.50 years, 78.26% female) with simplified International AIH Group (IAIHG) scores ≥ 6 were included. Thirty-nine (42.39%) with severe confluent necrosis (≥ 5), 18(19.57%) with advance fibrosis (≥ 5). The MRI features of hepatic fissure widening, reticular fibrosis and the volume ratio of Couinaud segment II-IV to the total liver were independently associated with severe confluent necrosis; the enlarged preportal space, reticular fibrosis and the volume ratio of Couinaud segment I to the total liver were independently associated with advance fibrosis; the ascites, gallbladder wall edema and transient hepatic attenuation difference were independently associated with insufficient response, with an area under the ROC curve of 0.827(95% CI 0.743-0.910) , 0.911(95% CI 0.848-0.973) and 0.796(95% CI 0.691-0.902) respectively. The C-statistics of the internal validation were 0.818 (95% CI 0.683-0.929) , 0.873(95%CI 0.730-0.973) and 0.757(95%CI 0.597-0.904) respectively.

Conclusion: The novel models including different MRI features for predicting histopathological severity and insufficient response were established in AIH.

Abstract Submission No. 101349

O-0040

Endoscopic Management of Primary Sclerosing Cholangitis: Clinical Outcomes at a Tertiary Center

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Background: Dominant strictures (DS) are a significant clinical feature in primary sclerosing cholangitis (PSC), and endoscopic treatment is crucial for managing DS and improving patient outcomes. This study aims to assess the clinical outcomes of endoscopic treatment for PSC-related DS.

Methods: A single-center, prospective study of consecutive PSC patients undergoing endoscopic treatment for DS management. The primary endpoint was the cumulative recurrence-free rate of the primary DS(s) within 24 months in patients who did not experience initial failure. Secondary endpoints were evaluated based on three parameters: 1) endoscopic treatment success, defined as no need for ERCP within three months after completing endoscopic treatment; 2) development of cirrhosis; and 3) recurrence of DS.

Results: A total of 35 patients were included. In total, 138 endoscopic treatment sessions were performed, with an average of 3.9 sessions per patient. DS was identified in 26 patients during cholangiograms. Endoscopic balloon dilation (EBD) was applied in 24 (68.6%) patients, while nine patients (25.8%) underwent bougie dilation. The average stent duration for the initial procedure was 17.9 days. 26 (78.8%) patients remained asymptomatic within three months of discharge and remained cirrhosis-free during a mean follow-up period of 36 months. This was the secondary endpoint of the study. The primary end-point

achievement rate was 45.4%. The complication rate was 8.0%, including pancreatitis, cholangitis, and perforation. The cholangiocarcinoma (CCA) development rate was 5.7%.

Conclusion: Endoscopic treatment, including stent placement and biliary dilation, effectively manages PSC-related DS, with high success and relatively low complication rates.

Abstract Submission No. 101430

O-0041

Scoring system is prognostic model of primary biliary cholangitis treated with UDCA and fenofibrate

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Background: Fenofibrate as the second-line therapy for ursodeoxycholic acid (UDCA)-refractory primary biliary cholangitis (PBC) patients is becoming widely used, but no model can test the efficacy of the second-line therapy. Thus, this study aimed to investigate the biochemical response model that can predict the efficacy and long-term prognosis for patients treated with fenofibrate add-on therapy.

Methods: We enrolled UDCA-refractory PBC patients treated with fenofibrate and UDCA. These patients were grouped into the good outcome group and the poor outcome group according to a combined endpoint (hepatic decompensation, liver-related death, and liver transplantation). Patients are followed up by medical records, outpatient service, and telephone reviews. The biochemical response (Barcelona, Paris-I, Paris-II, Toronto, Rotterdam, Mayo, Ehime, Lindor, GLOBE score, and UK-PBC risk score) compared after 6 or 12 months of fenofibrate added-on therapy, and to identify a biochemical response model that can predict long-term prognosis by Kaplan-Meier plotting and Delong test.

Results: Sixty-three patients were enrolled in this study, including the good outcome patients (n=52) and the poor outcome patients (n=11). The poor outcome patients had higher GLOBE scores and UK-PBC risk scores than the good outcome patients after 12 months of treatment (GLOBE score: 1.1925 ± 1.1061 vs. -0.2363 ± 0.6666 ($p < 0.01$), UK-PBC risk score: 0.1395 ($0.0702, 0.2285$) vs. 0.0311 ($0.0210, 0.0511$) ($p < 0.0001$)). And other biochemical response criteria including Barcelona, Paris-I, Paris-II, Toronto, Rotterdam, Mayo, and Ehime didn't show statistically significant differences between these two groups. More importantly, the GLOBE score and UK-PBC risk score had better predictive performance of long-term survival in patients with fenofibrate add-on therapy than these criteria. The area under the receiver operating characteristic (AUROC) of GLOBE score and UK-PBC risk score at 6 months of 0.871 ($95\%CI 0.741-0.951$) and 0.875 ($95\%CI 0.746-0.953$), and 12 months of 0.919 ($95\%CI 0.803-0.978$) and 0.878 ($95\%CI 0.751-0.955$). All other criteria were lower than 0.750 for the prediction of long-term survival after 6 or 12 months of treatment with UDCA and fenofibrate.

Conclusions: The GLOBE score and UK-PBC risk score were suitable for predicting the efficacy and long-term prognosis for PBC patients with fenofibrate and UDCA treatment.

Abstract Submission No. 101516

O-0042

Genetic link between Periodontitis and liver diseases: a Mendelian randomization study

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Background & aims: The relationship between periodontitis and liver disease has received increasing attention in recent years, but the causal relationship is unclear. The aim of this study was to assess the causal relationship between periodontitis and various liver diseases

Method: We performed two-sample Mendelian randomization (MR) analysis. Suitable genome-wide association study (GWAS) datasets were used to select potential candidate single nucleotide polymorphisms according to the study needs. Inverse variance weighting (IVW) was used as the primary analysis method, supplemented by four sensitive analyses to assess the robustness of the results.

Results: Among the included liver diseases, only the genetic variant of PSC was causally associated with the risk of chronic periodontitis. According to IVW estimates, the presence of PSC may increase the risk of chronic periodontitis by 1.079% (OR 1.079 , $95\%CI 1.027-1.134$, $P = 0.002$, MR-Egger, Weighted mode and Weighted median also produced similar results. Conversely, periodontitis did not have an impact on the risk of developing the liver diseases included in this study.

Conclusion: We investigated for the first time the association between several liver diseases and periodontitis using a Mendelian randomized study method and found that PSC increases the risk of chronic periodontitis.

Abstract Submission No. 101630

O-0043

Pyroptosis plays a key role in primary biliary cholangitis in mice

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Background and Aims: Primary biliary cholangitis (PBC) is an autoimmune intrahepatic cholestatic disease with both environmental and genetic participation. In this study, we aim to investigate the involvement of pyroptosis in PBC mice and provide possible treatment strategy.

Method: Twenty female C57BL/6 mice of 4-6 months old were evenly divided into PBC group and control group. PBC mice were induced with two doses of 2-nonyloic acid (2OA-BSA) and polycytidylic acid (poly I: C) for 12 weeks. Immunocyte type correlation analysis was performed on the GSE119600 dataset of GEO database with whole blood samples from PBC patients (n=90) and controls (n=47). Immunohistochemistry (IHC) staining and multiplex immunofluorescence (mIF) in liver samples of PBC mice were determined regarding the pyroptosis pathway and different cell types.

Results: Immunocyte type correlation analysis reported that the expression of key transcription factors of M1 macrophages were significantly higher in PBC patients (Figure A). For PBC mouse model, pyroptosis pathway was upregulated determined by qrt-PCR (Figure B) and western blotting (Figure C). IHC staining revealed improved GSDMD and Caspase-1 expression in PBC mice (Figure D), and macrophages were determined to be the main cell type expressing GSDMD by mIF (Figure E). Flow cytometry showed an increased M1/M2 macrophage ratio in liver samples of PBC mice, with the expression of M2 macrophage marker decreasing and the marker of M1 macrophage increasing in the western blotting.

Conclusion: Pyroptosis plays a key role in PBC patients and 2OA-BSA induced PBC mice, possibly macrophages being the most important executors.

Abstract Submission No. 102016
O-0044

Urinary Tract Infection and Pyuria in Primary Biliary Cholangitis

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Introduction: Primary biliary cholangitis (PBC) is a chronic cholestatic autoimmune liver disease primarily affecting women and urinary tract infection (UTI) have a role in pathogenesis.

Method: The study aimed to assess demographic characteristics, treatment responses, and the presence of asymptomatic pyuria or urinary tract infection in PBC patients across five different centers. Patients receiving 13-15 mg/kg UDCA treatment for at least one year and consenting to participate were included. Patients with symptomatic pyuria, currently using antibiotics, or having symptomatic UTIs were excluded.

Results: Among the 229 participants, 90.5% (Female: 207) were female, with a mean age of 59.4 (11.2) years. Treatment unresponsiveness was observed in 13.5% (n:31) of the patients. Regarding symptomatic UTIs, 25.4% (n = 55) experienced at least one UTI before PBC diagnosis, and 16.9% (n = 38) had two or more UTIs. Additionally, 17.5% (n: 40) had a history of UTIs more than once a year. No significant association was found between UTI history and treatment response (p: 0.64 and 0.93, respectively). Among the 229 patients, 105 (45.8%) had asymptomatic pyuria, and in 16 (7.4%), urine cultures showed bacterial growth, with *Escherichia Coli* being the predominant pathogen in 8 cases, followed by *Klebsiella pneumonia* and *Streptococcus Agalactica*. Analyses revealed that the frequency of asymptomatic pyuria was not higher in treatment-unresponsive patients but was more common in cirrhotic patients (p: 0.028).

Conclusion: In our study, no correlation was found between symptomatic UTIs and treatment unresponsiveness. Similarly, asymptomatic pyuria and positive urine cultures did not increase in unresponsive patients.

Abstract Submission No. 100062
O-0045

Spatiotemporal immunometabolic landscape driven by the Mas signaling in acute liver injury

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Objective: Drug-induced liver injury (DILI) is the most common cause of acute liver failure. Despite the importance of inflammatory microenvironment in the progression of DILI, which involves distinct cellular interactions and molecular pathways, the mechanisms are poorly understood. Mas is a G protein-coupled receptor, which could

regulate the function of immune cells. Here we aim to explore the changes of the immunometabolic microenvironment during the process of DILI and whether Mas is an important factor of liver pathology.

Design: Single-cell RNA sequencing (scRNA-seq), spatial transcriptomics (ST), multiplex Immunohistochemistry (mIHC), flow cytometry and intravital imaging were used to describe the immunometabolic landscape. Multiple cell-specific knockout mice were used to clarify the effector cells of Mas. *Cdh5^{cre}Pkm^{f/+}* mice, various mouse primary cells and human liver samples were used to validate the discoveries of bioinformatics analysis.

Results: Using joint analysis of scRNA-seq, ST and intravital imaging, we described the unique immunometabolic landscape composed of CD31⁺MYC⁺CD63⁺ endothelial cells (ECs), F4/80⁺MMP12⁺ macrophages (Mφ) and monocytes, which could be regulated by myeloid Mas. Glycolysis was identified as the critical metabolic pathway for cellular communications. Notably, this landscape was visualized by the intravital imaging in living mice, which perfectly mapped and enriched in human DILI, along with the well-demonstrated clinical relevance. Finally, mouse DILI models were applied *in vivo* to confirm the beneficial role of either the activated myeloid-Mas signaling or the suppressed glycolytic pathway.

Conclusion: Our study provides a novel perspective for the unique immunometabolic microenvironment during the progression of DILI, which is driven by the insufficient myeloid-Mas signaling with the enhanced glycolysis.

Abstract Submission No. 100983
O-0046

Genetic risks of “one-pill” NSAIDs induced liver injury: a real-world study

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Background: Drug-induced liver injury (DILI) is a liver disorder that refers to the acute or chronic response of the liver to specific drugs. Anti-inflammatory drugs (NSAIDs) can induce DILI in rare instances. Our study aimed to explore the genetic risks of “one-pill” NSAIDs induced liver injury in the rapid wave of infections by the Omicron variant during 2023 winter in China.

Methods: Four “one-pill” NSAIDs-DILI out of 25 DILI patients during Dec 2022 to Feb 2023 were enrolled. Whole genome sequencing (WGS) was performed and bioinformatic analysis identified the genetic variants in NSAIDs-DILI. Meanwhile, healthy controls, exposed to NSAIDs at least one pill, were enrolled to examine the specificity and pathogenicity of detected genetic variants.

Results: We identified 14 SNPs in genes of PDE4DIP (rs1747930, rs1359300, rs2762745), MUC20 (rs3762739), DYNC2I2 (rs4837292), GPRIN2 (rs4926045, rs3127819, rs11204658, rs11204659, rs4926046), SNX19 (rs681982), KCNJ18/12 (rs1657738, rs1714864, rs1657742) as strong predictors of “one pill” NSAIDs-DILI. Notably, several reported NSAIDs-related DILI gene variants, including PTPN22(rs2476601), ABCB11 (rs2287622), CYP2E1 (rs2515641), HLA-B (rs2308655, rs1140546, rs1051488, rs1050747), and HLA-DQB2 (rs1049110) were also detected in each of our patients. Finally, the occurrence of cholestasis induced by NSAIDs is mainly associated with dysfunction of BSEP encoded by ABCB11 mutations (rs2287622, rs118109635, rs497692).

Conclusion: “One pill” NSAIDs-DILI is associated with polymorphic expression of several genes. Our study not only verified reported gene variants but also revealed new SNPs contributing to NSAIDs-related DILI, which shed a new light on the genetic risks of NSAIDs-DILI.

Abstract Submission No. 101200
O-0047

Hepatic MUM1 expressions distinguish drug-induced liver injury from acute-onset autoimmune hepatitis

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Background: Perivenular necroinflammation is a common but easily confused histological characteristic in both drug-induced liver injury (DILI) and acute-onset autoimmune hepatitis (A-AIH). We aimed to evaluate multiple myeloma antigen 1 (MUM1) immunohistochemistry (IHC) stain in distinguishing DILI from A-AIH.

Method: DILI or A-AIH patients with liver biopsy matched by propensity score were retrieved from DILI (n=138) and AIH (n=125) database from 2016 to 2023. Liver biopsies were evaluated according to the modified histological activity index (mHAI). MUM1-expression cells were quantified by ImageJ. The diagnostic performance of MUM1 IHC stain was assessed by an area under the receiver operating characteristic curve (AUROC).

Results: Eligible DILI (n=10) and A-AIH (n=10) patients: the median age was 52 (38.3, 57.8) years, and females were 16 (80.0%). There was no significant difference of age, gender, aminotransferase, bilirubin and immunoglobulin G levels at onset and mHAI scores between two groups. In portal areas, both total and average number of MUM1-expression cells per square millimeter were significantly higher in A-AIH than that in DILI: 561.5 (226.8, 839.5) versus 226.0 (144.8, 445.5); 621.3(336.1,809.1) versus 260.2(163.2,428.6), respectively (all $P < 0.05$). Total or average number of MUM1-expression cells or their combination in portal areas yielded an AUROC of 0.79 (95% CI: 0.5844-0.9956), 0.86 (95% CI: 0.6977-1.0000) or 0.85 (95% CI: 0.6784-1.0000) respectively in distinguishing DILI versus A-AIH. A cutoff value of 472.8 for average MUM1-expression cells per square millimeter in portal areas had a specificity of 90.0% and a sensitivity of 70.0%.

Conclusion: The number of MUM1-expression cells in liver biopsy specimens can effectively distinguish DILI from A-AIH.

Abstract Submission No. 101201
O-0048

Current status and safety of ICI rechallenge for patients with IMH at our hospital

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[Background] Among immune-related adverse events (irAEs), immune checkpoint inhibitor (ICI)-induced immune-mediated hepatotoxicity (IMH) is one of the most important irAEs. The safety of ICI rechallenge after IMH is controversial. We aimed to propose the feasibility of ICI rechallenge to patients with IMH.

[Methods] We enrolled 453 patients who administered ICIs (Nivolumab, Pembrolizumab, Atezolizumab, Nivolumab+Ipilimumab, Durvalumab, or Avelumab) for malignant tumors at our hospital from November 2021 to October 2022. 102 patients with IMH were divided into grade 1-2 and grade 3-4 groups to investigate the current status of rechallenge and safety.

[Results] In grade 1-2, 59 of 79 patients (74.7%) continued to receive ICI, and 5 patients used UDCA or SNMC. Only 1 patient discontinued treatment due to subsequent worsening of IMH. Of the 20 patients who discontinued ICI, 8 were rechallenged and 2 (10%) had recurrent liver injury. 2 of 8 patients were taking 5 mg and 20 mg of PSL for other irAE, respectively. 7 of the withdrawn cases were using PSL for severe other irAE. 11 of 23 patients (47.8%) with grade 3-4 had ICI rechallenge. Among them, 3 patients received 10mg of PSL, another received 15mg. Only 1 patient (9.1%) had IMH relapse. In only grade 4, 1 of 6 cases was rechallenged with PSL.

[Conclusions] ICI administration or rechallenge after IMH should be performed with caution, considering other concomitant irAEs and the use of PSL. At our institution, ICI rechallenge for grade 4 IMH patients was not frequent, but IMH did not recur after rechallenge.

Abstract Submission No. 101864
O-0049

Clinical features of acute drug-induced liver injury with pathological severe hepatic inflammation

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Background: Research on biopsy-proven acute drug-induced liver injury (DILI) remains limited. This study aimed to identify clinical characteristics of acute DILI with pathological severe hepatic inflammation.

Methods: A prospective hospitalization-based cohort study was conducted on biopsy-proven acute DILI patients admitted to our hospital from 2009 to 2017, and followed up until October 2023. The clinical characteristics at the time of liver biopsy, discharge, and follow-up were collected. According to Scheuer scoring system, hepatic inflammation was categorized as mild (G0-2) and moderate/severe (G3-4) groups, and between-group comparisons and multivariate logistic regression analyses were performed.

Results: The median age of 157 enrolled patients was 40.4 years, with 65.6% female. The median length of stay was 18 (IQR, 12.0-26.0) days. Liver injury induced by traditional Chinese medicine, chemical synthetic drugs and mixed drugs accounted for 42.7%, 25.5% and 31.8%, and the median incubation period was 14.0 (IQR, 7.0-30.0) days. Logistic regression analysis revealed that female (OR: 2.420, 95% CI: 1.078-5.436, $P = 0.032$) and higher BMI (OR: 1.156, 95% CI: 1.019-1.311, $P = 0.024$) were independent risk factors for moderate-to-severe hepatic inflammation, while increasing HCL_C (OR: 0.360, 95% CI: 0.131-0.992, $P = 0.048$) was protective. During follow-up, 23 patients (14.6%) developed chronic DILI, with 9 patients (5.7%) progressing to cirrhosis, and 15 patients combined with autoimmunity (G0-2 group 3 vs G3-4 group 12, $P < 0.05$).

Conclusions: Being female and having high BMI are associated with a higher risk of developing severe hepatic inflammation, which can lead to chronicity when compounded with autoimmune factors.

Abstract Submission No. 101930
O-0050

Close relationship between hepatotoxicity and adverse events of other organ induced by ICI therapy

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Background: With the widespread use of immune checkpoint inhibitors (ICIs), the diagnosis and treatment of immune-related adverse events (irAEs) has become increasingly important. Although, immune-mediated hepatotoxicity (IMH) is a relatively common, clinical evaluation of IMH remains unclear. The aim of this study was to clarify the clinical characteristics in patients with IMN.

Methods: The patients with advanced cancer who received ICI from September 2014 to December 2022 in our department were enrolled for this retrospective study. In enrolled patients, the incidence and severity of IMH were evaluated. Additionally, clinical factors that related to the onset of IMH were analyzed by multivariable logistic regression analyses. The onset and severity of IMH and other organ irAEs were defined according to CTCAE ver5.0.

Results: A total of 617 patients (468 males, 149 females; median age, 70.0 years) were enrolled in this study. Of all, 61 patients (9.9%) developed hyperamylasemia: Grade 2 (G2), Grade 3 (G3), and Grade 4 in 34, 27, and 0 patients. In univariate analysis, ICI combination therapy ($p=0.038$), and the onset of other organ irAE ($\geq G2$) ($p<0.001$) were significantly related to development of IMH. In multivariate analysis, only the onset of other organ irAE ($\geq G2$) ($p<0.001$) was the independent factor associated for the onset of IMH. Also, the incidence of other organ irAE $\geq G3$ was higher in the case with G3 IMH than in the case with G2 IMH, resulting in a correlation between the severity of IMH and other organ irAE ($p=0.02$).

Conclusions: The onset and severity of IMH was closely related to these of other organ irAEs in patients with ICI therapy. This finding suggests that in cases with IMH, more intensive systemic management is required because of the potential for multiple organ irAEs.

Abstract Submission No. 100044
O-0051

FIVE-YEAR SINGLE-CENTER EXPERIENCE IN ACUTE HEPATOTOXICITY DUE TO HERBAL MEDICATIONS FROM PAKISTAN

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Background & aims: Injury to liver secondary to herbal medication is quite Common. It can cause acute liver injury and acute liver failure (ALF) requiring Liver transplantation. We investigated outcomes of patients with acute Hepatotoxicity due to herbal medications in our cohort.

Method: we prospectively evaluated characteristics of patients with liver toxicity due to herbal medications. We also investigated parameters related to mortality or liver transplantation.

Results: 30 patients (17/13: f/m, median age 50.4(22-73)) were included in study. 27 patients presented with nausea and vomiting. In addition, 14 patients had abdominal pain & 16 had diarrhea. These patients

were admitted to our intensive care unit within an average of 2.5 days (6 hours-8 days) after herbal Medication intake. In 15 patients (14 at admission, 01 during hospitalization), INR increased >1.5 , ALF developed in 4 patients (02 patients at admission, hepatic encephalopathy developed in two patients during follow-up). The peak levels of ALT, AST & total bilirubin were 2109 ± 1963 u/l, 1828 ± 1675 u/l, 4.92 (0.1-28.56 mg/dl), respectively. In hospital follow-up, highest INR levels were found to be an average of 2.29 (± 1.56). All patients were treated with n-acetylcysteine (NAC). One of the 04 patients with ALF underwent emergency liver transplantation. 01 patient who developed ALF recovered with medical treatment, while other 02 patients who could not be transplanted died. In multivariate analysis, INR, AST & ALT levels at hospital admission were found to be statistically significant factors for death & liver transplantation respectively; or: 17.8 and $p: 0.04$, or: 0.59 & $p: 0.03$ & or: 0.54 & $p: 0.04$

Conclusion: In our cohort, the mortality rate due to herbal medication intoxication was 10%. High INR levels, ALT & AST levels have been associated with serious outcomes such as liver transplantation or mortality, & these parameters may be predictive of urgent liver transplantation.

Abstract Submission No. 100569
O-0052

N-acetylcysteine can accelerate the recovery of drug-induced cholestatic liver injury

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Objective: To observe the effectiveness of N-acetylcysteine in the treatment of drug-induced cholestatic liver injury.

Method: A retrospective study was conducted on hospitalized patients with drug-induced cholestatic liver injury from West China Hospital between January 2019 to June 2023. On the basis of adenosylmethionine and ursodeoxycholic acid treatment, the effectiveness of adding or not adding N-acetylcysteine were investigated.

Result: A total of 265 patients were included, including 84 males and 181 females, with an average age of 51.3 years. In terms of etiology, there were 98 cases caused by acetaminophen, 102 cases of traditional Chinese medicine or dietary supplements, 53 cases caused by other chemical drugs, and 12 cases of other causes. Among 265 patients, 137 received N-acetylcysteine treatment (Group A), while 128 patients did not receive N-acetylcysteine treatment (Group B). The levels of TBil (314.6 ± 45.8 $\mu\text{mol/L}$ vs. 307.5 ± 43.5 $\mu\text{mol/L}$, $P=0.198$) were similar between the two groups at admission, but the levels of ALP (462.9 ± 48.6 IU/ml vs. 448.5 ± 50.2 IU/ml, $P=0.018$) and GGT (436.5 ± 52.7 IU/ml vs. 423.7 ± 40.1 IU/ml, $P=0.044$) in Group A were higher than those in Group B. Among group A, 42 patients were hospitalized for less than 2 weeks, while 95 patients were hospitalized for more than 2 weeks. Among group B patients, 26 patients were hospitalized for less than 2 weeks, while 102 patients were hospitalized for more than 2 weeks. The average hospitalization time of Group A patients was significantly shorter than that of Group B patients (9.3 ± 3.1 vs. 11.1 ± 2.2 day, $P<0.05$), and the 2-week discharge rate was significantly higher than that of Group B (42/137 vs. 26/128, $P<0.05$). At 2 weeks of hospitalization, the serum TBil of Group A were significantly lower than that of Group B (128.6 ± 24.9 vs. 142.7 ± 31.5 IU/ml, $P<0.001$), and the levels of ALP (103.5 ± 26.4 vs. 145.7 ± 30.3 IU/ml, $P<0.001$) and GGT (111.2 ± 24.8 vs. 128.9 ± 26.4 IU/ml, $P<0.001$) were also significantly lower than those of Group B.

Conclusion: On the basis of combined treatment with adenosylmethionine and UDCA, the addition of N-acetylcysteine can accelerate the recovery of damaged liver function.

Abstract Submission No. 100739
O-0053

Usefulness of RECUM as a diagnostic criterion for drug-induced liver injury in Japanese patients

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Background: In Japan, DDW-J2004 based on RUCAM is used as a diagnostic tool for drug-induced liver injury (DILI). Recently, RECUM was reported as a new diagnostic tool, but it has not been fully investigated in Asian countries, including Japan, and we aimed to investigate the usefulness and problems of RECUM in Japan.

Methods: We included 120 cases with a diagnosis of DILI or suspected DILI between January 2020 and October 2022, and added RECUM scoring retrospectively to evaluate the rate of concordance of diagnosis. We also examined the characteristics of cases in which there was a dissociation of diagnosis.

Results: There was a strong correlation between RECUM and DDW-J scores ($R_s=0.586$, $p<0.001$). All patients with a highly likely DILI on the RECUM were also categorized as likely on the DDW-J. On the other hand, among the cases diagnosed as highly likely by DDW-J, there were 5/37 cases (13.5%) diagnosed as excluded by RECUM. DILI was considered negative in both cases: 2 cases because of time of onset and 3 cases because of other diagnoses (HEV, AIH, other). In addition, there were 19/54 cases (35.2%) who were diagnosed as exclusionary by RECUM among those who had been diagnosed with undeniable possibility of DILI by DDW-J. When examining the reasons for the lower scores, data loss was predominant in the excluded diagnosis items (number of missing data items 3(0-4) vs. 4(2-6), $p<0.001$).

Conclusions: The results suggest that RECUM may be useful in Japanese patients; however, caution should be exercised in cases of high data loss, as RECUM has a point reduction due to missing data. It should be used with a thorough understanding of how to exclude competing diagnoses.

Abstract Submission No. 100906
O-0054

Efficacy of magnesium isoglycyrrhizinate in liver injury after receiving novel antineoplastic agents

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Background: Liver injury often occurs in patients treated with novel antineoplastic agents including molecular targeted agents and immune checkpoint inhibitors. Magnesium isoglycyrrhizinate (MgIG) is an anti-inflammatory agent with the potential to ameliorate liver injury.

Methods: We conducted a retrospective, multicenter, real-world study to evaluate the efficacy of MgIG in patients with liver injury after receiving any novel antineoplastic agent. Propensity score matching

(PSM) is used to match age, sex, and baseline alanine aminotransferase (ALT) between groups. The change from baseline, normalization rate and the proportion of patients with 50% reduction of ALT, aspartate aminotransferase (AST) and total bilirubin (TBIL) 7 days after treatment and before discharge were compared.

Results: A total of 979 cases are included and subsequently divided into 2 populations after PSM in a 1:1 and 3:1 ratio respectively: MgIG (n=152) vs. supportive care (SC) (n=152); and MgIG + SC (n=497) vs. SC (n=171). The normalization rates and 50% reduction rates of ALT, AST, and TBIL is significantly higher in MgIG group than those in SC group (n=152) before discharge, while only 50% reduction rates reached statistical significance at day 7. In MgIG + SC group, normalization rates of only ALT and AST is significantly higher than those in SC group (n=171) before discharge, while 50% reduction rates of all compared serum markers reached statistical significance both at day 7 and before discharge.

Conclusion: This study provided preliminary evidence for the efficacy of MgIG in patients with liver injury after receiving novel antineoplastic agents compared to supportive care.

Abstract Submission No. 100910
O-0055

Efficacy of MgIG compared to steroids in liver injury after novel antineoplastic therapy

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Background: Liver injury in patients treated with novel antineoplastic agents including molecular targeted agents and immune checkpoint inhibitors is often managed with glucocorticoids. Magnesium isoglycyrrhizinate (MgIG) is an anti-inflammatory agent with potential to ameliorate liver injury.

Methods: We conducted a retrospective, multicenter, real-world study to evaluate the efficacy of MgIG compared to glucocorticoids in patients with liver injury after receiving any novel antineoplastic agent. Propensity score matching (PSM) is used to match age, sex, and baseline alanine aminotransferase (ALT) between groups. The change from baseline, normalization rate and the proportion of patients with 50% reduction of ALT, aspartate aminotransferase (AST) and total bilirubin (TBIL) 7 days after treatment and before discharge were compared.

Results: A total of 918 cases are included and subsequently divided into 2 populations after PSM in a 1:1 and 2:1 ratio respectively: MgIG (n=57) vs. glucocorticoids (n=57); and MgIG + glucocorticoids + supportive care (SC) (n=249) vs. glucocorticoids + SC (n=164). MgIG group only showed a higher 50% reduction rate in TBIL over glucocorticoids group at day 7 and before discharge. However, the normalization rate of ALT and AST before discharge in MgIG + glucocorticoids + SC group are significantly higher than those in glucocorticoids + SC group. The 50% reduction rates of all compared serum markers are significantly higher at day 7 and before discharge.

Conclusion: This study provided evidence that MgIG may aid to improve recovery as add-on therapy to glucocorticoids and supportive care in patients with liver injury after receiving novel antineoplastic agents.

Abstract Submission No. 101082
O-0056

Late Onset Efavirenz Induced Liver Toxicity in a 17-year-old, Filipino, HIV patient

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Efavirenz, a commonly used non-nucleoside reverse transcriptase inhibitor (NNRTI) for HIV treatment, is generally well-tolerated. However, rare cases of hepatic adverse effects, including hepatotoxicity, have been reported. While mild liver enzyme elevations are relatively common (in about 10% to 20% of cases), severe hepatotoxicity leading to liver failure is infrequent, with reported incidences ranging from 0.5% to 4%. The exact mechanisms underlying efavirenz-induced liver toxicity are not fully understood but may involve oxidative stress, mitochondrial dysfunction, and immune-mediated reactions.

In this case report, a first in the Philippines, we present a known case of HIV started on Lamivudine, Tenofovir and Efavirenz who presented with jaundice and elevated liver enzymes after a year of treatment which has not happened before in any published case. A comprehensive workup ruled out various causes of acute liver injury, including infection, autoimmune factors, herbal medications, and toxins. Genetic testing did not reveal any abnormalities related to medication metabolism. The patient's condition was successfully managed with a combination of steroids, immunosuppressants, and switching from efavirenz to dolutegravir, leading to the resolution of jaundice and liver enzyme abnormalities.

This case highlights a delayed onset of efavirenz-induced liver toxicity, occurring after a year of HIV treatment initiation. It emphasizes the importance of early detection, comprehensive workup, and personalized management for rare adverse effects associated with antiretroviral therapy. Understanding efavirenz-induced liver toxicity, including its mechanisms, risk factors, and clinical management, is crucial for the safe and effective treatment of HIV patients.

Abstract Submission No. 101278

O-0057

CTCAE system upgrades severity of ICIs induced liver injury than DILI grading systems

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Background: Immune-mediated liver injury (ICILI) induced by immune checkpoint inhibitors (ICIs) are usually graded by the Common Terminology Criteria for Adverse Events (CTCAE) grading system. While the grading systems for drug-induced liver injury (DILI) include the US Drug-induced Liver Injury Network (DILIN) and the International DILI Expert Working Group severity indexes. It remains unclear which of these systems is most appropriate for assessing the severity of ICILI.

Method: This is a retrospective review at Beijing Friendship Hospital (2016-2022) collecting clinical data of ICI-treated patients. ICILI cases were graded using CTCAE and two other DILI indexes. Agreement and correlation between grading systems were analyzed using the weighted kappa coefficient and Spearman's rho coefficient.

Results: A total of 66 (4.94%) cases developed ICILI. In summary, 18(27.3%) cases exhibited ALT elevation, 23(34.8%) AST elevation, 9(13.6%) ALP elevation, and 16(24.2%) TB elevation exceeding grade 3 in terms of liver injury severity with CTCAE systems. CTCAE identified a higher proportion of severe cases compared to US-DILIN and International systems significantly (45.5% vs 16.7% and 16.7%, respectively, $P=0.001$). Correlation analysis showed higher agreement

between US-DILIN and International ($\kappa=0.642$, 95%CI 0.517-0.766) than with CTCAE ($\kappa=0.188$, 95%CI 0.091-0.285 with International; $\kappa=0.239$, 95% CI 0.108-0.371 with US-DILIN).

Conclusions: CTCAE graded more ICILI cases as severe cases compared to DILI grading systems. A comprehensive assessment incorporating clinical presentation, liver chemistries, coagulation function, and prognosis is crucial for accurate severity determination.

Abstract Submission No. 101402

O-0058

Clinicopathological features and outcomes of Scutellaria (Huang Qin)-induced liver injury

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Objective To investigate clinicopathological features and outcomes of liver injury induced by Scutellaria, a herb known as Huang Qin.

Methods This is a multi-center retrospective cohort study. Cases with Scutellaria-induced liver injury were collected from Beijing Friendship Hospital, Beijing You'an Hospital, and the Fifth Medical Center of PLA General Hospital, from January 2009 to June 2017. Clinicopathological data and follow-up final clinical outcomes were summarized.

Results Twenty-nine patients with Scutellaria induced liver injury were identified from 1444 herb-induced liver injury cases. The median age was 48 (37, 59) years and 75.9% (24/29) were women. The most common symptom was dark-color urine (79.3%, 23/29). The main clinical injury pattern was hepatocellular (72.4%, 21/29), followed by mixed (17.2%, 5/29) and cholestatic (10.3%, 3/29). Of nine patients with liver biopsies, six had acute hepatitic and three had mixed acute cholestatic-hepatitic histological injury pattern. Compared to the mild group (n=12), moderate and severe group (n=13), the acute liver failure (ALF) and fatal group (n=4) had significantly higher level of aspartate aminotransferase (515.5 and 655.04 vs 1064.5 U/L) and prolonged prothrombin time (11.5 and 12.0 vs 16.3 s), lower level of albumin (39.5 and 38.6 vs 33.8 g/L, all $P<0.05$). One patient in the moderate and severe group had chronic liver injury, whereas, one developed chronicity and one died of liver failure in the ALF and fatal group. **Conclusion** Scutellaria can induce liver injury, and the main clinicopathological injury pattern was acute hepatitis with or without cholestasis. Most patients recovered; however, chronicity and death may occur.

Abstract Submission No. 101480

O-0059

Non-alcoholic fatty liver disease following chemotherapy

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Introduction: Chemotherapy-induced liver injury is one of the most common causes of mortality in cancer patients. One of the mechanisms of the development of fatty liver is hepatic steatosis, induced by chemotherapeutic agents. In this study, we are evaluating the development of fatty livers during the therapy for ovarian cancer.

Method: A prospective study was conducted on cases of ovarian cancer with normal liver function tests who developed fatty livers after getting chemotherapy.

Result: We studied 200 cases of ovarian cancer, out of which 31 (15%) cases developed fatty liver secondary to therapy for ovarian cancer. The average age at which fatty liver develops is 49.2 years. Among various clinical parameters, only weight and body surface area (BSA) did show a statistically significant correlation ($p = 0.05$) with the development of fatty liver. The patients who had PFI for more than 15 months also showed the development of FL ($P = 0.03$) (table 1).

Conclusion: The development of fatty liver following chemotherapy follows the common mechanism, but the process is fast. This may be due to an altered metabolic process. Here also weight and BSA are associated with the development of fatty liver. Following chemotherapy, progression-free interval has also shown a significant correlation with the development of fatty liver.

Abstract Submission No. 101490
O-0060

Analysis of International Comparisons of Adverse Drug Reaction Reports in FDA and PMDA Databases

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Background: An international comparison was made in the liver-related drug adverse event databases of FAERS (Food and Drug Administration Adverse Event Reporting System) by the FDA in the USA and JADER (Japanese Adverse Drug Event Report) by the PMDA in Japan.

Methods: An international comparison in the databases of liver-related adverse drug events was conducted. Standardised medical terminology with high quality and specificity internationally Both databases available with seven types of Preferred terms reported as liver-related adverse events registered in MedDRA internationally.

Results: Warfarin was the drugs most associated with adverse liver events in 452,272 cases registered in FAERS from 1997 to 2019. Sorafenib in 38,919 cases registered in JADER from 2004 to 2019, nivolumab and herbal extracts were the drugs most associated with adverse hepatic events. There was no correlation between the rank rankings in both databases. In terms of post-report outcomes, FAERS accounted for 43% of severe cases, while JADER accounted for 83% of recovered or mild cases, indicating that post-marketing surveillance reports also accounted for the majority of cases.

Conclusion: In Japan, regulations give priority to the promptness of drug adverse event reporting in post-marketing surveillance. Appropriate databases and information collection mechanisms on the frequency of adverse drug reactions are needed.

Abstract Submission No. 101491
O-0061

Impact of Prior Drug Allergies on severity of DILI, a study from tertiary care hospital, Pakistan

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Background&aim: In light of steady increase in hospitalizations related to drug intake in past few years, study aims to evaluate role of

prior drug allergies in population of patients with well-characterized drug-induced liver injury (DILI).

Patients&methods: DILI cases were identified&categorized on basis of COIMS/RUCAM score&exclusion of other liver diseases. This study included two arms, one arm included DILI cases with no prior drug allergy history&other consisted of all those identified DILI who had experienced any prior drug allergies including itching, coughing, hives, abdominal pain, vomiting, & diarrhea.

Clinical&laboratory parameters were analyzed to identify predictors of morbidity (prolonged hospital stay >7 days) & mortality.

Results: Out of 460 patients, 120 (25.8%) cases of DILI had prior history of drug allergies& remaining had no prior history. DILI was classified as definite/highly probable in 31.1%, probable in 62.5%, & possible in 7.4% of cases. Pattern of liver injury was hepatocellular in 25.1%, cholestatic in 56.17%, & mixed in 18.72% of patients. The patients with prior drug allergy were mainly male (78%) & significantly older, with mean age of 54 vs 45 with no prior drug allergy ($P = .009$), & they were more likely to have an underlying chronic disease like diabetes & Hypertension ($P = .016$). Clinically, patients with prior drug allergy were more encephalopathic (21.6% vs 10; $P = 0.02$) & jaundiced (54.1% vs 38%; $p = 0.04$). Those with prior drug allergy also had significantly hepatocellular pattern of DILI (68% vs 35%; $P = 0.003$), lower median values of albumin (2.8 g/L vs 3.8 g/L; $P = 0.04$) & alkaline phosphatase versus no drug allergies (1.4 vs 1.6 × ULN; $P = .045$) & lower platelet counts (189 vs 226 × 10³/ml; $P = .011$), while aspartate aminotransferase (AST), bilirubin & INR showed trend towards increased levels in patients with prior drug allergy (9.4 vs 6.2 × ULN; $P = .047$), (8.5 vs 4.2 mg/dl; $p = 0.02$) & (5 vs 3.5; $P = 0.01$).

Among those with prior drug allergies again, leading drugs most commonly responsible for injury were Anti-tuberculosis drugs (ATDs) (20%), followed by herbal medicines. In-hospital mortality was more in patients with prior drug allergy as compared to other arm (26.5% vs 10; $p = 0.034$) & prolonged hospital stay (>5 days) was observed to be more in drug allergy arm but not statistically significant (35.93% vs 28.6; $p = 0.43$).

Conclusion: Patients presenting with a history of prior drug allergies, one have to be careful while prescribing medications & if any present with DILI, they require close monitoring for early detection of worsening clinical courses

Abstract Submission No. 101593
O-0062

N-Acetylcysteine Prophylaxis for Anti-Tuberculosis Drug Induced Hepatotoxicity: A Meta-Analysis

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Background: The benefit of prophylaxis to prevent the development of antituberculosis drug-induced hepatotoxicity (ATDH) is still unclear. One of the promising hepatoprotectants available is N-acetylcysteine (NAC). We aimed to evaluate the effect of NAC on the prevention of ATDH, on transaminase levels and on time to recovery after hepatotoxicity among patients receiving anti-tuberculosis treatment.

Methods: We searched MEDLINE, PubMed, Embase, and CENTRAL up to 30th October 2023. Randomized controlled trials (RCTs) and case control studies comparing NAC with control were included. Statistical analyses were conducted using RevMan 5.4 software. Risk ratio (RR) and mean difference (MD) with 95% confidence intervals (CI) were used to evaluate the effect of NAC. The quality of included studies was assessed according to Cochrane handbook. Sensitivity analysis was conducted to assess the influence of each study.

Results: A total of 987 patients from 6 RCTs and 1 case control (392 with NAC, 595 with control) were included. Overall, prophylactic NAC significantly reduced the occurrence of ATDH with a pooled RR 0.39 [CI (0.27, 0.58), $p < 0.00001$]. Patients given NAC also had lower transaminases at 2 weeks anti-tuberculosis treatment. The mean difference between NAC and control for ALT was -40.21 [CI (-65.31, -15.10), $p = 0.002$] and for AST was -33.96 [CI (-57.11, -10.81), $p = 0.004$]. Lastly, NAC shortened the time to recovery after hepatotoxicity with a MD -6.51 days [CI (-8.13, -4.89), $p < 0.00001$].

Conclusion: NAC serves as effective prophylaxis in preventing ATDH. It has protective effects on transaminase elevation as well as reduces the time to recovery after hepatotoxicity.

Abstract Submission No. 101684

O-0063

Usefulness of a new diagnostic criteria in patients suspected of drug-induced liver injury

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Background: For the diagnosis of drug-induced liver injury (DILI), DDW-J2004 Workshop criteria has been used for many years in Japan. In this study, usefulness of the new criteria, RECAM (Hayashi PH, et al, DOI: 10.1002/hep.32327), was investigated.

Methods: Patients who were hospitalized for suspected DILI between 2017 and 2022 were enrolled. There were 30 cases suspected DILI with ALT $\geq 5 \times$ upper limit of normal (N) or ALP $\geq 2 \times$ N. Diagnostic performance of DDW-J 2004 and RECAM were compared.

Results: Patient age was 63(20-95) years, 9 (30%) were male. Causal drugs were anticancer agent (3), antiviral/antibiotics (3), dermatological (3), herbal medicine(4), and others. Injury pattern was hepatocellular in 22 (64%), cholestatic in 10 (29%), and mixed in 2 (6%). Interpretation by DDW-J2004 and RECAM criterion were highly probable (3, 6), probable (16, 11), possible (9, 12), and unlikely (2, 1). Fairly agreement of 33.7% (kappa 0.34, $p < 0.01$) was observed. The lower scores in RECAM were mainly due to missing values. Twenty-three cases recovered after discontinuation of the causal medication, 6 recovered with corticosteroid therapy, and 1 developed acute liver failure requiring liver transplantation. Later, diagnosis of DILI was denied in 2 cases; one case (DDW-J2004 possible; RECAM possible) coincidentally re-administered the same drug without liver injury. The other case (JDDW2004 probable; RECAM highly likely) showed ANA x 80 and IgG 1.6g/dl. Later the level of IgG increased, and liver biopsy finding was consistent with AIH.

Conclusion: RECAM criteria requires strict differential diagnosis, but may leads to accurate diagnosis.

Abstract Submission No. 100041

O-0064

Dopamine analog inhibits the HBV surface and e antigen expression by upregulation JAK/STAT pathway

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Background: Hepatitis B virus (HBV) infection is a major risk factor for cirrhosis and liver cancer and its treatment has always been challenging. Although several nucleos(t)ide analogs are available for treatment of HBV infection, long-term treatment with these drugs can lead to the emergence of drug-resistant viruses. In order to carry out such combinational therapy against HBV, several new drugs should be developed. We previously expressed and purified the HBV TP-RT with high purity using an E. coli expression system and established an in vitro ϵ RNA-binding assay system. Then, we used TP-RT in cell-free assays to screen candidate inhibitors from a chemical compound library, and identified, dopamine analog inhibited the HBV DNA, HBV surface antigen (HBsAg) and HBV e antigen (HBeAg) expression level. However, the inhibition of HBsAg and HBeAg mode of action remained unclear. Here, we aimed to identify the mechanism underlying dopamine analog-inhibited HBsAg and HBeAg.

Methods: We used dopamine analog treated AAV-HBV-infected mouse model, HepG2.2.15 and human NTCP-expressing HepG2 cell lines.

Result: We found that dopamine analog inhibited HBsAg and HBeAg expression level in two cell lines; dopamine analog increased the expression level of ISG15 and the JAK-STAT pathway factor STAT1, p-STAT1 and JAK1 expression level; dopamine analog inhibited the HBsAg and HBeAg expression level in AAV-HBV mouse model.

Conclusions: Clarifying the regulatory relationship between the dopamine analog and JAK-STAT/ISG15 pathway is necessary for developing new targets for the clinical treatment of chronic hepatitis.

Abstract Submission No. 100497

O-0065

The factor affecting HBsAg reduction after nasal therapeutic vaccine in chronic hepatitis B patients

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Background: The treatment goal of chronic hepatitis B (CHB) is HBs antigen (HBsAg) elimination, however it is difficult to achieve the goal with interferon and nucleos(t)ide analogues (NAs). We have developed a nasal administrative therapeutic vaccine containing HBs/HBcAg mixed viscosity enhancer (CVP-NASVAC). We conducted a clinical trial of CVP-NASVAC against CHB and demonstrated its capacities of HBsAg reduction and anti-HBs induction. In this study, we explored a factor affecting HBsAg reduction.

Methods: Fifty CHB patients (21 with NAs and 29 without NAs) received total 10 doses of CVP-NASVAC via nose. We investigated the rate of HBsAg reduction/loss, IgA- and IgG-type anti-HBs induction by CLEIA and ELISA, and HBcAg-specific CTL by ELISPOT.

Results: At the 18 months after CVP-NASVAC administration, HBsAg was reduced to 80.6% compared with baseline in patients with NAs and 69.4% without NAs, and HBsAg loss was observed in 1/21 with NAs and 3/29 without NAs. Anti-HBs was induced in 14.3% (3/21) with NAs and 42.9% (12/28) without NAs. IgA type anti-HBs titer and the number of HBc-specific interferon γ producing CTL were significantly increased after CVP-NASVAC treatment in both with and without NAs. Interestingly, significant correlation was observed

between the CTL increase and HBsAg reduction in CHB patients with NAs ($p < 0.005$), however no correlation was observed between anti-HBs elevation and HBsAg reduction.

Conclusion: HBcAg-specific CTL induction might be an important factor of reducing HBsAg in CHB patients under NAs treatment.

Abstract Submission No. 100628

O-0066

Highly expressed CTLA4 on B cells defected BCR signal to inhibit the secretion of anti-HBs in CHB

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Background: The generation of anti-HBs is lacking in CHB patients. The cause is controversial. B cells activation state has a crucial effect on the secretion level of antibodies. Therefore, B cell status deserves more attention.

Methods: Single-Cell RNA-seq analysis was performed in peripheral B cells. Peripheral and liver infiltrated B cells were characterized by flow cytometry. BCR signaling was tested by Ca^{2+} flow and WB assay. Aimed to explore the inhibiting role of CTLA4, we did CTLA4-blocking test in vitro. Further, B6-Ighm-KO mice were injected with HBsAg preimmunized CTLA4^{-/-} B cell after establishing HBV transduction model and HBV serological indicators were detected. CO-IP assay and proteome analysis was made to explore the downstream proteins of CTLA4.

Results: CTLA4 was highly expressed in B cells of CHB patients and more obviously in HBsAg-specific B cells. Moreover, CTLA4 was highly expressed in about 50% of the infiltrating HBsAg-specific B cells. CTLA4⁺HBsAg⁺B cells tended to show activated markers. GO analysis, Ca^{2+} flow and WB assay showed that BCR signaling of CTLA4⁺B cells was defected. Moreover, CTLA4 blocking could partly restore the deflection and make B cells secreted more anti-HBs. In mice model, B6-Ighm-KO mice injected with HBsAg preimmunized CTLA4^{-/-} B cells showed decreased level of HBV serological indicators. Proteome assay showed SHIP-1 was the down stream of CTLA4.

Conclusions: The circulating and liver infiltrating B cells increased the expression of CTLA4 to defected the BCR signal which might contribute to the deficiency of viral specific humoral response during CHB course.

Abstract Submission No. 100691

O-0067

Comprehensive analysis of CHB concurrent with NAFLD : A Proteomics Report Based on Liver Samples

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Background and Aims: In recent years, NAFLD has become more prevalent in patients with chronic hepatitis B as the prevalence of obesity and metabolic syndrome has increased. Both diseases can lead to liver fibrosis and even HCC, but the pathogenesis of each disease and CHB concurrent with NAFLD have not been fully elucidated.

Methods: We characterized the protein expression in liver tissues among four groups of people with healthy control, CHB, NAFLD, and CHB concurrent with NAFLD by using proteomic profiling. Based on the obtained DEPs results, further bioinformatics analysis was performed. We also verified the expression of some DEPs in the livers of patients and model mice.

Results: We found that accelerated viral clearance in HBV-infected patients with concurrent fatty liver might be associated with an inflammatory response and activation of a large number of metabolic reactions in the organism, while the level of hepatic steatosis was associated with abnormalities in fatty acid degradation, glycolysis/gluconeogenesis and others, however the prognosis of CHB concurrent with NAFLD is probably not optimistic, which could be associated with the expression of ACAT1, ACY1, SERPINB3, MTCH2, ALDH2, ECHS1, S100A7 and LRP6.

Conclusion: The prognosis of CHB complicated with NAFLD may not be optimistic compared with that of hepatitis B and NAFLD alone, which is closely related to the differential expression of certain proteins in the liver after the complication of the two diseases. Our study provides new insights into the disease development and clinical mechanisms of CHB and NAFLD.

Abstract Submission No. 100855

O-0068

MiRNA106b-3p down regulates PCGF3 and inhibits cell metastasis in HBV-related hepatoma carcinoma

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Background: MicroRNA-106b (miRNA-106b) has been shown to play a paradoxical role in disease progressing from different studies. However, the specific role of miRNA106b-3p in hepatocellular carcinoma and the underlying mechanism remains unclear.

Method: Huh7 cell transiently transfected with HBV C2 subgenotype plasmid was co-cultured with miRNA-106b-3p mimics. HBsAg level was detected using Elisa assay. Target genes that potentially bind to miR-106b-3p were predicted using TargetScan software. Target analysis was conducted via a dual-luciferase reporter assay. Q-PCR was used to detect expression level of target genes. Scratch assay was performed to evaluate cell migration. Transwell assays was used to evaluate cell invasion. Western blot was used to detect the PI3K/AKT signaling pathway-related proteins.

Results: Huh-7-HBV/C2 cells co-cultured with miRNA-106b-3p mimics was significantly increased with miRNA-106b-3p expression and down-regulated with HBsAg level. MiR-106b-3p overexpression significantly decreased the luciferase activity of wild-type PCGF3 3'-UTR, but no significant effect on the luciferase activity of mutant PCGF3 3'-UTR. MiR-106b-3p mimic can dramatically decrease the expressions of PCGF3 mRNA and protein in Huh7-HBV/C2 cells. In addition, the migration and invasion ability of Huh7-HBV/C2 cells was significantly decreased and the PI3K-AKT pathway was inhibited by miRNA-106b-3p mimics.

Conclusion: This study revealed that miR-106b-3p could down-regulate the expression of PCGF3 and inhibit the activation of PI3K/AKT signaling pathway, thereby preventing HCC metastasis.

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Abstract Submission No. 101155
O-0069

The differentiation of Treg and Th17 cells in patients with chronic hepatitis B in different stages

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Regulatory T (Treg) and T helper 17 (Th17) cells modulate the immune response in chronic hepatitis B virus infection by promoting immune tolerance, restricting liver damage, stimulating inflammatory responses, and inducing hepatocyte injury. These cells act by signaling transcription factors and secreting cytokines. Our study aimed to observe the percentages of Treg and Th17 cells, as well as their mRNA levels of Foxp3 and ROR γ t, in chronic hepatitis B (CHB)-infected groups and CHB patients experiencing hepatitis flare (HF). We recruited 159 participants, including 137 CHB-infected cases and 22 healthy controls (HC) from Ho Chi Minh City. CHB cases were divided into three groups: HBeAg+ CHB infection (e+CHBI, n=52), HBeAg+ CHB (e+CHB, n=24), and HF (n=61). Treg and Th17 cells were measured by flow cytometry, and the mRNA levels of Foxp3 and ROR γ t were analyzed by Realtime PCR. The percentages of Treg, Th17, and a special subset - IL17A(+)-Foxp3(+)-Treg cells - were significantly higher in the HF group compared to the e+CHBI group. Meanwhile, there was no significant difference in the mRNA levels of Foxp3 and ROR γ t in CHB groups. These findings reveal that these immune cells increase with the severity of the liver injury, and the mRNA levels of transcription factors do not correlate with the percentages of their cells. Our results explain the diversity of T cells and their subsets in the immune response in CHB and suggest that the new subset should be further investigated as a specific tool in the HBV immune response.

Abstract Submission No. 101224
O-0070

Adenosine sulfamate analogs inhibit HBV RNA synthesis and accelerate the decay of viral transcripts

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Background: The neddylation pathway is required for HBV replication. Targeting neddylation inhibits both HBV gene transcription and surface antigen expression in preclinical models. However, the underlying mechanism of neddylation modulation and HBV gene transcription remains unclear.

Methods: Two adenosine sulfamate analogs (ASAs) were evaluated for their ability to target host components of the neddylation pathway and inhibit HBV gene transcription in susceptible cells, in addition to

explanted primary human hepatocytes (PHHs) from multiple donors. Nascent transcript production was determined by click chemistry. RNA sequencing of HBV-infected PHHs determined the effects of ASAs on viral and host transcriptomes.

Results: Both ASAs, MLN4924 and TAS4464, reduced the expression of NAE1, Ubc12, Cul4A and neddylated cullins in PHHs. Upon SMC5/6 gene knockdown or HBx absence, the inhibitory effects of ASAs on viral transcription were alleviated. To further investigate the mechanism, 5-ethynyl-uridine was incorporated into infected HepG2-NTCP cells, allowing the detection of nascent transcripts. MLN4924 and TAS4464 reduced the synthesis of HBV transcripts by 60% and 74%, respectively. Furthermore, compared to DMSO treatment (>24 hours), ASAs accelerated the decay of subgenomic transcripts ($t_{1/2}$ = 10.8 and 14.2 hours) in HepAD38 cells. Remarkably, RNA-sequencing results showed that ASAs modulate host transcriptomes upon HBV infection in PHHs by selectively regulating a small cluster of host genes.

Conclusions: We demonstrate that ASAs reduce the protein expression of host components of the neddylation pathway, inhibit HBV RNA synthesis and accelerate viral transcript decay. ASAs have potential for future development and repurposing as a novel class of anti-HBV therapeutic.

Abstract Submission No. 101227
O-0071

Multi-Omics Panoramic Analysis of HBV Integration in the HBV-Integrated Cell Line PLC/PRF/5

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Background: The clearance or transcriptional silencing of integrated HBV DNA is crucial for achieving a functional cure in patients with chronic hepatitis B (CHB) and reducing the risk of hepatocellular carcinoma (HCC) development. The PLC/PRF/5 cell line is commonly used as an in vitro model for studying HBV integration. In this study, we employed a range of multi-omics techniques to gain a panoramic understanding of the characteristics of HBV integration in PLC/PRF/5 cells.

Methods: Transcriptome long-read sequencing was conducted to analyze characterize the transcriptional activity of different HBV DNA integrations in PLC/PRF/5 cells. Additionally, data pertaining to epigenetic regulation such as whole-genome bisulfite sequencing (WGBS), ChIP-seq, and ATAC-seq were collected to investigate the potential mechanisms associated with the transcriptional regulation of integrated HBV DNA.

Result: Our findings indicate that transcriptional activity of integrated HBV DNA in PLC/PRF/5 cells is influenced by methylation levels of the surrounding host genome near the integration site. The result indicated that elevated methylation of the adjacent host genome adversely impacts transcription activity of integrated HBV DNA. Furthermore, we observed a positive association between histone modification H3K4me3 and the transcription of integrated HBV DNA. These results suggest that host may regulate transcriptional activity of integrated HBV DNA through DNA methylation and histone modifications. Potentially leading to the silencing of integrated HBV DNA.

Conclusion: Our study brought a better understanding on the transcriptional regulation of integrated HBV DNA. This knowledge can be valuable in the development of novel strategy for functional cure of CHB.

Abstract Submission No. 101244
O-0072

IGF2BP1 promotes HBV replication via regulating HBV RNA stability in an m6A-dependent manner

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Background & aims: Hepatitis B virus (HBV) infection is the primary cause of chronic hepatitis B, cirrhosis, and hepatocellular carcinoma world widely. During HBV replication, HBV RNA undergoes post-transcriptional regulation by host cells which primarily relies on various host RNA binding proteins. However, the detailed mechanisms underlying post-transcriptional regulation of HBV RNA remain unknown. Herein, we investigated the role of RNA binding protein IGF2BP1 in the process of HBV replication.

Methods: The host proteins associated with HBV Dane particles was analyzed by mass spectrometry. Gene silencing and ectopic overexpression were used to detect the function of IGF2BP1 in regulating HBV replication. RNA turnover, RNA pull-down, and RNA immunoprecipitation assays were used to investigate the stability and binding between IGF2BP1 and HBV RNAs.

Results: Our study identified IGF2BP1 as an RNA binding protein that can be encapsulated into HBV Dane particles. According to the HBV replication cell model, the HBV infection cell model, and the HBV replication mouse model, we confirmed that IGF2BP1 promotes HBV replication. To elucidate the underlying mechanism, we found that IGF2BP1 enhanced the stability of all five HBV RNAs through its KH domain. IGF2BP1 recognized and bound to m6A modification sites on HBV RNAs, consequently promoted HBV RNA expression. This increased HBV RNA expression led to elevated protein expression and the formation of rcDNA, ultimately enhancing HBV replication.

Conclusions: Our study demonstrated IGF2BP1 as a critical host factor in enhancing the stability of HBV RNAs and facilitating HBV replication which provided a novel target for the development of anti-HBV drugs.

Abstract Submission No. 101573
O-0073

Deep sequencing analysis of HBV evolution in elderly cases of interspousal transmission

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Background/Aim: Hepatitis B virus (HBV) is transmitted within a family, but an interspousal transmission in elderly cases is rare. To clarify the dynamics of HBV quasiespecies in such cases, we performed long-read deep sequencing of the HBV preS1/preS2/S domain in two elderly couples of HBV transmission from wife to husband.

Methods: Using serum samples from two male patients with acute hepatitis (AH1: 67 years old, AH2: 71 years old) and their HBV carrier wives (CH1: 67 years old, CH2: 66 years old), HBV full genome

sequences were determined by direct sequencing. In addition, a long-read deep sequencing was performed with PacBio Sequel II using preS1/preS2/S domain amplicons.

Results: As a result of whole genome direct sequencing, AH1 was 98.0-99.2% identical to CH1, and AH2 was 98.5-99.5% identical to CH2. The identity between AH1 and AH2 was 96.9%. When a phylogenetic tree analysis was performed using the long-read deep sequences, it was shown that CH1 and CH2 had heterogeneous clones but AH1 and AH2 had relatively homogeneous clones. It was also suggested that the transmitted viral clones might be distinct from the major populations in the HBV carriers. We speculated that the major population in the carriers did not fit to the spouses and this might be one of the reasons why the transmission had not occurred during younger age.

Conclusion: Deep sequencing analyses revealed clonal population changes during HBV transmission.

Abstract Submission No. 101939
O-0074

Primer Design of Isothermal Amplification for Detection of Hepatitis B Virus Core Gene in Indonesia

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Diagnostic of Hepatitis B in Point of Care Testing (POCT) is needed to monitor and screening this virus. Current test using serological and molecular methods, which time-consuming and tend to be costly. A strategy using isothermal-based amplification methods, such as Multiple Cross Displacement Amplification (MCDA) and Loop-Mediated Amplification (LAMP) required to detect specific gene in Hepatitis B. We designed the primer to amplify core gene as target region, using both MCDA and LAMP technique, based on the circulating HBV genotype in Indonesia. The primer for amplification was selected in the conserved regions of HBV core genes. The primer was designed in silico using primer designing web-based tools. We designed 10 primers for MCDA and 5 primers for LAMP technique. The primer sequences were checked using Nucleotide BLAST tools (NCBI) to ensure the specificity of amplification. Furthermore, we pre-liminary tested these primers in isothermal amplification. This study provides the primer design to amplify sequence target to developed HBV diagnostic testing. The isothermal amplification needs to be evaluated and optimized HBV Diagnostic for POCT.

Abstract Submission No. 100363
O-0075

Knowledge, Attitudes and Practices (KAP) of Adult Filipinos towards Viral Hepatitis

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Viral hepatitis is a major public health burden worldwide. The objective is to focus on patients' knowledge, attitudes, and methods regarding viral hepatitis B and C to improve awareness, attitudes, and procedures related to viral hepatitis, leading to better prevention and management of the disease. A validated descriptive, cross-sectional, self-reported questionnaire on knowledge, attitudes and practices (KAP) relating to hepatitis B and C was administered at the outpatient department in a tertiary hospital. Data were analyzed and compared with mean scores from 2015-2023. Majority of the participants (44%) were between 41-60 years old, residing in Metro Manila (81%), high school graduates (53%) and unemployed (64%) and 81% having a monthly income of less than 200 USD (Php 10,000.00). There was an increasing mean KAP score towards hepatitis B and C from 2015 to 2017, with a decrease in the mean KAP scores in 2023. There were also no significant differences in the mean KAP scores except for practice scores in terms of age ($p=0.049$), and knowledge and practice scores in terms of place of residence ($p=0.026$ and 0.03 respectively). With most medical services directed to contain the expanding COVID-19 pandemic, viral hepatitis programs face several challenges. The COVID pandemic has widened the gap in the KAP towards hepatitis preventive practices and knowledge. Targeted health education programs promoting disease awareness should be intensified to eradicate viral hepatitis as a global health concern.

Abstract Submission No. 100425

O-0076

IFN- γ ⁺ Th1 promotes HBsAg loss by activating intrahepatic TRM through inducing M1 polarization

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Background: The immune mechanism of ALT elevation and HBsAg loss during pegylated interferon (PEG IFN) therapy remains to be elucidated.

Methods: Eight-two NA (nucleos(t)ide analog) treated Chronic hepatitis B (CHB) patients sequentially received add-on PEG IFN treatment for less than 96 weeks. 41 patients got HBsAg < 0.05 IU/ml (cured group) within 48 weeks. Blood samples were collected from all patients for research. Liver tissue from 14 CHB patients was used to detect inflammatory markers. Liver perfusate from healthy individuals or chronic HBV-infected individuals was used for mechanism validation. THP-1, Jurkat and HepG2.2.15 cell lines were used in vitro experiments.

Results: Serum and intrahepatic levels of Th1 cell-associated chemokines (CXCL9, CXCL10, CXCL11) and the proportion of Th1 cells in peripheral blood kept higher in the uncured group. But the proportion of IFN- γ ⁺ Th1 cells was higher in the cured group (0-24 weeks), the latter was linearly correlated with HBsAg decline and ALT levels during treatment. However, weak association was found between CD8⁺ T cells and HBsAg loss. Serum from cured patients induced a higher proportion of M1 (CD68⁺CD86⁺ Macrophage) cells compared to uncured patients. Polarization of IFN- γ ⁺ Th1 cells as well as M1 macrophages could be induced by IFN- α . M1 polarization of intrahepatic Kupffer cells promoted HBsAg loss by enhancing the effector function of tissue-resident T cells with an elevation of ALT levels.

Conclusions: IFN- γ ⁺ Th1 promotes HBsAg loss by activating intrahepatic resident memory T cells through inducing M1 macrophage polarization.

Abstract Submission No. 100482

O-0077

Anti-PD-1 antibody combined with ETV and Peg-IFN- α enhances anti-HBV efficacy in AAV-HBV mice

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Background: This study aimed to find a safe and more effective therapeutic strategy for hepatitis B virus (HBV) infection by combining anti-PD-1 antibody (α PD-1), entecavir (ETV) and pegylated interferon-alpha (Peg-IFN- α).

Methods: A 4-week treatment was conducted in an adeno-associated virus (AAV)-HBV mouse model. To evaluate safety, efficacy and immune response, various indicators were compared between model control, ETV, ETV+ α PD-1, ETV+ α PD-1/Peg-IFN- α , and ETV+ α PD-1+Peg-IFN- α groups.

Results: All groups had stable weight, alanine aminotransferase and aspartate transaminase levels during treatment, and similar liver necroinflammatory activity ($P>0.05$). After 4-week treatment, plasma HBsAg decreased most significantly in ETV+ α PD-1/Peg-IFN- α group [Mean: 3.99 log₁₀ vs. 4.36 log₁₀ (Model control group), $P=0.023$]; Plasma HBV DNA and HBeAg, and hepatocyte HBeAg positivity rates significantly decreased, but no statistically significant difference was found between groups at 4 week. Myeloid, NK, B and T cell responses were detected. Notably, after 4-week treatment, frequencies of HBV surface-specific IL-4⁺/IL-21⁺/IFN- γ ⁺/TNF- α ⁺ CD8⁺ T cells increased significantly in liver and blood in ETV+ α PD-1/Peg-IFN- α group ($P<0.05$); Frequencies of PD-1⁺CD8⁺ T cells in liver and CD8⁺ effector memory T (TEM) cells in spleen increased significantly in ETV+ α PD-1/Peg-IFN- α group, and the former positively correlated with frequencies of CD38⁺CD8⁺ T cells ($P<0.05$); Frequencies of circulating T follicular helper 1 (cTfh1) cells increased more prominently in ETV+ α PD-1/Peg-IFN- α and ETV+ α PD-1+Peg-IFN- α groups. Furthermore, HBsAg decrease value correlated with frequencies of above surface-specific IL-21⁺CD8⁺, PD-1⁺CD8⁺ and CD8⁺ TEM cells, and cTfh1 cells ($P<0.05$).

Conclusions: ETV+ α PD-1/Peg-IFN- α sequentially combined therapy reduces HBsAg levels safely and more effectively, whose efficacy may be related to enhanced T cell responses.

Abstract Submission No. 100907

O-0078

Serum N-Glycan for Diagnosing Liver Fibrosis in Chronic Hepatitis B Patients with Normal ALT Levels

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Background: The aim of this study was to explore the role of serum N-glycomic-derived models in diagnosing significant liver fibrosis and cirrhosis in 285 chronic hepatitis B (CHB) patients with normal (< 40 IU/L) alanine aminotransferase (ALT) levels.

Methods: Liver biopsy stages were assessed using the Ishak scoring system. Serum N-glycan profiles were tested using DNA sequencer-

assisted fluorophore-assisted carbohydrate electrophoresis (DSA-FACE). A machine learning method, random forest (RF) analysis was adopted to construct more ideal serum N-glycan models in order to distinguish significant liver fibrosis and cirrhosis.

Results: From Jan 2013 to Dec 2020, 285 CHB patients were enrolled, 63.86% (182/285) and 16.49% (47/285) of patients had significant liver fibrosis and cirrhosis, 4.91% (14/285) of patients had significant inflammation. The diagnostic efficiency of the serum N-glycan RF model constructed for distinguishing significant liver fibrosis (F3; RF-A model) was excellent (area under receiver operating characteristic (AUROC): 0.94), and the coincidence rate of the serum N-glycan RF-A model compared with liver biopsy was 90.45%. The diagnostic AUROC of the serum N-glycan RF model constructed for distinguishing liver cirrhosis (F5; RF-B model) was 0.97, and the coincidence rate was 88.94%.

Conclusions: The diagnostic efficiency of the constructed serum N-glycan models (RF-A and RF-B) was superior to that of liver stiffness measurement (LSM), the fibrosis index based on the four factors (FIB-4), and the aspartate aminotransferase-to-platelet ratio index (APRI). Serum N-glycan models are promising markers for the differentiation of significant liver fibrosis and cirrhosis in CHB patients with normal ALT levels.

Abstract Submission No. 101036
O-0079

Alcohol induced dendritic cell and it's exosome promotes specific T cell immunity in HBV infection

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Background: Dendritic cell (DC) plays a crucial role in the immune system and its function was found to be significantly impaired in patients with chronic hepatitis B. Dendritic cell derived exosome (DEX) is an extracellular vesicle secreted by DC and has the same or similar immune function as DC. Therefore, this study investigated the therapeutic role of DC and DEX in HBV infection.

Methods: We systematically investigated the functional effects of alcohol and HBV infection on DC and DEX, and co-cultured DC and DEX induced by alcohol with lymphocytes from HBV transgenic mice and patients with chronic hepatitis B to observe the T-cell immune response.

Results: Alcohol effectively stimulated the maturation of mouse bone marrow-derived dendritic cells (BMDCs) and DCs from HBV patients, but had no significant effect on the DC2.4 cell line. HBV infection inhibited the activation and maturation of DC and DEX. More importantly, in HBV transgenic mice and chronic hepatitis B patients, alcohol-induced DCs effectively promoted specific T-cell immunity, and DEXs were able to exert the same effects as DCs.

Conclusions: Our findings provide a new and effective way to stimulate DC maturation. In the future, DEX may substitute for DCs as a new therapeutic approach for patients with chronic hepatitis B.

Abstract Submission No. 100077
O-0080

Kinetics of iTACT-HBcrAg and -HBsAg assays in chronic hepatitis B patients with HBsAg seroclearance

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Objectives: Two novel assays have been developed, iTACT-hepatitis B core-related antigen (iTACT-HBcrAg) and iTACT-hepatitis B surface antigen (iTACT-HBsAg) assays. We investigated the longitudinal profiles of iTACT-HBcrAg and -HBsAg in patients with HBsAg seroclearance (SC) (<0.05 IU/mL).

Methods: This study comprises 60 HBV-infected patients with HBsAg SC, 27 in chronic hepatitis/liver cirrhosis (CH/LC) group and 33 in inactive carrier (IC) group. Longitudinal profiles of iTACT-HBcrAg and -HBsAg were examined using stored serum samples.

Results: The median period from HBsAg SC to iTACT-HBcrAg loss or to the last observation was longer in the CH/LC group than the IC group (39 vs. -3 months, $P = 0.004$), but this tendency was not observed in that by iTACT-HBsAg. Comparing the times of iTACT-HBcrAg and -HBsAg loss, the rate of patients who lost HBcrAg first was significantly higher in the IC group ($P = 0.008$). The cumulative incidence rate of iTACT-HBcrAg loss after HBsAg SC was higher in the IC group than the CH/LC group ($P = 0.002$), but there was no difference in the cumulative incidence of iTACT-HBsAg loss after HBsAg SC between the IC and CH/LC groups.

Conclusions: Patients in the CH/LC group had higher rates of detectable iTACT-HBcrAg than those in the IC group after HBsAg SC, suggesting that the presence of HBcrAg possibly contribute to the progression of chronic hepatitis B.

Abstract Submission No. 100137
O-0081

Effects of Vitamin D and Calcium on Bones in Chronic Hepatitis B Patients Treated with TDF

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Background: Tenofovir disoproxil fumarate (TDF) is an important drug to treat chronic hepatitis B (CHB) patients. However, long-term TDF therapy decreases renal function and bone mineral density (BMD).

Objective: To compare bone turnover markers, BMD, and renal function in CHB patients treated with TDF who received vitamin D₂ and calcium supplements and those who did not receive supplement.

Methods: This open-label prospective, randomized trial was conducted in patients with CHB treated with TDF who were randomized to the vitamin D₂ and calcium supplement group (n=32) and no supplement group (control group) (n=32) for 48 weeks.

Results: At baseline, the mean age was 54.2 years, 57.8% were male, and 17.2% had cirrhosis. Demographic data were similar in both groups, except body mass index, AST, and ALT were higher in the

control group. At 48 weeks, there were no differences in parathyroid hormone, serum creatinine, procollagen-1 *N*-terminal peptide, and tubular reabsorption of phosphate in both groups. The BMD T score of the total hip did not decrease in the supplement group but significantly decreased in the control group. The C-terminal telopeptide of type I collagen increased in only the control group. Subgroup analysis was performed in participants with low baseline vitamin D, the result showed that the median difference in the T score for the total hip in the supplement group also showed a smaller decrease than in the control group.

Conclusions: In CHB patients treated with TDF, supplementation with vitamin D₂ and calcium for 48 weeks can prevent loss of BMD.

Abstract Submission No. 100157

O-0082

Unawareness of hepatitis B infection and severity of hepatocellular carcinoma

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Background: Unawareness of hepatitis B virus (HBV) infection and lack of surveillance may serve as major barriers to HBV control and contributors to severe hepatocellular carcinoma (HCC) at presentation. This study evaluated the risk of HBV unawareness and its relationship with HCC severity.

Methods: This retrospective study was conducted in a tertiary hospital in Taiwan. Patients with HBV-related HCC diagnosed from 2011 to 2021 were enrolled. The demographic, clinical, and HCC characteristics were collected and compared between patients with HBV unawareness and awareness with and without surveillance.

Results: Of 501 HBV-related HCC patients enrolled, 105 (21%) patients were unaware of HBV infection at the time of HCC diagnosis. Patients with HBV unawareness were significantly younger and had poorer liver function than those with HBV awareness. Patients with HBV unawareness also had a significantly higher rate of detectable HBV DNA and an advanced stage of HCC. Patients with HBV unawareness and awareness without surveillance shared similar clinical characteristics with more severe HCC status. Further regression analysis demonstrated that HBV awareness with periodic surveillance was associated with early-stage HCC. Meanwhile, we observed that there was no change in the proportion of HBV awareness over the past 10 years.

Conclusions: Patients with surveillance also had better HCC survival than patients without surveillance or unawareness. HBV unawareness and lack of regular surveillance correlated with advanced HCC at presentation. Efforts to improve HBV education, disease awareness, and HCC surveillance are needed.

Abstract Submission No. 100176

O-0083

STOPPING ORAL THERAPY IN CHRONIC HEPATITIS B USING HBSAG THRESHOLDS: METAANALYSIS & META-REGRESSION

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Background and aims: Recommendations for stopping nucleoside analogue (NA) therapy in HBeAg-negative Chronic Hepatitis B (CHB) are unclear. End-of-treatment quantitative HBsAg (EOT-qHBsAg) thresholds <100IU/ml or <1000IU/ml have been proposed as stopping criterion. We assessed this by meta-analysis and meta-regression.

Design: We searched PubMed, EMBASE and conference abstracts for studies of HBeAg-negative CHB NA discontinuation. Extracted studies were analysed for risk-of-bias, pooled risk of HBsAg loss, virological (VR) and biochemical relapse (BR). Significant heterogeneity (*I*²) was addressed by subgroup analysis and random-effects meta-regression with known important covariables, including EOTqHBsAg thresholds, ethnicity, duration of therapy and followup.

Results: We found 24 papers (3732 subjects), 9 low, 14 moderate and one with high risk of bias. The pooled risks of HBsAg loss, VR and BR for stopping therapy at EOTqHBsAg <100IU/ml were 41.8%, 33.4% and 17.3%, versus 4.6%, 72.1% and 34.6% respectively for EOTqHBsAg ≥ 100IU/ml. The pooled risks of HBsAg loss, VR and BR for stopping therapy at EOTqHBsAg <1000IU/ml were 22.0%, 52.7% and 15.9%, versus 3.4%, 63.8% and 26.4% respectively for EOTqHBsAg ≥ 1000IU/ml. Multivariable analysis for HBsAg loss showed ethnicity, followup duration and EOTqHBsAg <100IU/ml explained 85% of the variance in heterogeneity; Asians with EOT-qHBsAg <100IU/ml had 28.2%, while Caucasians with EOT-qHBsAg <1000IU/ml had 38.4% HBsAg loss. Multivariable analysis showed EOTqHBsAg <100IU/ml and other covariables only explained 43% and 63% of the variance in heterogeneity for VR and BR respectively, suggesting that other factors are also important for relapse.

Conclusions: While EOTqHBsAg thresholds, ethnicity and followup duration strongly predict HBsAg loss, this is not true for VR and BR, hence stopping NA therapy should be considered cautiously.

Abstract Submission No. 100203

O-0084

The correlation between Interleukin-6 and the progression of chronic Hepatitis B

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INTRODUCTION: Hepatitis B virus (HBV) is a dreadful virus with the potential to cause human liver diseases such as self-limiting acute hepatitis, chronic hepatitis, fulminant hepatic failure, liver cirrhosis and hepatocellular carcinoma (HCC). These complications result from an immune response of the host that affects both outcome and disease progression, rather than a direct cytopathic effect. Cytokines have been shown to be engaged in regulating hepatocyte functions, and play an important role in HBV infection immunopathogenesis.

METHODS: About 52 subjects ranging from 18 years old to 80 years old who were diagnosed with HBV were recruited into the studies. Their venous blood was taken and centrifuged at 4500rpm for 5

minutes to separate the blood components. The patient's sera were withdrawn and divided into two aliquots and kept in a special fridge with a temperature of -20 to -70 degrees. The first group of sera were subjected to a hybrid capture, tube-based signal amplification using HBV Digene Hybrid-Capture I, Digene Corporation, USA. While the second group of sera were subjected to a sandwich-ELISA test using LEGEND MAX Deluxe set human IL-6 kit to quantify the IL-6 levels. Both data were recorded and analysed using IBM SPSS version 26 software.

RESULTS: We found that there was a direct correlation between the severity of HBV viral load and the level of IL-6. The more severe the infection, the higher the IL-6 level ($P < 0.05$) taking the mean value of IL-6 as 132.6pg/ml. Demographical data distributions showed that men, aged between 40 and 60 years old and healthcare workers were the risk factors to develop chronic HBV. A linear scatter plot was derived between the levels of IL-6 and HBV viral load. Pearson correlation coefficient showed a linear correlation between the two variables. The patient's ALT enzyme was used to stratify the severity of the liver functions. Higher levels of IL-6 were detected in the subjects with HBV for longer than 6 months which proved that IL-6 levels correspond to the chronicity of the disease.

CONCLUSION: IL-6 is a vital mediator of inflammation and the acute phase response of the liver. Our studies proved that serum IL-6 levels were positively correlated with HBV disease severity and chronicity. Thus, IL-6 may be a useful indicator of disease activity and therapeutic efficacy in patients suffering from hepatitis B.

Abstract Submission No. 100214

O-0085

Establishment of a predictive model of myelosuppression in patients with CHB treated with Peg-IFN

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Objective: The aim of this study was to explore the risk factors for myelosuppression in chronic hepatitis B patients with peginterferon and establish a risk prediction model.

Methods: A total of 208 patients with chronic hepatitis B who were treated with peginterferon in the infection Department of the First Affiliated Hospital of Nanchang University from December 2019 to December 2021 were selected and divided into the modeling group (153 cases) and the verification group (55 cases) according to a ratio of about 3:1. Patients with degree II and above myelosuppression after 1 dose of interferon therapy were defined as myelosuppression group, and the rest were normal group. The risk factors of myelosuppression were discussed by multivariate logistic regression, and the prediction model was established and verified internally.

Results: The results of multi-factor logistic regression analysis and prediction model establishment show: BMI (OR=0.869, 95%CI 0.772-0.979, $P=0.021$), leukocyte (OR=0.704, 95%CI 0.508-0.976, $P=0.035$) and globulin (OR=0.904, 95%CI 0.823-0.992, $P=0.034$) was an independent factor of myelosuppression in CHB patients treated with peginterferon. Calculation formula: $\text{Logit}(P) = \ln[P/(1-P)] = -0.14 \times [\text{BMI (Kg/m}^2)] - 0.351 \times [\text{WBC (x10}^9/\text{L)}] - 0.101 \times [\text{GLB (g/L)}] + 7.606$; The AUC of the modeling group was 0.732, $P < 0.001$ (Figure 1); The AUC of the verification group was 0.762, $P = 0.001$ (Figure 2).

Conclusion: Low BMI, low white blood cell and low globulin at baseline were independent risk factors for myelosuppression in CHB patients treated with peginterferon, and a risk prediction model was established, which provided a basis for early identification of myelosuppression prone patients in clinical work and active preventive measures.

Abstract Submission No. 100226

O-0086

Tenofovir disoproxil fumarate raises long-term fracture risk in elderly chronic hepatitis B patients

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Background: The use of tenofovir disoproxil fumarate (TDF) is associated with a reduction in bone mineral density. However, data on clinical bone fractures remain limited. We evaluated the impact of TDF compared to entecavir on fracture risk in elderly patients with chronic hepatitis B (CHB).

Methods: Patients with CHB aged ≥ 60 years receiving entecavir or TDF between January 2008 and December 2022 were identified using a territory-wide database in Hong Kong. The risk of incident fracture in entecavir- and TDF-treated patients before and after month 24 were compared after propensity score (PS) matching.

Results: 41,531 patients with CHB (mean age 69.8 ± 7.8 years, 61.6% male) receiving entecavir ($n=39,897$ [96.1%]) and TDF ($n=1,634$ [3.9%]) were analysed. At a median follow-up of 25.3 (9.1-58.5) months, 1,733 (4.2%) patients developed incident fracture. Patients with incident fracture were more likely to have diabetes, hypertension, congestive heart failure, rheumatoid arthritis, osteoporosis, and a history of fracture. Compared with PS-matched entecavir-treated patients, the risk of incident fracture in TDF-treated patients was comparable in the first 24 months (weighted subdistribution hazard ratio [wsHR] 0.98, 95%CI 0.56-1.72, $p=0.946$) but increased after month 24 (wsHR 1.79, 95%CI 1.11-2.89, $p=0.017$). The 24-, 60-, and 96-month cumulative incidence (95%CI) of fracture in TDF-treated and entecavir-treated patients were 2.3% (1.6%-3.4%) versus 2.6% (1.9%-3.5%), 6.4% (5.0%-8.2%) versus 4.7% (3.8%-6.0%), and 10.2% (8.3%-12.6%) versus 6.8% (5.4%-8.5%) respectively (Figure).

Conclusions: Fracture risk increased with TDF treatment for ≥ 24 months in elderly patients with CHB. Selection of nucleos(t)ide analogues should be individualised based on age and comorbidities.

Abstract Submission No. 100228

O-0087

Lipid safety of tenofovir alafenamide during 96-week treatment in c

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Background: TAF was the first-line antiviral drug recommended by major clinical guidelines for the treatment of HBV infection. Antiviral

therapy requires long-term treatment, so long-term efficacy and safety of the drug are very important. This study was aimed at investigating the dynamics of lipid profile in naive CHB patients for 96 weeks.

Methods: Naïve CHB patients treated with TAF were enrolled in this study. The data of TC, LDL-c, HDL-c, TG, and TC/HDL ratio were collected at baseline, 24 weeks, 48 weeks, 72 weeks, and 96 weeks.

Results: 137 CHB patients treated with TAF were enrolled. Mean Age was 40.71 ± 10.41 years, 62.04% were male. During 96 weeks of TAF treatment, TC and HDL-c levels gradually increased during treatment with TAF until 24 W (TC: 168.56 vs 170.87 mg/dL; HDL-c: 46.39 vs 47.16 mg/dL; $P > 0.05$), and then decreased and showed no statistical difference at 96 weeks (TC: 155.41 mg/dL; HDL-c: 43.3 mg/dL; $P > 0.05$) compared with baseline level. LDL-c levels did not change significantly during 96 weeks of treatment with TAF (105.16 vs 99.36 mg/dL, $P > 0.05$). TG levels gradually increased from 87.71 mg/dL to 116.1 mg/dL at 48 W ($P = 0.009$), and then decreased to 88.6 mg/dL at 96 weeks and showed no significant change compared with baseline ($P > 0.05$). TC/HDL ratio increased from 3.56 at baseline to 3.89 at 96 W, but there was still no statistical difference ($P > 0.05$).

Conclusion: TAF treatment had a low effect on the lipid profile of Naïve CHB patients over the course of 96 weeks.

Abstract Submission No. 100270

O-0088

High normal ALT is an indicator for better response to antiviral therapy in chronic hepatitis B

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Background: Evidence showed patients with a normal ALT (40U/L as threshold) still have histological disease and there is still a lack of research on the prediction of antiviral benefits in these patients. The study aimed to investigate liver histologic disease in CHB patients with normal ALT, as well as to evaluate the potential benefits of antiviral therapy for these patients.

Methods: We retrospectively examined 1352 patients who underwent liver biopsy from 2017 to 2021 and then obtained their 1-year follow-up data to establish a predict model of 1-year HBVDNA clearance.

Results: ALT levels were categorized into high and low, with thresholds set at ≥ 30 for males and ≥ 16 for females through Youden's Index. In the high normal ALT group, more patients have significant histological disease (56.43% vs 43.82%, $p < 0.001$). The threshold of high normal ALT in our study has similar discriminative ability with the threshold of AASLD 2016 (male ≥ 30 , female ≥ 19). Multivariate logistic analysis showed that high normal ALT, defined by two different thresholds, were both identified as an independent predictor of 1-year HBVDNA clearance after antiviral treatment (OR 1.993, 95% CI 1.115-3.560, $p = 0.020$; OR 2.000, 95% CI 1.055-3.793, $p = 0.034$, Table 4). Both of the models had higher AUC compared with the current scoring system, and there was no obvious difference between two models (AUC: 0.8840 vs 0.8835).

Conclusions: Male ≥ 30 , female ≥ 19 or ≥ 16 are suggested to be better thresholds for normal ALT. CHB patients with high normal ALT have a potentially better benefit from antiviral therapy.

Abstract Submission No. 100274

O-0089

High burden of compensated advanced chronic liver disease (cACLD) in diabetic chronic hepatitis B

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Objective: Antiviral therapy with oral nucleos(t)ide analogues (NAs) is effective in suppressing serum hepatitis B virus (HBV) DNA and reducing the risk of hepatocellular carcinoma (HCC). We aimed to evaluate the disease burden of compensated advanced chronic liver disease (cACLD) in patients with chronic hepatitis B (CHB) and diabetes mellitus (DM) who have been receiving NAs.

Methods: Consecutive NA-treated CHB-DM patients were recruited for transient elastography examination. cACLD was defined as a liver stiffness measurement (LSM) > 10.0 kPa, and severe hepatic steatosis was defined as a controlled attenuation parameter (CAP) ≥ 280 dB/m.

Results: We recruited 269 CHB-DM patients; their mean age was 64 ± 11 years; 65.4% were male. The median (interquartile range) of LSM was 6.5 (4.8-9.6) kPa; that of CAP was 244 (208-292) dB/m. The prevalence of cACLD was 21.2%, and that of severe hepatic steatosis was 32.3%. Severe steatosis was tended to be more commonly observed among patients with cACLD (40.3%) compared to those without cACLD (30.2%; $p = 0.15$). Patients with cACLD had less satisfactory control of DM (HbA1c 7.9% vs. 6.6%, $p = 0.013$).

Conclusion: The disease burdens of cACLD and severe hepatic steatosis are both high in CHB-DM patients. Suboptimal glycaemic control associated with cACLD. New generations of antidiabetic agents, namely sodium-glucose co-transporter-2 inhibitors (SGLT2i) are promising in improving glycaemic control and potentially helpful in reducing adverse clinical outcome in CHB-DM patients with cACLD. **Financial support:** This work was supported by the General Research Fund from the Research Grant Council grant to Grace Wong (Reference: 14106922).

Abstract Submission No. 100308

O-0090

CHB patients receiving NAs therapy and achieving HBsAg loss can safely discontinue medication

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Objective: This study aims to investigate the HBsAg negative maintenance rate and possible predictive factors after discontinuation in non-cirrhotic CHB patients with serum HBsAg negative conversion after long-term nucleos(t)ide analogues (NAs) treatment.

Method: This is a single-center retrospective study targeting CHB patients who received NAs treatment and achieved negative HBsAg conversion in non-cirrhotic patients. These patients were all treated and followed up at the Hepatitis Clinic of West China Hospital of Sichuan University. The CHB patients finally included in the analysis must have complete demographic and clinical data, and all discontinued patients underwent serum HBVRNA and HBcrAg testing at the time of discontinuation.

Result: A total of 137 non-cirrhotic CHB patients with negative serum HBsAg were screened, 83 patients refused to discontinue the medication, and only 54 patients agreed to discontinue the medication. Among these 54 patients who agreed to discontinue medication, there were 43

males and 11 females; 42 patients were HBeAg positive and 12 patients were HBeAg negative before antiviral treatment; 44 patients received continuous monotherapy and 10 patients received combination therapy. All patients received antiviral treatment for more than 5 years. Among these 54 patients who agreed to discontinue medication, 79.6% (43/54) of them were accompanied by HBsAb positivity when discontinuing medication, and 59.3% (32/54) of patients had serum HBsAb levels above 200 IU/mL. All patients had serum HBVRNA lower than the detection limit when discontinuing medication, with 87.0% (47/54) of patients having serum HBcrAg < 3 log₁₀ U/mL. Within 24 weeks after discontinuation, a cumulative 3.7% (2/54) of patients showed HBsAg positivity. Within 48 weeks after discontinuation, a cumulative 9.3% (5/54) of patients showed HBsAg positivity, of which 3 patients were also accompanied by serum HBV DNA positivity. Patients who developed HBsAg positivity within one year after discontinuation of medication had serum HBcrAg levels greater than 3 log₁₀ U/mL at the time of discontinuation.

Conclusion: Non-cirrhotic CHB patients who receive long-term NAs treatment and achieve HBsAg negative conversion have a high maintenance rate of serum HBsAg negative after discontinuation of the medication. The serum HBcrAg level at the time of discontinuation may be related to whether the patient's serum HBsAg remains negative after discontinuation.

Abstract Submission No. 100309
O-0091

Safety of Biological Agents Used in Autoimmune Diseases Patients with inactive HBsAg carrier state

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Objective: To investigate the incidence of liver function damage and reactivation of HBV in autoimmune diseases patients with inactive HBsAg carrier state after using biological agents.

Methods: The patients with inactive HBsAg carrier status who have been diagnosed with autoimmune diseases and need biological agent treatment are included. All patients were treated with biological agents for no less than 12 weeks. The main outcome measures were the incidence of liver function damage and the rate of HBV reactivation.

Results: A total of 71 patients were included in this study, including 40 males and 31 females. There were 6, 19, and 46 inactive HBsAg carriers complicated with rheumatoid arthritis, ankylosing spondylitis and psoriasis, respectively. Among them, 18 patients were treated with adalimumab, 42 patients were treated with secukinumab, 7 patients were treated with ustekinumab, and 4 patients were treated with ixekizumab. Among these patients, the incidence of liver function damage was 19.72% (14/71); 2.82% (2/71) of patients experienced HBV reactivation, which occurred in patients treated with adalimumab. The serum HBsAg levels of patients treated with biological agents were significantly higher than before treatment ($P=0.002$), but there was no significant difference in the distribution of HBsAg levels between HBV reactivators and HBV non-activators ($P=0.288$). In addition, there was no significant difference in FIB-4 ($P=0.912$) and APRI ($P=0.627$) scores between HBV reactivators and HBV non-activators.

Conclusion: The autoimmune diseases patients with inactive HBsAg carriers state are at risk of liver function damage and HBV reactivation when treated with biological agents.

Abstract Submission No. 100333
O-0092

Longitudinal Changes in Renal Function in Patients with Chronic Hepatitis B on Antiviral Treatment

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Background & Aims: Patients with chronic hepatitis B (CHB) on nucleos(t)ide analogues (NUCs) often experience renal function decline. Conflicting results regarding the impact of NUC use and renal function have recently been reported. We aimed to examine longitudinal changes in renal function according to the NUC treatment type compared with untreated patients.

Methods: From 2014 to 2022, 10,642 patients with CHB were retrospectively analyzed. The primary outcome was chronic kidney disease (CKD) progression, which was defined as a minimum one-stage elevation. Propensity score (PS) matching was employed for outcome comparisons.

Results: In the PS-matched cohort of 1,996 pairs, the NUC-treated group (7.6/100 person-years [PYs]) had a significantly higher CKD progression risk than the untreated group (4.4/100 PYs), with a hazard ratio (HR) of 1.70 ($P<0.001$). The tenofovir disoproxil fumarate (TDF)-treated group (7.9/100 PYs) showed a 1.76-fold increased CKD progression risk compared with the untreated group (4.5/100 PYs) in the PS-matched cohort ($P<0.001$). Both the entecavir (ETV)- and tenofovir alafenamide (TAF)-treated groups showed CKD progression risks comparable to those of the untreated group in the PS-matched cohorts of 755 and 426 pairs, respectively ($P=0.132$ and $P=0.120$, respectively). No significant CKD progression risk was found between the ETV- (6.0/100 PYs) and TAF-treated (5.2/100PYs) groups in the PS-matched cohort of 510 pairs ($P=0.118$).

Conclusions: NUC-treated patients, especially those on TDF, faced a higher CKD progression risk than untreated patients. ETV- and TAF-treated patients presented comparable CKD progression risks to untreated patients. No difference was observed between ETV and TAF in the risk of CKD progression.

Abstract Submission No. 100382
O-0093

Effects of ETV and TDF on the incidence and severity of COVID-19 in chronic hepatitis B patients

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Background: Whether different anti-hepatitis B virus (HBV) drugs have different effects on COVID-19 is controversial. We aimed to evaluate the incidence of COVID-19 in chronic hepatitis B (CHB) patients receiving anti-HBV treatment, and to compare the impact of entecavir (ETV) and tenofovir disoproxil fumarate (TDF) on the severity of COVID-19.

Methods: CHB outpatients were enrolled from December 2022 to February 2023. Questionnaires were used to collect whether subjects had COVID-19 within the past 2 months, and the information of symptoms, duration, and severity if infected.

Results: 630 CHB patients were enrolled, 64.3% (405/630) patients had COVID-19. No COVID-19 patient required hospitalization,

intensive care unit admission, oxygen support or died. Majority of patients reported mild (32.8% [133/405]) and moderate (48.1% [195/405]) symptoms. After propensity score matching, 400 matched patients were obtained (ETV: 238; TDF: 162), among which the incidences of COVID-19 were comparable between ETV and TDF-treated patients (60.1% [143/238] vs. 64.2% [104/162], $p=0.468$). The proportion of patients complicated with any symptom caused by COVID-19 were also similar (ETV vs. TDF: 90.9% [130/143] vs. 91.3% [95/104], $p=1.000$). In addition, the severity of overall symptom was comparable between ETV and TDF-treated patients, in terms of proportion of patients complicated with severe symptom (9.8% vs. 8.7%, $p=0.989$), symptom duration (4.3 vs. 4.3 days, $p=0.927$), and symptom severity score (4.1 vs. 4.0, $p=0.758$). Subgroup analysis supported these results. **Conclusions:** During the current pandemic, the vast majority of CHB patients experienced non-severe COVID-19, and ETV and TDF did not affect COVID-19 severity differently.

Abstract Submission No. 100392
O-0094

Soluble PD-1 and BTLA proteins as biomarkers for predicting the anti-HBV treatment responsiveness

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Aim: This study aimed to evaluate the levels of soluble immune checkpoint proteins and their changes in patients with chronic hepatitis B during treatment with nucleos(t)ide analogues (NUCs) or pegylated interferon- α (PegIFN α) and to identify potential biomarkers for predicting treatment responsiveness.

Methods: This study included 32 patients with chronic hepatitis B: 20 patients received NUC (entecavir or tenofovir) in an infinite course ≥ 48 weeks, and 12 patients received PegIFN α monotherapy in a 48-week finite course. The concentrations of 16 soluble checkpoint proteins were measured using multiplexed fluorescent bead-based immunoassays in sera collected at baseline, 12 weeks, and 48 weeks of treatment.

Results: NUC treatment resulted in significant decreases in 10 of the 16 soluble (s) immune checkpoint proteins, most of which were important inhibitory factors including sPD-1, sCTLA-4, sTIM-3 and sCD40. In contrast, during PegIFN α treatment, two inhibitors, sTIM-3 and sLAG-3, increased, while the stimulatory factors sGITRL and sCD40 decreased. Treatment response, defined as a 0.5 log decrease in hepatitis B surface antigen (HBsAg) levels, was obtained in 6 of the 20 patients (30%) in the NUC group and in 5 of the 12 patients (42%) in the PegIFN α group. The fold changes of sBTLA and sPD-1 in responders by week 12 of PegIFN α treatment were significantly lower than those of the non-responders ($P=0.028$ and 0.042 , respectively).

Conclusions: We found different changes in soluble immune checkpoint proteins between NUC-treated and PegIFN α -treated patients. Circulating soluble PD-1 and BTLA proteins are potential biomarkers for prediction of PegIFN α responsiveness.

Abstract Submission No. 100454
O-0095

TAF and TDF for Chinese Assisted Reproductive Pregnant Women with HBV Infected: A Prospective Study

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Background: Aim to evaluate effective and safe of Tenofovir alafenamide fumarate (TAF) and Tenofovir disoproxil fumarate (TDF) in preventing mother-to-child transmission (pMTCT) of HBV for pregnant women with assisted reproduction.

Methods: Prospective study, from January 2020 to January 2022, pregnant women with HBsAg (+) and HBV DNA (+) who had normal ALT in assisted reproduction at the Second Affiliated Hospital of Hainan Medical College were enrolled. The mothers received TAF 25mg or TDF 300mg daily from gestational week 24 until 2 weeks postpartum. All infants received active immunization combined with passive immunization after birth and were followed up to 7 months after delivery. The primary outcome was the hepatitis B surface antigen (HBsAg)-positive rate at 7 months for infants. The secondary outcome was the safety of mothers and infants.

Results: Totally 67 pregnant women were enrolled, including 21 in the TAF group and 46 in the TDF group. The two groups are comparable in their baseline. At 7 months, the HBsAg positive rate of infants was 0% for both groups. During the follow-up period, neither group of pregnant women experienced any adverse reactions resulting in discontinuation or change of medication; Both groups of pregnant women had no birth defects in their babies, and their physical development were normal at birth.

Conclusion: It is safe and effective to administer TAF and TDF in HBV pMTCT for pregnancy women with assist reproduction and their infants, no significant difference between two groups.

Abstract Submission No. 100548
O-0096

Humoral responses after COVID-19 vaccination and breakthrough infection in CHB patients

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Background: The clinical and immunological features after COVID-19 vaccination and breakthrough infection (BTI) during Omicron wave in CHB patients were still unclear.

Methods: In this study, 101 patients with CHB were recruited from the Second Affiliated Hospital of Chongqing Medical University during the Omicron wave epidemic. Clinical data were collected by questionnaire survey and electronic medical record. Blood samples were used to determine the antibody responses, B and T cell responses.

Results: The most common symptoms of COVID-19 infection in CHB were upper respiratory symptoms, with 5 days median duration, and all of them were mild or moderate. CHB patients were more susceptible to develop symptoms of COVID-19 infection and presented with more severe symptoms than healthy controls. The liver function was not significantly damaged and HBV-DNA was not significantly increased after COVID-19 infection. CHB patients could establish a stronger immune barrier after BTI than every period after vaccination. The type of vaccine administered was the main factor affecting antibody response after BTI. Patients with CHB received the recombinant SARS-CoV-2 protein vaccine (ZF2001) generated a more robust

immune barrier after BTI than those received the inactivated vaccine. It is worth noting that B cell immune response against the wild strain was higher than the Omicron strain after Omicron BTI. CHB patients post BTI developed a similar antibody response compared with healthy controls, but weakened B cells response.

Conclusions: CHB patients followed favorable outcome post COVID-19 infection, in turn, COVID-19 infection will not result in CHB exacerbation. The immune responses were robust after BTI in CHB patients.

Abstract Submission No. 100566

O-0097

Comparing M2BPGi, APRI and FIB4 for Liver Fibrosis Diagnosis with Pathology in Chronic Hepatitis B

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Background: Serum Mac-2 Binding Protein Glycosylation Isomer (M2BPGi) levels correlate with liver fibrosis severity, but large-scale studies with histopathological confirmation are scarce in patients with chronic hepatitis B (CHB).

Methods: We retrospectively enrolled treatment-naïve CHB patients with liver biopsies from four hospitals in Taiwan, excluding those with hepatitis C virus or human immunodeficiency virus co-infection, or with malignancy. Serum M2BPGi, APRI, and FIB-4 levels were quantified at liver biopsy. Their performance for the diagnosis of fibrosis stage, which was evaluated by the METAVIR system, was assessed by the receiver operating characteristic (ROC) curves. Optimal cutoffs were determined for F2 or above, F3 or above, and cirrhosis. Subgroup analyses were performed.

Results: Among 670 eligible patients (median age: 45; 73.3% male), fibrosis stages were F0-1 (33.9%), F2 (22.4%), F3 (18.2%), and F4 (23.6%). The stage fell between F3 and F4 in 13 patients (1.9%). Mean and median M2BPGi levels rose significantly ($P < 0.001$) across fibrosis stages. M2BPGi demonstrated superior performance (area under the ROC) in diagnosing F2 or above (0.71), F3 or above (0.71), and F4 (0.72) compared to APRI (F2+: 0.58, F3+: 0.56, F4: 0.55; $P < 0.001$) and comparable performance to FIB-4 (F2+: 0.70, F3+: 0.70, F4: 0.69; $P > 0.1$). In patients with ALT flares (ALT $> 5 \times$ normal limit), M2BPGi was significantly better than FIB4 in identifying cirrhosis (0.82 vs. 0.67; $P = 0.015$). Optimal M2BPGi cutoffs were 1.03 for F2+ (sensitivity 71.6%, specificity 63.4%) and 1.20 for F3+ (sensitivity 70.0%, specificity 62.1%). Results remained consistent across subgroups.

Conclusions: M2BPGi significantly outperforms APRI in diagnosing fibrosis in CHB patients. As compared to FIB4, M2BPGi is comparable overall but more accurate in patients with ALT flares.

Abstract Submission No. 100587

O-0098

Sex, age and geographic disparities in hepatitis B randomised trials: a meta-epidemiological study

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Background: The prevalence of chronic hepatitis B (CHB) is unevenly distributed by sex, age, geography and socioeconomic status. The natural history of disease, and potentially treatment effectiveness, may differ among different populations. Identifying populations at risk of exclusions in clinical trials could guide policies to redress real-world gaps in treatment decision information. Therefore, we aimed to examine the representativeness of CHB trials.

Methods: We searched MEDLINE and EMBASE for randomised controlled trials recruiting people with CHB published January 2010 to July 2023. The demographic information of trial participants, specifically age, sex, race and ethnicity, and geographic regions was compared with the prevalence of CHB according to the Global Burden of Disease data. Trials' reporting of demographics, demographic-based trial exclusions, and demographic-stratified results were explored.

Results: We included 331 trials of 68,629 participants. Most reported participant age (328, 99%) and sex (321, 97%), but only 33.2% (110) trials reported race and/or ethnicity. Many trials had exclusions based on age (93.4% children, 38.4% older adults) or sex (48.6%). Female sex was under-represented (42% people living with CHB, but only 28% trial participants). Similarly, although 28% of people with CHB are African, and 3% from Western countries, their participation in trials (12% vs 18%, Figure 1) was distorted. Less than 1% of trials reported results by age, sex or race and ethnicity.

Conclusions: Clinical trials for people with CHB are poorly representative, with exclusions (children, older adults) and under-recruitment (female sex, African ethnicity). Researchers should actively consider equity and inclusion when designing trials.

Abstract Submission No. 100669

O-0099

Deep Sequencing of the HBV Genome in Taiwan: Risk of HCC from Primary and Secondary Genotypes

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Background: Several studies have demonstrated that the Hepatitis B virus (HBV) is a diverse DNA virus comprising 10 genotypes (A-J). Genotypes B and C are predominant in Asia, and patients can be co-infected with multiple HBV genotypes. While previous studies predominantly focused on primary genotypes, the impact of secondary genotypes on HCC has been largely overlooked. We investigated the impact of various HBV genotype combinations on the risk of HCC.

Methods: This study utilizes a longitudinal cohort of HBV chronic carriers (REVEAL-HBV) collected from 7 communities in Taiwan. PacBio sequencing technology was employed to deeply sequence HBV DNA from patients' serum. The proportions of primary and secondary genotypes of each patient were then identified. Subsequently, we analyzed the association between HCC and different genotype combinations.

Results: Our finding revealed that the HBV C2 subgenotype presented a higher risk of HCC (OR=4.73, 95%CI=2.85 - 7.85), aligning with previous studies (Table 1). To elucidate the impact of diverse HBV genotype combinations on HCC, we performed a detailed grouping analysis of primary and secondary subgenotypes. The results indicated

that among the groups with mixed C genotype infections, C+B and C+C, were the main combinations predominantly responsible for the elevated risk of HCC (C2+B2: OR=6.6, 95% CI=1.7-26.0, C2+C1: OR=11.9, 95% CI=3.1-45.4, C2+C6: OR=7.0, 95% CI=1.9- 26.1, C2+C8: OR=12.4, 95% CI=2.5-62.2, C2+C10: OR=8.4, 95% CI=2.4 - 29.7) (Table 2).

Conclusion: Our data indicates that groups co-infected with multiple HBV genotypes possess a higher risk of developing HCC compared to those with a singular infection.

Abstract Submission No. 100765

O-0100

Expected eight-week tenofovir alafenamide to prevent perinatal transmission of hepatitis B virus

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Background: The latest international guidelines recommended various durations of maternal antiviral prophylaxis to prevent mother-to-child transmission of hepatitis B virus (HBV-MTCT). We aimed to investigate safety and efficacy of short-course tenofovir alafenamide fumarate (TAF) therapy to prevent HBV-MTCT.

Methods: This multicentre, open-label, non-inferiority, randomized controlled trial was conducted at six Chinese referral hospitals. Eligible pregnant women with HBV DNA of 5.3-9.0 logs IU/mL received TAF from the first day of 33 gestational weeks to delivery date (33GW-DD, expected eight weeks) or to postpartum month 1 (33GW-PPM1, expected twelve weeks) were 1:1 randomly enrolled and followed until PPM6. All infants received standard immunoprophylaxis. The primary outcomes were birth defects and infants' HBV-MTCT rate at seven months of age. The secondary outcomes are safety concerns and virologic responses. This completed trial registered with ClinicalTrials.gov, number NCT04850950.

Results: Between April 26, 2021, and June 16, 2023, 119 and 120 intention-to-treat pregnant women were enrolled, and 110 and 112 per-protocol mother-infant dyads in 33GW-DD and 33GW-PPM1 groups completed the study. At delivery, 96.5% (111/115) and 97.4% (113/116) of intention-to-treat women achieved HBV DNA <5.3 log₁₀ IU/mL in two groups. No per-protocol infant had birth defect in either group (0% [0/115] versus 0% [0/116]). At PPM7, the infants' HBV-MTCT rate was similar between the two groups, both in the intention-to-treat analysis (7.6% [9/119] versus 6.7% [8/120], $p=0.788$) and the per-protocol analysis (0% [0/110] versus 0% [0/112]). TAF was well tolerated, and no one discontinued therapy due to adverse events; 15.1% (18/119) versus 18.3% (22/120) of women had mildly elevated alanine aminotransferase levels in two groups ($p=0.507$). The infants' physical and neurological development at birth and at seven months were normal in two groups.

Conclusions: An expected eight-week TAF treatment to prevent HBV-MTCT is safe, effective, and more cost-effective, which may change the clinical practice or thinking in this field. Future large-scale validation studies are warranted.

Abstract Submission No. 100768

O-0101

Evolution of HBV genomic structures without selective pressure of antiviral treatment

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Background: Hepatitis B virus (HBV) causes persistent infection to human bodies and develops genomic structural variants. However, the characteristics of these structural variants, such as localization in HBV genome, length, and long-term survivability during untreated persistent infection are not fully known.

Methods: Twenty-five sera were collected from 10 cases of treatment-naive chronic HBV infection. HBV-DNA was extracted from these sera and was sequenced using PacBio® third generation sequencer. The sequence errors were corrected using circular consensus sequencing.

Results: The nucleotide sequences of approximately 800-thousand copies of HBV genome were determined. Totally, 431 types of genomic structural variants were detected including 407 deletions, 22 insertions, and 2 duplications. The number of structural variants at the active hepatitis phase negative for anti-HBe were significantly larger than that at the anti-HBe-positive inactive hepatitis phase. Major structural variants with high allele frequencies in each case were in-frame deletions that cause nine to 91 amino acid deletions in PreS or C protein. Phylogenetic analysis indicated that these major structural variants can survive years and accumulate nucleotide substitutions independently from non-structural-variants during treatment-free persistent infection.

Conclusions: During persistent infection, genomic structural variants of HBV form quasispecies in the host bodies and each variant evolves independently for several years or longer.

Abstract Submission No. 100870

O-0102

Assessing liver cirrhosis progression under the Baveno VII definition using hidden Markov model

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Background: The Baveno VII consensus highlighted post-decompensation hepatic recompensation. However, ambiguities in its definition might lead to data inaccuracies. Our study identified predictors for cirrhosis progression and regression, accounting for misdiagnoses.

Methods: A Bayesian inhomogeneous hidden Markov model was developed among patients with chronic hepatitis B (CHB)-related cirrhosis in Hong Kong to determine transition probabilities among liver cirrhosis states: compensated, decompensated, recompensated, liver transplantation, and deaths. We considered 32 variables, including patient demographics, laboratory results, and comorbidities (Figure). Transitions from recompensated state to the compensated or transplantation states were prohibited. A one-month granularity was set to update cirrhosis states and variables.

Results: We evaluated 5,263 CHB-related cirrhosis patients. Initially, 4,690 (89%) were compensated, and 573 (11%) were decompensated.

At a mean follow-up of 32 ± 47 months, 2,317 (44%) remained compensated, 158 (3%) remained decompensated, 1,341 (25%) experienced non-liver deaths. Older age is associated with a higher likelihood of progressing to decompensated cirrhosis (odds ratio [OR]=2.41). Females are less likely to progress or deteriorate from a compensated state (OR ranges from 0.008 to 0.061). However, they have a higher likelihood of transitioning to recompensated cirrhosis (OR=8.50). The presence of hepatocellular carcinoma increases the likelihood of transitioning to decompensated cirrhosis and reduces the chances of progressing to recompensated cirrhosis.

Conclusions: Age, gender, and hepatocellular carcinoma were key determinants in disease transitions. Using the model's outcomes, we can deduce the importance of covariates across multiple transitions and estimate the future disease trajectory for each patient.

Abstract Submission No. 100877

O-0103

Dynamic liver volume changes predict re-compensation of HBV-related decompensated cirrhosis

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Background: NUCs treatment may change or even reverse the progression of HBV-related decompensated cirrhosis, that is, the realization of re-compensation. The change of liver volume can reflect the function and regeneration ability of liver. Nevertheless, the precise clinical implications of dynamic liver volume changes among patients with re-compensation remain uncertain.

Methods: This retrospective study involved the administration of NUCs treatment for a minimum of 48 weeks and a follow-up period of at least 2 years to all patients diagnosed with HBV-related decompensated cirrhosis. Two abdominal computed tomography (CT) scans were conducted at baseline and during the first two years of follow-up to measure the liver volume (LV₁, LV₂). The change in liver volume ($\Delta LV = LV_2 - LV_1$) was then calculated. Re-compensation was defined as the disappearance of decompensation complications and stability for a minimum of one year.

Results: A total of 159 patients were included, 38% of the patients achieved re-compensation, and the liver volume of the recompensated patients was significantly larger than that of the decompensated patients (1072.8 cm³ vs 848.11 cm³, $P < 0.001$). Logistic regression analysis screened the independent protective factors for predicting re-compensation of HBV-related decompensated cirrhosis as ΔLV , Hb, Na and Female, respectively, and established a prognostic model based on dynamic liver volume. The model demonstrated good performance in predicting re-compensation (C index 0.951, AUC value 0.959).

Conclusion: Effective antiviral therapy can reverse the liver volume of HBV-related decompensated cirrhosis. The model based on dynamic liver volume change is a reliable model for predicting re-compensation.

Abstract Submission No. 101046

O-0104

Investigation on current situation and trend of antiviral treatment for chronic hepatitis B in China

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Objective: To investigate the current situation and trend of antiviral therapy in patients with chronic hepatitis B (CHB) in China, and to analyze the factors affecting patients' acceptance of antiviral therapy and the choice of treatment methods.

Method: An electronic questionnaire was used to investigate patients with CHB in 12 hospitals including the First Affiliated Hospital of Jinan University and the Fifth Hospital of Shijiazhuang City in 2023. The contents included demographic characteristics, follow-up compliance, treatment compliance, knowledge of antiviral drugs and other influencing factors were analyzed by binary logistic regression.

Results: A total of 1360 patients with CHB were included in the questionnaire, of which 77.4% received antiviral therapy and 32.6% did not. Regression analysis showed that whether patients received antiviral treatment was related to education level, course of hepatitis B, HBV DNA results, follow-up compliance, treatment compliance, acceptance of antiviral treatment indications, understanding of antiviral drugs and price of long-acting interferon ($P < 0.05$). There were 399 patients over 30 years old with positive HBV DNA test, of whom only 30.6% received antiviral treatment. Regression analysis showed that whether the patients received antiviral treatment was related to their education level, follow-up compliance, treatment compliance, acceptance of antiviral treatment indications and understanding of nucleoside (acid) analogues ($P < 0.05$). Among 1052 patients who received antiviral therapy, 88.7% were oral nucleoside (acid) analogues, 11.3% were long-acting interferon monotherapies or combinations. And 913 patients (69.4%) had strong intention to pursue the clinical cure of CHB, but only 13.2% of them chose long-acting interferon. Regression analysis showed that the influencing factors of whether patients chose long-acting interferon were related to the understanding of long-acting interferon for clinical cure of CHB, the fear of HBV DNA results in liver cirrhosis or cancer, the understanding of nucleoside (acid) analogues and the treatment compliance ($P < 0.05$).

Conclusion: Whether patients with CHB choose antiviral therapy at present is influenced by many factors, such as educational level, compliance, understanding of diseases and drugs, etc. Doctors should strengthen the propaganda of clinical cure of hepatitis B and long-acting interferon treatment to improve the treatment rate and effective rate of CHB, which is beneficial to the early elimination of hepatitis B in China.

Abstract Submission No. 101055

O-0105

Exploratory biomarkers HBcrAg and HBV RNA: relationship with bepirovirsen response in B-Clear

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Background: Bepirovirsen (BPV) is an antisense oligonucleotide targeting HBV RNAs. B-Clear is a Phase 2b study (NCT04449029) assessing the efficacy and safety of BPV in participants (pts) with chronic hepatitis B. This post-hoc analysis looked at the presence and levels of hepatitis B core-related antigen (HBcrAg) and HBV RNA and their relationship with response to treatment.

Methods: B-Clear study pts were either receiving concomitant stable nucleos(t)ide analog therapy (On-NA) or not receiving NA (Not-on-NA). Pts were randomized (3:3:3:1) into 4 treatment arms receiving up to BPV 300mg weekly for up to 24wks with loading doses in Arm 1-3. HBcrAg and HBV RNA were assessed with Lumipulse G HBcrAg (Fujirebio) and custom RT-qPCR, respectively.

Results: HBV RNA was target not detected (TND) at baseline in 41.2% (93/228) Not-on-NA and 75.2% (170/226) On-NA pts. Mean HBcrAg and HBV RNA decreased from baseline to end of treatment (EOT) across both populations and all treatment arms (Table). Mean baseline HBcrAg and HBV RNA were lower in pts with sustained HBsAg loss (<0.05 IU/mL for 24wks post BPV treatment) compared with non-responders, respectively, but were not significant predictors of response.

Conclusions: HBV RNA was more likely to be TND at baseline in On-NA than Not-on-NA pts. Average EOT reductions were larger in Not-on-NA than On-NA pts. HBcrAg and HBV RNA at baseline were lower but not significantly associated with sustained HBsAg seroclearance. HBcrAg and HBV RNA may be worth exploring as early indicators of treatment response, primarily in patients not virally suppressed.

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Abstract Submission No. 101125

O-0106

Association of serum virology indicators with immune-mediated hepatic injury in chronic HBV

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Background & Aims: The natural history and disease progression of chronic HBV infection is dynamic, but the longitudinal landscape of virology indicators with immune-mediated hepatic injury remains undetermined. To this issue, we studied the association of virologic indicators with the severity of hepatic inflammatory damage and enumerated HBV specific CD8⁺T cells using the peptide-based cultured ELISPOT assay.

Approaches & Results: This retrospective study included 524 treatment naïve adult individuals with chronic HBV infection. The Spearman rank correlation analysis revealed that in HBeAg-positive patients, all HBV virologic indicators negatively correlated with liver inflammatory damage and fibrosis ($P < 0.01$). It was stronger in the subgroup of HBeAg-positive patients with HBV DNA $> 2 \times 10^6$ IU/mL ($P < 0.01$), whereas these negative correlations disappeared, in those patients with HBV DNA $\leq 2 \times 10^6$ IU/mL. Surprisingly in HBeAg-negative patients, the HBV DNA level was positively correlated with the hepatic inflammatory damage ($P < 0.01$). Furthermore, the anti-inflammatory cytokine IL-10 was negatively correlated with virologic indicators and correlated positively with the hepatic inflammatory activity, but only in a subgroup of HBV DNA $> 2 \times 10^6$ IU/mL. The relationship between the

interferon genes expression and HBV DNA levels revealed a direct shift from the initial negative to positive in HBeAg-positive patients with HBV DNA declined below 2×10^6 IU/mL. In addition, ELISPOT assay showed that the number of IFN- γ^+ SFCs/ 4×10^5 PBMC in HBeAg-positive and HBeAg-negative group progressively increase in ascending order.

Conclusions: The host's anti-HBV immunity is functional in HBeAg-positive patients with HBV DNA level exceeds 2×10^6 IU/mL, which can efficiently eliminate the infected hepatocytes and inhibit HBV replication. However, albeit the increasing number of HBV-specific IFN- γ^+ spot-forming cells, the host immune response shifts towards dysfunctional when the HBV DNA load drops below this threshold, which causes more pathological damage and disease progression.

Abstract Submission No. 101188

O-0107

Risk of MTCT after amniocentesis in pregnant women with HBV: A systematic review and meta-analysis

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Background: Amniocentesis is the most widely used invasive prenatal procedure for diagnosis or therapeutic purposes. Mother-to-child transmission (MTCT) is responsible for majority prevalent cases in the endemic area of hepatitis B virus (HBV). This study aimed to systematically evaluate the HBV MTCT risk under amniocentesis, as well as the risk factors.

Material and methods: In this systematic review and meta-analysis, we searched PubMed, Embase, China National Knowledge Infrastructure, ClinicalTrials.gov, and Cochrane Library databases for studies on MTCT in HBV infected pregnant women with or without amniocentesis published from database inception until September 13, 2023. MTCT was defined as HBsAg or HBV DNA seropositivity in the infants aged 6-12 months.

Results: Among 137 articles identified, the data encompassed 6509 participants from 6 studies were enrolled for final analysis. The MTCT rate of HBV was 6.39% (416 of 6509) overall, with individual rates of 10.29% (119 of 1156) for mothers who underwent amniocentesis and 7.42% (397 of 5353) for those who without amniocentesis. Compared with non- amniocentesis group, the summary relative risk (RR) was 1.65 (95%CI: 0.96-2.84, $P = 0.07$) in amniocentesis group. In the subgroup analyses, amniocentesis increases the risk of MTCT in pregnant women with HBV DNA $\geq 7.0 \log_{10}$ IU/mL (RR=7.26, 95%CI: 3.07-17.17, $P < 0.00001$) or HBeAg-positivity (RR=3.25, 95%CI: 1.5-7.01, $P < 0.001$).

Conclusion: Amniocentesis increases the risk of MTCT in pregnant with HBV DNA $\geq 7.0 \log_{10}$ IU/mL or HBeAg positivity. Pregnant women should be properly counselled before consenting for invasive procedures according to their HBV DNA levels.

Abstract Submission No. 101239

O-0108

Functional Delivery of miRNAs via HBsAg: Modulation of Monocyte and Inflammation Progression in CHB

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Objectives: The surface antigen of Hepatitis B virus (HBsAg) serves as an important immune-modulatory factor in chronic hepatitis B (CHB). One aspect of such modulation may act through monocytes which are the major antigen presenting cells (APCs) taking up HBsAg. There is evidence for the encapsulation of hepatocellular miRNAs by HBsAg particles, while its pathobiological significance is unclear. Here, we characterized the miRNA profile in CHB patients and probed their association with liver inflammation.

Design: We collected plasma from treatment-native CHB patients (n=110) and quantified total/HBsAg-enveloped miRNAs by qRT-PCR and serum cytokines by ELISA. The biological effects of HBsAg-delivered miRNAs in monocytes were evaluated by multiple systems. The clinical significance of candidate miRNAs and cytokines was corroborated in patients with HBV-associated advanced liver diseases.

Results: The plasma miRNA profile showed two major clusters, one associated significantly with HBsAg titer and the other correlated with liver inflammation. Among HBsAg-carried miRNAs, miR-939 displayed most significant correlation with IL-8 ($r=0.3039$, $p=0.0014$). Mechanistically, miR-939 in subviral particles enters monocytes and significantly augments IL-8 production via the MAPK p38 signaling pathway. Finally, the findings that miR-939 positively correlated with IL-8 level and inflammation/fibrosis stage in the cohort of HBV-associated advanced liver diseases support its direct role in the progression of liver diseases.

Conclusion: HBsAg particles carry hepatocellular miRNAs, including miR-939, which enter monocytes and alter their functional status such as IL-8 secretion. Our findings demonstrate that HBsAg-miR-939-IL-8 axis may play a crucial role in HBV-induced hepatic necro-inflammation and progression of advanced liver diseases.

Keywords: CHB infection, HBsAg subviral particles, miR-939, IL-8, monocytes, liver inflammation.

Abstract Submission No. 101385
O-0109

The GAAD score predicts HCC in HBV-related cirrhosis patients after 6-year antiviral therapy

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Background: In CHB-related cirrhosis patients on long-term antiviral therapy, hepatocellular carcinoma (HCC) risk persists, motivating the need for risk stratification. The GAAD score, encompassing gender, age, alpha-fetoprotein, and des-gamma carboxyprothrombin (DCP) measurements, is designed for early-stage HCC detection. This study investigates the predictive role of the GAAD score in HCC development in CHB-related cirrhosis patients on antiviral therapy.

Methods: We conducted a retrospective cohort study to include HBV-related cirrhotic patients undergoing long-term antiviral therapy with regular HCC surveillance. The on-treatment plasma samples were retrieved for alpha-fetoprotein and DCP measurements by the Roche Elecsys[®] system to calculate the GAAD score. Cox proportional hazard regression analysis identified risk predictors for HCC.

Results: A total of 499 patients were included and categorized into "prior HCC" (n=47), "HCC" (n=56), and "no HCC" (n=396) groups with a median GAAD score of 1.12, 0.84, and 0.54, respectively ($p<0.001$). Among the 452 patients without prior HCC, their median age was 60, and they received a median of 6.2 years of antiviral therapy. After a median of 3.3 years of follow-up, 56 patients developed HCC. A GAAD score of 0.71 and 1.64 significantly stratified the risk of HCC (log-rank $P<0.0001$). After adjusting for age, sex, and FIB-4 index, a GAAD score ≥ 1.64 and GAAD score 0.71-1.64 significantly increased the risks of HCC by 8.68-fold (95% CI: 3.50-21.55) and 2.25-fold (95%CI: 0.96-5.25) respectively, compared with a GAAD score of <0.71 .

Conclusions: After 6 years of antiviral therapy, a high GAAD score significantly stratified the risks of HCC development, and high-risk patients should receive intensive HCC surveillance.

Abstract Submission No. 101390
O-0110

High accuracy prediction model for HBsAg loss during long-term antiviral therapy in CHB patients

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Abstract

Background: Hepatitis B surface antigen (HBsAg) loss is the optimal outcome for patients with chronic hepatitis B (CHB) but rarely occurs

with currently approved therapies. We aimed to develop and validate a prognostic model for HBsAg loss on treatment using longitudinal data from a large, prospectively followed, nationwide cohort.

Methods: CHB patients on treatment were enrolled from 50 centers in China. Quantitative HBsAg (qHBsAg) were prospectively evaluated biannually per protocol. Longitudinal Discriminant Analysis algorithm was used to estimate the incidence of HBsAg loss.

Results: In total, 9437 CHB patients who had initiated antiviral treatment 55.2 (IQR:12.1,109.0) months prior to enrollment and had qHBsAg 2.8 (IQR:2.3,3.3) log₁₀IU/mL at entry were analyzed. With a median follow-up of 65.5 (IQR:50.5,84.7) months, the 5-year cumulative incidence of HBsAg loss was 3.0%. A prediction model integrating all longitudinal information of each patient during follow-up, designated GOLDEN model, was developed and validated. The AUCs of GOLDEN model were 0.978(95%CI:0.972-0.984) and 0.977(95%CI:0.973-0.981) in the training and external validation sets, respectively, and were significantly better than those of a single qHBsAg measurement. GOLDEN model identified 10.5-11.8% of patients with a high probability of HBsAg loss (5-year cumulative incidence: 19.3-31.1%), and excluded 88.2-89.5% of patients with zero incidence. Moreover, GOLDEN model consistently performed excellently among various subgroups.

Conclusions: This novel GOLDEN model, based on longitudinal information, accurately predicts HBsAg clearance, provides a reliable estimate of functional HBV cure and is valuable to identify favorable patients for benefiting from novel anti-HBV therapies.

Abstract Submission No. 101391

O-0111

Efficacy of combination treatment of TLR7 agonist and anti-PD-L1 in virally suppressed CHB patients

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Background: TQB2450, a PD-L1 antibody, inhibits PD-1/PD-L1 axis and rouses adaptive immune response to HBV. This study aimed to evaluate the safety and efficacy of nucleos(t)ide analog (NA) and TQA3334 combined with/without TQB2450 in CHB patients (pts).

Method: Totally 24 viral-suppressed (250 ≤IU/ml HBsAg ≤ 5000 IU/ml, HBV DNA < 20 IU/ml) CHB pts (HBsAg-positive: HBsAg-negative=1:2) were randomized to receive NA (monotherapy, n=6), NA+TQA3334 (dual therapy, n=9) or NA+TQA3334+ TQB2450 (triple therapy, n=9). TQA3334 (1.2mg or 1.5mg, QW) and TQB2450 (400mg, Q3W) were administrated for 24 weeks, and NA was given throughout this 48-week study. The HBsAg (Roche) reduction was evaluated.

Results: One participant received dual therapy withdrew at week 6. Adverse events (AEs) were more common in triple therapy, and the grade 1 thyroiditis was the most common immune-related AEs in pts received TQB2450. All the events were resolved before the end of follow-up (EOF). At the end of treatment (EOT), triple therapy was associated with greater HBsAg reduction compared to monotherapy and dual therapy (0.04 ± 0.08, 0.04 ± 0.16, and 0.37 ± 0.50 log₁₀ IU/ml). In triple therapy group, 1.5mg TQA3334 administration had a greater HBsAg reduction (0.46 vs 0.32 log₁₀ IU/ml) at EOT. HBsAg remained lower than those of EOT in 62.5% and 66.6% of pts received dual therapy and triple therapy respectively at EOF.

Conclusion: The combination of NA, TQA3334 and TQB2450 induced greater HBsAg decline in viral-suppressed CHB pts with good

safety. Moreover, high dose of TQA3334 promoted HBsAg reduction in triple therapy.

Abstract Submission No. 101413

O-0112

Detection of HBV DNA levels in untreated hepatitis B patients with low viral load by ddPCR

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Abstract: At present, real-time fluorescence quantitative PCR (qPCR) detection of HBV DNA is a routine method for diagnosing HBV infection. However, qPCR has many methodological limitations, including frequent false negative results for HBV copy numbers and the need for a standard curve for quantification. Droplet digital PCR (ddPCR) is used for absolute quantification of nucleic acids, which has high analytical sensitivity, high precision and no standard curve for quantification. Although detection of serum HBV DNA by ddPCR has been reported in patients receiving antiviral therapy, the clinical significance of ddPCR detection of HBV DNA in patients not receiving treatment has not been reported. In this study, we evaluated the performance of a ddPCR-based HBV DNA assay and compared the consistency of CAP/CTM assay and ddPCR assay for HBV DNA using clinical samples. The results show that ddPCR has good analytical sensitivity and can detect at least 1 copy. ddPCR assay has high specificity and accuracy. In addition, ddPCR assay has better repeatability than CAP/CTM assay, especially for HBV DNA samples with low viral load. The two methods showed good consistency in detecting HBV DNA. For patients who did not achieve HBsAg serologic conversion, 91.2%(34/37) of CAP/CTM v2.0 positive samples were 97.3% (36/37) tested positive for HBV DNA by ddPCR. However, HBV DNA was detected by ddPCR in 85.0% (17/20) of samples, compared with <20 IU/ml by CAP/CTM v2.0. ddPCR analysis detected HBV DNA in 97.3% (36/37) of the samples, while the CAP/CTM v2.0 method did not detect HBV DNA, with DNA levels ranging from 16.67 IU/mL to 3623.21 IU/mL. The viral load quantified by ddPCR was significantly higher than that by CAP/CTM v2.0 assay (P<0.01). ddPCR assay can be used as a good alternative diagnostic marker for HBV, thus revealing the accuracy of true viremia in HBV infection.

Abstract Submission No. 101450

O-0113

Risk factors for low level viremia in chronic hepatitis B patients receiving antiviral treatment

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Background: Available antiviral agents have demonstrated the ability to suppress HBV DNA replication and reduce the risk of liver-related complications and some patients continue to experience low-level

viremia (LLV) which is defined as HBV DNA <2000 IU/ml. In this study, we aimed to evaluate the incidence and the factors that influence low-level LLV in patients with CHB receiving antiviral treatment.

Methods: This multicenter retrospective observational study included CHB patients who had received antiviral treatment and univariate and multivariate logistic regression analyses were conducted to investigate the risk factors for LLV.

Results: A total of 2455 patients from 32 centers included in the study. At the end of 1 year, incidence of LLV was 13.6%. To evaluate the risk factors for LLV, patients were divided into two groups as LLV and sustained virological response (SVR). Results of the univariate and multivariate logistic regression analyses are given in Table 1. Multivariate logistic regression analyses showed that patients with HBeAg positive serostatus, cirrhotic status, higher albumin levels and pretreatment HBV DNA levels > 1.000.000 IU/ml has increased risk for LLV. No significant difference was observed between patients receiving entecavir and tenofovir in terms of LLV.

Conclusion: Studies have demonstrated that a significant proportion of CHB patients, ranging from 20% to 40 maintain LLV. Results of this study emphasize that patients with HBeAg positive serostatus, cirrhotic status, higher albumin levels or pretreatment HBV DNA > 1.000.000 IU/ml has higher risk for LLV and should carefully monitored.

Abstract Submission No. 101537

O-0114

Coffee consumption on advanced fibrosis and cirrhosis among hepatitis B patients: Meta-analysis

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Background: Coffee consumption has preventive effect on liver fibrosis and cirrhosis among patients with hepatitis C and NAFLD. Existing evidence on its effect on hepatitis B are limited and contradicting.

Methodology: Literature search was done through PubMed, MEDLINE and google scholar. Four studies with total of 6413 hepatitis B patients were reviewed which correlated coffee consumption on advanced fibrosis and cirrhosis using risk ratio (RR). The cut-off for high coffee consumption was > 2 cups of coffee per day in three studies and consumption of coffee 4 to 7 days per week in one study.

Results: The summary estimate for any coffee consumption vs no consumption on cirrhosis was RR 0.96 (95% confidence interval [CI], 0.73-1.27). Summary estimate for advanced fibrosis for any coffee consumption vs no consumption was RR 0.69 (95% CI, 0.45-1.03). Comparison of low coffee consumption vs no consumption on cirrhosis showed RR 1.10 (95% CI, 0.82-1.49) and on advanced fibrosis showed RR 0.90 (95% CI, 0.53-1.54). In terms of high coffee consumption on cirrhosis RR 0.71 (95% CI, 0.48-1.05) while on advanced fibrosis was RR 0.62 (95% CI, 0.39-0.99). Results showed that the presumed effect of coffee consumption on prevention of liver fibrosis and cirrhosis was not observed in this study.

Conclusion: Among hepatitis B patients, coffee consumption has no effect on prevention of cirrhosis, whereas there is a trend towards advanced fibrosis among coffee drinkers. Limitations of this meta-analysis include varied cutoff values of outcome measurement, treatment status of HBV and level of ALT.

Abstract Submission No. 101546

O-0115

Lower HBcrAg level associates with higher spontaneous HBeAg seroclearance rate in CHB patient

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Background and aims: Hepatitis B e antigen (HBeAg) seroclearance is crucial in the management of chronic hepatitis B (CHB). This study aimed to elucidate the role of hepatitis B core-related antigen (HBcrAg) level, a biomarker for cccDNA, in predicting spontaneous HBeAg seroclearance in treatment-naïve HBeAg-positive CHB patients.

Methods: This retrospective cohort study involved 484 treatment-naïve HBeAg-positive CHB patients with extended follow-up at the National Taiwan University Hospital. The study explored the association of baseline and kinetics of HBcrAg levels with spontaneous HBeAg seroclearance rate over time.

Results: Of 484 patients, 331 experienced spontaneous HBeAg seroclearance during 3376.73 person-years of follow-up, with a mean seroclearance rate of 8.76% per year. Lower baseline HBcrAg level (log rank $P < .001$) was associated with a higher chance of HBeAg seroclearance by univariate analysis. By multivariate analysis, persistently low (HR: 2.43; 95% CI: 1.53-3.85) and decreasing to below (HR: 2.53; 95% CI: 1.97-4.65) 10^5 KU/mL at year 3 of follow-up were independent factors associated with spontaneous HBeAg seroclearance. In a subgroup analysis of 208 immune-tolerant patients, lower baseline HBcrAg level and a decline of HBcrAg were independently associated with higher rates of spontaneous HBeAg seroclearance

Conclusions:

HBeAg-positive CHB patients maintaining HBcrAg levels below 10^5 KU/mL or achieving a decrease to below this threshold during follow-up are associated with a higher likelihood of clearing HBeAg spontaneously. These findings highlight the potential utility of HBcrAg as a prognostic marker in predicting the clinical course and directing management decision in HBeAg-positive CHB patients.

Abstract Submission No. 101591

O-0116

Efficacy and safety of tenofovir alafenamide fumarate in chronic hepatitis B patients in real world

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Background: Tenofovir alafenamide fumarate (TAF) has been treated in chronic hepatitis B (CHB) patients since 2018 in China. We aimed to assess the long-term efficacy and safety of TAF in a real-world setting.

Methods: Treatment-naïve and treatment-experienced CHB patients who received TAF were included. Serum levels of hepatitis B virus (HBV) DNA, hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) were analyzed at baseline, 24, 48, 72, 96, 120, 144, 168 and 192 weeks by immunoassays. Serum levels of alanine

aminotransferase (ALT), triglyceride (TG), total cholesterol (TC) and low-density lipoprotein-cholesterol (LDL-C) were measured by biochemistry assay. Kidney function was measured by estimated glomerular filtration rate (eGFR) as per Cockcroft-Gault. Controlled attenuation parameter (CAP) and liver stiffness measurement (LSM) were analyzed by transient elastography.

Results: In total of 144 CHB Patients were followed up for 204 weeks. Fifty (34.72%) patients were treatment-naïve (38% patients were HBeAg positive) and 94 (65.28%) patients switched from other NAs (47.87% patients were HBeAg positive). Among treatment-naïve patients, the ALT normalization rate was 96% (48/50), the complete virological response (HBV DNA <20 IU/ml) rate was 76% (38/50) and the HBeAg seroconversion rate was 5.26% (1/19) at 48 weeks. The levels of HBV DNA and HBsAg were significantly decreased from the $5.27 \pm 1.29 \log_{10}$ IU/ml at baseline to $1.32 \pm 0.27 \log_{10}$ IU/ml and from $3.63 \pm 0.72 \log_{10}$ IU/ml to $3.44 \pm 0.73 \log_{10}$ IU/ml, respectively. LSM was significantly decreased from 13.15 ± 8.01 kPa at baseline to 8.32 ± 4.93 kPa at 48 weeks of treatment. No significant differences were observed in the levels of TG, TC, LDL-C, CAP and eGFR. Among treatment-experienced patients, decline of HBV DNA and HBsAg levels were also found. Most of patients had renal deterioration during TDF (76%) who were with eGFR <60 mL/min reversed to eGFR increase after 48 weeks of TAF treatment ($P = 0.017$). In patients with eGFR between 60 and 89 mL/min, the estimated eGFR decrease during TDF was halted after switching to TAF ($P = 0.06$).

Conclusions: TAF was effective and well-tolerated in present CHB cohort in real-world setting. Switching to TAF is conducive to the decline in HBV DNA and the improvement of kidney function.

Abstract Submission No. 101657
O-0117

A Model to Identify the Starting of Antiviral Therapy in Gray Zone Patients with Chronic Hepatitis B

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Introduction: Individuals who do not fit to any stage of natural history of chronic hepatitis B (CHB) are classified as gray zone; however, the management of these patients remains unclear. Here, we developed and validated a nomogram to predict the starting of antiviral therapy in gray zone patients.

Methods: We retrospectively collected 200 gray zone patients as no need to start antiviral therapy using non-invasive parameters (uncertain antiviral therapy, UAT) from 2010 to 2023 in 6 medical centers. Uni-variate and multi-variate regression analysis were performed to identify the independent variables for establishing the nomogram to

predict the probability of patients who need antiviral therapy using the gold standard of liver biopsy. Furthermore, the nomogram was test by the area under receiver operating characteristic curve (AUROC), calibration plot and decision curve analysis.

Results: A total of 200 UAT patients were retracted and 78 patients (n=39%) were identified to start antiviral therapy. Age (OR 1.05, 95%CI 1.01-1.10), alanine aminotransferase (OR 2.53, 95%CI 1.14-5.62), lymphocyte percentage (OR 6.57, 95%CI 1.23-34.58), platelet count (OR 0.99, 95%CI 0.99-1.00), and international normalized ratio per (0.01) (OR 1.06, 95%CI 1.00-1.12) were identified to generate the nomogram, which showed the good discrimination (Development set: AUROC=0.755; Validation set: AURUC=0.707), calibration and clinical applicability. Patients with score >197 had high probability and those with score ≤132 had low probability for starting antiviral therapy.

DISCUSSION: Antiviral therapy should be considered in gray zone patients and the non-invasive nomogram is promising for rapid screening patients who need antiviral therapy.

Abstract Submission No. 101716
O-0118

Biochemical and Serological Characterization of Chronic Hepatitis B Infection in Sylhet

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Introduction: The World Health Organization (WHO) recognized hepatitis B virus globally as one of the commonest health problems [1]. Inactive or active chronic infection of hepatitis B virus can exaggerate the possibilities of hepatic insufficiency, end-stage liver disease including liver cirrhosis (LC) and hepatocellular carcinoma (HCC) [2].

Objective: This retrospective study was done to see biochemical and serological activity of hepatitis B virus in incidentally detected hepatitis B virus infected patients.

Methods: Available demographic and laboratory data of incidentally detected patients of chronic hepatitis B virus infection were retrieved from record and analysis using SPSS version 20. Mean and SD for continuous data and percentage of categorical data were calculated.

Result: Total 276 patients, age ranging from 13 to 60 years (mean 29.38), male 225 (81.5%) were enrolled. Of them 147 (53.3%) were in 26 - 40 years age group. In this series, 157 (56.9%) and 54 (19.6%) had history of saloon shave and family history of liver disease respectively. Alanine aminotransferase (ALT) of them varied from 15 to 367 IU/dl (mean 51.54). Of them 37 (13.4%) had HBeAg positive and 17 (6.2%) had fatty liver in ultrasound. HBV DNA was seen in 115 patients with 32 (27.82%) had DNA load above 100,000 copies per ml.

Conclusion: Asymptomatic and incidentally detected chronic hepatitis patients may have significant biochemical and serological viral activity requiring antiviral treatment.

Abstract Submission No. 101767
O-0119

Effectiveness of HBV Vaccination in Hemodialysis Patients negative for Anti-HBs

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Background: Despite the national HBV vaccination program, hepatitis B (HBV) infection remains a significant health concern in Taiwan, especially in hemodialysis patients because of potential viral exposure. This study aimed to assess the effectiveness of HBV vaccination in hemodialysis patients negative for anti-HBs.

Methods: Hemodialysis patients without protective anti-HBs were prospectively enrolled from the National Taiwan University Hospital and local clinics, categorized as “HBV-naïve” or “resolved-HBV” [HBsAg negative, anti-HBc positive]). Engerix-B 40 mg was administered at 0, 1, 2, and 6 months. Serum anti-HBs level was evaluated at the first, 6th, and 12th month post full vaccination, and participants were categorizing as responders or non-responders (anti-HBs < 10 mIU/mL). Selected patients with a pre-study vaccine history received a booster vaccination.

Results: Between March 2019 and September 2023, 106 patients, with 100 completing the 4-dose vaccination, were enrolled. Among them, 65 were HBV-naïve, and 35 had resolved-HBV. HBV-naïve patients achieved anti-HBs > 10 mIU/mL at 58% (N=24/41), 70.4%(N=31/44), 76.3%(N=29/38), and 75%(N=27/36) at 1, 6, 12, and more than 12 months post-vaccination, respectively. Resolved HBV patients exhibited vaccine responses of 67.7% (N=21/31), 66.7%(N=10/15), 80%(N=4/5), and 33.3%(N=2/6), respectively. For 6 patients (5 HBV-naïve, 1 resolved HBV) receiving a booster vaccination, the anti-HBs positive rate was 100% at the 12th month.

Conclusion: Hemodialysis patients lacking anti-HBs achieved 70% response rate to HBV vaccination in HBV-naïve and resolved HBV groups. HBV vaccination for hemodialysis patients without protective anti-HBs is thus feasible and should be routinely implemented.

Abstract Submission No. 101807

O-0120

ALG-000184 ± ENTECAVIR RESULTS IN SUBSTANTIAL HBV ANTIGEN DECLINES IN UNTREATED HBEAG+ HEPATITIS B

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ALG-000184 is a prodrug of the potent (EC₅₀=0.63 nM) capsid assembly modulator, ALG-001075.

Part 4 Cohorts 2 and B in Study ALG-000184-201 are evaluating oral daily 300 mg ALG-000184 doses ± entecavir (ETV) in a randomized, double blind, placebo-controlled (Cohort 2) or open label (Cohort B) manner, respectively, for 96 weeks. All Cohort 2 subjects receiving ETV monotherapy receive ALG-000184 + ETV beginning at Week 12. Here we report emerging data from untreated HBeAg+ CHB subjects who have received ALG-000184 ± ETV x ≤ 52 weeks.

22 subjects were enrolled in these 2 cohorts. At Week 52, ALG-000184 ± ETV resulted in mean DNA and RNA reductions of 6.6 log₁₀ IU/mL and 4.4 log₁₀ copies/mL, respectively. The proportion of subjects achieving ≥ 0.5 and ≥ 1.0 log₁₀ declines at Week 52 were 100% and 59% for HBcAg, 86% and 72% for HBeAg, 68% and 45% for HBsAg, respectively. No serious adverse events (AEs) or treatment emergent AEs (TEAEs) leading to discontinuation have been reported. The most frequent grade ≥ 3 TEAEs were transaminase elevations (n=6), all of which resolved, returned to baseline or improved in the setting of continued dosing with study drug.

Substantial declines in HBV DNA/RNA and antigens have been observed in untreated HBeAg+ CHB subjects receiving 300 mg ALG-000184 ± ETV x ≤ 52 weeks. These data suggest ALG-000184 may lower cccDNA levels and may play a central role in future regimens designed to achieve higher rates of functional cure.

Abstract Submission No. 101812

O-0121

Major obstacles to “functional cure” with novel anti-viral therapy for CHB - a systemic review

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Background: New novel therapies targeting different steps in hepatitis B virus lifecycle are in clinical development for “functional cure”. This systemic review highlights key unresolved challenges to achieve such a cure.

Methods: We searched clinicaltrials.gov for interventional HBV trials in phases 1-3 posted January 1, 2018 - December 1, 2023. We further examined published results for novel anti-HBV compounds, focusing on antiviral strategies.

Results: The search yielded 238 records with 143 relevant to current review, covering 103 unique compounds across 15 categories. Analysis of 13 compounds with published results indicated that novel anti-HBV compounds were generally safe, but lacked a clear dose-response relationship in efficacy. Eleven out of 13 failed to achieve clinically significant and sustained declines in HBsAg levels. On-tx HBsAg decline from baseline (mean: 3.6 log₁₀ IU/mL) varied: -2.6 to 0.11 log₁₀ IU/mL, with maximum decline ranging from -0.33 log₁₀ IU/mL for CAM, -2.6 for siRNA, -2.0 for ASO to -0.11 for ASPINs. Off-treatment HBsAg decline was generally not sustained. One siRNA compound showed a 1% functional cure rate EOF, while control group

displayed a 2.2% rate. For one ASO (bepirovirsen, the only one entering phase 3), the dose-response relationship was unclear, with response divergence at week 8 among intervention groups, suggesting unknown confounding factors.

Conclusion: Few novel drugs led to HBsAg loss at EOT and even fewer achieved sustained off-tx HBsAg loss. The lack of evidence for a dose-response relationship underscores the importance of identifying unknown confounding factors for a “functional” cure in chronic hepatitis B patients.

Abstract Submission No. 101813

O-0122

ALG-000184 (100 mg) + ETV leads to stronger antiviral effects compared to ETV alone in HBeAg+ CHB

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ALG-000184 is a prodrug of the potent ($EC_{50} = 0.63$ nM) HBV capsid assembly modulator, ALG-001075.

Part 4 Cohort 1 in Study ALG-000184-201 evaluated the safety and antiviral activity of 100 mg ALG-000184 + Entecavir (ALG-000184/ETV) vs. placebo + ETV for 12 weeks in a randomized, double blinded manner in untreated HBeAg+ CHB subjects. All subjects then received open label 100 mg ALG-000184 + ETV during Weeks 12-24 followed by an 8-week follow-up period, during which ETV monotherapy was administered.

Eleven subjects randomized into the ALG-000184/ETV (N=8) and ETV (N=3) arms; baseline characteristics were similar. At Week 12, HBV DNA and RNA change from baseline (CFB) in ALG-000184/ETV and ETV arms were -5.3 vs. -4.0 $\log_{10}$ IU/mL and -2.8 vs. -0.3 $\log_{10}$ copies/mL, respectively. After adding ALG-000184, ETV subjects demonstrated similar CFB at Week 24 as ALG-000184/ETV subjects, -6.4 vs -6.9 $\log_{10}$ IU/mL (HBV DNA) and -3.9 vs -4.1 $\log_{10}$ copies/mL (HBV RNA), respectively. After switching to ETV monotherapy, antiviral effects diminished; the Week 8 follow up visit CFB was -5.2 $\log_{10}$ IU/mL for HBV DNA and HBV RNA returned to baseline. Three ALG-000184/ETV subjects exhibited a ≥ 0.4 $\log_{10}$ IU/mL (maximum reduction = 0.74 $\log_{10}$ IU/mL) HBsAg decline; HBsAg returned to near baseline levels after stopping ALG-000184. No serious adverse events (AEs) or discontinuations due to AEs were reported. All AEs were grade 1-2.

Dosing of untreated HBeAg+ CHB subjects with 100 mg ALG-000184 + ETV x ≤ 24 weeks was well tolerated and had greater antiviral effects compared with ETV alone.

Abstract Submission No. 101816

O-0123

ALG-000184 has favorable antiviral effect & safety in untreated Asian/non-Asian HBeAg- CHB subjects

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ALG-000184 is a prodrug of the the potent ($EC_{50} = 0.63$ nM) capsid assembly modulator, ALG-001075.

Part 3 in Study ALG-000184-201 utilized a double-blind, randomized, placebo-controlled design and evaluated once daily oral dosing with 10-300 mg ALG-000184 x 28 days in untreated Asian/non-Asian CHB subjects who were HBeAg + or -. Previously, a favorable safety profile, dose proportional pharmacokinetics (PK), and significant HBV DNA and RNA declines were reported in Part 3. Here we report the comparative safety, PK, and antiviral activity profile of Asians versus non-Asians in Part 3.

9 Asian and 14 non-Asian HBeAg- CHB subjects were enrolled and received 10, 50, or 100 mg of ALG-000184 x 28 days; all HBeAg+ (n=25) subjects were Asian. ALG-001075 exposures were higher in Asians vs. non-Asians following correction for body weight. Mean baseline values of HBV DNA and RNA were similar across the 2 groups as were mean reductions (SEM) from baseline of HBV DNA and HBV RNA, which were 3.4 (0.2) $\log_{10}$ IU/mL and 1.6 (0.4) $\log_{10}$ copies/mL in Asians and 3.4 (0.1) $\log_{10}$ IU/mL and 1.5 (0.2) $\log_{10}$ copies/mL in non-Asians, respectively. No serious adverse events (AEs) or treatment emergent AEs (TEAEs) leading to discontinuation were reported in either population. All reported TEAEs were mild to moderate in severity with no meaningful imbalances across the 2 groups. Dosing x 28 days with 10-100 mg ALG-000184 had comparable safety, tolerability, PK and substantial antiviral activity among untreated Asian and non-Asian HBeAg- CHB subjects.

Abstract Submission No. 101836

O-0124

Mutational Effects on HBsAg in Occult Hepatitis B among Pregnant Women: In-silico Study, Indonesia

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Hepatitis B surface antigen (HBsAg) is used to detect hepatitis B virus (HBV) infection in most screening programs. This testing strategy may overlook occult hepatitis B infection (OBI), which is a growing concern because of its transmissibility, clinical impact, and wide global

distribution. HBV gene variants linked to OBI have been identified; however, expense and time preclude in vitro functional definition. Seven pregnant women with OBI and four with overt HBV were investigated. Among the OBI cases, three mutations (K122I, T126N, and V177M) were discovered in the HBsAg 'a' determinant region. Phylogenetic analysis showed that V177M, T126N, and K122I were HBV genotypes C and B, respectively. Serotyping showed adr for V177M, ayr for T126N, and unknown for K122I. Protein models were constructed using AlphaFold2, verified with Ramachandran plots, and refined with Galaxyrefine2. Based on detected mutations, mutagenesis created models with above 95% validity for each mutant. Molecular dynamics simulation of the model proteins identified four pathways that caused HBsAg detection failure: altered protein compactness, altered residue interactions, impaired HBsAg double loop formation, and altered protein-solvent interactions. This study represents the few to employ in silico modelling and molecular dynamics to assess OBI-associated mutations, providing valuable insights for future research.

Abstract Submission No. 101871

O-0125

HBV recurrence after liver transplantation associated with non-compliance to "Up to seven" criteria

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Aim: To investigate risk factors for hepatitis B virus (HBV) recurrence after liver transplantation (LT) in patients with hepatocellular carcinoma (HCC).

Methods: This retrospective study analyzed patients with HCC secondary to HBV infection and had LT from February 15th, 2015 to February 18th, 2019 at a referral hospital. Patients were classified into those with HBV recurrence and those without. HBV recurrence was defined as HBV DNA or HBsAg positive. Univariate and multivariate analysis were used to explore the risk factors for HBV recurrence.

Results: A total of 112 eligible patients from February 15th, 2015, to February 18th, 2019, were included. Those with HBV recurrence after LT had higher prevalence of preoperative detectable HBV DNA ($P = 0.001$), microvascular thrombosis ($P = 0.020$), beyond "Up to seven" criteria ($P < 0.001$), longer maximum tumor diameter (6.3 cm vs. 2.0 cm, $P < 0.001$), a greater number of tumors (2.5 vs. 1, $P = 0.017$), and a more advanced TNM stage (III+IV: 58.3% vs. 16.5%, $P = 0.001$). Twelve (10.71%) patients experienced HBV recurrence after LT. The median recurrence time was 15.0 (6.5, 21.1) months after LT. All HBV recurrence were accompanied with HCC recurrence. Multivariate analysis highlighted that beyond "Up to seven" criteria (OR:7.99, 95%CI:1.19-53.49, $P = 0.032$), cholangiocellular carcinoma (OR:116.7, 95%CI:6.06-2250.5, $P = 0.002$) were independent risk factors for HBV recurrence.

Conclusions: HBV recurrence was associated with HCC recurrence. Preoperative HCC patients with beyond "Up to seven" criteria had higher risk for HBV recurrence after LT.

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O-0126

Different guidelines on classification of grey zone in those with normal ALT and detectable HBV DNA

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Background and Aims: Patients with CHB who do not meet traditional natural immune phases are considered to be in grey zone (GZ). The criteria for this classification, specifically the thresholds for HBV DNA and ALT, vary among different guidelines. We explored the effect of different guidelines (CSH/CSID, 2022 version vs. AASLD, 2018 version) on classification of GZ in patients with normal ALT and detectable HBV DNA.

Method: A total of 1843 naive CHB patients with ALT<1×ULN undergoing liver biopsy during August 2013 through June 2023 from six hospitals were retrospectively analyzed. Hepatic histology was assessed by Scheuer scoring system, significant inflammation and fibrosis were defined as ≥G2 and ≥S2, respectively.

Results: The median HBV DNA of the 1843 patients were 4.3 (IQR 2.9-7.6) log₁₀ IU/mL. Overall, 38.0% and 52.3% of 1843 patients fell into GZ based on AASLD and CSH/CSID guideline, respectively. Over 30% of patients were classified into immune active phases as per CSH/CSID. Compared with GZ patients according to AASLD, those under CSH/CSID guidelines showed lower ALT, AST and rate of significant hepatic inflammation (20.2% vs. 26.2%, $p=0.005$) and fibrosis (38.8% vs. 45.5%, $p=0.007$). Higher AST, age > 40 and HBeAg positive are independent risk factors of significant fibrosis in GZ patients according to both AASLD and CSH/CSID guidelines.

Conclusion: In CHB patients with normal ALT, a greater proportion were categorized into GZ according to 2022 CSH/CSID guideline, though pathological changes are relatively mild. Among them, patients aged > 40 and with HBeAg positive need aggressive antiviral therapy.

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O-0127

Efficacy and safety of xalnesiran with and without an immunomodulator in chronic hepatitis B

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Background: PIRANGA (NCT04225715) is a phase 2 platform study designed to evaluate safety and efficacy of therapies including one or more new molecular entities in chronic hepatitis B (CHB) participants, to achieve higher functional cure rates than standard of care. We report primary endpoint results of xalnesiran, a small interfering ribonucleic acid (siRNA) in combination with nucleos(t)ide analogues (NUC), with or without an immunomodulator: pegylated interferon alfa-2a (Peg-IFN- α), or ruzotolimod (toll-like receptor 7 agonist).

Methods: HBeAg positive or negative virologically suppressed CHB participants on established NUC therapy were randomized into the study arms (see table) with a minimum of 12 participants per arm with HBsAg <1000 IU/mL. Participants were treated for 48 weeks and the primary endpoint was the proportion of participants with HBsAg loss (<0.05 IU/mL) 24 weeks post-end of treatment (EOT).

Results: 160 participants were enrolled. The majority were male (83%), Asian (94%), with a mean (range) age of 42 (24-65) years. At baseline, 70% were HBeAg negative, 98% had normal ALT levels with a mean (SD) serum HBsAg level of 2.82 (0.92) log₁₀ IU/mL. At 24 weeks post-EOT, HBsAg loss was observed in 2/30 (7%), 1/30 (3%), 7/30 (23%), 4/34 (12%) participants from Arms 1-4 and in no participants from the NUC control arm. All participants with HBsAg loss had undetectable HBV RNA and baseline HBsAg level <1000 IU/mL. Safety findings were consistent with the individual modalities.

Conclusion: Xalnesiran therapies were generally safe and well tolerated. HBsAg loss rates were higher when xalnesiran was combined with immunomodulators (Peg-IFN- α or ruzotolimod).

Abstract Submission No. 101933

O-0128

Clinical outcomes of HBeAg-negative CHB patients in indeterminate phase with normal ALT

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Background: A substantial proportion of patients with chronic hepatitis B (CHB) may fall into indeterminate phase. This study investigated the phase transition and disease progression of hepatitis B e antigen (HBeAg) negative CHB patients in indeterminate phase with normal alanine aminotransferase (ALT).

Methods: Four hundred and fourteen consecutive HBeAg-negative indeterminate phase CHB patients with normal ALT were retrospectively enrolled from three medical institutions. Significant liver fibrosis and cirrhosis were assessed by noninvasive indexes.

Results: The median age was 38.5 years and 54.3% were male. The proportion of patients transitioned to immune active phase, inactive

phase and remained in indeterminate phase were 21.3%, 26.3%, and 52.4% after a median follow-up of 21.0 months, respectively. HBV DNA $\geq 20,000$ IU/mL (HR 2.074, P=0.001) and HBsAg $\geq 1,000$ IU/mL (HR 1.626, P=0.031) were significant predictors of transition to active phase. Eleven (25.0%) and 5 (11.4%) patients who transitioned to active phase progressed to significant liver fibrosis and cirrhosis respectively, while only one patient (0.8%) who remained in indeterminate phase developed significant liver fibrosis. Patients who transitioned to active phase (HR 32.093, P=0.001) had a higher risk of significant fibrosis development than those remained indeterminate.

Conclusions: About one fifth of HBeAg-negative indeterminate phase patients with normal ALT transitioned to active phase, and half of these patients remained in indeterminate phase. The levels of HBV DNA and HBsAg were significant predictors of phase transition. Transitioning to active phase had a higher risk of liver fibrosis and cirrhosis development in these patients.

Abstract Submission No. 101944

O-0129

Clinical outcomes of HBeAg-negative CHB patients with HBsAg less than 100 IU/ml

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Background: HBsAg level <100 IU/ml and undetectable HBV DNA has been proposed as an alternate endpoint of "partial cure" in chronic HBV infection. We investigated outcomes of HBeAg-negative chronic HBV-infected patients with HBsAg <100 IU/ml and undetectable HBV DNA.

Methods: Consecutive untreated HBeAg-negative patients with chronic HBV infection with normal ALT and undetectable HBV DNA were enrolled from three medical institutions. Patients were divided into low HBsAg group (<100 IU/ml, "partial cure", n=501) and high HBsAg group (≥ 100 IU/ml, n=717). Liver fibrosis was assessed by noninvasive tests (NITs) including APRI, FIB-4 or transient elastography.

Results: Of 1218 patients, the median age was 41.5 years and 51.3% were male. Patients with low HBsAg were older (45.0 vs. 40.0 years, P<0.001) than those in high HBsAg group, while NITs parameters including APRI, FIB-4 or transient elastography were comparable between groups. A total of 309 patients without significant fibrosis at baseline had available follow-up data. During a median follow-up 25.7 months, patients with low HBsAg were more likely to achieve HBsAg clearance (13.0% vs. 0%, P<0.001), while had a lower risk of significant liver fibrosis development (2.2% vs. 7.0%, P=0.020) compared to high HBsAg group. No patients developed HCC in both groups. Serum HBsAg <100 IU/ml was associated with higher chance of HBsAg clearance (HR 76.034, P=0.026) and low risk of significant fibrosis development (HR 0.045, P=0.002).

Conclusions: Patients with "partial cure" had favorable outcomes with a high rate of HBsAg clearance and low risk of fibrosis progression.

Abstract Submission No. 101958

O-0130

HBeAg-positive CHB patients in indeterminate phase associated with high risk of significant fibrosis

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Background: The risk of liver fibrosis in HBeAg-positive chronic hepatitis B (CHB) patients with indeterminate phase remains unclear. We aimed to compare the risk of liver fibrosis in HBeAg-positive CHB patients between indeterminate phase and immune-tolerant phase.

Methods: This multi-center, retrospective cohort study included 719 treatment-naïve HBeAg-positive CHB patients with normal alanine aminotransferase (ALT). Patients with HBV DNA >10⁶ IU/mL were categorized into immune-tolerant phase according to the AASLD 2018 hepatitis B guidance, whereas those with HBV DNA ≤10⁶ IU/mL were classified into indeterminate phase. Significant liver fibrosis and cirrhosis were determined by APRI, FIB-4, transient elastography, or liver biopsy.

Results: The median age of patients was 33.0 years and 59.8% of patients were male. 81.5% and 18.5% of patients were in the immune-tolerant phase and indeterminate phase, respectively. The APRI (0.33 vs. 0.27, P<0.001), FIB-4 (1.08 vs. 0.72, P<0.001), and liver stiffness values (7.80 kPa vs. 5.65 kPa, P=0.011) were higher in the indeterminate phase than patients in the immune-tolerant phase. Patients in the indeterminate phase had higher proportions of significant fibrosis (27.1% vs. 11.3%, P<0.001) and cirrhosis (14.3% vs. 3.2%, P<0.001) compared to those in the immune-tolerant phase. In the multivariate logistic regression, indeterminate phase (OR 2.138, 95% CI 1.253, 3.649, P=0.005) was associated with higher risk of significant fibrosis, especially for patients aged ≥30 years.

Conclusion: HBeAg-positive CHB patients in the indeterminate phase had higher risk of significant liver fibrosis compared to immune-tolerant phase.

Abstract Submission No. 101964

O-0131

Multi-method analysis identifies genotypes in all evaluated participants on-NA, B-Together study

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Background: In B-Together, 9-15% of participants with chronic hepatitis B virus (HBV) infection on background nucleos(t)ide analogs (NAs) receiving sequential bepirovirsens and pegylated interferon-α-2a (bepirovirsen+Peg-IFN) therapy achieved the primary outcome of hepatitis B surface antigen (HBsAg) and HBV DNA

< lower limit of quantification maintained for 24 weeks off-treatment. This post hoc analysis investigated HBV genotype (GT) using a three-tiered genotyping methodology.

Methods: HBV GTs in virally suppressed participants were determined using medical history, HBV sequencing, and a serology method (IMMUNIS® HBV Genotype EIA by Institute of Immunology Co.).

Results: The three methodologies had a high degree of concordance (75-100%) and determined GT for 101/108 (94%) participants. By contrast, medical history and HBV DNA/RNA sequencing alone were only successful in identifying GT in 50% of participants. GT-C and GT-D were the most common; GT-B the least (**Table**). GT-B (n=3/4) and GT-C (n=30/37) were predominantly identified in Asia; GT-A (n=14/16) and GT-D (n=30/34) in Europe. Virological response to bepirovirsens was observed across all common HBV GTs. Baseline HBsAg varied markedly by GT. Analysis of the relationship between HBV GT and treatment response is currently ongoing across studies exploring the efficacy of bepirovirsens-containing regimens.

Conclusions: This innovative three-tiered approach identified HBV GTs in all tested participants on NAs. GT analysis of participants in trials for novel HBV therapies is an important tool to understanding disease heterogeneity in chronic HBV infection.

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O-0132

ScRNAseq reveals high expression of CXCL8 resident immune cells with fibrosis in low HBsAg patients

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Background and Aims: Chemokine ligand 8 (CXCL8) is suggested as a potential biomarker in assessing the progression and severity of nCHBV patients. Analysis of CXCL8 expression in naïve CHBV patient's liver and blood may provide insights of immune activation and inflammation.

Methods: We have included liver biopsies and plasma specimens from 36 naïve nCHB patients, stratified into two groups based on HBsAg levels: Group I (HBsAg^{lo}, n=9) with HBsAg < 2000 IU/mL and Group II (HBsAg^{hi}, n=27) with HBsAg > 2000 IU/mL. with HBV DNA < and >2,000 IU/mL, with increased ALT/AST >1.2 x ULN. Comprehensive histopathological analysis, quantification of plasma cytokine levels using cytokine bead array in all patients and single-cell RNA sequencing of liver biopsies in three patients in each group was performed.

Results: Patients with low HBsAg levels showed advanced mean fibrosis scores of 2.62±1.76, while high HBsAg patients had mean fibrosis scores of 0.68±0.87. Lower HBsAg levels correlated with increased IL-8 (p=0.027) compared to higher HBsAg levels in plasma. Single-cell RNA sequencing of liver biopsies from low HBsAg patients compared with high HBsAg patients revealed elevated CXCL8 expression (p=0.0007) associated with intrahepatic CD4 effector memory (p=0.038) and CD8 naïve (p=0.017) cells, contrasting with high HBsAg levels. Individuals with low HBsAg exhibited a correlation between high expression of CXCL8, IL-8, and a higher fibrosis score (p=0.008).

Conclusions: Intrahepatic CXCL8 from CD4 effector memory and CD8 naïve cells contribute to increased IL-8 secretion, contributing to advanced fibrosis in nCHB patients with low HBsAg.

Abstract Submission No. 102017
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Virological and histological characteristics of chronic hepatitis B virus patients with normal ALT.

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Background and aims: Patients with chronic hepatitis B virus (HBV) infection and persistently normal ALT levels have whether abnormal liver histology or not is crucial for treatment. At present worldwide available most of the guideline recommends treatment depending on serum ALT level, which may miss significant number of liver disease. We studied the ALT, HBV DNA levels, and spectrum of histologic lesions in such patients.

Methods: It was a cross sectional observational study among the chronic hepatitis B virus infected patients presented in the DMCH who shows persistently normal ALT and detected HBV DNA load. Total 104 patients were enrolled in the study and undergone liver biopsy (n=104; hepatitis B e antigen [HBeAg+], 82; hepatitis B e antigen [HBeAg-] 22).

Results: Among 82 HBeAg negative cases, there were 12(14%) moderate chronic hepatitis and 26(31%) showed mild chronic hepatitis. HBeAg positive cases also 8(27%) had moderate chronic hepatitis and 8(36%) had mild chronic hepatitis. 62% of HBeAg-positive and HBeAg-negative patients persistent normal ALT had baseline HBV DNA levels of >3.3 log copies/mL. Serum HBV DNA level and spectrum of histological changes doesn't correlate. 60 (73.1%) HBeAg negative and 14 (63.6%) HBeAg positive patients had Knodell score > 7.

Conclusion: A fair proportion of patients with chronic HBV infection with persistent normal ALT have HBV DNA >3.4 log copies/ml and significant histologic fibrosis in both HBeAg positive and HBeAg negative groups. Use of ALT and HBV DNA levels without liver biopsy may miss histologically significant disease in a proportion of patients.

Abstract Submission No. 102039
O-0134

Investigation of HBV cccDNA-bound proteins in liver biopsies from HBV for Therapeutic targeting

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Aims: Present study aims to examine the potential roles of cccDNA-bound proteins in HBV reactivation, silencing and contribution to viral replication in the progression of the infection. Identification of cccDNA-bound proteins in both HBeAg-positive (high replicating group) and HBeAg-negative patients (Low replicating group) may aid in better management of HBV patients.

Methods: We obtained 14 liver biopsies from patients with chronic hepatitis B. We divided into two groups: HBeAg negative (n=7) and HBeAg positive (n=7). We also measured blood HBsAg levels (log₁₀ IU/ml 3.21±1.09 >6 months) and HBV DNA levels (log₁₀ IU/ml 4±1.09). The single-stranded portion of HBV cccDNA was used as a template to synthesise biotinylated DNA oligos. Nano liquid

chromatography combined with mass spectrometry (nano LC/MS) was used after the pull down was used to extract cccDNA and binding proteins from the nuclear extract of liver tissues of HBeAg+ and HBeAg-patients.

Results: Out of the 300 bound proteins in the HBeAg+, a total of 900 were down-regulated (≤0.5-fold) and 300 were considerably elevated (≥2-fold). In HBeAg+ several proteins were found to be increased (≥2-fold), whereas others were downregulated (≤0.5-fold): cul4B, RACK1, DNA damaging binding protein 2, and repressor bound proteins DDx17, DDx5, METTL4, and PRDX1. Using siRNA in vitro (HepG2.2.15), we were able to identify the top three proteins DDB2, RACK1, and Cul4B expressed in HBeAg positive group. These proteins were shown to be directly associated to the expression of HBV parameters such as HBsAg (p<0.001), HBeAg (p<0.001), pgRNA (p<0.005), HBV DNA (p<0.005), and cccDNA (p<0.005).

Conclusion: A correlation between viral load and cccDNA-bound proteomes. The high viral replicating group validated the identification of DDB2, Cul4B, and RACK1 as new nuclear cccDNA-bound proteins

Abstract Submission No. 200111
O-0135

Functional HBsAb responses induced by BRII-179 are strongly associated with improved HBsAg loss

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Background: BRII-179, a therapeutic vaccine comprised of PreS1, PreS2 and S HBsAg, showed no new safety observation and improved HBsAg loss at end-of-treatment (PPS: 32.6% vs. 21.6%) and 12-week post EOT in a randomized, double-blind, placebo-controlled phase 2 study as an add-on therapy in CHB patients receiving PEG-IFNα. Here, we report the data on patients meeting NRTI discontinuation criteria.

Methods: 114 Chinese HBeAg negative virally suppressed CHB patients partially responding to 24-28 doses of PEG were randomized 1:1 to BRII-179 or placebo every 3 weeks for 7 doses with PEG continued for another 24 weeks. Eligible patients with HBsAg <0.05 IU/mL for 2 consecutive assessments at 12-24 weeks post EOT would be eligible to discontinue NRTI.

Results: 3 (5.3%) vs 1 (1.8%) patient in BRII-179 vs placebo group had AEs that led to BRII-179/placebo discontinuation. 4 treatment related SAEs were reported including 2 related to PEG and 2 related to PEG and BRII-179. By 24-week post EOT, BRII-179 group had higher percentage of patients met NRTI discontinuation criteria (FAS: 26.3% vs. 15.8%) and earlier NRTI discontinuation. In addition, higher percentage of patients in BRII-179 group had maximum HBsAb titer ≥10 (45.6% vs. 14.0%) and ≥100 IU/L (19.3% vs. 3.5%). As previously reported, HBsAb ≥10 IU/L was strongly associated with sustained HBsAg loss off-treatment.

Conclusion: BRII-179 add-on was generally safe and tolerated. It induced functional immune responses and may improve CHB functional cure.

Abstract Submission No. 200115
O-0136

Everest Project's 5-Year Update: Efficacy of PegIFN- α Therapy in HBeAg- CHB Patients in China

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Background and Aims: This study aims to evaluate the efficacy and safety of pegIFN α -based therapy in real-world nucleoside analog (NA) treated chronic hepatitis B (CHB) patients and identify predictors for HBsAg loss by pegIFN α .

Method: The Everest Project, a multicenter real-world study in China, was previously introduced, focusing on the HBsAg loss of CHB (NCT04035837). Patients with over a year of NA therapy, HBV DNA <100 IU/ml, HBeAg negative, and HBsAg $\leq$ 1500 IU/ml were recruited starting in 2018. PegIFN α -2b monotherapy or combination with NA was performed. The 5-year study enrollment has now concluded, and the latest research data is presented here.

Results: Out of the total 23,412 patients recruited, 15,896 were considered mITT group, 12,260 patients were included in PP group. Of the total patients over 48-week treatment, 77.47% were male, with an average age of 41.77 years and a mean HBsAg baseline of 378.05 IU/mL. 3864 patients achieved HBsAg loss. The HBsAg loss rates were 10.75%, 22.72%, 28.72% and 31.43% at 12, 24, 36, and 48 weeks in PP group, respectively, higher than that in mITT group (figure 1A, B). Factors predicting higher HBsAg loss included a lower HBsAg baseline, reduced HBsAg levels at 12 and 24 weeks, ALT flare at the 12-week mark, younger age, female gender, and a lower BMI (figure 1C).

There were no severe adverse events during this project.

Conclusion: HBsAg loss rate could be over 30% in NA - suppressed CHB patients by pegIFN α strategy. Baseline and on-treatment predictors can better guide the achievement of functional cure.

Abstract Submission No. 200148
O-0137

The correlation between HLA-DR⁺CD38⁺CD8⁺ T cell changes and efficacy during IFN-based CHB treatment

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Aims: To investigate changes in phenotype and function of CD8⁺ T lymphocytes in chronic hepatitis B (CHB) patients undergoing interferon (IFN) and correlation with clinical response.

Methods: CHB patients were divided into three groups according to antiviral treatment. Peg-IFN α was then administered to Naïve group and nucleoside (t) ide analogues (NAs)-treated group. For Plateau group, whose hepatitis B surface antigen (HBsAg) decline reached a plateau, IFN therapy was stopped and was resumed after an interval. Peripheral blood samples were collected to detect clinical indexes, and T lymphocyte related phenotypes and functions using flow cytometry at corresponding detection points of three groups.

Results: A prospective cohort of 151 CHB patients participated in this study. During IFN treatment, HLA-DR⁺CD38^{dim} subset of CD8⁺ T cells increased and then markedly decreased, while the HLA-DR⁺CD38^{hi} subgroup increased significantly in both Naïve and NA-treated groups (P all < 0.0001). For Plateau group, the HLA-DR⁺CD38^{dim}CD8⁺ T cells increased significantly and the HLA-DR⁺CD38^{hi}CD8⁺ T cells greatly decreased after IFN intermittent treatment (P all < 0.0001). The changes of HLA-DR⁺CD38^{dim} and HLA-DR⁺CD38^{hi} subsets during IFN intermittent treatment were strongly positively correlated with the changes of HBsAg during IFN retreatment, respectively ($r = 0.4843$, $P = 0.0066$; $r = 0.4588$, $P = 0.0315$). Compared with activated HLA-DR⁺CD38^{dim}CD8⁺ T cells, HLA-DR⁺CD38^{hi} subgroup expressed lower level of co-stimulatory molecules and killing ability.

Conclusions: IFN treatment made activated HLA-DR⁺CD38^{dim}CD8⁺ T cells gradually differentiated into HLA-DR⁺CD38^{hi} subset that indicated impaired killing function. IFN intermittent therapy can reverse this trend and help restore antiviral efficacy of IFN.

KEY WORDS: Chronic hepatitis B, Interferon, CD8⁺ T lymphocyte, Antiviral therapy

Abstract Submission No. 200285
O-0138

First-in-human, first-in-class, Phase 1B preliminary safety data of VRON-0200, a novel checkpoint modifier containing immunotherapy, for HBV Functional Cure

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Background: VRON-0200 is a therapeutic vaccine for hepatitis B virus (HBV) functional cure that contains a genetically encoded checkpoint modifier (herpes simplex virus type 1 (HSV-1) glycoprotein D), fused with HBV core and polymerase antigens, to induce enhanced, broadened, and prolonged CD8⁺ T cell responses. Here we report the first-ever preliminary clinical data of VRON-0200 in patients with chronic HBV.

Methods: Chronic HBV-infected adult, virally suppressed patients, with HBsAg levels <500 IU/mL, are randomized to receive 1x10¹⁰ vp of one of 2 different chimpanzee adenoviral vectors intramuscularly. Cohort 1a receives a prime, followed by a heterologous boost, on day 91; Cohort 1b receives only the prime. A higher dose cohort, Cohort 2 (5x10¹⁰ vp), following the same dosing schedule, will begin once 12 patients in Cohort 1 reach day 28. Study assessments include safety, virologic, and immunologic parameters through one-year post-prime vaccination.

Results: Six Cohort 1 patients have been randomized and received one dose of VRON-0200 (n=3 each viral vector); all male, 5 Asian, with mean age of 44 years (range: 41-49); 5 are HBeAg-. Patients are at varying stages of follow-up: all had Days 1, 7, and 14 visits, 5 had Day 28 visits, and 2 had Day 60 visits. As of Jan. 12, 2024 (Table 1), no AEs,

SAEs, TEAEs, or laboratory abnormalities (including clinically significant ALT elevations) have been reported.

Conclusions: In this first report of safety data from VRON-0200, the prime dose has been well tolerated, with no significant safety concerns to date. The study is ongoing, and additional Cohort 1 clinical data will be presented.

Abstract Submission No. 100319

O-0139

Efficacy of hepatitis B vaccine in liver cirrhosis patients

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Aim: The literature has shown that the vaccines against hepatitis B virus (HBV) are safe and effective in patients with liver cirrhosis (LC) but the data is lacking in our country. We aimed to evaluate the response to standard hepatitis B (HB) vaccination in LC of various etiologies and compare in different stages of LC.

Method: Consecutive patients of LC negative for hepatitis B surface antigen (HBsAg) and antibody to hepatitis B core antigen (Anti HBc total) were included. All patients received three doses of HB vaccine 20µgm intramuscularly at zero, one, and six months interval. Anti-HBs antibody was measured after 90 days of last vaccine.

Results: A total of 214 patients with mean age 59.28±11.23 years were studied. Overall response rate was 92%. Response rates as per Child Pugh classes A, B and C were 98%, 100% and 61%. Ethanol related LC had less antibody response (44%) than other causes of LC (p=0.003). Poor immunogenicity was associated with low albumin and malnutrition (p=0.003). The response rate was also found to be decreased in older age group. There were no side effects except for soreness at injection sites in few patients.

Conclusions: Vaccine against HBV is safe in LC patients. Low level of albumin and presence of malnutrition was significantly associated with decreased vaccine response. As the age and liver disease progress, the response rate for HB vaccination was found to be weaker. We recommend correction of malnutrition and build up albumin level before vaccination to Child C cirrhosis patients.

Abstract Submission No. 100356

O-0140

Maternal infection with hepatitis B and maternal and neonatal outcomes

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Background: The correlation between HBV carrier status and pregnancy, as well as neonatal outcomes is clinically concerned.

Methods: We conducted a retrospective cohort study to analyze the risk factors and independent predictors of maternal and infant outcomes. Propensity Score Matching (PSM) was performed using a 1:4 matching ratio between the HBsAg (+) group and the healthy group.

Results: A total of 5,871 pregnant women received perinatal services in our hospital from January 1, 2021, to December 31, 2022. After PSM, we included 445 mothers with HBsAg (+) and 1,780 healthy mothers. The two groups were comparable after PSM. Compared to

healthy group, HBsAg (+) mothers had a higher likelihood of preeclampsia (4.0% vs. 2.2%), gestational diabetes (16.9% vs. 13.0%), intrahepatic cholestasis of pregnancy (ICP) (2.25% vs. 1.0%), and umbilical cord prolapse (0.2% vs. 0%) and had a significantly lower occurrence of oligohydramnios (6.7% vs. 9.9%) and thyroid dysfunction during pregnancy (6.3% vs. 9.7%) (all P<0.05). In multivariate logistic regression analyses confirmed a higher risk of ICP with HBV infection (OR 2.35, 95% CI 1.12-5.44). (P<0.05). Newborns of HBsAg (+) mothers had a significantly lower occurrence of birth defects (0.4% vs. 2.9%, P<0.05) compared to babies of healthy mothers. In the multivariate logistic regression analysis, maternal HBV infection was not found to be associated with birth defects (P>0.05). (See Figure 1, Table 1-3)

Conclusions: HBsAg is an independent risk factor for ICP. HBV infection does not lead to an increased risk of birth defects.

Abstract Submission No. 100358

O-0141

ETV, TDF and TAF on recurrence after curative RFA in HBeAg-negative HBV-related HCC patients

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Background: In HBeAg-negative hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC), the effect of first-line antiviral agents on recurrence-free survival (RFS) after receiving curative radiofrequency therapy (RFA) remains unclear. We aimed to compare the outcomes of HBeAg-negative HBV-HCC patients receiving ETV or TDF or TAF after RFA.

Methods: This study consecutively collected 229 patients who were treated with ETV (n = 159) or TDF (n = 46) or TAF (n=24) after RFA from June 2018 to June 2020 at Tianjin Third Central Hospital. Kaplan-Meier and Cox regression analyses were performed to validate possible risk factors for RFS.

Results: In the full cohort, the overall 3-year RFS rate was 72.9%. The 1-, 2-, and 3-year RFS rates in the TAF group were 91.7%, 83.3%, and 75.0%, respectively, which were significantly higher than that in ETV group (71.6%, 44.0%, and 39.6%), and in TDF group (67.4%, 50.0% and 43.5%), P < 0.01. Patients in the TAF group had significantly higher RFS(months) than those in the TDF and ETV groups. (31.7 vs 22.9 vs 22.7, P=0.006). In HCC patients after RFA treatment, nucleotide analogue therapy is associated with higher 2-and 3-year relapse-free survival compared with nucleoside analogue therapy.(61.4% vs 44.0% P=0.015; 55.7% vs 39.6% p=0.024). CNLC stage I, ALT below lower limit at 48 weeks and nucleotide analogue therapy were independent protective factor for early recurrence(<2year) after RFA for HCC patients(CNLC p=0.026;ALT p=0.000;NUCs p=0.026).

Conclusions: Nucleotide analogue therapy was associated with a significantly lower risk of recurrence than nucleoside analogue therapy among patients who undergo curative RFA for HBeAg-negative HBV-related HCC.TAF treatment was associated with longer recurrence-free survival in HCC patients after RFA.

Abstract Submission No. 100375

O-0142

Switching to TMF is effective for ETV or TAF monotherapy in patients with hypoviremia

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Objective: Some patients treated with ETV or TAF monotherapy may experience hypoviremia. This study aims to observe whether switching to (tenofovir amibufenamide, TMF) monotherapy can further improve the antiviral treatment benefits of these CHB patients with hypoviremia.

Method: This is a retrospective study targeting CHB patients treated with ETV or TAF monotherapy for more than 1 year, but with serum HBV DNA consistently fluctuating between 20 and 2000 IU/mL. All enrolled patients voluntarily switched to TMF for further antiviral treatment and completed comprehensive examinations at least once every 6 months. The primary outcome measure was the undetectable rate of HBV DNA after 6 and 12 months of TMF treatment, while the secondary outcome measure was the incidence of renal tubular damage and dyslipidemia.

Result: A total of 73 patients were included, including 47 patients treated with ETV and 26 patients treated with TAF. Among them, there were 33 HBeAg-positive patients and 40 HBeAg-negative patients. After switching to TMF treatment for 6 months and 12 months, 69.9% (51/73) and 74.0% (54/73) of patients achieved HBV DNA <20 IU/mL, respectively. Compared to HBeAg-positive patients, HBeAg-negative patients switching to TMF treatment can achieve a higher proportion of complete virological response (19/33 vs. 32/40, $P=0.038$; 18/33 vs. 36/40, $P<0.001$). After 12 months of treatment, the abnormal rate of urinary b2 microglobulin was 16.4% (12/73), and the proportion of urinary b2 microglobulin increasing by three times the upper limit of normal value was 6.8%. The proportion of blood phosphorus below the lower limit of normal value is 19.2% (14/73). Although the levels of total cholesterol and low-density lipoprotein cholesterol increased compared to before treatment, the differences were not statistically significant.

Conclusion: CHB Patients treated with ETV or TAF experience hypoviremia, switching to TMF can help most patients achieve a complete virological response rate, with good patient tolerance.

Abstract Submission No. 100421

O-0143

HBV PreS1 Variant Mediates the Protective Effect of NTCP S267F Variant Against HCC in CHB Patients

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Background: The S267F variant (rs2296651) in the human hepatitis B virus (HBV) entry receptor, sodium taurocholate co-transporting polypeptide (NTCP), has been previously associated with a reduced risk of hepatocellular carcinoma (HCC) development in individuals with chronic hepatitis B (CHB) infection. However, the mechanism by which the NTCP variant decreases the HCC risk remains unclear. We examined the DNA sequence of HBV preS1 domain, known as the NTCP binding domain, to assess its association with the protective effect of the S267F variant against HCC.

Methods: The HBV DNA preS1 sequences of 366 CHB patients, sequenced through PacBio, were analyzed via Cox regression, logistic

regression, and mediation analysis to predict HCC risk and evaluate the mediation effect of the HBV preS1 allele.

Results: Within the HBV preS1 domain sequence, a significant difference in the allele frequency of the adenine nucleotide at position 2956 (2956A) was observed between individuals with S267F GG genotype (mean $\pm$ SD: 0.35 ± 0.47) and those with GA/AA genotype (0.60 ± 0.43 ; $p<0.001$). Moreover, individuals with a higher allele frequency of 2956A demonstrated a reduced risk of HCC development (HR: 0.45; 95% CI: 0.29-0.69). The subsequent mediation analysis revealed that the 2956A served as a mediator in the protective effect of S267F variant against HCC, with more significant protection in the average causal mediation effect (ACME; OR: 0.87; $p<0.001$) than the average direct effect (ADE; OR: 1.07; $p=0.28$).

Conclusions: The allele 2956A within the HBV DNA preS1 domain might mediate the NTCP S267F variant against HCC.

Abstract Submission No. 100430

O-0144

Histological Characteristics in Functional Cure Post PEG-IFN-based Therapy

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Background: HBsAg seroclearance is associated with disease remission after treatment cessation. However, the histologic characteristics in patients with PEG-IFN-inducing HBsAg seroclearance have not been explored before.

Methods: Liver tissues obtained from patients with functional cure post PEG-IFN-based therapy ($n=70$). Liver pathology was evaluated by Scheuer. Intrahepatic HBsAg and cccDNA were analysed.

Results: There were 61 patients with chronic hepatitis B (CHB) and 9 patients with compensated cirrhosis received PEG-IFN based therapy and attained functional cure. Notably, 1/9 patients with prior compensated cirrhosis achieved fibrosis regression which verified by both histopathology and B ultrasound after attaining HBsAg seroclearance. In patients who have achieved a functional cure from prior CHB, it demonstrated that 13.1% and 1.6% of them presented with moderate and severe intrahepatic inflammation, respectively. Furthermore, 36.1% and 1.6% of these patients illustrated moderate fibrosis and severe fibrosis, respectively. The age, gender, NAFLD, intrahepatic HBsAg and cccDNA level between intrahepatic inflammation and none-inflammation groups showed no statistic difference. Eight functionally cure patients experienced HBsAg seroreversion. HBsAg seroreversion group exhibited a higher level of cccDNA at cessation time of PEG-IFN, with a median (Q1, Q3) of 2.2 (0.79-2.84) log copies/ 10^3 cells, compared to none HBsAg seroreversion group (0.96, 0-2.06 log copies/ 10^3 cells, $P=0.028$).

Conclusion: HBsAg seroclearance contributes to fibrosis remission in patients with prior compensated cirrhosis however, part of patients with prior chronic hepatitis B remained inflammation and fibrosis, and it warrant further study to investigate the potential influencing factors of residual inflammation.

Abstract Submission No. 100447

O-0145

Antiviral therapy can improve the health-related quality of life in CHB patients with normal ALT

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Objective: To investigate the impact of chronic HBV infection on the quality of life of patients, and whether antiviral therapy can improve the quality of life of CHB patients

Method: This is a prospective study targeting CHB patients with persistent normal ALT, negative HBeAg, and positive HBV-DNA. The quality of life was evaluated using the Specific HBV Infected Person Quality of Life Scale (HBQOLV1.0). Patients need to complete the quality of life scale at baseline and 12 months after enrollment.

Result: A total of 244 patients finally included, with 59 in untreated group and 185 in treated group. At baseline, there was no significant difference in the total HBQOL scores between the treatment and untreated groups (2121.5 vs. 2140.6, $P=0.844$). The average scores of the two groups of patients in six dimensions of psychological status, expected anxiety, contagiousness and health vulnerability, vitality, and sense of shame were all less than 75 points, and the scores of the first four dimensions were less than 70 points. After 12 months of follow-up, the total HBQOL score of the untreated group increased compared to baseline (2121.5 vs. 2140.6, $P=0.380$), but the difference was not significant. Except for the dimension of shame, the other five dimensions were higher than the baseline, but the difference was not significant. After 12 months of treatment, the total score of HBQOL in the treatment group increased with statistical significance (2280.7 vs. 2121.5, $P<0.001$). Except for the vitality dimension, the average scores of the remaining five dimensions were all higher than the baseline, and the differences were statistically significant. Among them, expected anxiety (65.0 vs. 71.4, $P<0.001$), contagiousness (66.8 vs. 74.2, $P<0.001$), and sense of shame (74.4 vs. 79.9, $P=0.003$) showed significant improvement, with a score increase of 5 points compared to before treatment.

Conclusion: Chronic HBV infection reduces the health-related quality of life. Antiviral therapy can improve the negative effects of HBV infection on patients in terms of psychological status, expected anxiety, shame, contagiousness, and health vulnerability.

Abstract Submission No. 100453
O-0146

Anti-fibrosis effect of traditional Chinese medicine compound *Biejiaaruangan* in CHB patients

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Aims: Compound *Biejiaaruangan* (CBJRG) tablet can be used to treat liver fibrosis. This study aimed to investigate the anti-fibrosis effect of CBJRG in patients with chronic hepatitis B (CHB).

Patients and Methods: Eligible patients were divided into the Without group and the With CBJRG group based on whether the CBJRG was present in the treatment regimen. The differences of liver stiffness measurements (LSM) values, aspartate aminotransferase-to-platelet ratio index (APRI) scores and fibrosis index based on four factors (FIB-4) scores were compared between the baseline and the week 24 in the Without and the With CBJRG groups, and in the entecavir (ETV) and the ETV plus CBJRG groups.

Results: LSM values and APRI scores were significantly decreased in the With CBJRG group after 24-week treatment, while only LSM values were reduced in the Without group. The improvement of fibrosis stages was only observed in patients receiving 24-week CBJRG in the context of ETV antiviral therapy, not in patients receiving CBJRG plus other antiviral drugs. Moreover, LSM values at week 24 were

decreased as compared to the baseline in the ETV group, whereas no differences of APRI and FIB-4 scores were observed. LSM value, APRI and FIB-4 score were all statistically lower in patients treated with ETV plus CBJRG. The percentage of patient with fibrosis F4 were significantly lower in the ETV plus CBJRG group when compared to the ETV group.

Conclusion: The CBJRG plus ETV combination treatment shows a stronger anti-fibrosis efficacy than ETV alone in patients with CHB.

Abstract Submission No. 100485
O-0147

Pan-genotypic association of G1896A mutant with HBV DNA or advanced liver diseases: a meta-analysis

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Background: G1896A is one of the most common mutations in hepatitis B virus (HBV) genome, resulting in the abolishment of HBeAg production. Numerous studies focused on the replicative capacity and pathogenicity of G1896A mutant, but the conclusions were not consistent.

Methods: We searched Pubmed, Embase and Cochrane library up to June 18, 2022. Studies were screened according to inclusion and exclusion criteria. Extracted data were analyzed with the fixed- or random-effects model. Potential sources of heterogeneity were investigated using sensitivity and subgroup analyses.

Results: 63 studies were finally included to conduct meta-analyses. Results showed that G1896A mutant was more prevalent in HBeAg-negative patients (OR=5.57; 95%CI, 3.86–8.04; $P<0.001$). And G1896A was likely more common in genotype B and C than genotype D. Serum HBV DNA load of HBeAg-negative patients with G1896A mutant was 0.87 log₁₀copies/mL higher than those without mutant (WMD=0.87; 95%CI, -1.56–0.18; $P=0.014$). Moreover, G1896A mutant was closely associated with advanced liver diseases including liver cirrhosis (OR=1.96; 95%CI, 1.67–2.29; $P<0.001$) and hepatocellular carcinoma (OR=1.60; 95%CI, 1.20–2.12; $P=0.001$). These findings were constant in genotype B and/or C (liver cirrhosis: OR=2.47; 95%CI, 1.95–3.13; $P<0.001$; hepatocellular carcinoma: OR=1.61; 95%CI, 1.08–2.40; $P=0.021$).

Conclusions: HBeAg-negative patients with G1896A mutant might have higher HBV DNA level and G1896A mutant was closely associated with advanced liver diseases in chronic HBV-infected patients. In the area with high incidence of G1896A mutant, especially Eastern and Southeastern Asia, chronic HBV-infected patients should be monitored on mutants and expected to receive early antiviral treatment.

Abstract Submission No. 100544
O-0148

Development of a diagnostic model for hepatic inflammation in patients of CHB with HS based on ML

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Background: The coexistence of chronic hepatitis B (CHB) and hepatic steatosis (HS) is common, but simple non-invasive diagnostic methods to accurately assess hepatic inflammation severity are lacking. This study aimed to establish a non-invasive diagnostic model for hepatic inflammation in CHB patients with concurrent HS using machine learning (ML).

Methods: This study consecutively enrolled treatment-naïve CHB patients with concurrent HS who underwent liver biopsy from eleven medical centers between April 2004 and September 2022. Nine centers were used for training, while the other two centers were for external validation (validation cohort 1, validation cohort 2). Four ML algorithms (LR, RF, GBC, and ADB), were used to predict inflammation degree. Those patients with predicted inflammation grade (G) ≥ 3 were diagnosed. The optimal features for model development were selected by Shapley Additive explanation. Area under curve (AUC) was calculated to confirm the ability of the models.

Results: A total of 1,639 CHB patients with concurrent HS were enrolled in the study. In the training cohort, 157 (22.79%) patients reported hepatic inflammation $\geq G3$, respectively. In validation cohort 1, 31 patients (6.09%) had hepatic inflammation $\geq G3$. Meanwhile, in validation cohort 2, 76 (17.23%) patient exhibited hepatic inflammation $\geq G3$. The GBC model had the best performance in diagnosing inflammation $\geq G3$, with AUC of 0.856 (95% CI 0.830-0.883) in the training cohort, 0.892 (0.865-0.919) in validation cohort 1 and 0.775 (0.736-0.814) in validation cohort 2.

Conclusions: The GBC model reliably predicts inflammation $\geq G3$ in CHB patients with concurrent HS, improving disease diagnosis and management.

Abstract Submission No. 100545

O-0149

Determining of transient elastography cutoff for advanced fibrosis in patients of CHB with HS

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Background: Transient elastography (TE) is a non-invasive method for diagnosing hepatic fibrosis by measuring liver stiffness. However, the cutoff value of TE in CHB patients with concurrent hepatic steatosis (HS) remains unverified.

Methods: This study retrospectively enrolled CHB patients with concurrent HS who underwent liver biopsy and Fibroscan at Tianjin Second People's Hospital between 2016 and 2021. The study estimated the optimal TE cutoff for patients with concurrent CHB and NAFLD using the Youden index. AUC of contemporary TE cutoff for patients with CHB or NAFLD (9.7kPa) and optimal cutoff were calculated. Subgroup analysis by body mass index (BMI) was conducted.

Results: We enrolled 613 CHB patients with concurrent HS, with a median age of 36 years, of whom 442 (72%) were male and 12% had advanced fibrosis. The recommended TE cutoff for CHB or NAFLD patients was 9.7 kPa, with AUC was 0.681 (Table). At the optimal cutoff value (8.8 kPa), AUC was 0.733, significantly higher than 0.681 ($P=0.015$). Subgroup analysis showed that for patients with BMI < 25 kg/m², optimal cutoff AUC was 0.708, significantly surpassing the corresponding value of the contemporary cutoff value (AUC = 0.566) ($P=0.003$).

Conclusions: The optimal TE cutoff for assessing advanced fibrosis in CHB patients with concurrent HS was 8.8 kPa, lower than 9.7 kPa in CHB patients. In CHB patients with concurrent HS, a more stringent TE value is needed to enable more precise advanced fibrosis evaluation. The findings warrant further validation.

Abstract Submission No. 100560

O-0150

Immunogenicity of SARS-CoV-2 vaccination among patients with chronic liver disease

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Aim: We examined the humoral immune response and antibody dynamics after primary and booster vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) among patients with chronic liver disease (PCLD).

Methods: PCLD and completed primary or booster immunity of SARS-CoV-2 vaccination were recruited. Following primary or booster immunity, serological samples were gathered to detect neutralizing antibody and antibody against the receptor-binding domain (anti-RBD antibody).

Results: The positive rate of neutralizing antibody was 60.1% in Primary and 87.6% in Booster ($P<0.001$). The median titer of neutralizing antibody was 11.6 AU/mL in Primary and 31.6 AU/mL in Booster ($P<0.001$). The positive rate of anti-RBD antibody was 70.0% in Primary and 91.2% in Booster ($P<0.001$). The median titer of anti-RBD antibody was 21.7 AU/mL in Primary and 110.6 AU/mL in Booster ($P<0.001$). Compared to the antibody titer of primary immunity, 21 patients in whom SARS-CoV-2 vaccine antibodies were detected after both primary and booster immunizations showed an increase of 4.4 and 5.9 times in neutralizing antibody and anti-RBD antibody, respectively. Local and systemic adverse reactions after primary immunity and booster immunity were slight and resolved.

Conclusion: Humoral immune response after completing primary and booster immunity of SARS-CoV-2 vaccines was improved, while

booster immunity further improved the positive rate and antibody titer of PCLD, especially among patients with primary immunity failure. Local and systemic adverse reactions were slight.

Keywords: immune response; primary and booster immunity; SARS-CoV-2 vaccination; patients with chronic liver disease

Abstract Submission No. 100562

O-0151

Immunogenicity Of A Booster SARS-Cov-2 Vaccination In Patients With Chronic Liver Disease

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Objective: To investigate the safety and immunogenicity of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine booster in patients with chronic liver disease.

Design: Patients with chronic liver disease who received a SARS-CoV-2 vaccine booster were enrolled. Adverse events within 14 days of any dose of SARS-CoV-2 vaccine were recorded, simultaneously, serum samples were collected from enrolled patients at least 14 days after the booster dose and tested for SARS-CoV-2 neutralizing antibody (novel coronavirus neutralizing antibody, nCoV NTAb) and IgG antibody against SARS-CoV-2 spike binding domain (novel coronavirus Spike Receptor-binding Domain antibody, nCoV S-RBD) levels. The data of liver and kidney function, blood routine and coagulation function were collected and statistically analyzed before and after the booster injection of nCoV vaccine.

Results: A total of 114 patients with chronic liver disease were included. The positive rates of nCoV NTAb and nCoV S-RBD in patients with chronic liver disease were 87.72% and 91.23% after the booster injection of COVID-19 vaccine, and the positive rates of nCoV NTAb and nCoV S-RBD in non-cirrhotic group and cirrhotic group were 93.55%, 80.77% and 98.39%, 82.69%, respectively ($p < 0.05$); the median nCoV NTAb levels in non-cirrhotic group and cirrhotic group were 31.41 AU/mL and 32.64 AU/mL, and the median nCoV S-RBD levels were 102.94 AU/mL and 119.41 AU/mL, respectively. The results of continuous antibody level monitoring in 22 patients with basic immunization as well as booster injection of COVID-19 vaccine showed that after booster injection of COVID-19 vaccine, the positive rate of nCoV NTAb increased from 59.09% to 86.36%; the positive rate of nCoV S-RBD antibody increased from 68.18% to 90.91%. Antibody levels in patients with chronic liver disease increased significantly after the booster injection of COVID-19 vaccine compared to pre-injection levels. The nCoV-NTAb antibody levels increased evidently from 11.24 AU/mL (4.41 AU/mL -38.26 AU/mL) to 59.14 AU/mL (5.72 AU/mL -279.38 AU/mL) in 22 patients after the booster, with a mean increase of 5.26-fold. The median nCoV-SRBD antibody level increased significantly from 27.27 AU/mL (2.90 AU/mL -169.47 AU/mL) to 219.10 AU/mL (2.55 AU/mL -579.46 AU/mL) ($p < 0.01$), with a mean increase of 8.03-fold. The booster injection resulted in the production of nCoV-NTAb in 66.7% (6/9) of patients with chronic liver disease who failed basic immunization and nCoV-SRBD antibody in 71.43% (5/7). The overall tolerability of COVID-19 vaccine in patients with chronic liver disease was good, with a low incidence of adverse reactions, and most of the adverse reactions were mild or transient, with local pain at the injection site being the most frequent adverse reaction.

Conclusion: After basic SARS-CoV-2 immunization, the booster SARS-CoV2 vaccine can increase the serum conversion rate and antibody level of neutralizing antibodies and S-RBD IgG antibodies in patients with chronic liver disease (including patients with cirrhosis). The adverse reactions are mild and acceptable. The severity of liver disease is related to the immune response to COVID-19 vaccine.

Abstract Submission No. 100570

O-0152

A novel model for advanced fibrosis and cirrhosis diagnosis for CHB patients with hepatic steatosis

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Background: We previously developed a diagnostic model named PAP to assess advanced fibrosis ($\geq S3$) and cirrhosis ($=S4$) for chronic hepatitis B (CHB) patients with hepatic steatosis (HS). The PAP model was built on Gaussian naive bayes including prothrombin time, albumin and platelet. This study aimed to test the stability of the PAP model across five subgroups.

Methods: A total of 1,427 patients from nine clinical centers in China (NCT05766449) were enrolled. Patients were divided into five groups according to age (<40 and ≥ 40 years), sex (males and females), body mass index (<25 kg/m² and ≥ 25 kg/m²), hepatitis B e antigen (HBeAg) status (positive and negative) and hepatitis B virus deoxyribonucleic acid (HBV DNA) level ($<10^5$ and $\geq 10^5$ IU/mL).

Results: In the training cohort, the PAP model had the highest area under curves (AUCs) in patients with HBV DNA $\geq 10^5$ IU/mL at 0.827 (95% CI 0.749-0.905) for $\geq S3$ and 0.864 (95% CI 0.794-0.934) in patients aged ≥ 40 years for $=S4$, while it performed modestly in patients with HBV DNA $<10^5$ IU/mL when diagnosing $\geq S3$. In the validation cohort, it had the highest AUC of 0.824 (95% CI 0.765-0.883) in patients with HBV DNA $\geq 10^5$ IU/mL, and the lowest AUC of 0.687 (95% CI 0.619-0.755) in patients aged <40 years for $\geq S3$. The model performed best in female patients for $=S4$, with an AUC of 0.954 (95% CI 0.902-1.000).

Conclusions: In CHB patients with HS, the PAP model remained its stability for diagnosing liver advanced fibrosis and cirrhosis across various groups.

Abstract Submission No. 100582

O-0153

Novel algorithms for Predicting Advanced Fibrosis in CHB Patients with Concurrent Hepatic Steatosis

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Background: Non-invasive tests (NITs) are limited by having a significant proportion of indeterminate results for screening fibrosis in chronic hepatitis B (CHB) patients with concurrent hepatic steatosis (HS). Herein, we aimed to establish novel algorithms that call for improvements in current diagnostic workflow.

Methods: We consecutively recruited untreated patients who underwent liver biopsy from nine medical centers in China between April 2004 and September 2021 (Clinical Trials: NCT05766449). Fibrosis index based on the four factors (FIB-4), aspartate aminotransferase to platelet ratio index (APRI) and NAFLD fibrosis score (NFS), as well as their combinations were used to predict advanced fibrosis. Sensitivities, specificities, and positive and negative predicted values were calculated. Subsequently, we computed the proportion of patients with the correct classification (the sum of true positives and negatives) for different combinations of NITs.

Results: Among 926 treatment-naïve CHB patients with HS, 180 (19.44%) patients had advanced fibrosis. At the lower cut-off values, APRI exhibited the highest sensitivity of 65.56%, followed by FIB-4 (53.89%) and NFS (41.11%). At the higher cut-off values, NFS had the highest specificity of 97.99%, followed by FIB-4 (94.77%) and APRI (94.1%). Notably, APRI displayed the highest indeterminate rate of 30.99% compared to other NITs. The proportions of patients to receive a correct classification according to a single test were 64.7% for NFS, 64.1% for FIB-4, and 57.6% for APRI. When combining the test, the algorithm with NFS followed by APRI enabled most patients to receive a correct classification (73.7%), compared to FIB-4-NFS (71.3%), NFS-FIB-4 (71.8%), FIB-4-APRI (71.0%), APRI-FIB-4 (70.5%), APRI-NFS (71.8%).

Conclusion: The combined model NFS-APRI developed in our study showed better performance than individual NITs, which could reduce indeterminate zones and optimize referral pathways.

Abstract Submission No. 100595

O-0154

The diminished accuracy of non-invasive tests for significant fibrosis in CHB patients with MASLD

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Background: The co-existence of chronic hepatitis B (CHB) and metabolic dysfunction-associated steatotic liver disease (MASLD) has become popular, exacerbating the progression of hepatic fibrosis. However, the diagnostic performance of non-invasive tests (NITs), including the fibrosis-4 index (FIB-4), aspartate aminotransferase-to-platelet ratio index (APRI), and non-alcoholic fatty liver disease fibrosis score (NFS), remains uncertain in CHB patients with MASLD. This study aims to evaluate the accuracy of these NITs in identifying significant fibrosis in such population.

Methods: This multicenter, cross-sectional study was conducted at eleven Chinese hospitals. The whole population was classified as three groups, with group A of CHB patients combined with simple hepatic steatosis (HS), group B of CHB patients with MASLD involving 1-3 cardiometabolic risk factors (CMRFs), and group C of CHB patients with MASLD involving 4-5 CMRFs. According to Scheuer's classification, $\geq S2$ was defined as significant fibrosis.

Results: A total of 1,079 eligible patients were enrolled. In group A, the optimal cut-off values for FIB-4, APRI, and NFS in diagnosing $\geq S2$ were 1.263, 0.56 and -3.547, respectively, with corresponding area under curves (AUCs) of 0.784, 0.786 and 0.723. In group B, the AUC of FIB-4, APRI, and NFS was 0.655, 0.677 and 0.634, respectively. These AUCs further declined in group C, all falling below 0.640 (Figure 1).

Conclusions: The diagnostic accuracy of the three NITs diminished as the number of CMRFs increased. More studies are needed to develop tailored NITs for specific population.

Abstract Submission No. 100599

O-0155

Explore the decrease of HBsAg in patients with compensatory cirrhosis during Peg-interferon therapy

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Abstract Submission No. 100606

O-0156

Comparison of Markers for Diagnosing Significant or Advanced Fibrosis in Patients with CHB

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Background & Aims: The development of accurate non-invasive tests to detect liver fibrosis in patients with chronic hepatitis B (CHB) is crucial. We aimed to validate the performance of N-terminal type III collagen propeptide (PRO-C3), golgi protein 73 (GP73) and their combination for detecting significant (S2-4) and advanced (S3-4) fibrosis in CHB patients.

Methods: The serum level of Pro-C3 and GP73 were measured by ELISA. Scheuer scoring system was used to assess liver fibrosis. The diagnostic ability of PRO-C3, GP73 and PRO-C3 combined with GP73, to identify S2-4 and S3-4 in CHB patients, was estimated using ROC analysis.

Results: A total of 324 individuals with matched biopsy were enrolled, of whom 167 underwent FibroTouch. PRO-C3 and GP73 measurements were performed. Patients with S2-4 and S3-4 showed respectively increased levels of PRO-C3 and GP73 compared to patients with S0-1 and S0-2 ($P < 0.001$, respectively). PRO-C3 was independently associated with S2-4 and S3-4 when adjusted for clinical confounders. PRO-C3 combined with GP73 outperformed LSM, FIB-4 and APRI for detecting S2-4 in patients younger than 40 years ($P = 0.013$) and without steatosis ($P = 0.027$). The AUROC of PRO-C3, GP73 and their combination for identifying S2-4 and S3-4 was not significantly different from that of LSM in overall patients and other subgroups.

Conclusions: Overall, PRO-C3, GP73 and their combination were comparable with LSM for detecting S2-4 and S3-4 in CHB patients. These data supports their use as diagnostic tools for identifying CHB patients with S2-3 and S3-4.

Abstract Submission No. 100607
O-0157

HBsAg decline in Peg-IFN treated hepatitis B with fatty liver is similar to non-fatty liver patients

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Objective: To explore the decrease of HBsAg in patients with hepatitis B with fatty liver during Peg-interferon(Peg-IFN)therapy.

Methods: Patients treated with Peg-IFN for 48W were collected. According to the fat attenuation, the enrolled people were divided into fat attenuation<240dB/m group (n=116) and fat attenuation≥240dB/m group (n=150). Statistical analysis of data was performed by SPSS 26.0 software.

Results: The median age of our study was 40 (36-47) years old, including 201 males (75.85%), 138 treated patients (64.49%), 146 HBV-DNA negative patients (56.37%), 136 HBeAg negative (82.93%), and the median HBsAg was 3.02 (2.60-3.45) Log10IU/mL, the median ALT 24 (17-38.75) U/L; There were significant differences in gender and age between fat attenuation<240dB/m group and fat

attenuation≥240dB/m group. At follow-up up to 48W, there was no significant difference in the overall decline of HBsAg between the fat attenuation<240dB/m group and fat attenuation≥240dB/m group, and the decline slope was (-0.020 vs -0.016) respectively. However, the decrease rate of HBsAg in the fat attenuation <240dB/m group was greater than that in the fat attenuation≥240dB/m group at 24W (75.48% vs 52.05%). $P=0.05$; There was no significant difference in HBsAg clearance between the two groups at 12W, 24W, 36W and 48W. Stratified analysis showed that there were no significant differences in the overall decrease of HBsAg and the HBsAg clearance rate at 12W, 24W, 36W and 48W in terms of gender, age(>40 or not), treated/naïve patients, HBVDNA positive/negative, HBeAg positive/negative, and HBsAg (> 1500IU/ml or not), between fat attenuation<240dB/m group and fat attenuation ≥240dB/m group. Among the HBeAg negative patients, and the baseline ALT normal, the decrease of HBsAg in the fat attenuation<240dB/m group was significantly greater than that in the fat attenuation≥240dB/m group at 24W. For the baseline ALT abnormal, the 48W HBsAg decline in fat attenuation≥240dB/m group was greater than that in fat attenuation<240dB/m group, and the slopes were (-0.019 vs-0.011, $P=0.020$).

Conclusion: In the general population, compared with non- fatty liver group. there was no significant difference in HBsAg overall decline and the HBsAg clearance in patients with hepatitis B with fatty liver. For the baseline ALT abnormal, the 48W HBsAg decline in fatty liver group was greater than non-fatty liver group.

Abstract Submission No. 100608
O-0158

Analysis of PLT changes in patients with cirrhotic hepatitis B patients treated with Peg-interferon

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Objective: To explore the decrease of PLT in patients with compensatory cirrhosis during Peg-interferon therapy.

Methods: Patients treated with Peg-IFN for 48W were collected. liver stiffness measurement (LSM) was measured by instantaneous elastic imaging. The enrolled people were divided into LSM<9kPa group (non-cirrhotic patients) (n=171) and LSM≥9kPa group (compensatory cirrhosis group) (n=83). Statistical analysis of data was performed by SPSS 26.0 software.

Results: The median age of our study was 40 (36-48) years old, including 79 males (75.98%), 137 treated patients (67.82%), 143 HBV-DNA negative patients (59.09%), 121 HBeAg negative (80.13%), and the median HBsAg was 3.02 (2.58-3.42) Log10IU/mL, the median ALT 24 (17-38) U/L; PLT at 12W decreased significantly from baseline in both groups, The decrease of 12W PLT from baseline in LSM≥9kPa group was significantly higher than LSM<9kPa group (49.84% vs 45.48%, $P=0.010$). In the LSM≥9kPa group, the highest 12W decrease from baseline was 79%. PLT in 24W, 36W and 48W groups showed a slow upward trend compared with 12W, and the upward trend of PLT in the two groups was similar.

Stratified analysis showed that there were significant differences in the patients with male, age>40, naïve treatment, HBsAg>1500IU/mL, abnormal ALT in baseline, the decrease of 12W PLT from baseline in the LSM≥9kPa group was significantly higher than LSM<9kPa group. In these populations, we should pay more attention to the decline of 12W PLT and detect serious PLT reductions in time.

Conclusion: in the patients with male, age>40, naïve treatment, HBsAg>1500IU/mL, abnormal ALT in baseline, we should pay more attention to the decline of 12W PLT in the LSM≥9kPa group.

Abstract Submission No. 100641

O-0159

pgRNA and HBcrAg closely correlated with cytokines in HBeAg-positive pregnant patients in pregnancy

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Background: Previous studies indicated hepatitis B virus (HBV) serum markers are associated with host immunity. However, the relationship of novel HBV serum markers pregenomic RNA (pgRNA) and HBcrAg with host immunity in pregnancy CHB patients remains unclear. Therefore, we aimed to explore the relationship between novel HBV serum markers (pgRNA and HBcrAg) and cytokines in HBeAg-positive pregnant chronic hepatitis B (CHB) patients during pregnancy. **Methods:** In this retrospective real-world study, HBsAg, HBV DNA, pgRNA, HBcrAg and 28 cytokines were collected from 28 HBeAg-positive pregnant CHB patients at 24-28 weeks gestation.

Results: We found that neither HBsAg, HBV DNA, nor HBcrAg correlated with cytokines, but only pgRNA positively correlated with Th1 cytokines (IFN- γ , IL12p70, IL2 and TNF- α), Th2 cytokines (IL10 and IL5), Th17 cytokine (IL21), and cytokines regulating cell proliferation and differentiation (CTLA4, IL15, IL23 and TGF- β 1), and negatively associated with IL12p40 in 24-28 weeks gestation. In HBeAg-positive pregnant CHB patients younger than 30 years old, pgRNA correlated with Th1 cytokines (IFN- γ and IL12p70), Th2 cytokines (IL5), Th17 type cytokines (ICOS) and cytokines regulating cell proliferation and differentiation (CTLA4 and TGF- β 1), HBcrAg and HBsAg correlated with ICOS, and HBV DNA correlated with ICOS and CTLA4. In patients older than 30 years, pgRNA correlated with MIP-1 α , HBcrAg correlated with TNF- α , IL4, IL5, IL15, TGF- β 1 and IP10, HBsAg and HBV DNA did not correlated with cytokines.

Conclusions: pgRNA and HBcrAg showed more closely relationship with cytokines in HBeAg-positive pregnant CHB patients compared to traditional HBV serum markers.

Abstract Submission No. 100642

O-0160

IFN- α provides dual benefits of reducing HCC and facilitating HBsAg loss for NA-treated CHB patients

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Background: This study is to investigate whether peginterferon- α -2b (IFN) add-on Nucleos(t)ide analogs (NAs) can further reduce hepatocellular carcinoma (HCC) risk compared with NAs monotherapy in NAs-treated patients with chronic hepatitis B (CHB).

Methods: In this multi-center randomized controlled trial "PARADISE study" (NCT05671315), CHB patients with intermediate to high risk of HCC, who had undetectable HBV DNA after more than 24-week NAs pretreatment, were recruited, randomized to two groups at a ratio of 1:2 and followed up for 240 weeks. NAs group continued NAs monotherapy, while IFN+NAs group received IFN add-on NAs therapy for 48 weeks, then switched to NAs monotherapy. The changes of HBV serological markers at week 48 and the 96-week cumulative incidences of HCC were compared between groups.

Results: A total of 196 CHB patients were included in the interim analyses based on 96-week follow-up data (68 in NAs group, 128 in IFN+NAs group). The 96-week cumulative incidence of HCC was markedly lower in IFN+NAs group than NAs group (0% vs. 4.5%, log-rank test $p<0.05$). Compared with NAs group, IFN+NAs group had a significantly lower level of HBsAg at week 48 (1.553 ± 1.884 vs. 2.885 ± 0.714 log₁₀ IU/ml, $p<0.001$) and a notably greater HBsAg decline from baseline to week 48 (1.242 ± 1.333 vs. 0.095 ± 0.333 log₁₀ IU/ml, $p<0.001$). Rates of HBsAg loss and HBsAg seroconversion at week 48 were much higher in IFN+NAs group than NAs group (21.9% vs. 0%, $p<0.001$; 18.0% vs. 0%, $p<0.001$).

Conclusion: IFN add-on NAs therapy is superior to NAs monotherapy in reducing HCC risk and facilitating HBsAg loss among NA-treated virologically suppressed CHB patients with intermediate to high risk of HCC.

Abstract Submission No. 100701

O-0161

The Everest Project's 5-Year Update: Efficacy of PegIFN α Therapy in NA-suppressed HBeAg negative CHB

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Background and Aims: This study aims to evaluate the efficacy and safety of pegIFN α -based therapy in real-world nucleoside analog (NA)-treated chronic hepatitis B (CHB) patients and identify predictors for HBsAg loss by pegIFN α .

Method: The Everest Project, a multicenter real-world study in China, was previously introduced, focusing on the HBsAg loss of CHB (NCT04035837). Patients with over a year of NA therapy, HBV DNA < 100 IU/mL, HBeAg negative, and HBsAg $\leq$ 1500 IU/mL were recruited starting in 2018. PegIFN α -2b monotherapy or combination with NA was performed. The 5-year study enrollment has now concluded, and the latest research data is presented here.

Results: Out of the total 23,412 patients recruited, 15,896 were considered mITT group, 12,260 patients were included in PP group. Of the total patients over 48-week treatment, 77.47% were male, with an average age of 41.77 years and a mean HBsAg baseline of 378.05 IU/mL. 3864 patients achieved HBsAg loss. The HBsAg loss rates

were 10.75%, 22.72%, 28.72% and 31.43% at 12, 24, 36 and 48 weeks in PP group, respectively, higher than that in mITT group (figure 1A, B). Factors predicting higher HBsAg loss included a lower HBsAg baseline, reduced HBsAg levels at 12 and 24 weeks, ALT flare at the 12-week mark, younger age, female gender, and a lower BMI. There were no severe adverse events during this project.

Conclusion: HBsAg loss rate could be over 30% in NA-suppressed CHB patients by pegIFN α strategy. Baseline and on-treatment predictors can better guide the achievement of functional cure.

Abstract Submission No. 100730

O-0162

Clinical Study on the Efficacy and Safety of Interferon in Compensatory hepatitis B Cirrhosis

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BACKGROUND: There are limited data on the efficacy and safety of polyethylene glycolated interferon-alpha 2b (PEG-IFN α 2b) antiviral therapy in patients with compensated hepatitis B cirrhosis. In this study, we aimed to evaluate the efficacy of PEG-IFN α 2b in HBsAg-positive patients.

METHODS: A total of 52 HBeAg-positive patients with compensated hepatitis B cirrhosis who had not received antiviral therapy were divided into two treatment groups: Group A (12 patients): patients were injected with Peg-IFN α -2b (180 μ g) subcutaneously once a week; Group B (20 patients each): ETV (0.5 mg) or TDF (300 mg) was administered orally once a day for 48 weeks, and observed for 12 weeks. Group B (20 cases each). Blood samples were collected at baseline and every 12 weeks. ALT, AST, HBV DNA quantification and HBsAg, HBsAb, HBeAg, HBeAb, HBcAb levels were measured.

RESULTS: In group A, HBsAg levels decreased rapidly in the first 12 weeks and gradually declined over the next 36 weeks, the proportion of patients with undetectable HBV DNA was 100% during the observation period, and HBsAb increased significantly and stabilized. The rate of loss of HBeAg in group B was lower than that in group A. In group B, the rate of loss of HBeAg was lower than that in group B.

CONCLUSION: This real-world study demonstrated superior efficacy in HBeAg-positive patients after 48 weeks of treatment with PEG-IFN α 2b alone than with oral medications. However, this study needs to be validated with larger sample size studies.

Abstract Submission No. 100754

O-0163

ChB patients with extremely low-level viremia - clinical characteristics and prognosis.

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University Xi'an, Shaanxi China **Introduction:** After 48 weeks of treatment with nucleoside analogs (NAs), some chronic hepatitis B (CHB) patients can still detect HBV DNA by high-sensitivity polymerase chain reaction, but it can not be quantified accurately. This group requires further research to define their clinical characteristics and long-term prognosis.

Method: CHB patients received NAs treatment for over 48 weeks were divided into 4 groups based on virological response: sustained virological response group (SVR, HBV DNA undetected), extremely low-level viremia group (eLLV, 0.2000IU/ml). Analysis of baseline characteristics, long-term biochemistry, HBV markers, and disease progression was performed for each group.

Result: A total of 989 CHB patients were enrolled, including SVR (n=186), eLLV (n=468), LLV (n=295), and PVR (n=40). Serum ALT, the ratio of liver cirrhosis in eLLV and SVR are compared, which is different from LLV. HBsAg and the positive rate of HBeAg in eLLV were significantly lower than LLV while higher than SVR. After a median follow-up of 5 years, The incidence of hepatocellular carcinoma was observed with no difference in eLLV (9/468 1.92%) and SVR (4/186 2.15%), but it was lower than LLV (17/295 5.76%). Moreover, eLLV had a lower re-compensation rate for liver cirrhosis (27/170, 15.9%) than SVR (24/69, 34.8%), but comparable to LLV (12/76, 15.8%).

Conclusion: Extremely low viral load has little short-term effect on hepatitis patients' survival. Longer follow-up is needed for prognosis. Liver cirrhosis patients with LLV and eLLV should decrease viral load for improved prognosis.

Abstract Submission No. 100771

O-0164

The incidence of renal tubular absorption dysfunction among patients with NUC plus PegIFN α 2b therapy

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Objective: This study aims to evaluate the occurrence of renal tubular absorption dysfunction in CHB patients during NUC+PegIFN α 2b treatment.

Method: This study focuses on CHB patients who received NUC+PegIFN α 2b treatment at West China Hospital from February 2023 to July 2023, and evaluates the incidence of elevated urine β 2-microglobulin (β 2-MG) and decreased blood phosphorus during the treatment.

Result: A total of 92 patients were included, including 76 males and 16 females, with a median age of 37.5 years. After 12 to 24 weeks of NUC+PegIFN α 2b treatment, 73.9% (68/92) developed urinary β 2-MG increased, with 43.5% (40/92) less than 3 times the upper limit of normal (ULN), 6.5% (6/92) between 3-5 times ULN, 6.5% (6/92) between 5-10 times ULN, and 17.4% (16/92) more than 10 times ULN. In addition, 33.7% (31/92) of patients experienced a decrease in blood phosphorus, with 27.2% (25/92) showing a decrease of less than 20% and 6.5% (6/92) showing a decrease of 20% -60%. A total of 23 patients experienced simultaneous simultaneous β 2-MG increase and blood phosphorus decrease. Among patients with TAF+PegIFN α 2b, 27.3% (18/66) experienced urinary β 2-MG elevation >3 times ULN, and 33.3% (22/66) showed a decrease in blood phosphorus. Among patients with ETV+PegIFN α 2b, 41.7% (5/12) experienced urinary β 2-MG elevation >3 times ULN, and 41.7% (5/12) showed a decrease in blood phosphorus. Among patients with ETV+TAF+PegIFN α 2b,

35.7% (5/14) experienced urinary β 2-MG elevation >3 times ULN, and 28.6% (4/14) showed a decrease in blood phosphorus.

Conclusion: The incidence of renal tubular absorption dysfunction is relatively high among patients with NUC+PegIFN α 2b combination therapy.

Abstract Submission No. 100772

O-0165

Efficacy of antiviral therapy in ALT normal chronic HBV infection

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Objective: This study aimed to assess virological response efficacy and predictive factors in antiviral-treated patients with normal ALT levels.

Methods: We reviewed 164 treatment-naïve CHB patients receiving antiviral treatment (ETV, TDF, or TAF) at Beijing Ditan Hospital, Capital Medical University, between May and December 2020. Of these, 46 patients had normal ALT (ALT < 50 U/L), and 118 had abnormal ALT (ALT > 50 U/L). Baseline and 12, 24, and 48-week post-treatment clinical data were collected to compare virological indicators between groups. The ALT normal group was divided into complete and poor virological response subgroups based on the HBV DNA at week 48, and predictive factors were analyzed using binary logistic regression.

Results: The highest baseline ALT in the abnormal ALT group was 2106.7 U/L, the highest baseline value of Log HBV DNA was 9.2 Log IU/ml, with a mean Log HBV DNA value of 7.5 Log IU/ml. In the normal ALT group, the highest baseline Log HBV DNA was 8.5 Log IU/ml, with a mean value of 7.2 Log IU/ml. The difference of HBV DNA viral load at baseline between groups was not statistically significant ($p=0.183$). After 48 weeks antiviral treatment, the mean Log HBV DNA values decreased to 1.4 Log IU/ml for ALT abnormal and 1.7 Log IU/ml for ALT normal, with no statistically significant difference ($p=0.062$). Virological response (HBV DNA < 20 IU/mL) rates in the ALT abnormal group was 62.7% (74/118), compared to 43.5% (20/46) in the ALT normal group, showing statistical significance ($p=0.025$). No significant differences were observed at 12 and 24 weeks ($p=0.056$, 0.991). HBeAg serologic conversion rates after 48 weeks were 8.5% in the ALT abnormal group and 17.4% in the ALT normal group, with no statistical difference ($p=0.227$). Binary logistic regression indicated that high HBsAg and HBeAg positivity were predictive factors for poor virological response in the ALT normal group. **Conclusion:** At week 48 post-antiviral treatment, the ALT normal group exhibited a lower virological response rate than the ALT abnormal group. High HBsAg and HBeAg positivity were predictive factors for poor virological response in the ALT normal group. Larger studies are needed to validate these findings due to the small sample size.

Abstract Submission No. 100781

O-0166

Sexual dysfunction in female CHB patients with nucleoside(t) analogues therapy

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Objective: To investigate the sexual function of female chronic hepatitis B (CHB) patients treated with nucleoside (t) analogues (NUC).

Methods: Female CHB patients aged 18-60 who are receiving NUC antiviral therapy are invited to participate in this study. And those who have not had sexual activity in the past 4 weeks should be excluded. The validated Female Sexual Function Index (FSFI) is used to evaluate sexual function; and a score of 26.55 is used to determine whether there is sexual dysfunction.

Result: A total of 72 patients were finally included, with an average age of 39.83 ± 8.55 years and a median duration of antiviral treatment of 5 years. The majority of patients were college educated or above (66.7%), non-manual workers (73.6%), and received NUC monotherapy (83.3%). The average FSFI score was 24.48 ± 6.09 , with 61.1% of patients having FSFI scores less than 26.55, indicating a prevalence sexual dysfunction rate of 61.1% (44/72). In the surveyed population, there was no significant correlation between age, education level, occupational type, antiviral treatment drugs, and duration of antiviral treatment with FSFI scores. Compared with the non-FSD group, the FSD group is more inclined towards the population with higher education levels ($p=0.018$), but there is no significant difference in age, occupational distribution, duration of antiviral treatment, or quantity of antiviral treatment drugs between the two groups.

Conclusion: Sexual dysfunction is common in female CHB patients who receive NUC antiviral therapy. However, more large-scale studies are still needed to validate the current findings.

Abstract Submission No. 100862

O-0167

Liver volume re-compensation in HBV-related decompensated cirrhosis after NUCs therapy

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Background: NUCs therapy can effectively inhibit HBV replication and enhance the long-term prognosis of individuals with HBV-related decompensation, and some patients can achieve re-compensation. Liver volume serves as a crucial measure for assessing liver reserve function, the precise impact of liver volume on re-compensation remains uncertain.

Methods: We retrospectively included 159 HBV-related decompensated patients who received NUCs treatment. All patients underwent two abdominal CT scans. Software was utilized to measure the actual liver volume (LV), while the standard liver volume (ELV) was calculated by thoracic width. The liver volume ratio (LV/ELV%) was employed to eliminate individual differences. The changes of liver volume were dynamically observed during follow-up.

Results: The cumulative re-compensation rate over a period of two years was 37.7%. Prealbumin was linearly positively correlated with LV/ELV% ($r = 0.515$, $P < 0.001$), while prothrombin time was negatively correlated with LV/ELV% ($r = -0.411$, $P < 0.001$). After NUCs treatment, LV (979.13 ± 256.42 cm³ vs 1081.72 ± 273.67 cm³, $P < 0.05$) and LV/ELV% of HBV-related decompensated patients increased, while LV (985.02 ± 247.78 vs 883.38 ± 261.91 cm³, $P < 0.01$)

and LV/ELV% decreased in the persistent decompensated group. The risk of death was significantly increased in patients with LV < 950cm³ and LV/ELV% < 80%. The 5-year survival rate was significantly improved in patients with LV > 1000cm³ and LV/ELV% > 80%.

Conclusion: Patients with HBV-related decompensation can reverse liver fibrosis and enhance liver regeneration after receiving effectively NUCs treatment. Liver volume re-compensation is beneficial to long-term functional re-compensation.

Abstract Submission No. 100886

O-0168

Higher risk of disease progression in the grey zone relative to inactive Chronic hepatitis B

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Abstract;

Background & aims: Chronic hepatitis B (CHB) remains a global healthcare burden. Inactive CHB(IC) is the commonest immune state. There are also patients with normal alanine aminotransferase (ALT) and HBeAg negative, which guidelines refer to as the IC corresponding grey zone (GZIC). There is still confusion about the evolution of disease progression in the GZIC. So we aimed to study the natural history of IC and GZIC.

Method: This was a retrospective-prospective cohort study that included 300 patients with stage IC and GZIC. Conversion to HBeAg-negative immune-active CHB (IA) and IA corresponding grey zone (GZIA), initiation of antiviral therapy, and occurrence of end-stage liver disease events were defined as outcome events. The cumulative incidence of outcome events in the IC and GZIC groups was compared.

Results: At baseline, 201 (67.00%) patients were IC and 99 (33.00%) were GZIC. 18.9% of the 300 patients with IC and 46.4% of the patients with GZIC converted to IA or GZIA. 30 (10%) received antiviral therapy, of which 22 (77.3%) were patients with GZIC and 8 (22.7%) were IC patients. Nine (3%) developed end stage liver disease of which seven (77.78%) were GZIC and two (22.22%) were IC. The cumulative event rates for conversion to IA or GZIA, initiation of antiviral therapy, and occurrence of end-stage liver events were higher in GZIC than in IC ($p < 0.0001$, $p < 0.0001$, $p = 0.0018$) (Figure 1).

Conclusion: Patients with GZIC have a higher risk of disease progression than those with IC.

Abstract Submission No. 100889

O-0169

Antiviral effect in patients with chronic hepatitis B infection in the indeterminate phase

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Background: Emerging data suggest that a substantial proportion of patients with chronic hepatitis B (CHB) do not fall into any of the defined phases and are considered indeterminate. These CHB patients have a significantly high risk of hepatocellular carcinoma. Little is known about the effect of antiviral therapy for these patients. We

aimed to investigate liver histology and assess the effect of antiviral treatment on these patients.

Methods: We retrospectively analyzed the outcomes of antiviral therapy for CHB patients in the indeterminate phase who underwent liver biopsy and were treated with nucleoside/nucleotide analogues (NAs) or polyethylene glycol interferon (PEG-IFN) for up to 96 weeks.

Results: A total of 241 patients receiving NAs ($n = 206$) or PEG-IFN ($n = 17$) or NAs + PEG-IFN ($n = 18$) were included, 18.7% (45 of 241) were HBeAg positive. Approximately 80% of CHB patients in the indeterminate phase had significant histological changes. At week 96, the rate of undetectable HBV DNA in NAs group, PEG-IFN group or NAs + PEG-IFN group was ~99.0%, ~88.2% or ~100.0%, respectively. No patients were found to have viral resistance to therapy. In NAs group, HBeAg clearance rate were 10% (4 of 40) at week 48. No patient had loss of hepatitis B surface antigen.

Conclusion: Majority of CHB patients in the indeterminate phase had significant liver histological changes. Antiviral therapy can effectively inhibit HBV replication in these CHB patients, although rates of HBeAg seroconversion and hepatitis B surface antigen loss were low.

Abstract Submission No. 100921

O-0170

NAFLD comorbidity predicts higher ALT and liver stiffness: A longitudinal study in CHB patients

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Introduction: The impact of NAFLD in chronic hepatitis B virus (HBV) infection remains further exploration.

Methods: We enrolled 784 treatment-naïve HBV-infected patients who underwent liver biopsies. The presence of steatohepatitis was evaluated according to the NAFLD activity score (NAS). After the liver biopsy, biochemical measures and liver stiffness (LS) measurements were performed repeatedly. Mixed models were used to evaluate the associations of steatosis (NAS score 1-2) or steatohepatitis (NAS score 3-8) with longitudinal ALT, FIB-4 and LS.

Results: Among 784 patients without excessive alcohol intake, 174 (22.2%) had steatosis only and 110 (14.0%) had steatohepatitis. Steatohepatitis (versus no FLD) was associated with 1.90 times higher risk of advanced fibrosis at baseline (95%CI, 1.10-3.28) and also associated with 1.20 times higher ALT ($P < 0.001$), 1.11 times more frequent ALT elevation ($P < 0.001$), 1.17 times higher FIB-4 ($P = 0.021$) and 2.20 times higher liver stiffness ($P = 0.004$) across eight years follow-up. Although steatosis (versus no FLD) has no association with a higher risk of advanced fibrosis at baseline and higher FIB-4 (both $P > 0.05$) across follow-up, steatosis was associated with 1.16 times higher ALT ($P < 0.001$), 1.08 times more frequent ALT elevation ($P < 0.001$) and 1.70 times higher liver stiffness ($P = 0.017$) during the follow-up period. Similar results were found in the subgroup who received antiviral treatment within 6 months after liver biopsy.

DISCUSSION: The presence of NAFLD was associated with higher hepatic inflammation and fibrosis over time, whether antiviral treatment started or not. Therefore, besides viral suppression, prevention of the progression of fatty liver is also crucial in HBV.

Abstract Submission No. 100930

O-0171

Elevated Risk of in clinical outcomes Untreated HBeAg-Positive CHB Patients in Indeterminate Phase

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Background: The indeterminate phase of HBeAg-positive chronic hepatitis B (CHB) has not been covered by antiviral therapy in the current management guidelines. This study assessed hepatocellular carcinoma (HCC) and cirrhotic complication risks of these patients.

Methods: This was a territory-wide cohort study of untreated non-cirrhotic hepatitis B e antigen (HBeAg)-positive CHB patients with identifiable CHB phases based on their serial alanine aminotransferase (ALT) and hepatitis B virus (HBV) DNA. Patients with HBeAg-positive indeterminate phase were further classified into either the high HBV DNA group with a load of 20,000 to 1,000,000 IU/mL and normal ALT (i.e., high HBV DNA) or the low HBV DNA group with a load <20,000 IU/mL and elevated ALT (i.e., low HBV DNA).

Results: Among 11,288 patients, 54.7% were male with a mean age of 43.7 ± 13.8 years. 3,107 patients (27.5%) were in the indeterminate phase, with 78% in the high HBV DNA group. At a median follow-up of 6.2 [3.6,9.6] months, 2,441 (78.6%) remained indeterminate. In the HBeAg-positive indeterminate phase, the high HBV DNA group showed a 10-year cumulative HCC incidence of 6.7% vs. 4.2% ($P < 0.001$) and cirrhotic complications of 13.2% vs. 8.8% ($P < 0.001$) when compared to the low HBV DNA group.

Conclusions: HBeAg-positive indeterminate phase patients with high HBV DNA levels face significantly increased 10-year risks of HCC and cirrhotic complications. Further studies are vital to evaluate the benefits of early antiviral treatments.

Abstract Submission No. 100931

O-0172

Prolonged indeterminate phase in untreated chronic hepatitis B-infected patients

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Background: Indeterminate phase of chronic hepatitis B (CHB) has not been covered by antiviral therapy according to the current management guidelines. We aimed to determine the transition dynamics of the indeterminate phase.

Methods: This was a territory-wide cohort study of untreated non-cirrhotic CHB patients with identifiable CHB phases based on their serial alanine aminotransferase (ALT) and HBV DNA. Indeterminate phase was defined according to the European Association for the Study of the Liver guidelines. Follow-ups were censored at the earliest event among antiviral treatment initiation, last follow-up, December 2022, or death.

Results: Of 42,837 patients, 22,166 (51.74%) were in the indeterminate phase at study entry; 6,256 (14%) of them were HBeAg-positive, with a mean age of 51.8 ± 13.9 , and 56.5% were male. At a median follow-up of 11.5 [1.0,50.2] months, 15,367 (69%) remained indeterminate, while 3,573 (16.1%) and 3,226 (15%) transitioned to immune clearance and immune active phases, respectively. For the HBeAg-

positive indeterminate group, 78% stayed in the indeterminate phase at the last follow-up, with most of the rest transitioning to immune active phase. 67% of the HBeAg-negative indeterminate group remained indeterminate, with 0.13% and 18.15% transitioned to immune clearance and immune active phases respectively.

Conclusions: Most patients continue to remain in indeterminate phase over time, suggesting that this phase in CHB patients is not transient. The indeterminate phase warrants closer clinical attention, including evaluating the risks associated with clinical outcomes, specifically hepatocellular carcinoma and cirrhotic complications, in this patient population.

Abstract Submission No. 100960

O-0173

Long-term effects of tenofovir and entecavir cessation in HBeAg negative chronic hepatitis B

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Background: Recent studies found that nucleos(t)ide analogues (NA) stopping will lead to more rapid HBsAg clearance and safe. However, few studies reported the long-term outcomes after the discontinuation. This study aim to evaluate HBsAg loss, virological relapse (VR), clinical relapse (CR), and safety after cessation of tenofovir (TDF) or entecavir (ETV).

Methods: A total of 98 non-cirrhotic HBeAg negative chronic hepatitis B patients (CHB), treated with either TDF or ETV for at least three years and virally suppressed were enrolled into TDF discontinued (TDF-D, n=39), ETV discontinued (ETV-D, n=27) groups compared continued group (continue, n=32). All patients were followed for at least one year and up to 4 years after NA discontinuation.

Results: The median follow-up time was 146 weeks, and seven patients (10.6%) achieved HBsAg clearance after NA discontinuation. All of them had end-of-treatment (EOT) HBsAg levels <100 IU/ml. Cumulative incidences of VR and CR at week 48, 96 and 144 in both TDF-D, ETV-D were shown in Fig1A,B,C. The cumulative rate of HBsAg loss, VR, and CR in patients with EOT-HBsAg <100 IU/ml and ≥ 100 IU/ml were shown in Fig1(D,E,F). EOT-HBsAg level was significant predictor for HBsAg clearance (HR=0.21, 95% CI 0.05-0.89, $P=0.028$). Six patients in TDF-D had severe ALT flares, two required admission, and one death.

Conclusion: NA cessation led to achieving HBsAg clearance more than NA continuation and usually in the first year; however, it increased risk of VR and CR, especially TDF group, and patients with high EOT-HBsAg levels. Some resulted in early and more severe CR, which lead to hepatic decompensation and death.

Abstract Submission No. 100974

O-0174

The impact of long-term Entecavir treatment on renal safety in patients with chronic hepatitis B

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Introduction and objectives: Entecavir (ETV) is a preferred antiviral for chronic hepatitis B (CHB). However, its impact on renal function in patients with CHB remains inconclusive in the literatures. The aim of this study was to comprehensively assess the impact of ETV treatment on both glomerular and tubular function in patients with CHB and to investigate the potential risk of renal impairment associated with long-term ETV therapy.

Patients and methods: A total of 602 CHB patients were enrolled in this study. Propensity score matching (PSM) was utilized to balance confounding factors. Comparative analyses were performed between the ETV treatment group and non-antiviral treatment CHB group, the ETV treatment group and the tenofovir alafenamide (TAF) treatment group, as well as the ETV treatment group with more than 5 years of treatment (8.68±3.43 years) and the ETV treatment group with less than 5 years of treatment (2.31±1.22 years). Renal function indicators measured included eGFR, urinary albumin-to-creatinine ratio, urinary retinol-binding protein, urinary β 2-microglobulin, urinary α 1-microglobulin, serum phosphate, and serum cystatin C.

Results: After propensity score matching, no significant differences were observed in renal function indicators between the ETV treatment group and the non-antiviral treatment CHB group ($P > 0.05$), between the ETV treatment group and the TAF treatment group ($P > 0.05$), and between the ETV treatment group with more than 5 years of treatment and the ETV treatment group with less than 5 years of treatment ($P > 0.05$).

Conclusions: Long-term ETV treatment shows no evident renal impairment.

Abstract Submission No. 100977

O-0175

Study on replication-competent HBV DNA in hepatitis B cirrhosis with HCC patients

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Background: The purpose of this study was to determine the level of replication-competent HBV DNA A in liver tissue to investigate its role in decompensation events and recompensation in patients with hepatitis B cirrhosis complicated with primary liver cancer.

Methods: The level of replication-competent HBV DNA was detected by droplet digital PCR assay (ddPCR) method with mono-over-gap rcDNA primers. The value of replication-competent HBV DNA levels to decompensated events and recompensations was analyzed.

Results: Among the 40 patients with negative HBV DNA, the median and interquartile interval of the group with and without decompensated replication were 3.94(3.83-4.19) and 3.52(3.24-3.80), respectively, with a difference between the two groups ($P=0.042$). In the follow-up of 16 patients with decompensated hepatitis B cirrhosis complicated with primary liver cancer, the median and interquartile distance of replication-competent HBV DNA in patients with and without decompensation were 3.50 (3.23-3.96) and 4.25 (4.04-4.45), respectively, and there was a difference between the two groups ($P=0.026$).

Conclusion: In patients with hepatitis B cirrhosis complicated with primary liver cancer, the level of HBV DNA replication in liver tissue is higher in patients with decompensated events. The level of HBV DNA replicating universal in liver tissue was lower in patients with recompensation.

Abstract Submission No. 100982

O-0176

Multi-parametric MRI identified chronic hepatitis B patients with subclinical liver inflammation

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Background: Chronic hepatitis B (CHB) patients with ongoing necroinflammation have elevated risk of cirrhosis and hepatocellular carcinoma (HCC). Alanine transaminase (ALT), a key serum biomarker recommended by all clinical guidelines, is used to stratify patients for antiviral therapy or cirrhosis surveillance but is often inaccurate due to the heterogenous nature of hepatitis B virus (HBV) infections. Liver biopsy, the current reference standard, has significant well reported limitations. Iron-corrected T1 (cT1), a multi-parametric MRI (mpMRI) biomarker, correlates well with liver disease including inflammation and fibrosis, and can predict liver related outcomes. Our aim was to evaluate the utility of cT1 to identify subclinically active disease in non-cirrhotic CHB patients in biochemical remission.

Methods: This nested-cohort study within the ELEGANCE cohort (prospective multi-centre study enrolling patients at increased risk of HCC in Singapore, NCT04965259) included 77 non-cirrhotic CHB patients with paired mpMRI (LiverMultiScan®) and ALT scores. Ongoing inflammation and active disease was defined as cT1>800ms. Normal ALT was defined as ≤ 25 U/L.

Results: ALT and cT1 were positively correlated ($r=0.32$, $p=0.004$). Although the majority with ALT ≤ 25 U/L had low cT1 (≤ 800 ms), 8% with normal ALT had active disease with cT1>ULN (829ms [813ms-880ms]). ALT was suboptimal at ruling-out CHB patients with ongoing liver inflammation. (sensitivity: 42.9%, specificity: 65.7%, NPV: 92.0%, PPV: 11.1%).

Conclusion: ALT levels, while commonly used for monitoring CHB patients, will miss 8% of CHB patients with subclinically active disease. cT1 using mpMRI can identify ongoing liver inflammation which in turn prevents long-term liver-related complications.

Abstract Submission No. 100986

O-0177

The effect of tenofovir amibufenamide on lipid metabolism

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Objective: To analyze the effect of tenofovir amibufenamide (TMF) on blood lipid metabolism in CHB patients

Method: CHB patients treated with TMF monotherapy for more than 1 year were screened, and the blood lipid metabolism related indicators were quantitative tested before and after TMF treatment.

Result: A total of 109 patients with complete demographic and clinical follow-up data were included, and their peripheral blood cholesterol, triglycerides, high-density lipoprotein(HDL), very low-density lipoprotein(VLDL) and ApoB levels were within the normal range before receiving TMF treatment. After more than 1 year of TMF treatment, 28.4% (31/109) of patients had triglyceride levels exceeding the upper limit of normal(ULN), with 67.7% (21/31) of patients having an increase of no more than 30% of ULN; 15.6% (17/109) of patients had total cholesterol levels exceeding the ULN, with 52.% (9/17) of patients having an increase of no more than 30% of ULN; 11% (12/109) of patients had VLDL levels exceeding the ULN, with 66.6% (8/12) of patients having an increase of no more than 30% of ULN. In this group of cases, In this group of cases, 14.7% (16/109) of patients had HDL levels exceeding the ULN. There was no significant difference in the average level of ApoB between before and after TMF treatment, but approximately 11% (12/109) of patients had peripheral blood ApoB slightly exceeding the ULN after 1 year of TMF treatment.

Conclusion: Patients treated with TMF can experience slight abnormalities in some blood lipid indicators, but the clinical significance is not yet clear.

Abstract Submission No. 101045

O-0178

Diagnostic accuracy of FAST score, NFS, FibroScan, and FIB-4 in CHB patients with NAFLD

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Objective: To evaluate the diagnostic value of the FibroScan-AST (FAST) score, non-alcoholic fatty liver fibrosis score (NFS), FibroScan, and liver fibrosis index (FIB-4) for identifying fibrotic non-alcoholic steatohepatitis (NASH) in patients with chronic hepatitis B (CHB) with non-alcoholic fatty liver disease (NAFLD).

Methods: All patients with CHB and NAFLD who underwent liver biopsy.

Results: A total of 156 patients with CHB combined with NAFLD were included, including 69 with NASH and fibrosis stage 2 or higher (NASH+F_{≥2}), and 16 with NASH and cirrhosis (NASH+F₄). The AUC of FAST, NFS, liver stiffness measurement (LSM), and FIB-4 for diagnosing NASH+F_{≥2} was 0.739 (P<0.001), 0.643 (P=0.006), 0.754 (P<0.001), and 0.665 (P=0.003), respectively. The specificity of FAST, NFS, LSM, and FIB-4 was 67%, 51.8%, 78.6% and 76.8%, respectively, and the sensitivity was 75%, 78.6%, 67.9%, and 53.6%, respectively. No significant differences were found between groups. The AUC of FAST, NFS, LSM, and FIB-4 for diagnosing NASH+F₄ was 0.650 (P=0.038), 0.725 (P=0.001), 0.851 (P<0.001), and 0.560 (P=0.533), respectively. The specificity of the FAST, NFS, LSM, and FIB-4 was 55.9%, 50.0%, 71.6%, and 75.5%, respectively and the sensitivity was 80.0%, 100%, 100%, and 50.0%, respectively. The differences between AUCs of FIB-4 and FAST compared with LSM were 0.291 and 0.201, respectively (P<0.05).

Conclusion: In patients with CHB combined with NAFLD, FAST did not have better accuracy than NFS and FIB-4 for predicting fibrotic NASH, whereas LSM had better accuracy than FAST and FIB-4.

Abstract Submission No. 101094

O-0179

Engagement in care, not antiviral therapy for all, is important to reduce early mortality from HBV

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Background: Liver clinic established 1979, DW 2003 to present. Free healthcare includes: clinic visits, blood tests, imaging, elastography. Paper records (1979-2006) were migrated to Epic EMR (developed by DW). On June 4, 2022, all patient records were manually migrated to Epic EMR by DW. Summary analyses obtained from Slicer Dicer module within Epic. ALT and platelet counts from Jan 2010 to present were graphed and recorded in each patient chart.

Philosophy of care: 1. HBV is not complicated 2. Not everyone needs treatment 3. Stopping treatment might be beneficial.

Results: N=2,840 individual patient records were migrated to Epic from June 4, 2022 to October 28, 2023. N=1,306 (46%) had diagnoses related to chronic HBV infection. Compared to those without chronic HBV, those with HBV were less likely to have ALD (0.6% vs 14.6%), MASLD (7.5% vs 27.7%), cirrhosis (12.2% vs 30.2%), HCC (5.5% vs 8.0%) or death (1.4% vs 4.7%). Majority (53.7%) were not on antiviral therapy. Trends over time: smaller proportion of Chinese origin and HBeAg pos HBV (now 8.1%). HCC size at diagnosis was larger in those referred to clinic for HBV/HCC compared to those with HCC discovered while being followed in clinic. Of 18 deaths, only 5 died from liver-related causes. Of those followed in clinic, only 1 died from liver. He was 83, HCC first diagnosed in 2004, had multiple recurrences, death from HCC in 2023.

Conclusion: Patients with chronic HBV infection do very well when followed in clinic, even when not on antiviral therapy.

Abstract Submission No. 101115

O-0180

Characterization of genotypes,subtypes and prevalence of occult HBV in chronic liverdisease and HCC

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Introduction: The specific genotypes and subtypes of the hepatitis B virus (HBV) have various biological and epidemiological behaviors. The aims of the study were to understand the distribution of HBV genotypes among patients with chronic liver disease (liver cirrhosis) and hepatocellular carcinoma in Armenian patient population, as well as to investigate the possible association of HBV genotypes with different clinical outcomes.

Methods: We used the 3rd generation polymerase chain reactions technique, droplet digital PCR (ddPCR), to identify the presence of occult HBV virus infection in the plasma of patients, as well as identify the subtype belonging of the virus. The study included 91 cases of liver cirrhosis and 69 cases of hepatocellular carcinoma.

Results: Our study on 69 HCC cases and 91 cases of non-tumor chronic liver disease (CLD) revealed that 18.8% of HCC patients very positive for HBV (in contrast to 4.4% in CLD population). Furthermore, 46.6% of HCC patients very documented to have an occult HBV infection, as opposed to 24.1% of the CLD cases, The majority of HBV cases constituted the D subtype.

Conclusion: HBV isolates subtype variants correspond to the overall distribution of genotypes in this part of Eurasia, however are more prevalent than expected, especially as occult infections. Overall, circulating mutations in plasma are promising tools for diagnosis and monitoring treatment. We aim to conduct a complementary study, add on our previously found data, and specify genomic alterations to characterize them and establish relationships between the frequency of these alterations and HCC-related mortality

Abstract Submission No. 101121
O-0181

Non-invasive MRE Assessment of Liver Injury in HBeAg-negative Patient with CHB: a Case Report

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¹Department of Radiology, Drum Tower Hospital, Nanjing University Medical School Nanjing China, ²Department of Infectious Diseases, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University Nanjing China, ³Department of Radiology, Mayo Clinic Rochester MN USA **Background and Aims:** Current guidelines recommend liver biopsy in HBeAg-negative cases with normal ALT and hepatitis B virus (HBV) DNA >2000 IU/ml; however, patients at this stage typically are not willing to accept it due to its invasive nature. We reported a 59-year-old female with HBeAg-negative chronic hepatitis B virus (CHB) who visited us for CHB management; liver injury was a concern. Six months prior to this visit, the patient underwent a liver biopsy due to the concern of liver injury in another hospital where MRE was not available, and the histopathology showed G1S0. The patient never received any anti-viral treatment.

Methods: In this visit, the patient underwent a serum blood test, HBV DNA quantification, and MRE for liver injury evaluation. FIB-4 index was calculated based on the formula: $FIB-4 = \text{age [years]} \times \text{AST [IU/L]} / (\text{platelets [10}^9/\text{L]} \times \text{ALT [IU/L]})^2$.

Results: The serum HBV DNA level is high (6.52×10^3 IU/ml) and alanine aminotransferase (ALT) is normal (18 U/L). The mean liver stiffness measured by MRE is 1.97 kPa which indicates fibrosis stage 0. The FIB-4 index is 1.31. $FIB > 1.28$ indicates significant fibrosis with a positive predictive value of 41.4%.

Discussions and Conclusions: In HBeAg-negative patients with normal ALTs and high HBV DNA levels, it is important to evaluate liver injury for HBV management. FIB-4 shows lower sensitivity and specificity. As the most accurate noninvasive liver fibrosis diagnosis method recommended by AGA, ACR, AASLD and AAD, MRE can be used to follow up patients requiring liver injury assessment for HBV management.

Abstract Submission No. 101130
O-0182

Optimal ALT cut-off values in the grey zone of HBV infect

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Background and Aims: We aimed to define gender-specific, optimal alanine aminotransferase (ALT) cut-off values for the prediction of significant liver histological changes (SLHC) in grey zone (GZ) chronic hepatitis B (CHB) patients with normal ALT.

Methods: This retrospective study included 1101 consecutive GZ CHB patients with normal ALT assigned to training or internal validation cohorts. An independent cohort of 842 GZ CHB patients was included for external validation. Receiver operating characteristic (ROC) curve, smoothed curve fitting, and threshold effect analyses were performed to determine the optimal ALT cut-off values, and area under the curve (AUC) values were calculated to assess their predictive performance.

Results: SLHC was observed in 79.3% of GZ CHB patients with normal ALT (≤ 40 U/L). ROC curve analysis initially identified optimal ALT cut-off values of 29 U/L (male) and 22 U/L (female). After smoothed curve fitting and threshold effect analyses, the new optimal cut-off values for ALT were 27 U/L for males and 24 U/L for females. Notably, the AUCs for these values reached 0.836 (male) and 0.833 (female) in the internal validation cohort and 0.849 (male) and 0.844 (female) in the external validation cohort. Moreover, the accuracy and discriminative ability of the newly defined ALT cut-off values were greater than those of the current recommendations.

Conclusion: This study established novel optimal ALT cut-off values for more precise prediction of SLHC among GZ CHB patients with normal ALT levels. As such, the findings may help identify individuals in this patient population who will benefit from timely antiviral therapy.

Abstract Submission No. 101136
O-0183

The negative relationship between HBV DNA and liver damage loss before HBeAg clearance in CHB

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Background and Aims: The disease progression of chronic hepatitis B virus (HBV) infection is driven by the interactions between HBV, hepatocytes and the host immune. The dynamic changes in the

relationship between HBV replication and host immunity during disease progression need to be clarified.

Method: Two cross-sectional and one validation clinical cohort were recruited, and meta-analyses of cross-sectional cohorts were performed to explore the relationship between HBV replication and the severity of liver immunopathological inflammation. Gene expression profiling of liver biopsies in GSE84044 was used to explore the relationship between expression immune related gene and HBV DNA levels.

Result: A positive correlation between HBV replication and the severity of hepatic immunopathological inflammation was observed in HBeAg-negative patients but not in HBeAg-positive patients in each of the two cross-sectional cohorts, and this correlation was confirmed by meta-analysis. Further stratified analysis in these HBeAg-positive patients revealed distinct relationship patterns between serum HBV DNA levels and patients with relatively higher HBV DNA ($>2 \times 10^6$ IU/mL) and confirmed that in one validation cohort. Serum HBV DNA levels also correlated negatively with expression of immune-related genes, which was converted to a positive relationship in HBeAg-positive patients with relatively lower HBV DNA levels and in HBeAg-negative patients.

Conclusion: This study suggests that in patients with chronic HBV infection, a negative relationship between the serum HBV DNA level and liver injury, might already transformed to positive before HBeAg loss in HBeAg-positive patients with HBV DNA levels below 2×10^6 IU/mL.

Abstract Submission No. 101174

O-0184

A validation study of FAL-1 score for predicting HCC risk in CHB patients treated with NAs

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Backgrounds: Assessing the risk of hepatocellular carcinoma (HCC) in chronic hepatitis B (CHB) patients who are treated with nucleos(t)ide analogs (NAs) is clinically important. The aim of this study is to evaluate the utility of a previously reported FAL-1 score for stratifying HCC risk in NA-treated patients.

Methods: Clinical data of 303 NA-treated CHB patients from 6 hospitals were collected. After excluding patients with incomplete data, patients with a history of HCC, patients who developed HCC within one year of starting NA, and patients who were superheavy drinkers, 212 patients (male/female: 135/77, median age: 58.5, median follow-up: 7 years) were retrospectively analyzed.

Results: The median levels of T-bil, AST, ALT, PLT, and HBV DNA were 0.8 mg/dl, 38 U/L, 44 U/L, and 175,000/μL, respectively. The HBeAg positivity rate was 20.7%. 2/67/51 patients were infected with HBV genotype A/B/C. 15/137/24/34 patients were treated with LAM/ETV/TDF/TAF as a first-line NA. HCC developed in 12 (5.7%) patients, and the cumulative HCC incidences were 2.8%, 9.2%, and 11.4% at 5, 10, and 15 years, respectively. When FAL-1 scores were calculated using data at 1 year after starting NA (ALT ≥ 31 : +1; FIB-4 ≥ 1.58 : +1), the cumulative HCC incidences for 5 years were 0/2.2/13.7% for score 0 (n=76)/score 1 (n=106)/score 2 (n=25) (P=0.021). Notably, there was no HCC development in patients with score 0, consistent with the derivation cohort.

Conclusion: This study validated the usefulness of a simple FAL-1 score calculated from FIB-4 index and ALT at 1 year of NA.

Abstract Submission No. 101222

O-0185

Reactivation of HBV in Patients With Resolved HBV Infection After Receiving DAA Treatment for HCV.

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Background and Aims: study to determine the risk of HBV infection reactivation while treating with direct anti-viral therapy.

Patients And Methods: This study was carried out on 80 patients with chronic Hepatitis C infection who were candidates for treatment with direct-acting antiviral therapy. The patients identified to carry HBsAg at baseline or with positive HBc Antibodies were further assessed for other HBV markers: hepatitis B e antigen and serum HBV DNA quantitative measurement at baseline, at week four of starting treatment, and at the end of treatment. All patients ≥ 18 years of age and gender with Chronic HCV infection with inactive HBV or resolved infection were included in the study. Patients were followed for every 4-week interval for 24 weeks.

Results: Of our study participants, the majority were males 51 (63.7%), and females 29 (36.2%) with a mean age of 48 ± 9.5 years. At the beginning of the study, there were 32 (40%) patients who were co-infected with HCV and HBV with HBeAg + quantitative PCR for HBV DNA ≤ 20 IU/ml. 23 (29%) patients with Inactive carriers and 24 (31%) patients with resolved HBV infection.

After DAAs therapy, reactivation of HBV infection was detected in 5 cases of resolved HBV infection, and 6 cases of Inactive carriers showed increased HBV DNA viral load from ≤ 2.5 log IU/mL to 7.7 log IU/mL after completion of DAAs therapy. Treatment outcome Of HCV infection 75 (94%) patients achieved SVR.

Conclusion: HBV screening is strongly recommended for co-infected HCV/HBV patients before initiation and during DAA therapy. HBV reactivation can be prevented with pre-treatment screening and prophylactic treatment when necessary.

Abstract Submission No. 101265

O-0186

Tenofovir alafenamide for treatment-naïve and nucleos(t)ide with hepatitis B virus infection

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Background and Aims: Tenofovir alafenamide (TAF) has been approved for the treatment of chronic hepatitis B (CHB). We aimed to assess the effectiveness and safety of TAF-based therapy in treatment naïve (TN) or experienced (TE) CHB patients.

Methods: This multicenter, prospective, real-word study included 500 CHB patients treated with TAF monotherapy or combining with

entecavir (ETV) for 144 weeks. Virological and biochemical responses and safety were evaluated (clinicaltrials.gov: NCT03752658).

Results: 404 patients (TN, 146; TE, 258) with available data were included in this interim analysis. 13.6% had cirrhosis at baseline. All TN patients and 164 TE patients received TAF alone, and 94 TE patients received TAF plus ETV. Of TN patients, 88.7% achieved virological response (HBV DNA <20 IU/mL) at week 96. 81.8% achieved biochemical response (ALT<40 U/L) at week 96. Among TE patients switching to TAF, virological response rate was significantly increased, from 67.8% at baseline to 91.7% at week 96 ($P<0.05$), and biochemical response rate was 79.7% at baseline and 92.1% at week 96. Among TE patients receiving TAF+ETV, virological response rate was significantly increased from 42.0% at baseline to 91.3% at week 96 ($P<0.05$), and biochemical response rate was significantly increased from 80.0% at baseline to 92.9% at week 96 ($P<0.05$). Of 75 TE patients with low level viremia at baseline (HBV DNA <2000 IU/mL), 61 achieved virologic response at week 96. Among patients with estimated glomerular filtration rate (eGFR) below 90 mL/min/1.73m² at baseline, eGFR was significantly improved at week 96 ($P<0.05$). Total cholesterol levels significantly increased at week 96 ($P<0.05$). TAF-based therapy was well-tolerated.

Conclusions: TAF-based therapy was effective in both TN and TE CHB patients, as well as those with low level viremia. TAF therapy show a sustained improvement in renal glomerular function in patients with prior impaired renal function.

Abstract Submission No. 101357

O-0187

On-treatment liver stiffness measurements predict liver-related events in patients on HBV therapy

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Background & Aims: Baveno VII proposed a criterion based on liver stiffness measurements (LSM) to identify compensated advanced chronic liver disease (cACLD). LSM decreased significantly after antiviral therapy in chronic hepatitis B (CHB) patients. However, whether the on-treatment LSM-defined cACLD has prognostic relevance is unclear among CHB patients receiving antiviral therapy.

Methods: LSM was collected after at least 1-year of antiviral therapy. cACLD was defined (LSM > 15 kPa) or excluded (LSM < 10 kPa) based on Baveno VII criteria. LSM between 10 and 15 kPa were in grey zone. Liver-related events (LREs) were defined as the first hepatic decompensation, hepatocellular carcinoma, and death.

Results: A total of 694 CHB patients were included in this analysis. Patients were predominantly male (539, 77.7%) with a median age of 44 years. The median on-treatment LSM values were 7.6 (5.6, 10.7) kPa, with 494 (71.2%) patients in the non-cACLD group, 127 (18.3%) in the grey zone, and 73 (10.5%) in the cACLD group. In total, 12 decompensations and 16 HCC occurred during a median follow-up of 5.0 (3.0 - 6.8) years after the on-treatment LSM. The 5-year cumulative incidence of LREs were 1.8%, 6.3%, and 19.3% in non-cACLD, grey zone, and cACLD group, respectively (Log-rank, $P < 0.001$). Compared to non-cACLD patients, those with cACLD had a higher risk of LREs after adjusting for age, sex, and platelet counts (adjusted HR = 3.98, 95%CI: 1.34-11.83, $P = 0.013$).

Conclusions: The on-treatment LSM could predict LREs in CHB patients during antiviral therapy.

Abstract Submission No. 101382

O-0188

M2BPGi stratifies HCC risks in chronic HBV-related cirrhosis patients after 6-year antiviral therapy

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Background: In chronic hepatitis B (CHB)-related cirrhosis patients receiving long-term antiviral therapy, despite effective suppression of HBV viremia, the risk of hepatocellular carcinoma (HCC) persists. To personalize HCC surveillance, it is crucial to stratify the HCC risk. Mac-2 binding protein glycosylation isomer (M2BPGi), a serum liver fibrosis marker, was evaluated for its predictive role in this context.

Methods: We conducted a prospective cohort study to include HBV-related cirrhotic patients who received long-term antiviral therapy. They received continuous antiviral therapy with regular HCC surveillance. The M2BPGi were measured by Sysmex HISCL M2BPGi Assay. Cox proportional hazard regression analysis was applied to identify risk predictors for HCC.

Results: A total of 501 patients were included and grouped in the "prior HCC" (n=47), "HCC" (n=56), and "no HCC" (n=398) groups at the time of M2BPGi measurement, with a median M2BPGi levels were 1.7, 1.3, and 1.0, respectively ($p=0.001$). Among the 454 patients without prior HCC, their median age was 60, and received a median 6.2 years of antiviral therapy. After a median of 3.3 years of follow-up, 56 patients developed HCC. M2BPGi levels <1, 1-3, and >3 mAU/mL significantly stratified the risk of HCC (logrank $P=0.079$). After adjusting for age, sex, and AFP, M2BPGi levels of 1-3 mAU/mL and >=3 mAU/mL increased the risks of HCC by 1.98 (95% CI: 1.05-3.74) and 2.55-fold (95% CI: 1.19-5.48), respectively, compared with M2BPGi <1 mAU/mL.

Conclusions: After 6 years of antiviral therapy, a high M2BPGi level proves valuable in predicting the development of HCC.

Abstract Submission No. 101428

O-0189

To determine the risk factors of Hepatitis B in children at Jinnah Postraduate Medical Center

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Place and Duration of Study: Gastroenterology Department, JPMC, Karachi from January 2019 to April 2022.

Methodology: A total of 134 children of age < 16 years with hepatitis B were recruited in this study. Demographic information was recorded. Screening for HBV was done in all patients. Investigations including liver biochemistry, HBsAg, and HBV DNA Polymerase chain reaction were conducted in the hospital along with a complete blood count and Ultrasound whole abdomen. All information was collected on a pre-designed proforma and evaluated using SPSS version 25.

Results: The mean age of patients was 11.02±2.19 years. There were 57.46% male. The frequent risk factor was blood transfusion in 23.9% of children followed by vertical transmission in 47%, horizontal transmission in 13.4%, and a prior history of surgical or dental intervention was present in 17.2% of children.

Conclusion: In this study, vertical transmission was the most common route of transmission followed by vertical transmission. Additionally, 11% of family members were HBV positive. None had concomitant HCV and HDV infection. All pregnant females should be screened. Children on chronic blood transfusion therapy should be screened annually. Additionally, birth dose Hepatitis B vaccination should be implemented as a key step in HBV prevention among Pakistani children.

Key Words: Hepatitis B virus, blood-borne transmission, perinatal transmission, Horizontal transmission

Abstract Submission No. 101437

O-0190

The effect of Peg-IFNα2b on metabolic status in patients with CHB combined with NAFLD

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¹Department of Hepatology of The Third Central Hospital of Tianjin, China Tianjin China, ²The Third Central Clinical College of Naikai University Tianjin China, ³Tianjin Key Laboratory of Extracorporeal Life Support for Critical Diseases of Tianjin Tianjin China, ⁴Institute of Hepatobiliary Disease Tianjin China **Background:** To investigate the effects of different antiviral treatment regimens on virological and metabolic related indicators in patients with chronic hepatitis B combined with NAFLD.

Methods: This is a prospective observational study. The patients with CHB who met the indications of antiviral treatment of the Guidelines were collected as the research objects, and were followed up for at least 24 weeks. The therapeutic effect and impact on metabolic related indicators of Peg-IFNα2b and nucleotide analogs (NA), as well as the combination therapy group were analyzed.

Results: There are 491 CHB patients who meet the inclusion criteria, including 240 patients combined with NAFLD. The group with NAFLD had higher BMI, CAP, TG and serum uric acid values ($p < 0.05$). 56 patients achieved clinical cure, including 30 cases combined NAFLD. All cured patients were treated with Peg-IFNα2b based therapy (Peg-IFNα2b alone or combined with NA). In the Peg-IFNα2b based treatment process, there was no significant statistical difference in virological indicators, including HBsAg and HBVDNA, between CHB and CHB combined NAFLD group at baseline, 12 weeks, and 24 weeks. However, metabolic related indicators, including BMI, CAP value, uric acid and TG, were significantly increased in the CHB combined NAFLD group at baseline, but there was no statistical difference between the two groups at 24 weeks ($p < 0.05$).

Conclusions: There was no doubt that Peg-IFNα2b treatment plays an important role in the clinical cure of CHB, and it also significantly

improves BMI, CAP and metabolic disorder of chronic hepatitis B combined with NAFLD.

Abstract Submission No. 101454

O-0191

ALL THAT GLITTERS IS NOT GOLD : THINKING BEYOND CAMS

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Introduction- A 55-year-old homemaker, presented with history of 2-weeks jaundice, 1-week pruritus and 1-day altered sensorium.

Past History- Received Ayurvedic medicines for 3-weeks for arthralgia. At 2-weeks, noticed jaundice, pruritus, nausea and fatigability.

16-years back, jaundice noticed after consuming same medicine, resolved after discontinuation.

Physical examination:- Icterus, Grade-II encephalopathy.

Investigations:- Bilirubin-28.9/14.6, SGOT/SGPT- 1095/1283, Alkaline Phosphatase-224, INR-2

Ultrasound abdomen - Acute hepatitis.

Etiological work-up done twice: negative.

With worsening to ALF, superurgent listing for Liver Transplantation planned, but donor unavailable. Plasma Exchange (3 sessions) performed as bridge procedure, INR and sensorium improved, she underwent trans-jugular liver biopsy (TJLB).

On Follow-up, LFT waxing and waning, not <25 mg% even after 1 month, gradually worsened.

Histo-Pathology:- Not only revealed DILI and acute hepatitis; hepatocytes showed Hepatitis B-core-antigen (HBcAg) in cytoplasm.

Tenofovir Adefovir 25mg was initiated.

Subsequently LFT improved dramatically, became asymptomatic in two weeks, discharged with near-normal-LFT and INR.

We suspect that the CAMS/Indigenous medicine, the initial purported culprit, must have been laced with steroids, during the second (current) ingestion, that precipitated a flare of the occult-HBV, along with DILI. Learning points:-

History of CAMS intake can be a confounder, leading the clinician away from real diagnosis.

HBV Meso-endemic countries may actually be hyperendemic.

Nation-wide studies are required (Serology- HBsAg /IgG antiHBc; and Autopsy studies -Liver biopsy to look for Occult HBV)- to consider empirical antivirals for HBV in patients with Cryptogenic Acute Hepatitis /ACLF.

The time has arrived for Population-based intervention strategies for Mass screening and HBV vaccination.

Abstract Submission No. 101484

O-0192

Neutrophil to lymphocyte ratio and mean platelet volume in predicting HBV DNA negativity

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Background: Evaluation of the role of neutrophil to lymphocyte ratio (NLR) and mean platelet volume (MPV) in predicting hepatitis B virüs (HBV) DNA negativity in patients with hepatitis B on nucleoside analogs treatment.

Methods: A total of 99 patients with hepatitis B were included in the study. Blood count was taken from each patient before nucleoside analog treatment, and after detecting HBV DNA negativity.

Results: Most of the patients had F2 (46; 46.5%) and F3 (30;30.3%) liver fibrosis according to the Metavir scoring system. The average HBV DNA was 6.43 ± 1.37 log copy/mL. Tenofovir was given to 54 (54.5%) patients, entecavir to 27 (27.3%) patients, and lamivudine to 18 (18.2%) patients. NLR and MPV were significantly lower after achieving HBV DNA negativity when compared to pretreatment values ($p < 0.018$; $p < 0.001$, consecutively)

Conclusions: NLR and MPV may be used for predicting or monitoring HBV DNA negativity and the effectiveness of nucleoside analogs in chronic hepatitis B patients.

Keywords: Neutrophil to lymphocyte ratio, mean platelet volume, HBV DNA, nucleoside analogs

Abstract Submission No. 101488

O-0193

Development and validation of new predictive model for immune tolerance of

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Objective To modify more accurate clinical and viral indicators and establish the new model for differentiating the different stages of chronic hepatitis B virus (HBV) infection based on liver histopathological changes.

Methods: The clinical and liver pathology data of chronic hepatitis B (CHB) patients undergoing liver biopsy were collected for retrospective analysis in the test and validation group. The area under the curve (AUC) of the receiver operating characteristic (ROC) was used to evaluate the diagnostic value for differentiating the different stages of chronic HBV infection.

Results A total of 118 patients and 73 patients who met the diagnostic and exclusion criteria were selected as the test group and validation group. Multivariate analysis showed that HBeAg independently correlated with the IT and IC stages. The cutoff value of HBeAg used to quantitatively differentiate between IT and IC was 1335 S/CO and the AUC was 0.921 (95% confidence interval (CI): 0.836 to 0.971). A new prediction model of IT stage was established by using three indicators including HBeAg, HBsAg and HBV DNA. The AUC is 92.3% (95% CI: 86.4-98.2, $P < 0.001$) using this prediction model. The sensitivity and specificity are 85.5% and 95.2%.

Conclusions: The high levels of HBeAg(1335s/co) rather than HBeAg positive might help to identify patients with the "true" IT stage. A predictive model for immune tolerance stage are established by combining three indicators. The new prediction model has significantly reduced the error rate compared with others standards.

Abstract Submission No. 101489

O-0194

sPD-1 and sPD-L1 levels predict functional cure in CHB patients after NAs and Peg-IFN α therapy

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Background: The role and expression of sPD-1 and sPD-L1 in hepatitis B research have become topics of debate.

Aim: To investigate the correlation between serum sPD-1/sPD-L1 levels and functional cure in CHB.

Methods: This retrospective study was conducted at a single center and involved 220 patients. After adjusting for age, gender, and baseline HBsAg level using propensity score matching, 80 patients were enrolled. Serum samples were collected at four time points (baseline, 12 weeks, 24 weeks, and 48 weeks) and tested for sPD-1 and sPD-L1 using ELISA kits.

Results: Serum levels of sPD-1 and sPD-L1 were lower in the cured group (sPD-1: 287.0 [224.1, 381.1] pg/mL; sPD-L1: 96.1 [36.0, 258.3] pg/mL) compared to the uncured group (sPD-1: 363.6 [312.6, 410.2] pg/mL, $P = 0.015$; sPD-L1: 269.0 [212.2, 336.6] pg/mL, $P < 0.001$). Additionally, while sPD-1 levels increased rapidly in both groups, sPD-L1 levels only increased in the cured group. In the entire cohort, there was a positive correlation between the reduction of HBsAg and the growth of sPD-1 at both 24 and 48 weeks. The combination of baseline sPD-L1 level with HBsAg reduction at 12 or 24 weeks demonstrated a predictive performance for functional cure at 48 weeks, with a receiver operating characteristic of 0.800 (95% CI: 0.700 - 0.900, $P < 0.001$) or 0.911 (95% CI: 0.841 - 0.982, $P < 0.001$) respectively.

Conclusions: It was found that the baseline sPD-L1 level and the drop in HBsAg were significant predictors of achieving functional cure at 48 weeks.

Abstract Submission No. 101520

O-0195

Achieving hepatitis B elimination in the Pacific Islands: test/treat is the way forward in Kiribati

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Background: In 2016, WHO declared that hepatitis B is a global health threat with elimination targets set to be achieved by 2030.[1] Progress towards elimination is slow[2]. One barrier to progress is the lack of screening and linkage to care in isolated populations where WHO guidelines cannot be applied. The remote islands of Kiribati are geographically isolated by vast stretches of ocean. Since 2019 our group has been providing hepatitis treatment in South Tarawa, where 50% of the country's population lives.[6] Starting in 2022, a "test and treat" program has been initiated in the outer islands.

Methods: Eleven outer islands, totalling 5497 individuals, were screened with 867 positive tests. All positive females older than 15 years were offered tenofovir alafenamide which, despite its higher cost, can be started without routine creatinine testing. This age was chosen to include all potential mothers. Males testing positive were offered treatment at age 18.

Results: The overall prevalence was 15.8%; one-third of persons 24 years or younger tested positive. Highest rates were in the 30-34 age group with a prevalence of almost 30%. The program was well-accepted by positive patients after education about the benefits/risks of treatment. Local providers found the protocol easy to implement.

Conclusions: Hepatitis B elimination using current guidelines is not achievable in remote locations such as the outer islands of Kiribati, and a new paradigm is needed. Despite its limitations, the "test and treat" strategy appears to be the most practical and cost-effective solution to meeting elimination goals in resource-limited regions.

Abstract Submission No. 100975

O-0196

Liver volume re-compensation in HBV-related decompensated cirrhosis after NUCs therapy

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Background: NUCs therapy can effectively inhibit HBV replication and enhance the long-term prognosis of individuals with HBV-related decompensation, and some patients can achieve re-compensation. Liver volume serves as a crucial measure for assessing liver reserve function, the precise impact of liver volume on re-compensation remains uncertain.

Methods: We retrospectively included 159 HBV-related decompensated patients who received NUCs treatment. All patients underwent two abdominal CT scans. Software was utilized to measure the actual liver volume (LV), while the standard liver volume (ELV) was calculated by thoracic width. The liver volume ratio (LV/ELV%) was employed to eliminate individual differences. The changes of liver volume were dynamically observed during follow-up.

Results: The cumulative re-compensation rate over a period of two years was 37.7%. Prolabum was linearly positively correlated with LV/ELV% ($r = 0.515$, $P < 0.001$), while prothrombin time was negatively correlated with LV/ELV% ($r = -0.411$, $P < 0.001$). After NUCs treatment, LV (979.13 ± 256.42 cm³ vs 1081.72 ± 273.67 cm³, $P < 0.05$) and LV/ELV% of HBV-related decompensated patients increased, while LV (985.02 ± 247.78 vs 883.38 ± 261.91 cm³, $P < 0.01$) and LV/ELV% decreased in the persistent decompensated group. The risk of death was significantly increased in patients with LV < 950cm³ and LV/ELV% < 80%. The 5-year survival rate was significantly improved in patients with LV > 1000cm³ and LV/ELV% > 80%.

Conclusion: Patients with HBV-related decompensation can reverse liver fibrosis and enhance liver regeneration after receiving effectively NUCs treatment. Liver volume re-compensation is beneficial to long-term functional re-compensation.

Abstract Submission No. 101627

O-0197

Little liver disease progression after long-term drug withdrawal in HBeAg positive postpartum woman<st

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Background: There is controversy over whether to discontinue treatment postpartum in HBeAg positive woman received prophylactic NAs treatment in the third trimester of pregnancy. And data on the long-term safety of the drug withdrawal after delivery is limited.

Methods: We conducted a retrospective-prospective real-world study to explore the progression of liver disease after long-term drug withdrawal in HBeAg positive postpartum woman. Finally, sixty HBeAg positive postpartum woman discontinuing treatment for more than six months, 10 HBeAg positive postpartum woman continuing treatment after delivery and 12 HBeAg positive postpartum woman received NAs treatment pre-pregnancy were eventually included.

Results: The baseline characteristics between three groups are comparable in terms of age, platelets count, APRI and FIB-4. The median follow-up time for postpartum woman discontinuing treatment was 28.8 months (6.0 - 89.2), which was comparable with the 27.6 months (6.6 - 111.7) for postpartum woman continuing treatment after delivery and 33.0 months (6.0 - 75.5, $p=0.963$) for postpartum woman received NAs treatment pre-pregnancy. No postpartum women developed to liver cirrhosis or hepatocellular carcinoma in three groups. The liver stiffness value was 4.75 kPa (2.8 - 13.9) in postpartum woman discontinuing treatment, 4.1 kPa (2.7 - 6.7) in postpartum woman continuing treatment after delivery and 4.65 (3.7 - 6.4) in postpartum woman received NAs treatment pre-pregnancy, which was comparable in three groups ($p = 0.360$). Moreover, APRI and FIB-4 were comparable in three groups ($p > 0.05$).

Conclusions: It is relatively safe for HBeAg positive postpartum woman to discontinue NAs treatment after delivery.

Abstract Submission No. 101705

O-0198

Optimal Threshold of M2BPGi for Predicting Minimal HCC Risk in CHB Patients with Antiviral Therapy

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Background & Aims: Mac-2 binding protein glycosylation isomer (M2BPGi) is a surrogate marker for liver fibrosis, predicting hepatocellular carcinoma (HCC) risk in chronic hepatitis B (CHB) patients receiving long-term antiviral treatment. However, the optimal threshold of M2BPGi to identify the minimal risk in these patients remains unclear.

Methods: We combined 2 cohort studies including 1283 Taiwanese CHB patients receiving long-term oral antiviral treatment. The primary endpoint was the development of HCC.

Results: Over a 7.4-year follow-up, 100 patients developed HCC. Our data showed that baseline M2BPGi level was positively associated with HCC development. Stratifying patients into quartiles with cutoffs of 0.55, 1.03, and 2.45 demonstrated escalating HCC risks in groups

II, III, and IV compared to group I with hazard ratio (95% confidence interval, CI) of 2.7 (1.0-7.0), 4.5 (1.8-11.1), and 14.6 (6.3-33.8), respectively. This association remained significant when limiting the analysis to patients without liver cirrhosis at baseline. When stratifying these non-cirrhotic patients using single M2BPGi value of 0.55, patients with higher M2BPGi level (vs. lower M2BPGi level) were associated with increased HCC risk with age- and sex-adjusted hazard ratio of 4.3 (95% CI: 1.0-18.5). The annual HCC incidence of the non-cirrhotic patients with M2BPGi level <0.55 was 0.08% (95% CI: 0.02-0.3%).

Conclusion: In CHB patients receiving long-term antiviral treatment, our study identifies a serum M2BPGi threshold of 0.55 as a valuable marker for identifying individuals with minimal HCC risk.

Abstract Submission No. 101743

O-0199

Effects of tenofovir alafenamide on the risk of hepatocellular carcinoma in Hong Kong

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Background and Aims: Tenofovir alafenamide (TAF) is a novel pro-drug of tenofovir. We aimed to evaluate the one-year and two-year cumulative incidence of hepatocellular carcinoma (HCC) in patients with chronic hepatitis B (CHB) receiving TAF treatment.

Method: This is a retrospective cohort study in Hong Kong. CHB patients who were initially treated with TAF for at least six months were included. The baseline was defined as the start date of TAF treatment. Kaplan-Meier's method was used to evaluate the cumulative incidence of HCC with 95% confidence interval (CI).

Results: We analyzed 444 CHB patients who initially received TAF for more than six months with a mean age of 54 years old, among whom 262 (59.0%) patients were males. The median TAF treatment duration was 24 months. During a median follow-up duration of 28 months, 10 TAF-treated patients developed HCC. We then censored the time at two years to evaluate the one-year and two-year cumulative HCC incidence. The one-year and two-year cumulative incidences of HCC in TAF-treated patients were 1.2% (95%CI: 0.5% - 3.0%) and 2.9% (95%CI: 1.4% - 5.7%), respectively (Figure). The one-year HCC incidence was comparable with that of entecavir (ETV)-treated CHB patients (1.3%, 95%CI: 1.1% - 1.4%) and higher than tenofovir disoproxil fumarate (TDF)-treated CHB patients (0.1%, 95%CI: 0.01% - 0.4%), which were reported by another retrospective cohort study in Hong Kong.

Conclusion: TAF treatment is associated with a comparable HCC risk with ETV treatment, but higher than TDF treatment.

Abstract Submission No. 101756

O-0200

A random survival forest model for predicting HBeAg seroconversion in CHB patients treated with NAs

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Background: Achieving Hepatitis B e-antigen (HBeAg) seroconversion is a pivotal treatment goal for patients with chronic hepatitis B (CHB) received nucleos(t)ide analogues (NAs) treatment. We developed a novel model to predict HBeAg seroconversion in CHB patients utilizing the Random Survival Forest (RSF) algorithm.

Methods: A total of 655 CHB patients who underwent NAs treatment from Nanjing Drum Tower Hospital (Nanjing cohort) and Huai'an No. 4 People's Hospital (Huai'an cohort) were retrospectively analyzed. The Nanjing cohort was split into a training set (n = 320) and an internal validation set (n = 138) randomly with the ratio of 7:3. The Huai'an cohort formed as an external validation set (n = 197). A predictive RSF model was constructed and validated through discrimination and calibration. The Kaplan-Meier method was employed for evaluating the risk stratification of patients.

Results: The overall HBeAg seroconversion rates were 21.9%, 18.1%, and 11.7% in the training set, internal validation set, and external validation set, respectively. The RSF-based model exhibited good calibration and relatively high accuracy for predicting HBeAg seroconversion with a C-index of 0.873, 0.734, and 0.795 in the three sets, respectively. The model effectively stratified patients into high and low-points groups, with those scoring ≥ 14.1 demonstrating a significantly higher cumulative incidence of HBeAg seroconversion compared to those with scores < 14.1 (P < 0.0001).

Conclusions: We trained and externally validated a novel RSF-based model using commonly available predictors for accurately predicting HBeAg seroconversion in CHB patients receiving NAs treatment.

Abstract Submission No. 200019

O-0201

Impact of different ALT thresholds on the treatment eligibility of patients with CHB

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Background: Treatment initiation thresholds of alanine aminotransferase (ALT) differ among international guidelines for chronic hepatitis B (CHB). The study aimed to investigate the impact of different ALT treatment thresholds on the antiviral treatment eligibility of patients with CHB.

Methods: Clinical, biochemical, and serological information of untreated patients with CHB was retrieved from a nationwide hepatitis B registry database named China Registry of Hepatitis B. The rates of treatment eligibility according to the newly updated China guidelines for these patients were estimated based on different ALT treatment thresholds.

Results: A total of 5018 patients with CHB were included, comprising 3152 males (62.81%) and 1866 females (37.19%). The overall rate of treatment eligibility per the updated Chinese guidelines would increase from 86.89% to 93.74% if the ALT treatment threshold decreased from 50/40 U/L to 30/19 U/L (males/females). For patients aged ≤ 30 years and without a family history of HCC or cirrhosis, the rates of treatment eligibility would be increased by 13.7%, 36.5%, and 55.5% if the ALT treatment threshold decreased from 50/40 U/L to 40 U/L, 35/25 U/L,

and 30/19 U/L, respectively. Furthermore, lower treatment thresholds were associated with lower fibrosis burden as measured by APRI and FIB-4 scores.

Conclusions: Lowering the ALT treatment threshold could benefit more patients who are already at higher risk of disease progression. Expanding treatment in China would contribute to achieving the global goal of reduction in HBV-related mortality by 2030.

Abstract Submission No. 200097
O-0202

Enhancer 1 unevenly activates the preS1 promoter of integrated HBV DNA and impacts HBsAg secretion

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Background & Aims: The expression of HBsAg from integrated HBV DNA limits the achievement of functional cure for chronic hepatitis B. Thus, characterizing the unique expression and secretion of HBsAg derived from integrated HBV DNA is of clinical significance. **Approach & Results:** A semi-quantitative analysis of intrahepatic HBsAg protein level in 563 treatment-naïve patients revealed that, in contrast to the significantly lower serum HBsAg levels, no significant decrease of intrahepatic HBsAg protein was observed in the HBeAg-negative patients, as compared to that in HBeAg-positive patients. *In vitro* studies of integrated HBV DNA mimic and long-read RNA sequencing of liver biopsy from patients revealed that, the lower HBsAg secretion efficiency seen in HBeAg-negative patients might be attributed to a relative increased proportion of 2.4 kb HBV RNA derived from integrated HBV DNA than covalently closed circular DNA (cccDNA), which resulted in L-HBsAg over-expression and the subsequent impaired HBsAg secretion. Mechanistically, the change of 2.4 kb HBV RNA proportion was caused by retargeting and uneven activation on preS1 (SP1) than preS2 (SP2) promoters by HBV enhancer 1 (EnhI) element, largely due to the loss of core promoter (CP) in integrated HBV DNA.

Conclusions: The secretion of HBsAg originated from integrated HBV DNA was impaired. Mechanistically, functional deficiency of CP leads to the promoter(s) retargeting of EnhI and uneven activation of SP1 over SP2, resulting in an increase in proportion of L-HBsAg.

Abstract Submission No. 200252
O-0203

Clinical Predictors of Functional Cure in CHB Patients Treated with Pegylated Interferon Alpha-2b

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BACKGROUND & AIMS: Functional cure of chronic hepatitis B (CHB) is now the goal of treatment, but is rarely achieved with current therapy, such as pegylated interferon or long-term nucleos(t)ide analogues (NUCs). In this study, we aimed to explore the novel biological indicators in peripheral blood that can predict the efficacy of pegylated interferon alpha-2b (PEG-IFN α -2b) treatment for CHB and its clinical significance.

Methods: This observational study retrospectively enrolled CHB patients who were treated with PEG-IFN α -2b at the Fifth People's Hospital of Suzhou from January 2020 to May 2023, a total of 151

patients. We comprehensively analyze the expression levels of 83 indicators at the baseline in the patients, including hemocyte indicators, biochemical indexes and serum virologic markers. According to the achievement of functional cure (FC group, n = 43) or non-achievement of functional cure (NFC group, n = 108) at End-of-treatment, the data were analyzed and grouped. Statistical analysis using GraphPad Prism 9.5.1, SPSS 26.0, and MedCalc.

Results: Thirteen blood markers such as Hepatitis B surface antigen (HBsAg), hepatitis B e antigen (HBeAg) and hepatitis B virus-deoxyribonucleic acid (HBV DNA) at baseline showed differences between the FC groups and NFC groups treated with PEG-IFN α -2b ($p < 0.05$). In contrast, women are more likely to achieve a functional cure with interferon therapy. HBsAg and lipoprotein(a) (Lp(a)) were associated with FC, with AUROCs of 0.87 (0.750 - 0.914, $p < 0.0001$) and 0.77 (0.657 - 0.846, $p < 0.0001$). A combination of HBsAg $< 2.09 \log_{10}$ U/ml and Lp(a) > 123.3 mg/L at baseline had a effective predictive for FC with an AUROC of 0.902 (0.824 - 0.953, $p < 0.001$). In the advantaged groups treated with PEG-IFN α -2b, Lp(a) and Mononuclear cell ratio (MONO %) also can be used to predict FC with AUROCs of 0.74 (0.587 - 0.981, $p = 0.004$) and 0.71 (0.552 - 0.842, $p = 0.001$) besides HBsAg, HBsAb and HBV-DNA.

Conclusions: The Higher Lp(a) at baseline with PEG-IFN α -2b, the easier to achieve functional cure. A predictive model constructed using baseline HBsAg and Lp(a) in CHB patients had good predictive value for achieving functional cure treated with PEG-IFN.

Keywords: PEG-IFN α -2b, functional cure, lipoprotein(a), HBsAg, CHB

Abstract Submission No. 101165
O-0204

Cost of Hepatitis C Virus self-testing in Malaysia: A micro-costing study

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Background: The seroprevalence of Hepatitis C virus (HCV) is 0.3%-2.5% in Malaysia's general population, with 4.6% prevalence in men who have sex with men (MSM), and 74.0% among people who inject drugs (PWID) on methadone maintenance treatment. A cohort study led by FIND, Malaysian AIDS Council and Malaysian Ministry of Health in 2021-2022 provided HCV self-tests (HCVST) through an existing online platform (Jom-Test) for HIV self-testing. We calculated the economic cost of HCVST in this study.

Methods: Participants were randomized to the intervention (249 in oral-fluid-based HCVST group, 250 in blood-based HCVST group, each receiving HCVST kits and instructions delivered by mail) and control groups (250, received information about facility-based HCV testing). Costs were gathered from program expenditure records in local currency units and converted to 2021 US Dollars. Research-specific costs were excluded.

Results: Most participants (92%) identified as MSM and 1% as PWID. There was 98% uptake of HCV testing in the HCVST arms compared to 51% in the control group. Total fixed costs were \$113,463 (63.4% staff, 19.3% start up, 11.0% recurrent, 1.9% equipment, 1.3% overheads), with \$4,125 total variable costs (test kit and delivery costs). Mean HCVST costs per patient were \$165 (oral-fluid; \$151 fixed and \$14 variable) and \$154 (blood; \$151 fixed and \$3 variable).

Conclusion: This micro-costing estimates the cost of HCVST in Malaysia, but cost-effectiveness of HCVST will depend on screening yield/prevalence, and numbers reached for testing. Few PWID participated, indicating that reaching this population may require different targeted approaches.

Abstract Submission No. 101894

O-0205

Hepatitis C Virus (HCV) Transmission among Japan's Limited Risk Groups

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Background: In Japan, despite low nationwide hepatitis C incidence, new infections persist among people who inject drugs (PWID) and men who have sex with men (MSM), hindering HCV eradication. Therefore, this study aimed to explore the status of HCV transmission among those groups in Japan.

Methods: Hiroshima University and the Gastroenterology Department of National Hospital Organization, Osaka, conducted a retrospective cohort study, recruiting HCV-infected patients from January 2009 to December 2023. Patients were recruited both prospectively and retrospectively, with serum samples collected before anti-HCV treatment. HCV RNA was extracted, and the full core region (576 base-pairs) was sequenced using the Sanger method. Genotype distribution was determined by phylogenetic analysis.

Results: We have already received 108 samples with additional 17 samples awaiting analysis. The updated results will be presented at the conference. As of now, the subjects were divided into four groups: non-MSM PWID (27), MSM PWID (15), MSM non-PWID (23), and non-MSM non-PWID (43). Of the 108 samples analyzed, 107 could be sequenced. The most common genotype among non-MSM PWID was 2a (56%), while in the MSM PWID, MSM non-PWID, and non-MSM non-PWID groups, it was 1b (87%, 65%, and 70%, respectively). By phylogenetic tree, clusters were found only in MSM but not in PWID. Moreover, non-MSM non-PWID were not closed to either MSM or PWID.

Conclusion: The transmission route for PWID is determined by MSM status, whereas the MSM group exhibited the same transmission route regardless of PWID, emphasizing prioritized control measures among MSM for HCV elimination in Japan.

Abstract Submission No. 200246

O-0206

Improving HCV Diagnosis: Precision Classification with Data Mining for Identify Suspected Patients

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The global prevalence of chronic hepatitis C virus (HCV) infection affects an estimated 58 million people, with approximately 1.5 million new infections reported annually. Consequently, the development of precise prediction models utilizing machine learning techniques is highly valuable. This study aimed to employ data mining techniques to classify individuals suspected of having HCV infection through various classification models. The research incorporated multiple methods, including data visualization with clean data, standard-scaler for data normalization, and the creation of dummy variables. Additionally, the study involved transforming and splitting data for training and testing, applying the Synthetic Minority Over-Sampling Technique (SMOTE) on the training dataset, and evaluating model performance using various metrics. Research outcomes were detailed based on patient-specific variables such as Age, Sex, ALB, ALP, ALT, BIL, CHE, CHOL, CREA, GGT, and PROT. The application of machine learning to a dataset of HCV-suspected patients demonstrated notable progress in healthcare precision. The Random Forest (RF) algorithm emerged as superior, exhibiting high accuracy and AUC values. This study underscores the importance of data mining, particularly highlighting the efficacy of the RF model, in advancing the detection of HCV. The integration of SMOTE effectively addressed imbalances in datasets, contributing to an improved model performance.

Abstract Submission No. 100316

O-0207

Improvement of Hepatitis C Virus Care Cascade by In-hospital Reflex tEsting ALarm-C (REAL-C) model

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Background: WHO has set targets to eliminate viral hepatitis, including HCV infection, by 2030. Achieving these goals necessitates improved rates of diagnosis and treatment. We present the results of the in-hospital Reflex tEsting ALarm-C (REAL-C) model, which incorporates reflex HCV RNA testing and sending alarming messages for physicians.

Methods: We conducted a retrospective study at Asan Medical Center in Seoul, Republic of Korea, focusing on 1,730 patients newly testing positive for anti-HCV between March 2020 and June 2023. Three distinct periods were defined: pre-REAL-C (n=696), incomplete REAL-C (n=515), and complete REAL-C model periods (n=519). The primary outcome measured was the rate of HCV RNA testing throughout the study period. Additionally, the referral rate to GI department, linkage time for diagnosis and treatment, and the treatment uptake rate.

Results: Rate of HCV RNA testing increased significantly from 51.0% (pre-REAL-C) to 95.6% (complete REAL-C). This improvement was consistent across clinical departments, regardless of patients' comorbidities. Among patients confirmed with HCV infection, the GI referral rate increased from 57.1% to 81.1% after the implementation of the REAL-C model. Treatment uptake rates among treatment-eligible patients was 92.4% during the study period. The mean days from anti-HCV positivity to HCV RNA testing decreased from 45.1 to 1.9. The mean days from the anti-HCV positivity to direct-acting antiviral treatment also decreased from 89.5 to 49.5 with the REAL-C model.

Conclusion: The REAL-C model, featuring reflex testing and alarming messages, effectively increased HCV RNA testing rates and streamlined care cascades. Our model facilitated progress toward achieving the WHO's elimination goals for HCV infection.

Abstract Submission No. 100467

O-0208

Factors of aggravation of esophagogastric varix after DAA in HCV decompensated cirrhotic patients

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Background: Sustained virologic response (SVR) rate of direct-acting antiviral (DAA) therapy has been reported to be approximately 90% in patients with hepatitis C virus (HCV) associated decompensated cirrhosis. However, the factors associated with the aggravation of esophagogastric varix after DAA in patients with decompensated cirrhosis is unclear.

Methods: A total of 116 patients with HCV associated decompensated cirrhosis who started DAA therapy from February 2019 to December 2021 and for whom esophagogastric varix could be evaluated before and after DAA were included. We defined the aggravation of esophagogastric varix as rupture of varix and treatment for varix, and investigated the cumulative rate of and the factors associated with the aggravation of esophagogastric varix.

Results: The median age was 67 years, and 78% of patients were Child-Pugh B. The SVR rate was 95.7% (111/116). During the median observation period of 17.9 months from the start of DAA, 15 patients underwent treatment for varix and two underwent varix rupture. The 3-year cumulative aggravation rate of varix was 22.4%. In multivariate cox proportional hazard analysis, baseline status of esophagogastric varix of F2 or more ($p=0.002$), higher baseline γ -glutamyl transpeptidase levels ($p=0.018$) and virologic failure ($p=0.015$) were significantly associated with the aggravation of esophagogastric varix. On the other hand, Child-Pugh class and alcohol intake were not.

Conclusions: Among patients with HCV associated decompensated cirrhosis treated with DAA, careful attention for the aggravation of esophagogastric varix are needed in patients with esophagogastric varix of F2 or more, higher baseline γ -glutamyl transpeptidase levels or virologic failure.

Abstract Submission No. 100531

O-0209

A government-leading multi-organization collaborative model for HCV elimination in Yuxi, Yunnan

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Objective: Aim to explore a model to call back the patients diagnosed by HCV-Ab(+) but untreated (DBU) in Yuxi prefecture, Yunnan Province.

Methods: Yuxi Center for Disease Control(CDC) collaborated with hospitals, civil affairs and polices center to developed a model to increase relinking rate for DBU population. Peer-to-peer education was utilized to patients' family members for screening. Primary health centers responses testing and treatment of referred HCV-Ab(+) patients. The police centers support to relink DBU patients who were in compulsory drug rehabilitation facilities. The civil affairs department coordinate financial assistance.

Results: From June to September 2023, 14 medical educations were hold by CDC for HCPs and government workers from 9 countries and 11 hospitals. From July to September, 3380 HCV-Ab(+) patients were contacted. 2465 patients (72.9%) were called back and completed HCV RNA testing. 40.4% patients (995/2465) were HCV RNA-positive. 33.7%(335/995) patients received SOF/VEL treatment, including 9 inmates and 36 individuals in drug rehabilitation centers. 100% (221/221) achieved SVR12. Through peer-to-peer patient education, another 374 sexual partners and 201 offspring received HCV-Ab screening. 14%(77/548) were HCV-Ab(+) and 100%(77/77)received HCV RNA testing. 28.6%(24/77) were HCV RNA(+) and 83.3%(20/24) received SOF/VEL treatment.

Conclusion: This collaborative model successfully relink DBU HCV patients.

Abstract Submission No. 100612

O-0210

Liver Stiffness Measurement and Risk of Hepatocellular Carcinoma After HCV Eradication in Cirrhosis

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Background & aims: Patients with cirrhosis secondary to chronic hepatitis C (HCV) are at risk for hepatocellular carcinoma (HCC) despite a sustained virological response (SVR). We examined whether post-SVR liver stiffness measurement (LSM) could be used to stratify HCC risk.

Methods: This was a retrospective cohort study of 1,850 participants identified from the Veterans Health Administration, with HCV cirrhosis and SVR, followed up over 5099 person-years, from the time of post-SVR elastography until death, HCC, or the end of the study.

Results: The risk of HCC increased by 3% with every 1 kPa increase in LSM (adjusted Hazard Ratio [aHR] 1.03, 95% confidence interval [CI] 1.01-1.04, $p<0.001$) and decreased with the number of years from SVR (aHR 0.79, 0.70-0.90, $p=0.0003$). The adjusted annual risk of HCC was 2.03% among participants with post-SVR LSM <10 kPa, 2.48% in LSM 10-14.9 kPa (aHR 1.71, 95% CI 1.01-2.88, $p=0.046$), 3.22% for LSM 15-19.9 kPa (aHR 1.59, 95% CI 0.78-3.20, $p=0.20$), 5.07% among LSM 20-24.9 kPa (aHR 2.55, 95% CI 1.30-5.01, $p=0.01$), and 5.44% in LSM ≥ 25 kPa (aHR 3.03, 95% CI 1.74-5.26, $p<0.0001$). The adjusted annual risk of HCC was $<0.4\%$ in participants with LSM <5 kPa and without diabetes mellitus.

Conclusions: LSM predicts rates of HCC in patients with HCV cirrhosis after SVR at multiple cutoff levels and offers a single test to predict portal hypertension-related complications and HCC. Patients with LSM <5 kPa in the absence of diabetes mellitus had a low risk of HCC where surveillance could be discontinued.

Abstract Submission No. 101032
O-0211

Long term outcome following HCV treatment with Glecaprevir/Pibrentasvir in people who use drugs

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Background: Long-term outcome data after HCV treatment are limited, especially for individuals who use drugs. In this study, we investigated the long-term outcomes of patients who achieved SVR12 with G/P treatment.

Methods: We followed up with patients who achieved SVR12 (2019-22). Participants were documented to be viremic with any HCV genotype, non-cirrhotic, previously untreated for their infection, and actively using or injecting drugs before initiating treatment and all received G/P as three tablets daily for eight weeks within the context of a multidisciplinary model of care.

Results: We identified 108 subjects with a median age of 47 (22-75) years, 27.8% female, and 21.3% Indigenous. Nearly half (46.7%) did not have stable housing. Active drug use was confirmed in 97.2% of cases, and all participants achieved SVR12 during the study. Among the cured participants, 104 (96.3%) remained alive, and 4 individuals died of an opioid overdose. Out of the 104 patients, 98 (94.2%) remained HCV-free, and 6 (5.8%) were re-infected (rate of 0.006/100 person years). All 6 have recently initiated therapy and outcomes of repeat therapy are pending.

Conclusion: To achieve the goal of HCV elimination by 2030, a systematic approach to diagnosing and treating infections in PWUD will be crucial, including maintenance in long-term follow-up after cure. Most patients remain alive and cured, with a small number of overdose deaths in the context of an ongoing opioid crisis. Maintenance in follow up allowed us to identify all cases of reinfection and re-initiate therapy within our program.

Abstract Submission No. 101158
O-0212

Association of metabolic abnormalities with HCC development and survival in CHC patients after SVR

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Aims: The risk of carcinogenesis and liver-related or -unrelated death after SVR among patients with HCV has not been fully elucidated. Lifestyle factors have recently received attention as a risk factor, and we aimed to elucidate the association of metabolic abnormalities with liver carcinogenesis and prognosis after SVR with DAA.

Patients and Methods: A multicenter registry study, 1089 of 1267 patients without a history of HCC prior to DAA treatment enrolled from September 2014 to August 2023 who had achieved SVR were included in the study. The start date of follow-up is defined as the date of achieving SVR. Cox proportional hazards regression model was used to determine factors associated with the development of cancer and death among patients with and without prior history of HCC by using STATA 16 (StataCorp LP, College Station, TX, USA)

Results: The median number of follow-up was 3.8 years. Fifty-two patients (4.8%) without a prior history developed HCC. The following factors were identified as contributors to carcinogenesis: male (HR 2.0,

$p=0.018$), diabetes (HR 2.1, $p=0.023$), SVR-Plt < 150,000 (HR 2.1, $p=0.009$), SVR-GGT (HR 2.5, $p=0.015$), and hypovascular nodule (HR 8.4, $p<0.001$). extracted in univariate analysis. Even after adjustment for diabetes, dyslipidemia, alcohol consumption, obesity, and fatty liver, high SVR-GGT was associated with carcinogenesis (HR 2.4, $p=0.030$), and high SVR-GGT was a risk of carcinogenesis in the no alcohol consumption and no diabetes group ($n=560$) (HR 10.6, $p<0.001$). Next, life expectancy analysis revealed 45 deaths (4.1%) after SVR, 9% from liver cancer, 22% from other organ cancer, and 42% from cardiovascular death or CPA/drowning. Univariate analysis extracted factors involved in death as age >70 (HR 1.8, $p=0.044$), diabetes (HR 2.0, $p=0.044$), and Alb <3.5 (HR 5.3, $p<0.001$), although only low Alb was significant (HR 3.6, $p=0.023$) after adjustment for metabolic abnormalities. When stratified by platelet level, diabetes (HR 3.1, $p=0.017$) and high SVR-GGT (HR 6.1, $p=0.002$) were associated with death in the group with platelets over 150,000.

Conclusion: Patients with elevated GGT after SVR are at high risk of HCC regardless of their metabolic abnormalities and lifestyle, and are also at high risk of death including cardiovascular events and malignancies of other organs. GGT levels after SVR may reflect hepatitis C-specific oxidative stress as well as induction by lifestyle factors such as alcohol consumption and diabetes mellitus.

Abstract Submission No. 101286
O-0213

Real world outcomes of sofosbuvir/velpatasvir/voxilaprevir in naïve chronic hepatitis C patients

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Background: Pan-genotypic Sofosbuvir/Velpatasvir/Voxilaprevir (SOF/VEL/VOX) for 8-12 weeks has been shown highly effective, safe, and well-tolerated in treating patients with chronic hepatitis C (CHC) in POLARIS studies, however, there are no real-world setting data are available especially in treating naïve patients. This is the first opportunity from all over the world to demonstrate SOF/VEL/VOX efficacy and safety in Real World setting for the naïve patients.

Methods: SOF/VEL/VOX was approved in Turkey to use pan-genotypically for noncirrhotic naïve, cirrhotic naïve, treatment experienced patients for 8, 12 and 12 weeks respectively. We presented preliminary results of naïve CHC patients.

Results: Of the 180 patients 89.4% ($n=161$) were naïve, 42.9% ($n=69$) completed 12nd week follow-up after the completion of the 8 ($n=65$) or 12 weeks treatment. Of these 69 patients 47.8% were female, median age was 59 (24-85), 77.3% were genotype 1 and 68.2% were genotype 1b. Median HCVRNA at the time of diagnosis were 1.310.000 IU/mL (19.426-10.000.000). Undetectable HCVRNA levels at the first month, end of the of treatment were 87.3% and 100% respectively and SVR12 were 98.6% (68/69). One relapsed patient was genotype 4. Median ALT levels were 36.0, 17.0 and 15.0 IU/L at diagnosis, end of the treatment and at the SVR12 follow-up respectively. There were not any treatment interruption or adverse event leading to treatment cessation.

Conclusion: SOF/VEL/VOX combination treatment is safe and presenting high SVR12 rates for the naïve CHC patients, further results with the high number of patients will be needed to prove this preliminary results.

Abstract Submission No. 101668

O-0214

Elevated GGT with metabolic factors enhances HCC development after HCV eradication

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Background: Gamma-glutamyltransferase (GGT) is known as an oxidative stress marker, but its association with the development of hepatocellular carcinoma (HCC) after sustained viral response (SVR) in patients infected with hepatitis C virus (HCV) is still unclear. We investigated the risk stratification using GGT after SVR.

Methods: The study enrolled 4773 patients who had achieved SVR with antiviral treatment and had no prior history of HCC. The definition for normal GGT was ≤ 32 IU/L in female and ≤ 64 in male. We analyzed the impact GGT and some metabolic factors at SVR 24 on subsequent HCC incidences.

Results: The median observation period was 6.7 years. Annual HCC rate was 4.7 per 1000 person-years. To examine the impact of GGT on the development of HCC, we classified the subjects into 4 groups; Group A: normal GGT with no alcohol and low BMI, Group B: normal GGT with alcohol or high BMI, Group C: high GGT with no alcohol and low BMI, Group D: high GGT with alcohol or high BMI. The 10-year cumulative HCC rates were in the order of Group D > B > C > A (8.2%, 4.9%, 1.8%, and 1.5%, respectively) ($P < 0.001$). Similar results were observed in multivariable Cox regression.

Conclusion: HCC incidence was lower in patients with normal GGT even if they had a history of alcohol consumption and obesity. On the other hand, elevated GGT enhance HCC development in those with a history of alcohol consumption or obesity. Further investigation is needed to clarify its mechanism.

Abstract Submission No. 101877

O-0215

Real-world effectiveness and tolerability of interferon-free DAA for HCV patients with genotypes 1-6

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Objectives: As practice pattern and HCV genotypes (GT) vary geographically, a global real-world study from both East and West covering the range of GTs can help inform practice policy towards the 2030 HCV elimination goal. This REAL-C study characterized patients

receiving direct-acting antivirals (DAA) including older regimens in routine practice, focusing on GT3/6.

Methods: We analyzed sustained virological response (SVR12) of 15,849 CHC patients from 39 REAL-C clinical sites from Asia Pacific, North America and Europe.

Results: The mean age was 62 ± 13 years, with 49.6% male, 91.1% Asian (52.9% Japanese, 25.7% Chinese/Taiwanese, 5.4% Korean, 3.3% Malaysian and 2.9% Vietnamese), 6.4% White, 1.3% Hispanic/Latino and 1% Black/African-American, 34.8% with cirrhosis, 8.9% HCC, and 24.9% treatment-experienced (TE:20.7% interferon, 4.3% DAA). The largest group was GT1 (10246[64.6%]), then GT2 (3686[23.2%]), GT3 (1151[7.2%]), GT6 (457[2.8%]), GT4 (47[0.3%]), GT5 (1[0.006%]), and untyped GTs (261[1.6%]). SVR12 was 96.9% overall, >95% for GT1/2/3/6, but 91.5% for GT4. SVR12 for GT3 was 95.1% overall, and 98.2%/94.0% for GT3a/3b. SVR12 was 98.3% overall for GT6, lower for cirrhosis and TE (93.8%) but $\geq 97.5\%$ for treatment-naïve regardless of cirrhosis status (Fig.1). On multivariable analysis, advanced age, prior treatment failure, cirrhosis, active HCC and GT3/4 were independent predictors of lower SVR12, while Asian was a significant predictor of achieving SVR12.

Conclusion: In this diverse multinational real-world cohort of patients with diverse GTs, the overall cure rate was 96.9%, despite large numbers of cirrhosis, HCC, TE, and GT3/6. SVR12 for GT3/6 with cirrhosis and TE was lower but still excellent (~90%).

Abstract Submission No. 101882

O-0216

Mortality rates among patients successfully treated for HCV: A real world multinational cohort study

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Objectives: HCV cure with SVR following DAA treatment reduces mortality risk, but data on risk factors associated with mortality following DAA-associated SVR are sparse. We aimed to fill in this gap.

Methods: 11,451 patients with SVR were enrolled in a real-world multinational cohort from 39 REAL-C clinical sites, and divided into four liver disease severity groups: non-cirrhosis (group 1), compensated cirrhosis (group 2), decompensated cirrhosis (group 3) and HCC (group 4). Follow-up started 24 weeks after antiviral treatment completion and ended on date-of-death or end-of-study follow-up (31/08/2023), whichever came first.

Results: 704 (6.2%) participants died during a 4.6 ± 2.4 years follow-up: 124/207/133/240 in group 1/2/3/4, respectively, yielding corresponding all-cause mortality rates per 1000 person-years (95%CI) of 5.06 (4.24-6.03), 10.2 (8.86-11.6), 46.5 (39.2-55.1), and 49.4 (43.5-56.1). For patients without HCC at baseline, mortality rates stratified by sex, age, DM and liver fibrosis severity were shown in Fig.1A. For patients with HCC at baseline, mortality rates stratified by sex, age and presence of active HCC were shown in Fig.1B. In multivariable analyses, older age (>65 years:3.1 times), male(1.4 times), fibrosis severity (4.7/1.7 times for decompensated/compensated cirrhosis), HCC

(4.0/2.0 times for active/inactive HCC) were significantly associated with higher mortality.

Conclusion: Patients with SVR after DAAs face different risks of death, with mortality strongly influenced by pre-DAA liver disease severity and patient factors such as age, sex, and DM comorbidity. These findings highlight the need for individualized risk assessment and continued monitoring of high risk patients after successful HCV treatment to maximise the impact of HCV cure.

Abstract Submission No. 102060
O-0217

Attention not only to hepatocellular carcinoma but also to carcinogenesis of all organs.

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Objective: To prospectively observe the development of all-organ malignancies in hepatitis C patients treated with DAA and to observe overall survival.

Methods: A prospective observational study was conducted on hepatitis C patients treated with DAA from July 2013 to November 2023. The primary endpoint was the occurrence of all malignancies, and the secondary endpoint was overall survival.

Results: All 689 patients were prospectively observed from the start date of DAA treatment until November 30, 2023. The median observation period was 6.0 years. During the observation period, 141 malignancies occurred in 128 patients. These included 70 cases of hepatocellular carcinoma (HCC), 64 cases of malignancy of other organs (non-HCC). The overall cancer incidence was 4.6% at 1 year, 12.3% at 3 years, 19.4% at 5 years, and 24.0% at 7 years. The HCC incidence was 3.2%, 7.4%, 11.2%, and 12.9%, showing a trend of down of carcinogenesis after 5 years. The incidence of non-HCC continued to occur at 1.6%, 5.2%, 9.2%, and 12.6%. Forty-seven patients died during the follow-up period: 1-year survival rate 98.9%, 3-year survival rate 96.2%, and 5-year survival rate 94.1%.

Conclusion: The incidence of HCC tended to slow down over time. On the other hand, it was observed that carcinogenesis of non-HCC continued to occur. It is important to follow up with caution not only for HCC but also for all organs.

Abstract Submission No. 100106
O-0218

Impact of DAAs on HCC Risk in Chinese Hepatitis C Patients: A 10-Year Follow-Up Study

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Background/Aims: The long-term benefit of direct-acting antiviral agents (DAAs) therapy after achieving sustained virological response (SVR) has not been clearly established, particularly in the Chinese population. The incidence of hepatocellular carcinoma (HCC), decompensated cirrhosis and all-cause mortality were compared between patients treated with DAAs to achieve SVR and those who did not in a cohort of Chinese hepatitis C patients.

Methods: We used data from a cohort of Chinese patients with hepatitis C, which included those diagnosed with HCV since 2011. Those who received DAA were followed up until the outcome event or 31 December 2022. The primary outcomes were HCC, decompensated cirrhosis and all-cause mortality. Multivariate proportional hazards model was performed to assess the impact of DAAs and cirrhosis status on morbidity.

Results: The study comprised 1272 (92.1%) patients with SVR and 109 (7.9%) patients with no-SVR. Median follow-up time of 61.0 (IQR:39.0-81.0) months. The incidence of HCC was 5.1/1000 person-years (HCC=30) in the SVR group and 15.0/1000 person-years (HCC=12) in the no-SVR group. In multivariate models, SVR was associated with a significant reduction in HCC compared with no SVR (adjusted hazard ratio [aHR]: 0.32; 95% CI: 0.16-0.67). Cirrhosis was associated with a high risk of developing HCC and decompensated cirrhosis. Patients achieving SVR had a higher risk of reduced HCC in the group with cirrhosis than in the group without cirrhosis.

Conclusions: Achieving SVR is associated with a significantly reduced risk of HCC and calls for early treatment of DAAs in patients with cirrhosis.

Abstract Submission No. 100142
O-0219

Dynamic serum M2BPGi to predict hepatic fibrosis in HCV patients achieving SVR to DAAs

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Background: Little is known about the role of dynamic serum Mac-2 binding protein glycosylation isomer (M2BPGi) levels to assess hepatic fibrosis in hepatitis C virus (HCV)-infected patients who have achieved sustained virologic response (SVR₁₂) to direct-acting antivirals (DAAs).

Methods: Serum M2BPGi levels and liver stiffness measurement (LSM) using transient elastography (TE) were evaluated in 638 patients who achieved SVR₁₂. Receiver operating characteristic (ROC) curves were generated to assess the diagnostic accuracy of baseline and SVR₁₂ M2BPGi levels in distinguishing a fibrosis stage of $\geq$ F2, $\geq$ F3, and F4. The selected M2BPGi cutoff levels at baseline and SVR₁₂ were determined based upon the maximal Youden index, and optimized positive and negative likelihood ratios (LRs).

Results: Compared to baseline level, the median serum M2BPGi level at SVR₁₂ significantly decreased (1.55 versus 0.92, $p < 0.001$), irrespective of the fibrosis stage. The areas under ROC curves (AUROCs)

of M2BPGi in predicting a fibrosis stage of $\geq F2$, $\geq F3$, and $F4$ were 0.854, 0.914, and 0.947 at baseline, and 0.814, 0.913, and 0.937 at SVR₁₂, respectively. M2BPGi, with cutoff values of 2.05, 2.83, and 3.98 at baseline, and 1.49, 1.58, and 1.75 at SVR₁₂ exhibited predictive power for the presence of $\geq F2$, $\geq F3$, and $F4$, with positive likelihood ratios (LRs) of ≥ 10 . The diagnostic accuracy of M2BPGi appeared to increase with the severity of hepatic fibrosis.

Conclusions: The dynamic serum M2BPGi level can monitor the severity of hepatic fibrosis in HCV-infected patients before and after SVR₁₂ to DAA treatment.

Abstract Submission No. 100194
O-0220

Non specialist training : an effective method for micro-elimination of hepatitis C in hospital

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Background/aims: WHO aims to eradicate HCV infection by 2030. However, the current situation of eliminating hepatitis C is not satisfactory, as many patients were missed. The purpose of this study was to explore an effective method for micro-elimination of hepatitis C in hospital.

Methods: Online questionnaire was used to investigate the HCV knowledge of the non specialists from 7 medical centers in Tianjin. Then they received a brief training for the diagnosis and treatment of hepatitis C. Then the effect of training was investigated by rate of referral, diagnosis and treatment of HCV patients.

Results: More than half of hepatitis C antibody positive patients are distributed in non liver disease departments. 459 questionnaires were retrieved and we found that only 26.4% non specialists who found hepatitis C antibody positive were familiar with the following screening step (HCV RNA). Additionally, 8.7% of doctors were familiar with the DAA drugs for hepatitis C treatment, and 78.4% were completely unaware of the hepatitis C medical insurance policy. The rate of HCV screening, diagnostic and treatment in non liver disease departments were 67.2%, 41.1% and 47.3% before training, however, the rates were 92.3%, 92.1% and 94.4% after the training (P all <0.001).

Conclusions: There was a huge obstacle to the elimination because the low awareness of hepatitis C in non specialists. A brief training could significantly improve the effect of diagnosis and treatment. This may be an effective and fast way for us to achieve the 2030 goals.

Abstract Submission No. 100250
O-0221

Clinical utility of HCV core antigen measurement for HCVAb-positive patients towards HCV elimination

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The cascade of hepatitis C virus (HCV) cure/care depends on the linkage of medical examination and treatment initiation to eliminate HCV. We conducted a prospective, non-interventional, observational study from April 2022 to March 2023 targeting patients who underwent HCV antibody testing during hospitalization or outpatient visits. HCV core antigen levels were additionally measured using residual serum from HCV antibody-positive cases. We encouraged patients to receive medical care if both samples were positive. The HCV antibody positivity rate was 4.4% (390/8,805 cases), with a significantly higher rate in outpatient testing (4.6%) than in inpatient testing (2.3%) ($P=0.002$). Among the 378 HCV antibody-positive patients with sufficient residual serum, HCV core antigen positivity rate was 8.2% (31/378 cases) and significantly higher in patients with HCV antibody level ≥ 10 COI ($n=249$) than in those with <10 COI ($n=129$) (11.6% vs. 1.6%, $P=0.002$). The median age of the HCV core antigen-positive individuals (14 male and 17 female) was 76 years (range: 18-92 years). Apart from 2 patients with no scheduled visits, the remaining 29 patients were urged to undergo detailed examination and follow-up. One patient tested negative for HCV RNA. Nine of the remaining 28 cases (32.1%) were prescribed direct-acting antiviral (DAA) treatment, 13 (46.4%) were deemed DAA-ineligible due to such complications as hepatocellular carcinoma, and 6 (21.4%) had no interest in therapy. Performing HCV core antigen measurement with residual serum from HCV antibody-positive individuals may be useful for identifying HCV carriers and directing them towards additional examination and treatment.

Abstract Submission No. 100326
O-0222

Long-term Serum Ferritin Dynamics in Patients Receiving Antiviral Treatment for HCV Infection

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Background: Data regarding the long-term serum ferritin dynamics and factors associated with the trends of changes in patients receiving antiviral treatment for hepatitis C virus (HCV) infection are limited.

Methods: Serum ferritin levels were evaluated biannually in 1538 HCV-infected patients receiving direct-acting antiviral (DAA) or interferon (IFN)-based treatment after confirming sustained virologic response (SVR₁₂) or not. We compared the ferritin dynamics in patients with factors of interest using the generalized estimating equation (GEE). Univariate and multivariate analyses were performed to identify predictors associated with serum ferritin evolutions.

Results: By univariate analysis, patients achieving SVR₁₂, aged > 50 year, having metabolic dysfunction-associated steatotic liver disease (MASLD), or pre-treatment HCV RNA level $> 2,000,000$ IU/mL were associated with different ferritin dynamics. Multivariate analysis showed that patients achieving SVR₁₂ (adjusted slope coefficient difference: -7.50 ng/mL/year [95% CI: -3.37 to -11.63], $p < 0.001$), and those with MASLD (adjusted slope coefficient difference: 4.16 ng/mL/year [95% CI: 0.41 to 7.91], $p = 0.0022$) were independently associated with ferritin evolutions. In patients achieving SVR₁₂, the

ferritin evolution was not affected by DAA or IFN-based treatment (crude slope coefficient difference: -3.33 ng/mL/year [95% CI: -12.78 to 6.12], $p = 0.49$), while the presence of MASLD was associated with an unfavorable ferritin evolution (adjusted slope coefficient difference: 2.86 ng/mL/year [95% CI: 0.33 to 5.39], $p = 0.021$).

Conclusions: HCV-infected patients had a decreasing trend of ferritin levels once achieving SVR₁₂, irrespective of types of antiviral treatment. Concurrent MASLD may worsen the ferritin levels even if patients achieved SVR₁₂.

Abstract Submission No. 100504

O-0223

Collaboration with community and hospital contributes to HCV elimination in database

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Background: Still a big gap in HCV patients who diagnosis-but-untreated (DBU) in China. It is the priority for HCV elimination in China.

Methods: The Centers for Disease Control and Prevention (CDC) in Wuming District of Nanning City and Tengxian County of Wuzhou City in Guangxi collaborate with community hospitals and community service centers, worked on recalling all the patients with HCV-Ab (+) from 2004 to 2021 in their data pool. Once the patients come back to the community hospital, doctors will perform the blood sampling for HCV RNA testing for them. The doctor in community hospital will phone the patients about the result and referred the patients with HCV RNA (+) to hepatologist. And then the patients will receive DAA treatment after communication with hepatologists.

Results: In the past 10 months, 4995 previously reported hepatitis C positive cases were recalled, and 1610 cases were contacted successfully. Among them, 1006 patients were tested for HCV RNA testing. The positive rate of nucleic acid was 36.5 % (367/1006). At present, 16.34 % (60 / 367) of CHC patients have been successfully referred to hepatologists for further assessment, of which 13.35 % (49 / 367) have received DAA treatment. Another 318 patients were still in the telephone follow-up and had agreed to go to the liver disease clinic for treatment in the near future.

Conclusion: CDC collaborates with community hospital and community service center contribute to HCV elimination for the DBU patients.

Abstract Submission No. 100528

O-0224

HCV Micro-elimination in private Hemodialysis center

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Objective: This study aimed to explore standard operation procedure (SOP) of HCV elimination in private hemodialysis centers.

Methods: This was a multi-center study. A Survey would be provided to medical workers and HCV-Ab(+) patients to access the awareness of the people regarding no patients accepted HCV RNA testing and

anti-viral treatment in 5 private hemodialysis centers. Then HCV knowledge education would be held. After education, HCV RNA testing will be recommended for anti-HCV(+) patients. Finally HCV RNA(+) patients will be accompanied by dedicated medical workers throughout "green channel" to hepatologists for SOF/VEL treatment.

Results: From October to November 2022, 247 medical workers and 45 anti-HCV(+) patients completed survey. 89% medical workers and 100% patients have no idea about HCV and only 7~9% medical workers would recommend patients to receive HCV screening and treatment. All the medical workers and HCV-Ab(+) patients were educated through 9 medical education tours. From March to May 2023, 100% (44/44) HCV-Ab(+) patients received HCV RNA testing, with a positivity rate of 38.6% (17/44). Till September 2023, 84.6% (11/14) patients received SOF/VEL treatment. The sustained virological response rate at 12 weeks of treatment (SVR₁₂) was 100% (11/11).

Conclusion: This SOP can greatly contribute to HCV elimination in private hemodialysis centers

Abstract Submission No. 100542

O-0225

Real-world study of Sofosbuvir/Velpatasvir for cirrhotic patients with genotype 3 HCV infection

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Objective: To explore the efficacy and safety of Sofosbuvir/Velpatasvir ± ribavirin (SOF/VEL±RBV) in the treatment of genotype 3 (GT3) chronic hepatitis C cirrhotic patients.

Methods: Patients diagnosed as GT3 HCV infection and treated at the Third People's Hospital of Kunming City from June 2018 to February 2023 were included. All patients had liver cirrhosis and treated with SOF/VEL±RBV for 12 weeks. Virologic response, liver and kidney function and adverse effects (AE) were analyzed.

Results: A total of 319 patients were included, including 308 with SOF/VEL+RBV group and 11 with SOF/VEL group (RBV intolerable). After 12 weeks off-treatment, the sustained virological response (SVR₁₂) rate in SOF/VEL+RBV group was 98.37% (303/308), and the levels of APRI score and FIB-4 index were decreased compared with baseline ($P < 0.05$). The levels of total bilirubin, AST and ALT were all decreased compared with baseline ($P < 0.05$). SVR₁₂ rate of SOF/VEL group was 72.73% (8/11). Most common AEs were mild hemolytic anemia (15.26%), fatigue (8.12%) and rash (8.77%) in SOF/VEL+RBV group, and fatigue (9.09%) in 1 case in SOF/VEL group.

Conclusion: SOF/VEL+RBV could achieve higher SVR₁₂ and well tolerated for GT3 HCV infected patients either with compensated cirrhosis or decompensated cirrhosis patients.

Abstract Submission No. 100592

O-0226

Baseline FIB4 is superior to FIB4 at SVR12 to predict HCC occurrence following DAA-attained SVR12

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INTRODUCTION: Direct-acting antiviral (DAA) has cured millions of patients with chronic hepatitis C (CHC). The need for hepatocellular carcinoma (HCC) surveillance after DAA-attained SVR12 among non-cirrhotic CHC patients remained a matter of debate. We sought to compare the performance of baseline and FIB4 at SVR12 to predict the HCC occurrence in CHC patients after DAA-attained SVR12.

Methods: This is a post-hoc analysis including all consecutive genotype 3 CHC patients treated with sofosbuvir/velpatasvir between 2018-2019 in our institution (PMID: 3321740). Primary predictor was FIB4 at baseline and SVR12 (FIB4-SVR12). Primary outcome was new HCC.

Results: A total of 779 CHC patients with SVR12 were included. Over median follow-up of 4 years, 2.3% developed HCC after SVR12. All HCC developed in patients with cirrhosis and male gender. Patients who developed HCC were older with prior history of HCC (44.4% vs 1%, $p < 0.001$) and higher median FIB4 score at SVR12 (3.9 vs 1.5, $p < 0.001$). HCC risk increases with both baseline FIB4 (low-risk: 0%, moderate-risk: 0%, high-risk: 9.8%, $p < 0.001$) and SVR12-FIB4 (low-risk: 0%, moderate-risk: 2.0%, high-risk: 18.4%, $p < 0.001$), with excellent AUC (Baseline: 0.92, SVR12: 0.88). Using FIB4-SVR12 > 3.25 to select post-SVR CHC patients for HCC surveillance significantly reduce the proportion of patients requiring HCC surveillance (87.8% vs 80.7%, $p = 0.0018$) at the expense of missing more HCC than baseline FIB4 (1.6% vs 0.2%, $p = 0.0123$).

Conclusion: FIB4 accurately risk stratify post-SVR HCC in CHC patients, however a small but persistent risk of HCC remained when post SVR12 FIB4 was used to select patients for HCC surveillance.

Abstract Submission No. 100784
O-0227

Evaluating HCV Point-of-Care Testing - a Real-World Study on People Who Inject Drugs in Singapore

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Background: The target for HCV elimination is set at $\geq 90\%$ of Chronic HCV diagnosed. Point-of-care testing (POCT) has the potential to increase diagnosis. We critically evaluated the performance of POCT using OraQuick® HCV Rapid Antibody Test.

Method: People who inject drugs (PWID) from 4 Halfway Houses in Singapore were recruited from March 2022-April 2023. Participants were concurrently screened for HCV via blood for Anti-HCV Serology and using fingerstick capillary whole blood (FSWB) and oral mucosal transudates (OMT) for POCT interpreted by trained personnel. A blinded study team-member independently assessed images of POCTs.

Results: Of 207 participants, 37.3% were Anti-HCV positive. Compared to anti-HCV serology, POCT performance on FSWB and OMT

were: Sensitivity 81.8 (73.2 - 90.4), 74.0 (64.2 - 83.8), $p = 0.014$; Specificity 100.0 (100.0 - 100.0), 98.5 (96.3 - 100), $p = 0.157$. Sub-group analysis of 30-minute pre-test nil-by-mouth instruction in 103 subjects reported Sensitivity 77.5 (64.6 - 90.4), 77.5 (64.6 - 90.4) and Specificity 100.0 (100.0 - 100.0), 98.4 (95.3 - 100.0). OMT positivity and false-negative had no correlation with sample analytical cutoff index signal distribution of Anti-HCV Serology. Inter-class correlation between real-time and imaging readings of POCT for FSWB/OMT at 20 min/40 min were Kappa 0.9666, 0.9674; 0.8803, 0.8940.

Conclusion: We observed a lower-than-reported sensitivity of OraQuick® POCT with comparable performance for FSWB and OMT. Factors such as difference in oral fluid immunoglobulin secretion, sample collection, could affect POCT reading. Nevertheless, POCT OMT remains a promising diagnostic tool for its adaptability, ease-of-performance in serial or self-testing for HCV naïve population.

Abstract Submission No. 101031
O-0228

COMPARING SOFOSBUVIR/VELPATASVIR & GLECAPREVIR/PIBRENTASVIR FOR HCV TREATMENT IN DRUG USERS

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Background: To eliminate HCV infection as a public health concern by 2030, there is a need to develop comprehensive programs among key populations such as PWUD. Two highly effective regimens are available for initial therapy: S/V given as 1 tablet/day for 12 weeks; G/P given as 3 tablets/day for 8 weeks. Data evaluating the safety, efficacy and factors determining a choice of one regimen over another in a population of PWUD is limited.

Methods: Patients were identified through outreach events in single room occupancy dwellings. Viremic patients were offered HCV treatment within a multidisciplinary. This analysis focuses on the last 120 sequential individuals who chose either treatment, correlating treatment choice with safety, efficacy, and other outcomes.

Results: Among 240 subjects enrolled, the median age was 47 for both treatment groups. We note 37.5% female, 24% Indigenous, 98.2% active drug use, 93.5% opiates/fentanyl, and 68% unstable housing. Overall, 117 and 119 patients completed therapy on G/P and S/V. Virologic relapse was documented in 3 and 4 participants on G/P and S/V. The mITT cure rate for G/P and S/V were 97%, and 2 drug overdose deaths occurred among those who initiated treatment, one on S/V and one on G/P.

Conclusion: We have evaluated two highly effective regimens in a group of inner-city PWUD. By mITT, 97% of participants were cured, with no difference between treatments. Our data supports the offer of both treatments within the setting of this program for the treatment of HCV-infected PWUD, irrespective of the level of stability.

Abstract Submission No. 101064
O-0229

Sexual transmission was common in recently acquired HCV infected patients with HIV

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Background: Diagnosis and treatment of recently acquired HCV in people living with HIV (PWLH) was still limited in China.

Methods: This prospective study would identify acquired HCV patients in the HIV outpatient clinic in Jiulongpo Hospital of Chongqing. During regular follow-up, PWLH with abnormal liver function took HCV-Ab screening, and HCV RNA testing was provided for the HCV-Ab positive patients. HCV RNA positive patients would receive Sofosbuvir/Velpatasvir (SOF/VEL) treatment for 12 weeks.

Results: From May 2021 to October 2023, 76 patients with recently acquired HCV were identified among PLWH. All the patients were HCV-Ab within 6 months. 93.4% (71/76) was sexual transmission. Homosexual and heterosexual were 71% (54/76) and 22.4% (17/76), respectively. 6.6% (5/76) was transmitted by drug injection. After 12 weeks post-treatment, 100% patients achieved SVR12, and 86% (65/76) patients had ALT normalization. All the patients (76) treated with EFV/TDF/3TC or AZT/3TC/LPVr were switched to B/F/TAF before anti-HCV treatment. SOF/VEL treatment was well tolerated. No serious adverse events (AEs) reported.

Conclusion: More attention should be paid for recently acquired HCV infection among PLWH, especially for patients with actively sex. Regular HCV screening and prompt anti-HCV treatment could effectively prevent HCV transmission in PWLH.

Abstract Submission No. 101072

O-0230

Frequency of cognitive impairment in patients with chronic HCV and its correlation with CTP Score.

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Introduction: It is estimated that approximately 100 million persons have been infected with HCV. HCV is detected in CSF raising the possibility of its extra hepatic replication resulting in cognitive impairment. CHC patients already have reduced health related quality of life and cognitive impairment will even make it worse.

Methods: This was a cross sectional study, conducted from January 2023 to June 2023. All patients with hepatitis C fulfilling the inclusion criteria were included. Baseline characteristics were collected on pre-designed proforma. Montreal Cognitive Assessment was used to assess the cognitive impairment in HCV patients. Patients with score of 18-25 were classified as having mild, 10-17 as moderate and less than 10 as severe cognitive impairment.

Results: Total 78 consecutive patients were enrolled. Mean age of patients was 43.6 ± 12.2. Males and females were 59% & 41%. Overall, 14 (17.9%) patients had normal cognitive function, while mild, moderate and severe CI was seen in 28.2%, 33.3% and 20.5%. Normal cognitive function was found in 11 patients of CTP class A, 3 in CTP class B and none in CTP class C while none of the patient in CTP class A had severe CI followed by 4 and 12 patients in CTP class B & C.

Conclusion: We concluded that majority of the patients having HCV associated cognitive impairment were males and more patients in CTP class C had severe cognitive impairment. So actions are needed for early detection and treatment of HCV for better health outcomes.

Abstract Submission No. 101287

O-0231

The Risk for Tumor Progression of HCV-related Hepatocellular Carcinoma after curative treatment

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Background: HCC shows poor prognosis after progression to intermediate or advanced stage (BCLC stage B-D). However, tumor progression risk and the effect of DAA therapy after curative HCC treatment remain unclear. **Methods:** We conducted a retrospective cohort study of patients with HCV-related HCC with BCLC stage 0/A diagnosed for the first time and treated by curative resection or ablation. We estimated the risk of tumor progression (defined as progression to BCLC stage B-D) by time-varying Cox regression analysis. **Results:** Among 558 patients with HCV-related HCC, 165 patients were included in the analysis. The median age was 72 years, 96 were men, 53 received surgical resection, and 72 received DAA therapy after HCC treatment. FIB-4 index and liver-to-spleen (L/S) ratio for CT attenuation were calculated, and the median were 5.21 and 1.16, respectively. We recorded 56 incidences of tumor progression (29, 13, 8 and 6 cases were due to multiple nodules, portal invasion, extrahepatic metastasis, and deterioration of hepatic reserve, respectively). In univariate analysis, DAA-induced SVR (HR 0.27, p<0.001), FIB-4 index (HR 1.10, p<0.001), L/S ratio (HR 0.67, p<0.002), history of IFN therapy (HR 0.40, p=0.02) and ALBI score (HR 2.39, p=0.02) were associated with the risk of tumor progression. Multivariate analysis showed DAA-induced SVR, FIB-4 index and L/S ratio were associated with the risk. **Conclusions:** This study suggested DAA-induced SVR reduced, and liver fibrosis (FIB-4 index) and liver steatosis (L/S ratio) increased the risk for tumor progression.

Abstract Submission No. 101298

O-0232

TREATMENT OUTCOME OF PATIENTS UNDERGOING HEMODIALYSIS WITH CHC ON THE SOF AND VELPA REGIMEN

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Aims: This study aims to determine the outcome associated with combination therapy (sofosbuvir/velpatasvir) in HCV patients with end-stage renal disease and undergoing hemodialysis.

Materials and methods: All HCV patients with ESRD and undergoing maintenance hemodialysis with having age of more than 18 years were included in our study. The study population was enrolled from the Nephrology Gastroenterology and hepatology wards of a tertiary care hospital in Karachi. A structured questionnaire was used to obtain the data regarding baseline demographics & clinical profile and outcomes associated with combination therapy (SOF (400 mg once daily) and VEL (100 mg once daily). Outcome was assessed at the end of treatment (week 12) and at week 24.

Results: The final analysis was performed on 34 patients out of 122, among all, more than 91% (n = 31) of the patients achieved sustained

virological response at week 24. Treatment relapse was very low and only five patients showed treatment relapse which was statistically insignificant. The most common cause of ESRD was hypertension (44.1%, n = 15/34) and the most common side effect observed by the end of treatment was fatigue (47.1%, n = 16/34).

Conclusion: Treatment with sofosbuvir and velpatasvir is a safe choice for achieving SVR after 24 weeks in patients with ESRD undergoing hemodialysis.

Abstract Submission No. 101345

O-0233

37 years with Malmö Needle Exchange Program at the center: From HIV prevention to HCV elimination

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Background: Malmö needle exchange program (MNEP) opened at the Infectious disease department at the Skåne University Hospital in 1987 to prevent HIV transmission among people who inject drugs. Since then, MNEP has evolved according to the needs of the participants.

Methods: MNEP has reached > 5200 persons, with 600 individuals conducting 6000 visits per year. Injection material and risk reduction counselling, medical care and psychosocial support are provided. Interviews on sociodemographic facts and substance use are combined with testing for HIV, hepatitis A (HAV), B (HBV) and C (HCV). Vaccinations against HAV and HBV are provided. HCV treatment and Take Home Naloxone was introduced on site in 2018.

Results: While HIV and HBV transmission remained low, HCV prevalence (80% anti-HCV positive, of whom >50% viremic) and incidence (31.5/100 pyr in 1997-2005) were previously high. A pilot study offering HCV treatment on site (2018, n=50) found high rates of adherence (94%) and sustained virological clearance (90%), with 9 reinfecting so far. By large scale treatment the overall HCV prevalence among MNEP participants has declined to <20%. Naloxone is now distributed by all NEPs and OAT clinics in Skåne region. To date, 900 kits out of the 5700 distributed have been used to reverse opioid overdoses.

Conclusion: A NEP with ID expertise can constitute a center for the hepatitis elimination process. Addressing both HCV and opioid overdoses is essential in reducing morbidity and mortality in this high-risk population.

Abstract Submission No. 101394

O-0234

HCV screening in general populations and high-risk population in areas with low prevalence in China

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Background: Most of HCV screening were taken in high-risk population. We aim to provide more information for future HCV screening strategy decisions.

Methods: We conducted two HCV screening programs, one (STAT program) was taken in general individuals taking routine physical examination or free mobility clinic screening, and the other (Pudong program) was taken in individuals with methadone treatment, HIV VCT outpatients and STD outpatients. After informed consent, the residual plasma was collected from routine laboratory testing and conducted Anti-HCV testing and following HCV RNA testing if with positive anti-HCV. This analysis is taken based on interim data.

Results: A total of 9379 in general population (642 in Shanghai [South], 734 in Shenyang [North] and 8003 in Yichang [Middle]) and 864 in high-risk population (453 people who inject drugs [PWID], 166 people live with HIV [PLWH], 245 STD outpatients) in Shanghai were screened. In general population, the positive HCV antibody prevalence was 0.16%, 0.04 and 0.41% in Shanghai, Yichang and Shenyang, respectively. The HCV RNA viraemic rate was 100% in those with positive antibody. The risk factor of HCV infection in general group was drug-use history. The positive HCV antibody prevalence in high-risk population were 21.85% in PWID, 1.81% in PLWH, 1.22% in STD outpatients. The rate of HCV RNA viraemic was 42.68% among anti-HCV positive in high-risk population

Conclusions: Approach to concentrate the individuals needing HCV screening should be seek for in general population in low HCV-prevalent areas. PWID is the main risk group of HCV infection in both populations.

Abstract Submission No. 101459

O-0235

EFFICACY OF VELPATASVIR AND SOFOSBUVIR COMBINATION THERAPY IN CHRONIC HCV PATIENTS.

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Abstract:

Introduction: Chronic Hepatitis C is a prevalent infection in Pakistan. It can lead to complications like cirrhosis of liver, liver failure, hepatocellular carcinoma and death. Oral antiviral therapy has revolutionized the treatment of Hepatitis C. It can achieve eradication of HCV in the form of sustained virological response in HCV patients. We conducted a study to analyze the efficacy of Sofosbuvir, Velpatasvir combination therapy with Ribavirin except when there was a contraindication.

Materials and methods: It was a prospective single cohort study including all chronic Hepatitis C patients who underwent treatment for Chronic hepatitis C virus (HCV) with Sofosbuvir (SOF) and Velpatasvir (VELPA) combination therapy with Ribavirin. All patients were more than 18 years old.

Results: 64% patients were males and 36% were females. 6.1% patients were cirrhotic and all patients received Ribavirin.SVR was achieved in 111/114 (97.36%) patients.

Conclusion: Sofosbuvir, Velpatasvir combination therapy with Ribavirin is an effective antiviral therapy for the treatment of chronic hepatitis C.

Key Words: Hepatitis C, Sofosbuvir, Velpatasvir, Ribavirin, Naïve, HCV Treatment in Faisalabad, Cirrhosis, Sustained Virological Response

Abstract Submission No. 101478

O-0236

CHANGES IN THE DEGREE OF LIVER STEATOSIS AND LIPID PROFILE OF HEPATITIS C PATIENTS AT SVR12

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Background: The relationship between hepatitis C patients' SVR12 incidence, lipid profile, and liver steatosis remains unclear. The results of existing publications are still inconsistent regarding changes in the value of these parameters after SVR12. This study aims to examine changes in the degree of hepatic steatosis and lipid profile in hepatitis C patients during SVR12 and look for their relationship.

Methods: Longitudinal design, before and after a study conducted at Cipto Mangunkusumo Hospital (RSCM). The study was conducted for one year. Patients who met the inclusion criteria were included and examined for lipid profile and controlled attenuated parameter values before and after therapy.

Results: The mean SD CAP value increased before therapy 196 ± 49.36 dB/m and after therapy 227 ± 47.11 dB/m. There is significant increase in mean SD value of total cholesterol (166 ± 40.30 mg/dL vs 190 ± 42.58 mg/dL), triglycerides (94 ± 45.39 mg/dL vs 109 ± 49.83 mg/dL), and LDL (109.48 ± 39.57 mg/dL vs 130.88 ± 34.32 mg/dL). There was a negative correlation between CAP values in hepatitis C patients before therapy and changes in CAP values after DAA therapy. No correlation exists between changes in total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides with the degree of liver steatosis at SVR12.

Conclusion: There is a difference in the degree of liver steatosis, total cholesterol, HDL cholesterol, LDL cholesterol, and triglyceride levels before therapy and at SVR12 in hepatitis C patients receiving DAA therapy. There was negative correlation between CAP values at baseline and SVR12

Abstract Submission No. 101505

O-0237

The State of the Oral Mucosa in Patients with Viral Hepatitis C in Armenia for the Period 2021-2022.

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Background: Signs of chronic viral hepatitis C in the oral cavity are various changes in the mucous membrane of the inflammatory-dystrophic nature. Professional infection with HCV by dentists in Armenia is 25%. The aim of the study was to study the oral mucosa in HCV.

Material and methods: 96 patients with HCV who were treated at the Department of Infectious Diseases of the Mikaelyan Institute at YSMU for the period from 2021 to 2022 were examined. The average age of patients is 50.05 ± 13.29 years. Men 61 (63.5%), women -35 (36.5%). The comparison group included patients without HCV

Results: In patients with HCV, upon objective examination, erosions were observed in 13.5%, cracks in the corners of the mouth in 42.7%, and disturbances in the relief of the mucous membrane in 89.6% ($p < 0.001$). In the control group it was 1%. Hemorrhages on the buccal mucosa and hard palate were 78.1%, and telangiectasia in 67.7% ($p < 0.001$), a bright red tongue was detected in 71.9%, plaque on the surface - 93.8% ($p < 0.001$). Obviously, these signs are pathognomonic for HCV. For the first time, it has been reliably established that the high frequency of detection of hyposalivation - 91.9% ($p < 0.001$) may be an indirect sign of the sialotropic nature of hepatitis C viruses.

Conclusions: Thus, patients with HCV develop inflammatory changes in the oral mucosa: stomatitis, glossitis, cheilitis. Lesions of the OM aggravate the course of disease and serve as an important addition to the characteristic of the overall clinical picture of HCV.

Keywords: oral mucosa, cracks, hemorrhages, HCV

Abstract Submission No. 101884

O-0238

Characteristics of Hepatitis C Patients Undergoing Oral Antiviral Therapy at Our Institution

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Background and Aims: Direct acting antiviral therapy (DAA) has shown high efficacy for HCV infection. However, untreated cases of chronic hepatitis C remain a domestic problem. This study analyzes treatment outcomes and patient characteristics during different time periods, aiming to identify issues in acquiring untreated patients and improve acquisition strategies.

Methods: 257 DAA cases (Oct 2015 - Sep 2023) were categorized into early (2015-2017) and later periods (2018-2023) with glecaprevir/pibrentasvir. We examined factors such as consultation reasons, efficacy, follow-up, prognosis, and mortality causes.

Collaboration between our institution and regional healthcare facilities in DAA therapy cases was investigated.

Results: Of 257 cases, 149 were in the early period, and 108 in the later period. Median ages were 68 and 69.5, with male: female ratios of 71:78 and 43:65. Genotypes 1, 2, and others were 105:44:0 and 68:38:2 in early and later periods. SVR rates were 99.3% and 100%. Cases under treatment versus referrals were 96:53 and 60:48. Liver disease-related deaths were 1/5 for both periods, with 12 and 4 lost to follow-up cases.

101 referrals came from various healthcare institutions, with 1-4 patients per facility (median: 1).

Discussion: Around 40% of DAA cases were referred, 53.6% in the early and 48.8% in the later period. DAA therapy showed high SVR and survival rates, with a low lost-to-follow-up rate, emphasizing the importance of regional collaboration.

Conclusion: Enhancing collaboration with regional healthcare institutions and strengthening intra-institutional coordination is crucial. Efforts should be made to expand DAA therapy to more chronic hepatitis C patients.

Abstract Submission No. 102018

O-0239

Concurrent Management of Chronic Hepatitis C and Advanced Hepatocellular Carcinoma: A Case Report

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There is paucity of data concerning the concurrent management of patients with active Hepatitis C virus (HCV) infection and hepatocellular carcinoma (HCC). Guidelines regarding the timing and duration of HCV treatment in patients with advanced HCC are still ill-defined. We present a case of advanced HCC with concomitant HCV infection who was successfully downstaged following immunotherapy and direct-acting antiviral treatment. A 71-year-old Filipino male was referred for evaluation of recently diagnosed HCV infection and liver mass. Dynamic imaging showed infiltrative mass at the right hepatic lobe with portal vein thrombosis (PVT). He received concurrent treatment with sofosbuvir-velpatasvir and atezolizumab-bevacizumab. Sustained virologic response 12 weeks post-treatment was achieved. Radiologic evaluation revealed a significant decrease in tumor size. Patient underwent successful curative microwave ablation and is currently tumor- and drug-free for 21 months. Our case shows that patients with advanced HCC and HCV infection may attain excellent responses with simultaneous treatment. Data from prospective, randomized-controlled trials are needed to identify patients who will benefit most from this strategy.

Abstract Submission No. 200090

O-0240

Nomogram for Predicting Hepatocellular Carcinoma in HCV-associated Cirrhosis Patients

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Background and objectives: Hepatitis C virus (HCV) associated cirrhosis are in high risk of hepatocellular carcinoma (HCC), and this study aimed to explore the risk factors, and establish and validate a novel nomogram.

Methods: A total of 309 inpatients with HCV-associated cirrhosis from Tianjin Second People's Hospital were selected as the training cohort, and 363 patients from Beijing You'an Hospital were selected as the validation cohort. Both cohorts received Direct-Acting Antiviral Agents (DAAs) treatment and achieved sustained virological response (SVR). Laboratory parameters were collected at baseline and duration of follow-up. Cox regression analysis was used to explore risk factors of HCC, and a nomogram for prediction was developed and validated.

Results: HCC incidence was 5.45 100PY (95% CI, 3.91-7.40) in patients of the training cohort. Age, nonspecific liver nodules, the albumin-Bilirubin (ALBI) score and end of treatment (EOT)-AFP are independent risk factors for HCC by Cox regression analysis. A nomogram was used to predict the 1-year, 3-year and 5-year incidence of HCC, with the areas under receiver operating characteristic curves (AUROCs) of 0.866, 0.813 and 0.764, respectively. The AUROCs in validation cohort at 1, 3, and 5 years were 0.884, 0.783 and 0.692 in this nomogram, respectively.

Conclusion: This novel nomogram had a good predictive ability for HCC in patients with HCV-associated cirrhosis after eliminating virus with direct-acting antiviral agents, especially in 3 years.

Abstract Submission No. 200091

O-0241

"Stiffness" resolution is uncompleted with the HCC incidence reduction in advanced fibrosis.

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Objective: To prospectively observe hepatocarcinogenesis in hepatitis C patients treated with DAA and to examine the relationship between fibrosis remission and carcinogenesis.

Methods: A prospective observational study was conducted on hepatitis C patients treated with DAA from July 2013 to November 2023. The primary endpoint was the occurrence of liver cancer, and the secondary endpoint was the change in liver stiffness. Liver stiffness was measured by Fibro-scan and divided into 4 groups (Group 1: <4 kPa, Group 2: 4 to 8 kPa, Group 3: 8 to 12 kPa, Group 4: 12 kPa or higher). The most improved values before and after DAA were compared.

Result: All 689 patients were prospectively observed. The median observation period was 6.0 years. During the observation period, hepatocellular carcinoma occurred in 70 patients (10%). Liver stiffness trends were group 1 (1-1 80%, 1-2 20%), group 2 (2-1 14%, 2-2 84%, 2-3 1%, 2-4 1%), group 3 (3-113%, 3-2 50%, 3-3 36%, 3-4 1%), and group 4 (4-14%, 4-2 24%, 4-3 20% 4-4 52%). The incidence of liver cancer was group 1 (1-1 0%, 1-2 0%), group 2 (2-1 0%, 2-2 4.8%, 2-3 0%, 2-4 50%), group 3 (3-1 5.9%, 3-2 3.0%, 3-3 12.5%, 3-4 50%) and group 4 (4-1 28.6%, 4-2 15.2%, 4-3 30.0%, 4-4 25.5%). Up to group 3, the incidence of liver cancer tended to be low as fibrosis remitted, but in group 4, the incidence was high even when fibrosis remitted.

Conclusion: Patients with high liver stiffness before DAA treatment should be aware of the risk of carcinogenesis even after fibrosis remission.

Abstract Submission No. 200192

O-0242

VIETNarms: A strategic post-licensing randomised trial of direct acting Hepatitis C antivirals

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Background: No randomised trials have compared WHO-recommended first-line hepatitis C treatments. More evidence is needed to support therapeutic strategies to deliver expanded treatment access.

Methods: We enrolled adults with chronic hepatitis C infection without evidence of significant liver disease (Fibroscan < 9.0 kPa) from two centres in Vietnam (Ho Chi Minh City, Hanoi). Patients were stratified into genotype-6/non-genotype-6 and randomly allocated one of two treatment combinations: sofosbuvir 400mg/daclatasvir 60mg (SOF/DCV) or sofosbuvir 400mg/velpatasvir 100mg (SOF/VEL), and then one of four treatment strategies (i) standard-of-care 12 weeks (SOC) (ii) four weeks' DAA therapy with 4 weekly PEGylated interferon (PEG-IFN) doses from week-1 (iii) induction/maintenance therapy with two weeks' standard therapy followed by 10 weeks' therapy 5 days/week and (iv) response-guided therapy of 4, 8 or 12 weeks determined by viral load on day-7 of treatment. Primary outcome was sustained virological response 12 weeks after treatment completion (SVR12).

Results: Primary outcome data were available for 644 of 646 randomised participants. 296 (47%) were genotype-6; 328 (53%) non-genotype 6 were mostly genotype-1/2. Overall SVR12 was 294/302 (97%) for SOF/DCV and 292/307 (95%) for SOF/VEL combinations. SVR12 for strategies were (i) 148/150 (99%) in SOC (ii) 143/152 (94%) with 4 weeks' with PEG-IFN (iii) 151/152 (99%) with induction/maintenance and (iv) 144/155 (93%) with response-guided therapy. Overall severe adverse events were rare (3%) with no significant differences between treatment combinations or strategies.

Conclusions: High efficacy rates were achieved for both sofosbuvir/daclatasvir and sofosbuvir/velpatasvir as well as three different strategies that may be suitable to improve access for harder-to-reach treatment populations.

Abstract Submission No. 100276

O-0243

CRISPR/Cas13a-Assisted Accurate and Portable Hepatitis D Virus RNA Detection

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Background & Aims: Hepatitis delta virus (HDV) infection accelerates the progression of chronic hepatitis B virus (HBV) infection, posing a large economic and health burden to patients. At present, there remains a lack of accurate and portable detection methods for HDV RNA. Here, we aim to establish a convenient, rapid, highly sensitive and specific method to detect HDV RNA using CRISPR-Cas13a technology.

Methods: we established fluorescence (F) and lateral flow strip (L) assays based on CRISPR-Cas13a combined with RT-PCR and RT-RAA, respectively. we conducted a cohort study of 144 patients with HDV-IgG positive to evaluate the CRISPR-Cas13a diagnostic performance for identifying HDV in clinical samples, compared to RT-PCR and RT-ddPCR.

Results: For synthetic HDV RNA plasmids, the sensitivity of RT-PCR-CRISPR-based fluorescence assays was 1 copy/μL, higher than that of RT-qPCR (10 copies/μL) and RT-ddPCR (10 copies/μL); for HDV RNA-positive samples, the sensitivity of RT-RAA-CRISPR-based fluorescence and lateral flow strip assays was 10 copies/μL, as low as that of RT-qPCR and RT-ddPCR, and the assay took only approximately 85 minutes. Additionally, the positivity rates of anti-HDV IgG-positive samples detected by the RT-qPCR, RT-ddPCR, RT-PCR-CRISPR fluorescence and RT-RAA-CRISPR lateral flow strip methods were 66.7% (96/144), 76.4% (110/144), 81.9% (118/144), and 72.2% (104/144), respectively.

Conclusions: We developed a highly sensitive and specific, as well as a portable and easy CRISPR-based assay for the detection of HDV RNA, which could be a prospective measure for monitoring the development of HDV infection and evaluating the therapeutic effect.

Abstract Submission No. 100465

O-0244

Hepatitis Delta Virus Testing and Prevalence Among Veterans with Chronic Hepatitis B in the USA

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Background: Poor awareness of hepatitis delta virus (HDV) contributes to suboptimal testing, delayed diagnosis, and increased morbidity/mortality. We aim to evaluate HDV testing patterns and HDV prevalence among a national cohort of United States (US) Veterans with chronic hepatitis B (CHB).

Methods: Using longitudinal data on all Veterans receiving care within Veteran health systems (1/1/2010-9/30/2023), HDV testing (HDV antibody, HDV RNA, HDV antigen) among CHB patients, and the proportion positive among those tested, were compared using chi-square methods. Multivariable logistic regression models evaluated predictors of HDV testing (entire CHB cohort) and HDV test positive (among those tested).

Results: Among 27,548 CHB patients (93.2% male, 92.5% non-Asian, 2.8% HIV, 22.3% HCV, 32.8% drug use, 10.5% cirrhosis), 16.1% completed HDV testing and 3.25% were positive. HDV testing was higher among Asians vs. non-Hispanic white (29.0% vs. 14.9%, aOR 1.49, 95%CI 1.32-1.68), men vs. women (16.2% vs. 14.5%, aOR 1.24, 95%CI 1.07-1.43), and HIV positive vs. negative (17.8% vs. 16.1%, aOR 1.32, 95%CI 1.07-1.64), p<0.01 for all. Among those tested, HDV positive was higher in HCV-positive vs. HCV-negative (8.45% vs. 2.35%, aOR 3.24, 95%CI 1.94-5.42), cirrhosis vs. non-cirrhosis (7.71% vs. 2.80%, aOR 2.27, 95%CI 1.47-3.53), and drug use vs. non-drug use (5.30% vs. 2.49%, aOR 2.04, 95%CI 1.14-3.63), p<0.01 for all.

Conclusion: Among US Veterans with CHB, HDV testing is alarmingly low, particularly among patients with HDV risk factors. HDV test positive was highest in patients with cirrhosis, HCV, and drug use. Greater HDV awareness is needed to improve timely diagnosis and treatment.

Abstract Submission No. 100802

O-0245

Bulevirtide improves virologic & biochemical response in non or partial responders with CHD

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Background: Bulevirtide (BLV) is approved in Europe for chronic hepatitis delta (CHD). It's unclear whether BLV monotherapy benefits patients with early virologic nonresponse (NR) or partial response (PR) after 24 weeks (Wks).

Methods: Patients completed 96-Wk BLV monotherapy. Virologic response (VR) was defined as undetectable hepatitis delta virus (HDV) RNA or $\geq 2 \log_{10}$ IU/mL decline from baseline (BL); NR and PR were defined as HDV RNA declines of $<1 \log_{10}$ IU/mL and ≥ 1 but $<2 \log_{10}$ IU/mL, respectively. Biochemical responses (alanine aminotransferase [ALT] within normal limits [WNL]) were compared.

Results: At Wk24, 92/141 patients had VR (ALT WNL, 53), 34/141 had PR (ALT WNL, 19), and 15/141 had NR (ALT WNL, 2) (Table). Of the 34 PR patients at Wk24, 25/35 PR patients had VR and 24 had ALT WNL by Wk96. Of the 15 NR patients at Wk24, 7 had VR and 3 had PR by Wk96. More NR at Wk24 achieved VR at Wk96 with BLV 10mg [4/5] vs BLV 2mg [3/10]. Median BL ALT was higher in patients with NR and PR at Wk96. The mean (SD) $\log_{10}$ IU/mL HDV RNA change at Wk96 among VR/PR/NR was -3.6 (1.1), -1.4 (0.3), and -0.2 (0.7) for VR, PR, and NR at Wk96. Median (Q1, Q3)ALT (U/L) change at Wk96 among VR/PR/NR was -48 (-73, -12), -42 (-83, -6), and -67 (-102, -33). Among NR at Wk96, ALT declined $>50\%$ from BL in 7/11 patients.

Conclusion: Results support continued BLV monotherapy despite early suboptimal virologic responses.

Abstract Submission No. 100812
O-0246

Efficacy & safety of bulevirtide in combination with pegylated interferon α -2a in patients with CHD

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Background: Bulevirtide (BLV) is approved for chronic hepatitis delta (CHD). Phase 2 MYR204 evaluated the safety and efficacy of BLV (2 and 10mg) with/without pegylated interferon α -2a (pegIFN) in patients with CHD and compensated cirrhosis (CC).

Methods: Based on CC status, 174 patients were randomized (1:2:2:2) to receive (A) pegIFN for 48 weeks (Wks); (B) BLV 2mg + pegIFN; (C) BLV 10mg + pegIFN for 48 Wks, then BLV 2 or 10mg monotherapy for 48 Wks; or (D) BLV 10mg for 96 Wks. The primary endpoint was sustained virologic response (SVR) at Wk24 (SVR24) after EOT (end of treatment) defined as undetectable hepatitis delta virus (HDV) RNA with comparison between Arms C and D.

Results: Overall, 35% had CC, mean liver stiffness was 13.1 (7.72) kPa, mean HDV RNA was 5.3 (1.2) $\log_{10}$ IU/mL, mean alanine aminotransferase (ALT) was 114.0 (94.8) U/L, 28% were on nucleos(t)ide analogue therapy, and 48% were IFN experienced. SVR24 was achieved by 17% (Arm A), 30% (Arm B), 46% (Arm C), and 12% (Arm D) ($P = 0.0003$; Arm C vs D) (Table). ALT normalization and composite endpoint at Wk24 after EOT were superior with BLV 10mg + pegIFN vs monotherapy. Hepatitis B surface antigen loss was observed in the combination groups. Adverse events (AEs) observed for the BLV + pegIFN arms were similar to pegIFN monotherapy. Six patients (3%) discontinued treatment (unrelated to BLV).

Conclusions: Combination therapy was effective and well tolerated. Longer-term data will help define durability of BLV + pegIFN for CHD.

Abstract Submission No. 100970
O-0247

BULEVIRTIDE IN PATIENTS WITH CHRONIC HEPATITIS D - REAL WORLD EXPERIENCE

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We analyzed retrospective data from 61 chronic hepatitis D (CHD) patients, including 27 with compensated cirrhosis, treated with bulevirtide, HBV and HDV entry inhibitor, 2 mg/day sc as

monotherapy or dual therapy (combined with peginterferon) up to 144 weeks in Moscow region and Dagestan centers. A 48-week treatment resulted in a significant decrease in HDV RNA levels from 6.9 log₁₀ to undetectable ($p < 0.001$, median reduction in HDV RNA levels from baseline -5.0 log₁₀ (monotherapy -4.0 log₁₀, dual therapy -5.7 log₁₀), alanine aminotransferase (ALT) levels - from 68.0 to 31.0 U/l ($p < 0.001$), high virological response rate (95%, monotherapy 93%, dual therapy 96%, full virological response (aviremia) 58%), ALT normalization (69% vs 20% at baseline). Virological efficacy improved over the course of treatment. In patients with compensated cirrhosis similar virological response dynamics were observed compared to the overall group. The treatment was well tolerated, without serious adverse events, cases of treatment withdrawal. CHD treatment with bulevirtide in real-world practice demonstrated high efficacy, safety and good tolerability, including patients with compensated cirrhosis. Further development of an optimal treatment algorithm is needed.

Abstract Submission No. 100990
O-0248

Compassionate use of REP 2139-Mg in HBV/HDV infection with advanced liver disease

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Background: In fibrotic patients, REP 2139-based combination therapy achieves high rates of functional cure of HBV and HDV. An ongoing compassionate use program (NCT05683548) provides REP 2139-Mg therapy for cirrhotic HBV / HDV co-infection with viral non-response or rebound with pegIFN and or bulevirtide therapy.

Methods: Add-on therapy with 250mg REP 2139-Mg qW SC and 90ug pegIFN (with compensated cirrhosis) was scheduled for 48 weeks. Safety and biochemical response were monitored weekly and virologic response every 4 weeks using standard assays for quantitative HBsAg and anti-HBs, HBV DNA, HDV RNA, HIV RNA and HBcrAg.

Results: Currently 27/32 patients have completed > 24 weeks of REP 2139-Mg therapy. Transient grade 1 injection site reactions occur in a majority of patients. Four ALT flares > 5 X ULN accompanied pegIFN; 3 self-resolving and one resolved after removal of pegIFN. ALT has normalized in 12/32 patients.

HDV RNA decline > 2 log₁₀ from baseline (22/32) and HDV RNA loss (15/32) is accompanied by HBsAg decline > 2 log₁₀ (12/32), HBsAg loss (6/32) and anti-HBs seroconversion (6/32). HDV clearance was observed in 1 liver explant after 10 weeks of therapy. Functional cure of HBV with HDV cure (n=1) and persistent HBsAg and HDV RNA loss on TDF monotherapy (n=2) have occurred after removal of REP 2139-Mg.

Conclusions: REP 2139-Mg is safe and effective against HBV/HDV infection in advanced liver disease. REP 2139-Mg can clear HDV RNA from the blood and liver and can establish HBV functional cure and HDV cure in advanced liver disease.

Abstract Submission No. 100610
O-0249

High prevalence of Hepatitis D by double reflex testing of HBsAg positive individuals in Pakistan

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Background: Hepatitis D caused by the hepatitis delta virus (HDV) is a serious health problem in many regions of the world. We aimed to determine the prevalence of HDV infection by double reflex testing on HBsAg-positive visitors of screening camps in Usta Muhammad and Dera Allah Yar, two high-prevalence neighbouring towns in the Eastern part of Baluchistan province of Pakistan.

Methods: 1643 people were examined for HBsAg and anti-HCV antibodies using ICT methods. HBsAg-positive individuals were further tested for antibodies to HDV (anti-HDV) using enzyme immunoassay (EIA). Samples with detectable anti-HDV were further examined for HDV RNA using real-time PCR.

Results: Of the 1643 individuals examined, HBsAg was reactive in 277 (16.9%) individuals. The reflex test for anti-HDV antibodies of these HBsAg positives was positive in 186 (67.1%); 133 were men and 53 were women. The mean age (years) was 32.2±11.3. HDV RNA was detectable in 108 (58.1%) of the anti-HDV-reactive patients. Log₁₀ HDV RNA levels (IU/ml) were 6.69±1.34. Anti-HCV was detected in 227 (13.8%) of all examined individuals. Of these, four anti-HCV-positive individuals were also positive for HBsAg and one was positive for anti-HCV, HBsAg, and anti-HDV but negative for HDV RNA.

Conclusions:

Reflex testing of HBsAg-positive individuals for HDV in an endemic area revealed that 67% of HBsAg-positive individuals had HDV exposure and 58.1% of anti-HDV-positive individuals had HDV viremia. Our study highlights the need for double-reflex testing in HBsAg-positive individuals for anti-HDV antibodies and HDV RNA in anti-HDV-positive individuals.

Abstract Submission No. 101229
O-0250

Development of a network for hepatitis D registration and study in Taiwan: TADR - An update in 2023

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Backgrounds: HBV and hepatitis delta (HDV) dual infections leads to more severe liver disease, with increased rates of cirrhosis and hepatic decompensation, and hepatocellular carcinoma (HCC). We aim to establish a nationwide epidemiological study of HDV in Taiwan.

Methods: We follow the successful launching of TACR (TASL hepatitis C Registration) in Taiwan and invite the corresponding medical centers to join TADR (TASL Hepatitis D registration). TADR use this existing platform and to set up and manage the platform and blood samples of HDV patients (hospital cohort). A community cohort and special population (HIV/HBV co-infection) cohort will be also included for comparison. TADR already kicked off in February 2022, and includes 14 medical centers so far.

Results: At the end of OCT 2023, there have been 318 HDV cases registered. The prevalence of HDV in hospital cohort is approximately 1.2%. In a subgroup analysis of HBV related cirrhotic patients undergoing nucleos(t)ide therapy (NUC), the prevalence of HDV infection is 1.79 % (14/780). There is no significant association between HDV and baseline clinical characteristics of patients (except age), as well as

Results: Two groups were similar for baseline characteristics except for age (48.5 ± 12.7 vs 40.3 ± 10.3 ; $p < 0.01$), HBeAg positivity (32.6% vs 16.9% $p < 0.01$), platelets (188.5 ± 76.7 vs 162.3 ± 55.6 ; $p < 0.01$) and ALT (80.2 ± 113.4 vs 103.7 ± 101.7 ; $p = 0.05$) for CHB and CHD, respectively. HCC developed in 23 (9.5%) of CHB and in 21 (16.9%) of CHD patients during median 8 years of follow-up (FU). Cumulative HCC

development probability was 0.4%, 6.4%, 10.5% and 0.9%, 10.8%, 14.0%, at 1, 5 and 10 years of FU for CHB and CHD, respectively. HCC was more common in CHD vs. CHB ($p<0.01$). When CHB patients were compared to CHD with VR, cumulative HCC development probability did not differ (10% for CHB and 10% for CHD at end of FU, $p=0.88$).

Conclusions: Data confirm higher HCC risk for CHD. Higher risk is likely due to lack of effective treatment in CHD as HCC incidence rates were similar in CHB and CHD patients with VR.

Abstract Submission No. 102023

O-0254

Lonafarnib-based regimens associated with long-term apparent cures in chronic hepatitis delta

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The farnesyl transferase inhibitor lonafarnib is in advanced clinical development for chronic hepatitis delta virus (HDV) infection, having been studied in multiple phase 2 and 3 studies. Several patients who participated in these studies have now been followed for over eight years following clearance of HDV RNA and ALT. Here we report on four patients who following a single, or one brief retreatment, course of LNF-based therapy of 3 to 12 months duration demonstrated off treatment virologic and biochemical responses lasting beyond 5 years of treatment discontinuation. In 3 of the 4 patients, long-term off-treatment efficacy was induced after a post-treatment beneficial enzymatic flare leading to regression of liver fibrosis while in one patient HDVRNA negativity was achieved on-treatment. One patient also cleared HBsAg. In 2 additional patients quantitative HBsAg levels at last visit were below 100 IU/mL. In conclusion, lonafarnib-based treatment appears to be an option for finite treatment in CHD where post-treatment month 6 viral response may be at least as important as end of treatment as a guide of treatment efficacy.

Abstract Submission No. 102053

O-0255

The course of COVID-19 infection in patients with chronic hepatitis delta

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COVID-19 disease led to 7 Million deaths. Older age, co-morbidities such as cirrhosis are associated with mortality. Among liver disease etiologies, only alcoholic liver disease was associated with mortality. Chronic hepatitis delta (CHD) has not been studied in this context.

Method: Chronic hepatitis B (CHB) and CHD patients followed in 2 academic hospital gastroenterology departments were compared retrospectively. COVID-19 diagnosis was made by PCR detection of SARS CoV-2 RNA in nasopharyngeal swap specimens.

Results: Total of 618 patients (343M/275F), 540 with CHB and 78 with CHD, were analyzed. 70 patients had cirrhosis. 40 CHD and 427 CHB patients were taking nucleos(t)ide analogs (NAs). Among CHB

patients (n:540, 27[5%] cirrhotic), 47 (4 with cirrhosis) developed COVID-19. CHB patients with and without COVID-19 infection did not differ according to age, gender and laboratory parameters. No CHB patient had COVID-related death; none required intensive care. ALT-AST reactivation, defined as increase of ALT to $> 3 \times$ ULN, occurred in 3 patients (6.4%) including hepatic decompensation in 1 cirrhotic patient. Among CHD patients (n:78; 43 (55%) cirrhotic), COVID-19 was diagnosed in 12 patients and 4 had documented hepatic reactivation. Hepatic reactivation during COVID 19 occurred more often in CHD vs CHB patients (4/12[33%] vs 3/47[6.4%], $p=0.016$). COVID[CY1] -19 developed in 6 cirrhotic CHD patients, of whom one died and one developed hepatic decompensation[CY2].

Conclusion: The course of COVID-19 appears to be more severe in CHD vs CHB. This may be due to an effective antiviral treatment in CHB but lack of it in CHD.

Abstract Submission No. 200187

O-0256

Pegylated Interferon α for patients with chronic hepatitis D in Mongolia

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Introduction: Mongolia faces a high prevalence of chronic viral hepatitis, contributing to severe liver diseases like cirrhosis and hepatocellular carcinoma. This retrospective study analyzes the response rate of chronic hepatitis delta (CHD) patients treated with pegylated Interferon alpha (peg-IFN α).

Materials and Methods: Thirty-six CHD patients (mean age 37.4; male: 63.9%) receiving at least 24 weeks of peg-IFN α (between 2014-2019 in Intermed hospital) were analyzed. Virological response was assessed at the end of treatment and during follow-up at 24 and more than 48 weeks post-therapy.

Results: At the end of treatment, biochemical and virological responses were observed in 19.4% (n=7) and 27.8% (n=10) of patients, respectively. At 24 weeks follow-up, 50% (n=18) and 22.2% (n=8) of patients showed biochemical and virological responses. Sustained virological responses were observed in 22.2% (n=8) at 48 weeks, with HDV RNA reappearance in 4 patients. HBsAg-positive patient exhibited seroconversion. Antiviral treatment for over 48 weeks resulted in responses in 11.1% (n=4), including two with HBsAg loss.

Conclusions: Our study reveals sustained HDV clearance in approximately one-ninth of CHD patients. Reduced HBsAg levels, not only during treatment but also in the follow-up period, emerged as a primary predictor for long-term treatment response. These findings underscore the importance of monitoring HBsAg levels for effective CHD management.

Abstract Submission No. 100655

O-0257

Apolipoprotein J facilitates diabetic nephropathy progression via mTOR-TFEB-autophagy axis

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Background: Ectopic lipid accumulation in kidney leads to lipotoxicity and contributes to development of diabetic nephropathy (DN). Recently, Apolipoprotein J (ApoJ) is recognized as a hepatokine and participates in lipid and glucose homeostasis. Herein, we reported that accumulation of ApoJ in renal tubule promotes renal injury and facilitates DN progression.

Methods: The pathways involved in ApoJ-associated pathogenesis were identified by Omics analysis and validated using in vitro gain- or loss-of-function assays and in vivo tissue-specific ApoJ knockout mice. A co-immunoprecipitation assay was applied to verify the interactions between ApoJ, mammalian target of rapamycin (mTOR), and transcription factor EB (TFEB). The autophagy-lysosome pathway was dynamically addressed by live image analysis and autophagic flux assay. The efficacy of ApoJ antagonist peptide on DN was evaluated in mouse models of obesity and diabetes.

Results: Elevating in ApoJ levels were found in serum and renal tubules and exerted positive correlations with renal tubular injuries in mouse models of DN. Functionally, ApoJ facilitated mTOR-TFEB interaction, leading to disturb lipid homeostasis and promote epithelial-mesenchymal transition of proximal tubular cells. Coordinated with endogenous ApoJ, accumulation of hepatocyte-derived ApoJ in renal tubule was found to accelerate DN progression. Moreover, targeting ApoJ reactivated TFEB, restored autophagy, and prevented accumulation of lipid and reactive oxygen species. Finally, a peptide antagonizing ApoJ chaperone activity reversed lipid deposition and fibrosis in mouse models of DN.

Conclusion: ApoJ promotes renal injury by inducing lipid and ROS accumulation through mTOR-TFEB-autophagy axis and proposed ApoJ antagonist peptide as a novel therapeutic strategy against DN.

Abstract Submission No. 100890

O-0258

All pediatric fatty liver diseases are not non-alcoholic fatty liver disease (NAFLD)

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Background and objectives: Fatty liver is the most common cause of chronic liver disease in adults due to obesity, whereas pediatric Fatty liver disease has wide spectrum of etiology apart from obesity. In this study we aimed to identify all causes of fatty liver in children.

Methods: From June 2021 to June 2023 all liver biopsies done under 18 years of age were screened retrospectively. Of the total 150 biopsies 25 showed hepatic steatosis.

Results: Out of 25 liver biopsies, 15 were of infants. Median age at the time of biopsy was 7 years (Range 1 month-15 years) and 10 were females. Median weight and BMI (Median, IQR) were 38(20-48) & 26 (16-32) respectively. Median Platelet count, AST, ALT, Total Bilirubin was (Median, IQR) 202 (180-250), 165(100-236), 178(97-267), 6 (2-8) respectively. Etiologies of fatty liver were metabolic syndrome and obesity in 4, Wilson's disease in 4, Glycogen storage disorders in 4, tyrosinemia in 2, celiac disease in 2, malnutrition in 2, Lysosomal acid lipase deficiency in 1, hereditary fructose intolerance in 1, Zellweger syndrome in 1, Cystic fibrosis in 1, steroid toxicity in child with nephrotic syndrome in 1, methotrexate toxicity in child with leukemia in

1, congenital generalized lipodystrophy in 1. All children were managed according to standard practice guidelines. Except Zellweger, congenital lipodystrophy and tyrosinemia all showed clinical improvement on follow up.

Conclusion: All pediatric fatty liver diseases are not due to metabolic syndrome & obesity. All efforts should be made to identify clear etiology to improve outcome.

Abstract Submission No. 101056

O-0259

Clinical characteristics, genotype and outcome of type 2A hereditary hemochromatosis in China

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Background: Hereditary hemochromatosis (HH) is mainly caused by *HFE* p.C282Y in the Caucasians. HH is rare in Chinese, and non-*HFE* mutations constitute the major cause. We aimed to analyze clinical characteristics, genotype, and outcome in Chinese patients with type 2A HH.

Methods: Patients with primary iron overload enrolled at the China Registry of Genetic/Metabolic Liver Diseases were analyzed for mutations in *HFE*, *HAMP*, *HJV*, *TFR2* and *SLC40A1* genes by Sanger sequencing. The clinical characteristics, genotype, and outcome of patients with *HJV* mutations were analyzed.

Results: Ten of 37 patients were identified with *HJV* mutations, including 4 homozygotes, 5 compound heterozygotes and 1 heterozygote, the most common mutations were p.Q6H+p.C321X (8/10,80%). The average onset age was 30.7±14.7 years. The mean serum ferritin (SF) level and transferrin saturation were 5267±905 ng/ml, 94.3%±1.2%, respectively. Iron overload was shown in liver, pancreas, and myocardium on MRI. Liver biopsy showed iron deposited predominantly in hepatocytes. The end-organ manifestations included liver disease, cardiac disease, diabetes, hypogonadism, skin pigmentation and fatigue. They were followed up for a median of 6 years. Six underwent phlebotomy, their SF level decreased to 100ng/ml. Two were treated with oral iron chelator, their SF level did not reach the target. One died of acute heart failure. One lost to follow up.

Conclusions: *HJV* gene may be one of the major causes of HH in Chinese, and *HJV* p.Q6H+p.C321X may be the hot mutations. Type 2A is a severe type of HH, and the prognosis is good if diagnosed early and treated by phlebotomy.

Abstract Submission No. 101318

O-0260

Can we predict outcome in galactosemia?: Experience from a tertiary c

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Background: Galactosemia constitutes 2% of all neonatal cholestasis. Despite early diagnosis and dietary exclusion, there may be adverse liver and neuro-ophthalmic outcomes. We analysed the risk factors of outcome in galactosemia patients.

Methods: Diagnosis was based on galactose-1-phosphatase uridyl transferase (GAL-1-PUT) enzyme <10 U/gHb or mutation of GALT gene. Risk factors of death or neuro-ophthalmic morbidity (poor neuro-cognition, learning disability persistent cataract or amblyopia despite cataract surgery) were analysed from a prospectively maintained database.

Results: Fifty-one galactosemia patients presented as infantile cholestasis. Their median age of symptom onset and diagnosis were 10(1-90) and 45(7-450) days respectively. Figure 1 shows the natural history on lactose-free diet. Among the 43 survivors, 28 had follow-up with >6 months were analysed for long term outcome. All had normalisation in liver functions. Ten(36%) had adverse neuro-ophthalmic outcome. Eighteen patients are currently asymptomatic in follow up till now. Multivariate analysis of non-survivors(n=8) versus survivors(n=28) identified risk factors: refractory ascites (88% vs.18%, p=0.012), persistent coagulopathy at 4 weeks (88% vs.25%; p=0.02), and culture-positive sepsis (63% vs 43%; p=0.04). In addition, pediatric end-stage liver disease (PELD) score<21 (sensitivity 78%; specificity 50%, p=0.02) and Child score <7.5 (sensitivity 89%; specificity 61%, p=0.01) predicted survival. PELD score correlated with culture-positive sepsis (p=0.05). In the 10 patients with poor neuro-ophthalmic morbidity, no risk factors could be identified.

Conclusion: Refractory ascites, uncorrectable coagulopathy at 4 weeks of diagnosis and sepsis were associated with poor liver outcome. PELD and Child score predict survival. Long term neuro-ophthalmic morbidity is not associated with disease severity at onset.

Abstract Submission No. 101486

O-0261

Serum iron overload activates SMAD pathway and hepcidin expression of hepatocytes via SMURF1

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Background: Liver iron overload can induce hepatic expression of bone morphogenic protein (BMP)6 and activate the BMP-SMAD pathway. However, serum iron overload also can activate SMAD while does not induce BMP6 expression. Therefore, the mechanisms whereby serum iron overload activates the BMP-SMAD pathway remain unclear. The aim of this study is to clarify the role of SMURF1 in serum iron overload and BMP-SMAD pathway.

Methods: Cell model of serum iron overload was established by hepatocytes treated with 2 mg/mL Holo-transferrin (Holo-Tf). Serum iron overload mice model and liver iron overload mice model were established by intraperitoneal injection of C57BL/6 mice with 10 mg Holo-Tf and by administration of high iron diet for 1 week followed by a low iron diet for 2 days, respectively. Western blot and Real-time PCR were performed to evaluate the activation of BMP-SMAD pathway and the expression of hepcidin.

Results: Holo-Tf could augment the sensitivity and responsiveness of hepatocytes to BMP6. E3 ubiquitin-protein ligase SMURF1 mediated the Holo-Tf-induced SMAD1/5 activation and hepcidin expression, specifically, SMURF1 dramatically decreased when serum iron was overloaded. Additionally, the substrates of SMURF1, important molecules that transduce BMP-SMAD signaling, were significantly upregulated. Furthermore, *in vivo* analyses confirmed SMURF1 specifically regulates the BMP-SMAD pathway in serum iron overload.

Conclusions: SMURF1 can specifically regulates the BMP-SMAD pathway by augmenting the responsiveness of hepatocytes to BMPs in serum iron overload.

Abstract Submission No. 101653

O-0262

Hepcidin-inducer Laennec® can sorely improve congenital iron and copper metabolism disorder

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Aimes: Recent studies indicate that hepcidin deficiency underlies most known forms of hereditary hemochromatosis(H.H.). The high affinity of hepcidin for copper also suggests that hepcidin could bind copper *in vivo*. Thus Laennec® which can induce hepcidin may be effective not only for H.H. but for Wilson's disease by regulating iron and copper metabolism through the action of hepcidin.

Case1 H.H.: 55years-old male patient that developed type2 diabetes mellitus had elevated serum ferritin level(10,191ng/ml). Liver biopsy revealed remarkable iron deposition. Chromosomal analysis revealed the presence of Tfr2 mutations. As the substitute for the repeated phlebotomy, the infusion with Laennec® (672mg/d,3times/w) has been done for 11 years. Recent serum ferritin levels were constantly below 550ng/ml. HbA1c also improved with the same dose of insulin(8.8±6.8%). Liver biopsy revealed the improvement of liver fibrosis (F3&F1).

Case2 Wilson's disease: 45years-old male patient with compensated liver cirrhosis presented neuropsychiatric signs. Liver biopsy revealed the presence of the deposition of copper and iron. The infusion with Laennec® has been done for these10 years. Liver biopsies revealed the remarkable improvement of both in fibrosis (F3&F1) and metal deposition.

Conclusion: The discovery of hepcidin and its role in heavy metal metabolism could lead to the development of novel therapies for H.H. and Wilson's disease. The placenta-derived Laennec® which can induce hepcidin solely improved iron overload of H.H. patient, and the impaired copper metabolism through chelating excessive copper in Wilson's disease. The results suggest that Laennec® can take the place of venesection for H.H. and other hepcidin-deficient diseases.

Abstract Submission No. 101990

O-0263

Evaluation of genetic markers contributing to disease predisposition in patients with MAFLD/NAFLD

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Introduction: The rising incidence of mortality and morbidity due to metabolic associated fatty liver disease (MAFLD) indicates towards genetic markers and their interplay with lifestyle factors to modulate the disease progression. Generally, 4 or 7 gene signatures are studied for the development and progression of MAFLD/NAFLD. The present study assesses the 68 MAFLD/NAFLD related genes in patients with different disease severity.

Methods: We sequenced 68 genes related to MAFLD/NAFLD phenotypes in 124 patients. The raw data after standard QC were mapped to GRCh38 and variants were called and annotated. The clinical impact of selected mutations was assessed by HGMD Professional and public databases for pathogenicity scores. Few of the genes included, APOB, APOE, FTO, PCSK9, PNPLA3, SAMM50 and TM6SF2.

Results: Out of 124 patients, 42 (34%) had clinical diagnosis of cirrhosis (NAFLD), 43 (35%) had NASH, 19 (15%) had steatohepatitis, 11 (8%) had MAFLD and 2 (2%) cryptogenic cirrhosis with miscellaneous in 7 (6%) of cases. Total of 168 variations were detected in the 118 patients which were relevant to the clinical phenotype with 6 cases reported no associated polymorphisms. The genes PNPLA3, PCSK9, GCKR and APOB together accounted for 88% of the observed genetic variations (n=148). Other genes included SAMM50, GPAM, TM6SF2 etc. (n=23, 12%). The major mutations included PNPLA3:Lys434Glu (n=43), PCSK9:Glu670Gly (n=25), GCKR: Pro446Leu (n=30) and APOB: Pro2739Leu (n=15).

Conclusion: Although PNPLA3 was most mutated gene, the mutations in GCKR, APOB and PCSK9 may also play a crucial role in MAFLD/NAFLD development and progression in Indian population.

Abstract Submission No. 101993
O-0264

Diagnostic genetic markers implicated in prothrombotic phenotypes in liver disease patients

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Introduction: There could be risk of thrombosis in chronic liver disease both at inflow and outflow vessels. Previous reports from India have shown a very low frequency of inherited prothrombotic disorders in patients with vascular diseases. A thorough evaluation of predisposing prothrombotic genetic markers via sequencing is warranted in these patients.

Methods: We sequenced 44 genes related to thrombosis regulation in 88 patients (from Feb-Sep,23) with diagnosed vascular liver disorders. The genes included MTHFR, F5, F9, ADAMTS13 and VWF etc. Following standard QC measures, the clinical impact of selected mutations was assessed by HGMD Professional and public databases for pathogenicity/functional effects.

Results: Out of all, 70 cases had liver cirrhosis with partial/complete/chronic thrombosis of the portal vein, five patients had Chronic Budd-Chiari syndrome (BCS), and 12 patients had extra-hepatic portal vein obstruction (EHPVO). Upon analysis, 58% (n=51, Table) of the cases showed polymorphism associated with vascular thrombosis.

In the thrombosis group, most mutations were in GCKR, GP6 and F13B (55%) e.g. GCKR:Pro446Leu, GP6:Ser219Pro and F13B:His115Arg. Similarly In the EHPVO group, F5 and FGA were most mutated (43%) e.g. FGA:Thr331Ala and F5:Arg534Gln. In BCS,

CPB2:Thr347Ile: F13B:His115Arg, GP6:Ser219Pro and MTHFR:Ala222Val were observed.

Out of total 63 mutations, GP6, GCKR and F13B (n=34, 54%) were most frequent. The other genes included F5, FGA, CPB2 and MTHFR etc. The prominent variations included GP6:Ser219Pro (n=13), GCKR: Pro446Leu (n=12) and F13B:His115Arg (n=9).

Conclusion: The data presented here might prove useful in elucidation of molecular mechanism altering the regulation of coagulation factors, leading to risk of thrombosis.

Abstract Submission No. 100104
O-0265

The remission strategy for EPP accompanied with severe abdominal pain and liver injury

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Patients with severe abdominal pain and jaundice are often misdiagnosed as acute abdomen which require surgical intervention. The Erythropoietic Protoporphyrria (EPP) can also lead to severe abdominal pain and jaundice which is often neglected. Meanwhile, there are no particular therapeutic strategy for the disease with severe abdominal pain and jaundice. This case report presented a 29 year old male patient with a persistent intermittent severe abdominal pain for more than one month, accompanied by jaundice. After liver pathology and gene detection, the patient was diagnosed as EPP. The patient recovered after combined treatment with blood purification treatment, glucocorticoid, ursodesoxycholic acid and high sugar diet. In conclusion, when confronted with severe abdominal pain and jaundice for unknown reason, EPP, should be considered. The treatment strategy combining blood purification treatment, glucocorticoid, ursodesoxycholic acid and high sugar diet was effective for remission this disease.

Abstract Submission No. 101211
O-0266

Hepatomegaly from Poorly Controlled Type 1 Diabetes: A Rare Case of Mauriac Syndrome

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Glycogenic hepatopathy is an underrecognized complication poorly controlled Type 1 Diabetes. Excessive glycogen accumulation in the hepatocytes may lead to massive liver enlargement. When hepatomegaly is accompanied by growth failure, a cushingoid appearance, and dyslipidemia, it is referred to as Mauriac syndrome.

We describe a case of a 21-year-old female who was diagnosed with type 1 diabetes mellitus at the age of 8 and was maintained on insulin with poor compliance. She had recurrent hospitalizations for diabetic ketoacidosis since diagnosis. The patient also developed chronic kidney disease from diabetic nephropathy and has been on maintenance hemodialysis for 2 years. On examination, the patient was noticeably shorter compared to her parents with a height of 149cm and had visible abdominal enlargement with cushingoid facial features. The initial consideration for the abdominal enlargement was volume overload

from under dialyzed state. However, imaging revealed hepatomegaly (liver span 20cm) with no free fluid. She had regular follow-up at the outpatient clinic but had difficulty achieving adequate glycemic control from inconsistent insulin administration due to financial constraints. The patient eventually succumbed to complications of catheter-related bloodstream infection.

Strict glycemic control is the mainstay of treatment for hepatic glycogenesis. Complete reversal of hepatomegaly may be possible with improved control. Our case highlights the importance of recognizing the clinical features that comprise this rare syndrome to initiate timely management for this reversible condition.

Abstract Submission No. 101508

O-0267

The role of Vitamin E in the treatment of nonalcoholic steatohepatitis(NASH)

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Oxidative stress plays a vital role in the transition from simple steatosis to nonalcoholic steatohepatitis (NASH). An effective therapeutic strategy is to target the reduction of oxidative stress in these patients. Vitamins with antioxidant properties have the ability to act through multiple mechanisms to decrease the levels of reactive oxygen species in the body and prevent oxidative damage in the cell that can lead to cellular senescence and apoptosis. These properties may halt the progression of liver injury and facilitate the reversal of hepatic fibrosis in patients with NAFLD who are at risk for developing NASH. Thus, the aim of this study is to explore the functions of vitamin E in the treatment and recovery of patients suffering from NASH.

Abstract Submission No. 101783

O-0268

HEPATIC AMYLOIDOSIS: UNRAVELING THE MYSTERY !!!

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INTRODUCTION: Budd chiari syndrome (BCS) is considered as a disorder which mimic other disorders like constrictive pericarditis. We came across a case which was diagnosed and treated as BCS for 2 months, but it actually turn out to be a case of hepatic amyloidosis.

CASE REPORT: We present a case of 35-year-old female with complains of right upper quadrant pain for 1 year and insidious onset abdominal distension for 2 months. On examination patient was pale, had tachycardia, bilateral pedal edema and facial puffiness. Per abdominal examination revealed distended abdomen, shifting dullness and hepatomegaly. She was diagnosed as BCS based on her Triple phase CT abdomen findings and was being treated for same. However patient did not respond to the treatment. Patient was re-evaluated in our institute and her CT images were reviewed which showed thinned out hepatic veins, hepatomegaly and ascites however features like coma shape collaterals, regenerative nodules were not present. To confirm the diagnosis of BCS patient was taken up for hepatic venography which surprisingly revealed, no obstruction in hepatic veins. It was concluded that the false appearance of thinned out hepatic vein is likely due to extrinsic compression due to massive hepatomegaly. A liver biopsy was performed which confirmed the diagnosis of Amyloidosis.

CONCLUSION: This case is difficult and rare as triple phase CT abdomen was diagnostic of BCS but hepatic venography refuted the diagnosis and liver biopsy was performed which clinched the diagnosis of hepatic amyloidosis

Abstract Submission No. 200039

O-0269

Wilson disease: Our observations over the past five years

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Background: Wilson disease (WD) occurs worldwide with an average prevalence of ~ 30 affected individuals per million population. WD is due to mutations of the ATP7B gene on chromosome 13, which encodes a copper-transporting P-type ATPase (ATP7B) and responsible for decrease excretion of copper into bile and reduce synthesis of functional ceruloplasmin resulting accumulation of copper in affected tissues. Clinical presentation varies widely commonly liver, brain, eyes, and blood.

Objectives: To evaluate clinical and laboratory presentation over the past five years.

Methods: This is a hospital based observational study carried out in the Department of Hepatology, Shaheed Ziaur Rahman Medical College Hospital (SZMCH), Bogura over a period of five years, from January 2017 to December 2021. Twenty-four index patients of Wilson disease were enrolled in the study. We followed Leipzig Score for Wilson's disease diagnosis. Total score 4 or more, diagnosis established as WD.

Results: Among 24, 46 % were female (n=11) and mean age was 16.4 year with range from 07 to 34. Liver presentation were Isolated splenomegaly 8.3% (n=2), Persistently elevated serum aminotransferase activity (AST, ALT) 8.3% (n=2), Fatty liver 20.8% (n=5), Cirrhosis: compensated 8.3% (n=2) or decompensated 20.8 (n=5), Acute liver failure 29.2% (n=7). Hospital mortality of acute liver failure were 70.2 (n=5) without liver transplantation. Among them Neurological and Psychiatric manifestation were 16.6 % (n=04) and 45.8 % (n=11) respectively.

Conclusions: The spectrum of liver disease in WD are highly variable. If unexplained hepatic, neurologic or psychiatric Symptoms present we should carefully look for WD.

Abstract Submission No. 100088

O-0270

Lipid-Associated Macrophages Fuel NAFLD Fibrosis via CD36-Mediated Lipid Uptake & OPN Release

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Background and Aims: In the context of non-alcoholic fatty liver disease (NAFLD), a progressive transition occurs, replacing resident Kupffer cells (KCs) with distinct lipid-associated macrophages (LAMs) characterized by CD36 upregulation. However, the precise roles and mechanisms of CD36-expressing LAMs in NAFLD pathogenesis remain elusive.

Methods: We investigated LAM traits through single-cell RNA sequencing (scRNA-seq). Oleic acid (OA)-treated THLE-2 cells were co-cultured with THP1 macrophages to mimic LAMs and explore their *in vitro* functions. We also used high-fat diet (HFD) and methionine-choline-deficient (MCD) NASH mouse models.

Results: ScRNA-seq and *in vitro* data showed elevated CD36 expression in LAMs, linked to an immunosuppressive profile. By utilizing a co-culture system, we were able to confirm that the increased expression of CD36 in LAMs facilitated a more efficient uptake of lipids from hepatocytes with steatosis, subsequently triggering osteopontin (OPN) release via peroxisome proliferator-activated receptor gamma (PPAR γ) pathway. ChIP-seq data and ChIP-qRNA experiments confirmed PPAR γ regulation of SPP1, encoding OPN. OPN-stimulated hepatic stellate cells (HSCs) exhibited elevated alpha-smooth muscle actin (α -SMA) and collagen type I alpha 1 (COL1A1), driving liver fibrosis. CD36 silencing or inhibition in LAMs reduced lipid uptake and OPN release, mitigating fibrosis, observed *in vitro* and in mice. Combining a CD36 inhibitor with pioglitazone synergistically curbed fibrosis in murine models.

Conclusion: CD36 aids lipid transfer from hepatic cells to macrophages, activating hepatic stellate cells, and promoting liver fibrosis. Identifying CD36 as a potential therapeutic target holds promise for treating advanced NAFLD-associated fibrosis.

Abstract Submission No. 100307
O-0271

GLP-1RAs regulate lipid metabolism and induce autophagy through AMPK/SIRT1 pathway to improve NAFLD

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Background: Non-alcoholic fatty liver disease (NAFLD) is a leading cause of cirrhosis and a major risk factor for hepatocellular carcinoma and liver-related death. Diabetes medications have been studied as potential treatments for NAFLD. Glucagon-like peptide-1 agonists (GLP-1RAs) have been rarely reported in the treatment of NAFLD alone as an anti-diabetic drug, and its specific mechanism of action is unknown. We investigated whether the therapeutic effect of liraglutide (LRG, a representative drug of GLP-1RAs) on hepatic steatosis is related to regulating lipid metabolism and enhancing autophagy in the hepatocytes.

Methods: We examined the effect of LRG on fat accumulation in fatty hepatocytes, and discussed its effects on enzymes related to lipid metabolism and autophagy. Meanwhile, knockdown of SIRT1 in free fatty acids (FFA)-treated cells was used to detect the influence of LRG on lipid metabolism and autophagy by regulating of AMPK/SIRT1 signaling.

Results: Our findings showed that free fatty acids (FFA) induced hepatocyte steatosis, which was significantly reversed by LRG. Meanwhile, LRG significantly regulated the expression of hepatocyte lipogenesis and cytosolic lipolysis-related proteins (FAS, ACC1, ATGL, HSL, LAL). Furthermore, LRG enhanced FFA-induced suppression of autophagy and SIRT1 expression, reducing intracellular lipid accumulation. It is evident that LRG regulates lipid metabolism and induces autophagy in an (AMPK)-dependent manner. Moreover, SIRT1 knockdown inhibited the autophagy-inducing and lipid-lowering effects of LRG.

Conclusion: GLP-1RAs may improve hepatic steatosis by regulating lipid metabolism and enhancing autophagy in an APMK/SIRT1-

dependent manner, which providing a new target for the treatment of NAFLD.

Abstract Submission No. 100313
O-0272

Amitriptyline inhibits NLRP3 inflammasomes activation via suppressing the ASM/CE pathway in NAFLD

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Background: Both Acid sphingomyelinase (ASM)/ceramide (CE) and NLRP3 inflammasome pathway are involved in the occurrence and development of NAFLD. However, it has not been reported whether ASM / CE pathway promote the occurrence of NAFLD by acting on the NLRP3 inflammasome pathway *in vitro*. Therefore, we conducted relevant cytological research.

Methods: NAFLD model cells were divided into 5 groups. The changes of intracellular lipid droplets and cell viability was detected, the biochemical metabolism indexes were determined. Western blot was used to measure ASM, NLRP3, caspase-1 protein expression; ELISA was used to detect the level of CE and ASM; the mRNA expression of ASM and IL-1 β was tested by RT-PCR; the apoptotic rate of cells was evaluated by flow cytometry (FCM).

Results: ASM and CE levels in the NAFLD model group were significantly increased, along with the increase of the expressions of NLRP3, Caspase-1, IL-1 β , and TG, TC, ALT, AST and MDA. These indicators further increased in the TNF- α group. Amitriptyline suppressed ASM and CE, decreased the levels of all the above biochemical and inflammatory biomarker, and reduced lipid droplets accumulation and improved apoptosis. MCC950 down-regulated the expressions of NLRP3, caspase-1 and IL-1 β , improved lipid deposition and apoptosis in the cell of NAFLD.

Conclusions: ASM / CE-NLRP3 inflammasome pathway is a pivotal mechanism of hepatocyte steatosis, inflammation, and cell damage in NAFLD. Amitriptyline can inhibit this pathway from the source and exert the anti-lipid deposition and anti-inflammatory effects, suggesting that ASM/CE-NLRP3 pathway is a key target in the treatment of NAFLD.

Abstract Submission No. 100512
O-0273

Elucidating the role of complement C3 in metabolic-associated fatty liver disease

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Background: Metabolic-associated fatty liver disease (MAFLD) affects 30% of adults and is the leading cause of liver transplantation. Despite the growing threat, no approved treatment exists. Accumulating evidence suggests an important role of the complement system in causation of MAFLD. As the axial component of the complement

system, C3 is predominantly produced in the liver, the metabolic 'engine' of the body; however, its metabolic role remains little known.

Methods: This study comprehensively characterized C3 expression in normal and MAFLD livers using single nuclei RNA sequencing and bulk RNA sequencing. Data were validated in free fatty acid-induced steatotic human hepatocytes, and a mouse model.

Results: C3 exhibited zonal expression, abundant in periportal hepatocytes. Cellular deconvolution showed that MAFLD disrupted hepatic zonal structure, depleting pericentral hepatocytes while expanding periportal ones in a severity-dependent manner involving progenitor activation. RNA sequencing data from 408 liver biopsies confirmed C3 alterations during MAFLD. C3 expression was upregulated in all forms of NAFLD and positively correlated with liver fat load in patients with steatohepatitis. C3 expression increased in steatotic human hepatocytes and livers from the mouse MAFLD model. C3 knockout protected against diet-induced hepatic lipid accumulation, repressing hepatic de novo lipogenesis and triglyceride synthesis by downregulating lipogenic regulators.

Conclusion: We demonstrate the impact of lipid accumulation on C3 expression in hepatocytes and show that C3 knockout impacts hepatic lipid handling. Overall, our study provides new insights into the role of C3 in MAFLD pathogenesis and suggests its potential as a therapeutic target for the treatment of MAFLD.

Abstract Submission No. 100557
O-0274

Donor and recipient genetic interactions: improving post-transplant diabetes outcomes

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Post-transplant diabetes mellitus (PTDM) is a prevalent complication after liver transplantation and is linked to the emergence of cardiometabolic complications. We studied the consequences of the genetic interactions between liver donors and recipients on PTDM outcomes. Liver transplant recipients without pre-transplant diagnosis of type 2 diabetes mellitus (T2D) and their paired donors underwent genome-wide genotyping. Polygenic risk scores (PRS) for T2D, insulin secretion, and insulin sensitivity were calculated using observations available from independent large-scale genome-wide association studies.

Results: 1115 recipient-donor pairs were included. For recipients who had the lowest T2D genetic risk, donor livers with the highest T2D-PRS contributed to the development of PTDM (OR (95% CI) = 3.79 (1.10 - 13.1), p=0.035). Recipient risk was linked to factors associated with insulin secretion and β -cell function (OR (95% CI) = 0.85 (0.74-0.98), p=0.02), while the donor liver contributed to PTDM via gene pathways involved in insulin sensitivity (OR (95% CI) = 0.86 (0.75-0.99), p=0.03).

Conclusion: Recipient and donor PRS independently and collectively serve as predictors for the onset of PTDM. The genetically influenced biological pathways in recipients primarily pertain to insulin secretion, while the genetic makeup of donors exerts an influence on insulin sensitivity.

Knowledge of recipient and donor T2D-PRS could potentially enhance metabolic genetic matching, particularly in the context of living donor liver transplantation.

Abstract Submission No. 100849
O-0275

A social media listening study of patients' experiences toward NAFLD (LISTEN-NAFLD)

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Background: Patients increasingly use social media (SM) to share and access health-related information and experiences. Social listening identifies and assesses online conversations about a topic on SM platforms. This study used social listening to gain patient-centric insights into non-alcoholic fatty liver disease (NAFLD).

Methods: Data from blogs, forums, SM platforms were collected, using keywords through licensed aggregator tools between November 2020 and November 2022, for 8 countries. The dataset was filtered using manual and automated algorithms; data were summarised by thematic analysis.

Results: A total of 1600 relevant posts were identified. Patients' journey posts (n=1479) included ongoing disease management (72%), diagnosis and tests (50%), causes and risk factors (36%). Most frequently discussed management techniques (n=1061) included dietary changes (55%), exercise (39%) and weight loss methods (25%). Key diagnostic tests (n=553) included ultrasound (31%), blood (24%) and liver function (16%) tests. Perceived key causes of NAFLD (n=534 posts) were unhealthy diet (39%), overweight/obesity (32%) and medication effects (12%). NAFLD's impact on quality of life was discussed in 12% of posts. Emotional analysis (84% of posts) revealed patients were worried (20%) and frustrated (19%) about NAFLD, but hopeful (14%) and determined (20%) to improve their health. Unmet needs, highlighted in 19% of conversations, included access to knowledgeable healthcare professionals (16%) (driven by European countries), better education (25%) and management options (13%) (both driven by Asian countries).

Conclusion: This study highlights challenges, coping strategies and unmet needs of patients with NAFLD. These insights can improve communication and patient care through education and support.

Abstract Submission No. 100963
O-0276

New AI-digital pathology indices predict adverse clinical outcomes in patients with MASLD

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Background: Single-Harmonic-Generation/Two-Photon-Excitation (SHG/TPE) imaging reduces observer-related variability in histological assessment of Metabolic-dysfunction Associated Steatotic Liver Disease (MASLD). Other digital pathology methods provide ordinal scores, and clinical outcomes are strongly correlated with fibrosis stage. We applied SHG/TPE imaging to cases in the SteatoSITE multimodal MASLD dataset (www.nature.com/articles/s41591-023-02602-2) to generate new indices predicting clinical outcomes, without fibrosis stage as a surrogate, using collagen morphological features unapparent to human observers.

Methods: n=452 biopsies (training n=300, validation n=152) were imaged by SHG/TPE. Following sequential feature selection, 10, 10, and 5 of 184 fibrosis parameters were chosen and linear regression used to construct individual indices for all-cause mortality and hepatic decompensation risk. Time-to-event analyses used the Kaplan-Meier estimator method, distributions were compared by og-rank test, and Cox-proportional hazards model calculated hazard ratios (HRs). Predictive power of risk indices were compared with NASH-CRN fibrosis stage (F0/1/2 vs. F3/4) and SHG/TPE imaging-derived qFibrosis stage (qF0/1/2 vs. qF3/4).

Results: Figure 1 shows that the newly-defined "All-cause Mortality Index" had greater predictive power for all-cause mortality risk (HR=4.49) than NASH-CRN (HR=3.41) or qFibrosis stage (HR=3.07), and the "Decompensation Index" had greater predictive power for decompensation events (HR=5.96) than NASH-CRN (HR=3.65) or qFibrosis stage (HR=3.59).

Conclusion: We used a training and internal validation set of clinically-annotated MASLD biopsies to develop novel SHG/TPE imaging-based tissue-to-outcome risk indices that accurately predicted all-cause mortality and hepatic decompensation events. If externally validated, these indices could be leveraged to enhance patient stratification in clinical care pathways or MASLD drug trials.

Abstract Submission No. 100976
O-0277

Liver fibrosis is associated with burden of cardiovascular disease in non-alcoholic steatohepatitis

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Background: This study assessed the burden of cardiovascular (CV) disease (CVD) in patients with non-alcoholic steatohepatitis (NASH), using real-world US healthcare data (TriNetX).

Methods: Patients were identified using the International Classification of Diseases code (ICD-10-CM) for NASH (index date) and required the following: ≥ 1 fibrosis-4 index (FIB-4) measurement(s); ≥ 12 months of data prior to index date; and no history of CV events or cirrhosis at baseline. CV events were analyzed with FIB-4 continuous measurement and risk categories (low [<1.30], intermediate [$1.30-2.67$], and high [>2.67]). CV risk was analyzed by cumulative incidence, incidence rate (IR), and hazard ratios (HRs).

Results: Of 529 patients, 66 had high, 145 had intermediate, and 318 had low FIB-4 scores. IRs for any CV event were 24.6, 17.2, and 10.4 per 100-person year for high, intermediate, and low FIB-4. For continuous baseline FIB-4 measurements, a significantly increased risk of any and individual CV events was observed as FIB-4 increased

(Figure). The risk of any CV event increased by 1.3% (HR 1.013; 95% confidence interval [CI] 1.006, 1.02; $p=0.0003$) and 14% (HR 1.14; 95% CI 1.06, 1.22; $p=0.0003$) for each 0.1- and 1-unit increase in FIB-4, respectively. For high and intermediate vs low FIB-4, adjusted HRs (95% CI) for any CV event were 2.05 (1.23, 3.41); $p=0.006$ and 0.87 (0.55, 1.37); $p=0.5405$.

Conclusions: Fibrosis assessed by baseline FIB-4 scores is associated with increasing clinical burden due to CVD, in terms of risk for CV events.

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Abstract Submission No. 101057
O-0278

Ferroptosis is a cell death at an early stage of MASLD in a mouse model

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Background: Ferroptosis is a new form of cell death, characterized by the iron-dependent accumulation of lipid hydroperoxides to lethal levels. However, little information is available on the association between ferroptosis and MASLD.

Methods: Male hepatocyte-specific PTEN KO (PTEN KO) mice were used as a MASLD model. Huh7 was used in vitro experiment. Ferrostatin-1, a ferroptosis inhibitor, and apomorphine, a drug for Parkinson's disease that has anti-ferroptotic function were used.

Results: PTEN KO mice at 10-week-old showed a moderate grade of steatosis but few hepatocyte ballooning, a hallmark for necrosis. In addition, PTEN KO mice showed increased oxidative stress markers, elevated serum transaminases, and increased proinflammatory and profibrogenic genes in the liver. There were few apoptotic cells and a certain number of hepatocytes positive for propidium iodide (PI), a marker for necrosis. Treatment of ferrostatin-1 and apomorphine for 2 weeks ameliorated the features of MAFLD. There were no significant changes in hepatic iron contents in mice treated with ferrostatin-1 or apomorphine. Although necrosis inhibitor did not decrease the number of PI-positive hepatocytes, both ferrostatin-1 and apomorphine decreased the number of PI-positive hepatocytes. In vitro experiments, ferroptosis inducer RSL-3 induced cell death. This cell death was inhibited by ferrostatin-1 and apomorphine but not by a necrosis inhibitor. In addition, cell death induced by RSL-3 were positive for PI, which were suppressed by ferrostatin-1 and apomorphine but not a necrosis inhibitor.

Conclusions: Ferroptosis contributes to cell death in an early stage of MASLD. Inhibition of ferroptosis is a potential treatment for MASLD.

Abstract Submission No. 101263
O-0279

NPC1 deficiency mediates autophagy impairment in NAFLD and serves as a target for NAFLD treatment

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Background: One important pathogenesis of NAFLD attribute to the imbalance of lipid metabolism, autophagy serves as a critical lipid metabolism pathway, but it impaired in NAFLD. We found Niemann-Pick

C1 (NPC1), a transmembrane protein related to autophagy function, decreased dramatically in NAFLD, we aimed to investigate the role of NPC1 in NAFLD pathogenesis.

Methods: NAFLD mice model was established by feeding with high fat diet (HFD), pharmacological interventions were administrated by intraperitoneal injection. Palmitic acid (PA) was used to stimulate cells to establish NAFLD cell model, agents to regulate autophagy were added in the beginning of PA treatment. Lipid metabolism and autophagy function were tested.

Results: Autophagy flux was impaired in downstream in NAFLD which indicated by the increase of LC3II and P62. A dramatic decrease of NPC1 was detected, by using HP-b-CD, DOPG or Thioperamide to compensate NPC1 function, we observed increased autophagy flux in vitro. Furthermore, Thioperamide increased the level of NPC1 in vivo, but only when coupled with upstream activator RAPA, the lipid deposition could be eliminated. So, we sought for a strategy to stimulate autophagy both in upstream and downstream, and found the TFEB activator could improve autophagy flux and eliminate lipid deposition in NAFLD by stimulate autophagosome formation and NPC1 expression.

Conclusions: NPC1 deficiency serves as a critical role in downstream autophagy impairment in NAFLD. Stimulating both upstream and downstream autophagy is a feasible strategy to reverse the progression of NAFLD in vivo. TFEB activator seems to be an ideal approach to reverse NAFLD.

Abstract Submission No. 101275

O-0280

Mesenchymal stem cells restore NASH by ameliorating ER stress in the local environment of the liver.

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Background: Mesenchymal stromal cells (MSCs) are expected to be the next novel therapy for liver diseases. Endoplasmic reticulum (ER) stress progresses NASH by cellular dysfunction and apoptosis of hepatocytes. In this study, we investigated the modulatory effect of MSCs on ER stress in a NASH model mouse.

Methods: MSCs, isolated from inguinal adipose tissue of C57Bl/6J mice, were injected into the splenic sub-capsule of NASH mice established by high-fat atherogenic (HF-AT) diet feeding. Liver tissues were collected for gene and protein expression analysis and immunohistochemistry. *In vitro*, murine immortalized hepatocytes (H2.35) were cultured with conditioned media of IMS/N alone or IMS/N-MSC co-culture. Cell viability of H2.35 was assessed, and RNA or proteins were isolated from H2.35 or IMS/N.

Results: In response to HF-AT diet feeding, expression of Perk-related molecules was upregulated in the NASH liver, and MSC treatment ameliorated the Perk-related genes compared to control. In addition, MSC treatment decreased the apoptotic cells and alpha SMA-positive activated stellate cells in the liver of NASH mice. *In vitro*, IMS/N-culture media induced expression of the Perk molecule. The IMS/N-culture media enhanced the Perk expression of H2.35, meanwhile, the media of IMS/N co-cultured with MSCs did not. Alpha SMA staining showed the de-activation of IMS/N co-cultured with MSCs. DNA microarray analysis revealed that IMS/N co-culture with MSCs attenuated the expression of 1182 genes related to CCL2, IL17, IL1, and HMGB1/RAGE signaling.

Conclusion: Adipose tissue-derived MSCs novel treatment ameliorated the NASH condition by alleviating the ER stress induced by hepatic stellate cells in hepatocytes.

Abstract Submission No. 101720

O-0281

Development of a novel cell line using gene editing to study steatotic liver disease

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Background: The patatin-like phospholipase domain-containing protein 3 (PNPLA3) p.I148M variant is associated with metabolic-associated steatotic liver disease (MASLD) and metabolic-associated steatohepatitis (MASH). Conflicting studies indicate that the variant could be gain- or loss-of-function, or neomorphic. Cancer-derived hepatoma cell lines used to study MASLD already carry the homozygous PNPLA3 p.I148M variant. In this study we aimed to develop a novel in vitro model that would better reflect PNPLA3-associated MASLD/MASH. The PNPLA3 p.I148M gene variant was knocked into a normal immortalised human hepatocyte (IHH) cell line using CRISPR prime editing.

Methods: Quantitative real-time PCR was used to analyse expression of lipid metabolism genes in control and mutant cell lines plus or minus free fatty acid (FFA) treatment. Genes included: PNPLA3, cluster of differentiation 36 (CD36), fatty acid synthase (FASN), sterol regulatory element binding transcription factor 1 (SREBF1), carnitine palmitoyltransferase 1A (CPT1A), peroxisome proliferator activated receptor α and γ (PPARA and PPARG).

Results: Heterozygous and homozygous PNPLA3 p.I148M IHH cell lines were generated. Differences in gene expression were observed between the mutant IHH cell lines and normal IHH, HepG2, C3A and Huh7 cell lines. Noticeably, mutant cell lines, compared to controls treated with FFA, had increased CD36 gene expression and decreased CPT1A gene expression.

Conclusion: We show that the homozygous PNPLA3 p.I148M variant resulted in decreased PNPLA3 gene expression, and increased lipid uptake (CD36) and decreased lipid oxidation (CPT1A) in both heterozygous and homozygous mutant cell lines. We have developed a novel resource to help us understand the mechanisms involved in MASLD/MASH.

Abstract Submission No. 101850

O-0282

Edaravone promotes the AMP-activated protein kinase to relieve nonalcoholic steatohepatitis in mice

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Objective: The global burden of nonalcoholic steatohepatitis (NASH) is increasing. Edaravone (EDA) has various biological and pharmacological activities, including anti-inflammatory and anti-oxidant activities. However, the effects of EDA on NASH remain unclear.

Methods: Steatosis cells were induced by palmitate/oleic acid (PO) in vitro. To establish the NASH animal model, C57BL/6J mice were fed a high-fat/high-cholesterol (HFHC) diet for 24 weeks. Furthermore, EDA were administered by intragastric gavage every day for 16 weeks. Glucose and insulin tolerance tests were used to investigate insulin sensitivity. Serum enzymes and lipids were assayed by a biochemistry analyzer. Histological analysis of the liver included HE, Oil red, and Sirius red staining. RNA-sequencing, real-time qPCR, and western blotting were used to investigate the expression of genes associated with lipid metabolism, inflammation, and fibrosis.

Results: EDA alleviated lipid accumulation and inflammation in both HepG2 and AML12 cells after PO stimulation. In addition, EDA prevented HFHC-induced insulin resistance, lipid accumulation, liver inflammation, and liver fibrosis in NASH mice. Mechanistically, RNA-sequencing and western blotting suggested that EDA could promote AMPK-signaling pathway activation in vitro and in vivo, and this finding was further verified by determining the phosphorylation levels of AMPK α at the site of T172. Furthermore, the protective effects of EDA on lipid accumulation and inflammation in hepatocytes and livers induced by PO or HFHC disappeared under the effects of the AMPK inhibitor.

Conclusions: EDA protects against metabolic-stress-induced NASH progression through activation of AMPK signaling, indicating that EDA had the potential to be a promising drug for NASH therapy.

Abstract Submission No. 102054

O-0283

iNKT cells are key players in the progression of murine steatohepatitis caused by Western diet

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Aim: We investigated the role of type I (iNKT cells) and type II NKT cells in age-related exacerbation of metabolic dysfunction-associated steatotic liver disease (MASLD).

Method: C57BL/6 mice, iNKT cells KO mice (V α 14KO), and all NKT cells KO mice (CD1dKO) aged 8 w.o (young) and 55 w.o (elder) mice were fed a high-fat/high-cholesterol diet (HFHC) or a control diet for 8 weeks.

Results: Whereas HFHC-fed wild young mice developed trivial hepatic steatosis with slight elevation of serum ALT levels to 54 $\pm$ 11 IU/L, HFHC-fed wild elder mice showed severe macrovesicular steatohepatitis with marked elevation of serum ALT levels to 406 $\pm$ 46 IU/L. Serum ALT levels significantly decreased to 268 $\pm$ 45 IU/L in V α 14KO elder mice, and further decreased to 159 $\pm$ 23 IU/L in CD1dKO elder mice. HFHC increased hepatic TNF α and TLR4 mRNA twice as much in elder mice as in young mice. HFHC-induced upregulation of TNF α and TLR4 in elder mice was equally significantly suppressed in both V α 14KO/CD1dKO. Sirius-Red staining showed pericentral fibrosis in elder mice fed an HFHC, while fibrosis was not observed in HFHC-fed V α 14KO/CD1dKO. Expression of TGF β mRNA was enhanced only in HFHC-fed elder mice and was equally significantly suppressed in both HFHC-fed V α 14KO/CD1dKO.

Conclusion: These findings indicated that iNKT cells are more deeply involved in the induction of inflammatory cytokines and fibrogenesis although both iNKT cells and type II NKT cells are promoting involved in steatohepatitis in aged mice. It was concluded that iNKT cells play an important role in age-related exacerbation of MASLD.

Abstract Submission No. 200128

O-0284

Tartaric Acid Ameliorates MAFLD by Activating the AMP-Activated Protein Kinase Pathway

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Background: Tartaric acid (TA) has been shown to have beneficial effects on blood pressure and lipid levels. However, its effect on metabolic-associated fatty liver disease (MAFLD) remains unknown. This study aims to investigate the role of TA in MAFLD.

Methods: Mice were fed a western diet for 8 weeks, followed by administration of TA or a vehicle for an additional 12 weeks while continuing on the western diet. Glucose tolerance test, liver tissue RNA sequencing (RNA-seq), lipid assay and pathological staining were then conducted. The HepG2 cell line was used to explore the mechanism by which TA regulates lipid metabolism.

Results: Our findings demonstrate that TA significantly improved weight gain, insulin resistance, hepatic steatosis, inflammation and fibrosis in mice with western diet-induced MAFLD. Through comparing gene expression differences between the TA-treated and vehicle-treated western diet mouse models, we confirmed that TA affects biological pathways related to lipid metabolism, inflammatory response, and fibrosis. Furthermore, TA effectively reduced oleic acid-induced lipid accumulation in HepG2 cells. We observed a significant reduction in genes associated with fatty acid synthesis in the TA-treated group, which were enriched in the AMP-activated protein kinase (AMPK) signaling pathway. Additionally, TA enhanced the phosphorylation level of AMPK, while the AMPK inhibitor Compound C blocked the inhibitory effect of TA on lipid accumulation in HepG2 cells.

Conclusion: Our study suggests that TA inhibits the progression of MAFLD by activating the AMPK signaling pathway. These findings indicate that TA may serve as a potential therapeutic component for the treatment of MAFLD.

Abstract Submission No. 200265

O-0285

Spatio-temporal immune landscape of tertiary lymphoid structures in non-alcoholic steatohepatitis

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Background: The global epidemic of non-alcoholic fatty liver disease (NAFLD) and its more severe form, non-alcoholic steatohepatitis (NASH), represents a significant health and economic burden with no approved pharmacotherapy. Therapeutic promotion of sustained suppression of inflammation holds great promise for NASH, while the adaptive immunological mechanisms controlling hepatocyte injury in NASH remain largely unknown.

Methods: In this study, we horizontally investigated the immune landscape of NASH in both clinical samples and preclinical models by comprehensive multi-omic profiling, including spatial transcriptomics (ST), single-cell RNA sequencing (scRNA-seq), bulk RNA

sequencing, tandem mass tagging (TMT)-based proteomics, multiplex immunohistochemical (mIHC) staining and H&E staining. C57BL/6J wild-type (WT), B-cell-deficient and transgenic mice were fed different NASH-inducing diets, after which NASH and fibrosis were assessed and analysed.

Results: We profiled the spatially resolved transcriptomic architecture of the NASH microenvironment and identified the presence of tertiary lymphoid structures (TLSs) with characteristic spatial patterns and involving genes associated with immune metabolism, cytokine and chemokine signalling, and extracellular matrix remodelling. These TLSs formed a functional hub and contributed to an active *in situ* process of B cell maturation towards plasma cell (PC) formation, autoantibody accumulation and the initiation of IgG-dependent hepatocyte apoptosis. Meanwhile, robust preclinical evidences demonstrated that B-cell depletion, BTK deficiency and acalabrutinib were effective in blocking B-cell activation, reducing IgG levels and ameliorating NASH phenotypes.

Conclusions: Our comprehensive immune profiling confirms the dark side of B-cell-rich TLS in both clinical NASH patients and highly translatable preclinical NASH models, highlighting the need for clinical evaluation of BTK inhibitors in NASH.

Abstract Submission No. 100063

O-0286

Mechanistic study of tyrosine kinase inhibitors against metabolic-associated fatty liver disease

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The pre-eminence of metabolic-associated fatty liver disease (MAFLD) in the general population calls for more targeted efforts to address this growing problem. While some tyrosine kinases (e.g. EGFR and MET) have been linked to the regulation of lipid homeostasis within the liver, their strategic advantage as pharmacological target has not been evaluated comparatively across the different sub-types of receptor tyrosine kinases. Hence, our lab addressed this research question head-on by using classical inhibitors for different receptor tyrosine kinases and apply them on both drug-induced and diet-induced models of lipid accumulation in liver cell lines. We evaluated their pharmacological potential by measuring the reduction in lipid accumulation as our phenotype-based assay. Thereafter, we explored the mechanism of action by investigating specific biochemical processes relevant to the disposition of lipids: fatty acid uptake, *de novo* lipogenesis, fatty acid oxidation, VLDL secretion and lipophagy. From this effort, two distinct tyrosine kinases were found to be pivotal in the regulation of lipid accumulation, namely EGFR and AXL. They play significant roles in modulating *de novo* lipogenesis and fatty acid oxidation, but they differ in the utilization of cell signaling pathways to achieve this. Critically, they present opposing effects on lipophagy which raises questions on the criticality of this process in the overall regulation of lipid homeostasis. Subsequent study using mice on MCD diet ascertained the manifestation of overall lipid reduction in the liver, as well as an attenuation of liver injury. These findings support further work to evaluate the feasibility of this therapeutic strategy.

Abstract Submission No. 100078

O-0287

CD18 deficiency ameliorates NASH by inhibiting lipid synthesis and downregulating Th1 cells in mice

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Background & Aims: Nonalcoholic steatohepatitis (NASH) is the progressive stage of nonalcoholic fatty liver disease, which has a higher chance of progressing to end-stage liver disease, and there is an urgent need to find new molecular mechanisms and therapeutic targets. Contemporary studies have indicated the potential involvement of CD18 in governing cellular metabolic pathways. We aimed to explore the function and mechanisms of CD18 in NASH.

Methods: The investigation of the expression levels of CD18 in the liver tissue of NASH patients applied the GEO database. Then WT mice and CD18^{-/-} mice were given a normal chow diet or a western diet (WD) for 16w to produce NASH model. A series of experimental methods were used to assess the expression of CD18 in NASH mice and its effect on NASH-related phenotypes. Flow cytometry and RT-qPCR were used to explore the possible regulatory mechanisms of CD18.

Results: Both NASH patients and mice showed remarkably elevated levels of CD18. In WT mice, the western diet causes obesity, steatosis, insulin resistance, fibrosis, and inflammation. CD18 deficiency significantly reduces these effects. Compared with WT WD mice, CD18^{-/-} WD mice had decreased expression of lipid synthesis genes, increased expression of lipid oxidative catabolic genes, and lower numbers of Th1 cells in liver tissue.

Conclusions: The expression of CD18 was significantly increased in NASH patients and mouse models. Through the inhibition of lipid synthesis and a decrease in Th1 cell infiltration in liver tissue, CD18 deficiency reduces obesity, steatosis, insulin resistance, and inflammation in NASH mice.

Abstract Submission No. 100182

O-0288

MicroRNA 29a ameliorates NAFLD by attenuating the MAVS pathway and mitigating liver steatofibrosis.

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Aim: Non-alcoholic fatty liver disease (NAFLD), the most common cause of chronic liver disease, consists of fat deposited (steatosis) in the liver due to causes other than excessive alcohol use. NAFLD is also hepatic manifestation of the metabolic syndrome.

Methods and Materials: We utilized miR-29a transgenic mice (miR-29a) and wild-type (WT) mice, subjecting them to a 36-week high-fat Western diet (WD) regimen to induce the NAFLD model. Hepatocellular steatosis was assessed through histopathological analysis, and dsRNA was detected via immunofluorescence staining, and other biochemistry assays.

Key Findings: The findings indicated that overexpression of miR-29a significantly curtails weight gain, lowers elevated AST/ALT levels, and reduces steatofibrosis in WD diet-treated mice. Moreover, miR-29a overexpression inhibits GSK3 β expression, enhancing HSP60 levels and decreasing dsRNA in WD mice. Additionally, miR-29a overexpression diminishes the mitochondrial antiviral-signaling (MAVS) pathway in WD mice. This suppression of MAVS expression occurs through direct binding to its 3'UTR. In the HepG2 cell line, miR-29a mimics directly inhibits MAVS expression.

In conclusion: Our results support that miR-29a improves NAFLD by dampening the mitochondrial antiviral-signaling (MAVS) pathway and alleviating liver steatofibrosis.

Abstract Submission No. 100249
O-0289

GSK-3 β inhibition for stimulation of liver regeneration in partially hepatectomized rats

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Background: The primary treatment for Chronic Liver Disease (CLD) involves dietary and non-dietary interventions. However, when CLD progresses to end-stage liver disease, liver transplantation becomes the only viable option, despite challenges such as donor shortages, transplant rejection, immunosuppressive drug complications, and high costs. To address the urgent need for post-transplantation liver regeneration, the growing focus is emphasized on stimulation of liver regeneration by pharmacological intervention, even in non-transplanted individuals or those with early liver complications.

Method: Present study aimed to stimulate the Wnt/ β -catenin signaling pathway by inhibiting GSK-3 β to promote hepatocyte replenishment and liver regeneration. A partial hepatectomy was performed on 44 rats, with the animals divided into six groups and assessed from postoperative days one to eight. The effects of the GSK-3 β inhibitor CHIR99021 (6.25mg/kg/b.w.) on hepatocyte regeneration and hepatoprotection were evaluated using biochemical, histopathological methods, and docking studies.

Results: it was indicated that both single and repeated doses of CHIR99021 significantly improved lipid profiles, liver function, and reduced oxidative stress in partial hepatectomized rats on the 3rd and 7th day as compared to those without drug treatment. Histopathological assessments confirmed substantial hepatocyte regeneration after CHIR99021 treatment, supported by docking studies that showed significant binding interactions with essential amino acids of the protein. Mitotic cell phase determination also validated the histopathological findings in different rodent groups (Fig1).

Conclusion: In conclusion, pharmacological stimulation of the Wnt/ β -catenin pathway through GSK-3 β inhibition with CHIR99021 demonstrated promising results in promoting hepatocyte regeneration, potentially offering a new treatment strategy for liver regeneration.

Abstract Submission No. 100283
O-0290

Transcriptome analysis revealed FABP5 as a serum marker of metabolic associated fatty liver disease

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Abstract:

Objective: The pathogenesis of metabolic (dysfunction) associated fatty liver disease (MAFLD) is very complex, which has not been fully revealed as so far. In our study, the third-generation ONT (Oxford nanopore technologies) sequencing platform was used to explore the key differentially expressed genes involved in the pathogenesis of MAFLD. **Methods:** In the present study, we firstly fed male C57/BL6N mice with high fat and high fructose (HFHF) diet for 19 weeks to induce MAFLD model while setting up a normal diet control group (Chow).

Secondly, we collected the liver tissues of the two groups and used the ONT technology to perform transcriptome analysis. Finally, we verified the sequencing results by quantitative polymerase chain reaction (qPCR) and measured the serum concentrations of fatty acid-binding protein 5 (FABP5) in mice and patients with MAFLD by Enzyme linked immunosorbent assay (ELISA).

Results: By transcriptome analysis, we found that there were 400 differentially expressed genes between the two groups, 12 of which participated in lipid transport and metabolism. Furthermore, we discovered that the serum level of FABP5 decreased significantly in patients with MAFLD, compared with healthy controls.

Conclusion: Involved in lipid transport and metabolism, FABP5 could be used as a serum marker of MAFLD.

Abstract Submission No. 100288
O-0291

Pharmacological exploration of FAS inhibitors for managing diabetic & non diabetic-liver injury

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Objective: The onset and development of liver damage is considered to be influenced by drugs and bad dietary habits.

Methods: The current study also aims to investigate the relation between paracetamol and high fructose + high fat produced diabetic and non-diabetic liver damage in context of innovative pharmacological therapies (Pterostilbene, Arbutin and Purpurin) with respect to their anti-adipogenic and hepatoprotective effect (Figure 1). The various biochemical, oxidative stress and qRT-PCR parameters were considered for the evaluation of selected interventions.

Results: High fat and fructose diet intake for 28weeks markedly ($P < 0.05$) upsurge the level of glucose as compared to control diet treated experimental rodents. The scenario was reversed in the case of paracetamol treated rodents there was no significant ($P < 0.05$) increase in the level of glucose which depicted the difference of diabetic and non-diabetic liver injury models. The lipid, liver, inflammatory (IL-6) level, oxidative stress and serum free fatty acid parameters was shown to possess significant ($P < 0.05$) improvement in PTS, ARB and PUR treated groups as compared to the disease treated rodent groups. **Conclusion:** It is hypothesized that reducing free fatty acid levels by Fatty Acid Synthase inhibition will improve insulin resistance and attenuate diabetic and non-diabetic Liver Injury.

Abstract Submission No. 100402
O-0292

Oxidative-cellular bioenergetics governs the telomerase inhibition-induced senescence in hepatocytes

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Background: Cellular senescence is a state where cells resist growth signals and apoptosis, ceasing proliferation. This leads to a prolonged 'zombie-like' state, impacting regenerative tissues like the liver. Senescent cells undergo metabolic shifts, affecting liver function. Heterogeneity among the senescence characteristics makes targeting senescent cells difficult. This study focuses on the link between telomerase inhibition-induced senescence and liver cell metabolism.

Methods: Primary hepatocytes or hepatocyte-derived organoids were cultured *in vitro*. Both were treated with 20 μ M BIBR-1532 (telomerase inhibitor) for 12-72 hours. Senescence was assessed through SA- β -galactosidase, immunofluorescence, immunoblotting (p53, p21, γ H2Ax), and senescence-associated secretory phenotype (SASP) markers. Cellular bioenergetics were measured using the XFe Seahorse analyzer.

Results: BIBR-1532 increased phosphorylation of histone (γ H2Ax), a DNA damage marker, by 10-fold ($p < 0.001$), and SA β -galactosidase activity by 11-fold ($p < 0.001$) (Figure 1A). Arrested proliferation is an important feature of senescence cells and the primary hepatocytes have limited proliferation in 2D culture. To overcome this limitation, we validated the results in hepatocyte-derived organoids and observed similar findings (Figure 1A). Coincided with DNA damage, BIBR1532 stabilized p53, increased p21 levels, and SASP expression. In contrast to the studies in immortalized cell lines, telomerase inhibition initially (up to 24 hours of treatment) increased oxidative phosphorylation capacity, however, in the later senescence phase, the cellular bioenergetics became predominantly glycolytic (Figure 1B).

Conclusion: BIBR-1532 (telomerase inhibitor) induces senescence phenotype in mouse primary hepatocytes. Cellular bioenergetic capacity transitions from oxidative phosphorylation to glycolysis in BIBR-1532 treated hepatocytes, which may affect the hepatocytes' response to toxins and inflammation.

Abstract Submission No. 100503
O-0293

PAK1 protects against nonalcoholic fatty liver disease via suppression of PPAR γ

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Background: Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease worldwide characterised by an increase in hepatic accumulation of triglycerides. The p21 activated kinase 1 (PAK1) participates in the regulation of many cellular processes such as cell growth, survival and migration. However, the role of PAK1 in NAFLD remains unclear. This study aims to identify the function and mechanism of PAK1 in NAFLD.

Methods: The mice fed high fat or methionine and choline deficient L-amino acid diet and mouse hepatic cells treated with oleic acid were used to detect the change of PAK1 in the progression of NAFLD/NASH. Lentivirus, siRNA and small molecular chemicals were used to overexpress or suppress targeted genes in mouse hepatic cells. Triglyceride content was detected by oil red O staining. The gene expression was measured by western blotting and RT-qPCR.

Results: The expression and phosphorylation of PAK1 were significantly increased *in vivo* and *in vitro* after metabolic stimulation. PAK1 knockdown in hepatocytes exacerbated lipid accumulation in response to metabolic challenge. PPAR γ mediated the regulation of lipid metabolism by PAK1. PAK1 directly interacted with PPAR γ to promote its

phosphorylation and decreased its nuclear distribution. Changes in lipid accumulation caused by PAK1 overexpression or knockdown could be reversed by PPAR γ agonists or inhibitors.

Conclusions: PAK1 functions as a negative regulator in NAFLD by suppressing PPAR γ . Targeting PAK1 can be a potential therapeutic strategy for NAFLD treatment.

Abstract Submission No. 100543
O-0294

Antioxidative Activity of Orange Water Kefir to Improve Liver Tissue in The Hyperlipidemic Rat Model

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Background: This research aims to know the antioxidative activity of orange water kefir drink to improve oxidative stress of liver tissue and lipid profile level in the hyperlipidemic rat model.

Material and Methods: This research used 30 rats divided into 3 groups (K+, K-, B). Group of K+ and B were given quail egg yolk for the first 4 weeks to make hyperlipidemia condition. For the next 4 weeks, K+ and K- groups were only fed *ad libitum*. Group B was given an orange water kefir drink with a dose of 5 ml/200grBW. Orange water kefir drink was made by good manufacturing product (GMP) standards and the procedure for making water kefir. All of this intervention was administered to rats with the sonde method. Blood sampling was taken to measure lipid profile (Total Cholesterol/TC and High-Density Lipoprotein/HDL) and the animal model was terminated to get liver organs to measure the Malondialdehyde (MDA level) and Superoxide Dismutase (SOD activity). Data will be expressed as mean $\pm$ SD and significant differences when the P value < 0.05 .

Results: The Mean of TC (mg/dL) was 203.50 $\pm$ 0.96 (K+), 77.80 $\pm$ 1.52 (K-), and 131.32 $\pm$ 2.38 (B). Mean of HDL (mg/dL) was 25.98 $\pm$ 0.58 (K+), 82.31 $\pm$ 0.88 (K-), 51.50 $\pm$ 1.24 (B). MDA level (nmol/gr) was 11.80 $\pm$ 0.17 (K+), 2.5 $\pm$ 0.12 (K-), and 4.56 $\pm$ 0.12 (B). The mean of SOD activity (%) was 21.43 $\pm$ 2.52 (K+), 71.43 $\pm$ 3.91 (K-), and 71.42 $\pm$ 2.70 (B). The results showed significant differences between all groups after the intervention with orange water kefir drink ($P < 0.001$).

Conclusion: The antioxidative activity of orange water kefir drink has been proven to improve oxidative stress of liver tissue and lipid profile levels in the hyperlipidemic rat model.

Abstract Submission No. 100552
O-0295

Entacapone Abrogate Steatotic Liver Disease Progression by Modulating FTO Gene Expression

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Background: Steatotic Liver Disease (SLD) is a metabolic dysfunction-associated liver disease that arises in the context of obesity and metabolic disorders, and poses a substantial health burden. The fat mass- and obesity-associated (FTO) gene, initially identified through genome-wide association studies, is positively correlated with obesity and metabolism in both humans and mice. However, the metabolic regulation of FTO in SLD remains unclear. Furthermore, *in silico* and *in vitro* investigations have shown that inhibiting FTO's enzymatic

activity of FTO leads to the dysregulation of genes involved in energy metabolism. In this study, we used entacapone, a drug for Parkinson's disease treatment and known as an FTO inhibitor, to alleviate SLD in a murine obesity model.

Methods A murine obesity model was established by feeding C57BL/6/J male mice a high-fat, high-calorie (HFHC) diet for 13 weeks, with some mice receiving intraperitoneal entacapone injections of varying doses and durations. Key metabolic parameters, including glucose and insulin tolerance, liver histology, serum biochemistry, adiponectin and leptin levels, and hepatic FTO expression, were meticulously assessed using microscopy, ELISA, RT-qPCR, immunohistochemistry, and western blotting.

Results: Compared with their entacapone-treated counterparts, HFHC-fed mice exhibited impaired glucose regulation, increased body weight, heightened liver index score ($p < 0.0001$), and periportal fibrosis. Disease severity, reflected by SLD activity scores ($p < 0.0001$), emphasized exacerbated liver pathology in the HFHC-fed group. Elevated serum biochemical markers, such as alanine transaminase, aspartate transaminase, triglycerides, and total cholesterol, were evident in HFHC-fed mice. In contrast, the entacapone-treated group displayed more favorable metabolic profiles ($p < 0.01$).

Additionally, entacapone-treated mice demonstrated elevated serum adiponectin levels and reduced serum FTO expression ($p < 0.0001$). In contrast, higher levels of serum leptin and FTO were observed in HFHC-fed mice. RT-qPCR, immunohistochemical analysis, and western blot validation confirmed increased FTO expression ($p < 0.0001$) in the livers of HFHC-fed mice compared to that in the treatment groups.

Conclusion: These findings suggest that entacapone has the potential as a therapeutic agent for the management of obesity and SLD by interfering with the progression of MASLD. This study introduced entacapone as a repurposing drug to address metabolic liver disorders associated with obesity, thereby offering novel therapeutic avenues in this demanding medical domain.

Abstract Submission No. 100744

O-0296

METTL14 Promotes Liver Glucose Production and Liver Steatosis in Obesity by RNA m6A modification

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Hepatic glucose production (HGP), a pivotal process mediated by glycogenolysis and gluconeogenesis, maintains energy metabolism during fasting and exercise. However, an excessive amount of HGP can lead to diabetes. Glucose-6-phosphatase (G6pase) is a key enzyme that regulates HGP through both glycogenolysis and gluconeogenesis. N6-methyladenosine (m6A) modification controls RNA processing, trafficking, decay, and translation. Mettl14 binds to Mettl3 and forms a m6A transferase complex to modify RNA. Recent studies have shown that the Mettl3/Mettl14/m6A pathway plays a crucial role in health and disease, but its function in HGP remains unknown. Here, we identify

Mettl14 as m6A writer for G6pase transcripts. Obesogenic factors increase expression of Mettl14 and Mettl3 in hepatocytes, thereby increasing RNA m6A modification in the liver. Deletion of hepatic Mettl14 decreases hepatic gluconeogenesis, liver glucagon response, and blood glucose in mice with HFD-induced obesity while not altering HFD-induced obesity. Mettl14 overexpression has the opposite effects. Moreover, Mettl14-deficient male mice are resistant to HFD-induced liver steatosis, and Mettl14 deficiency does not alter liver insulin and glucagon signaling. Notably, HFD feeding increases liver G6pase transcript m6A content and G6pase levels. Overexpression of Mettl14 increases, whereas ablation of Mettl14 decreases G6pase transcript m6A content in hepatocytes. Deletion of Mettl14 decreases G6pase transcript stability and translation, thereby lowering G6pase levels, gluconeogenesis, and glycogenolysis. These data unravel a hepatic Mettl14/m6A/G6pase/gluconeogenesis and glycogenolysis axis contributes to increased hepatic glucose production and diabetes progression in obesity.

Abstract Submission No. 100780

O-0297

Role of Serum Ferritin Level in The Diagnosis of Non-Alcoholic Fatty Liver Disease

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Background: Non-alcoholic fatty liver disease (NAFLD) is characterized by excessive liver fat accumulation and is a major cause of progressive liver disease. Serum ferritin is a biochemical parameter which is elevated in several clinical conditions including both acute and chronic liver diseases. It may indicate hepatic inflammation, necrosis and fibrosis progression in NAFLD due to its association with iron buildup and inflammation.

Aims: To assess the role of serum ferritin as an effective marker in the diagnosis of NAFLD.

Materials and Methods: This cross sectional study was conducted at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic disorders (BIRDEM) General Hospital, Dhaka on patients attending department of Gastrointestinal, Hepatobiliary and Pancreatic Disorders (GHPD). Purposive sampling technique was applied to enroll the subjects according to selection criteria. Statistical significance were set at 0.05 level and confidence interval at 95% level.

Result: This study included 206 patients. They were divided into two groups on the basis of ultrasonogram of abdomen. Among them 136 patients had NAFLD (Group-A) and 70 patients had normal liver (Group-B). Serum ferritin level was measured in all patients. The mean±SD of serum ferritin was significantly higher among Group-A (326.88±203.94) than Group-B (57.23±14.55) ($p < 0.001$). ROC analysis for serum ferritin level yielded an AUC of 0.993. Sensitivity, specificity, PPV, NPV and accuracy at cut off value 77 ng/ml were 94%, 97%, 94%, 97%, 96%; at 78.5 ng/ml were 95%, 97%, 94%, 97%, 96%; at 81.5 ng/ml were 98%, 95%, 92%, 99%, 97%; at 82.6 ng/ml were 94%, 98%, 99%, 89%, 95% and at 86 ng/ml were 92%, 98%, 90%, 92% and 90% respectively. The cut-off value of serum ferritin ≥81.50 ng/ml showed the highest accuracy.

Conclusion: The findings of this study suggest serum ferritin is an important biochemical test of NAFLD.

Abstract Submission No. 100818

O-0298

A GOOGLE TRENDS™ ANALYSIS ON NON-ALCOHOLIC FATTY LIVER DISEASE: A RETROSPECTIVE INFODEMIOLOGY STUDY

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Background: Non-alcoholic fatty liver disease (NAFLD) is a prevalent and growing health concern globally, coinciding with the rise of metabolic disorders. Understanding the search patterns related to NAFLD can provide insights into public interest for this condition. This research aims to analyze global online interest using Google Trends™.

Methods: Google Trends™ data for search terms related to fatty liver over a period of five years was downloaded and analyzed. Spearman's rank-order correlation correlated NAFLD, diabetes and obesity prevalence data, GDP per capita and internet penetration rate with search volume index.

Results: There was a significant reduction in online search interest during the COVID-19 pandemic (2020) however, there was an increase of approximately 30% in search terms related to fatty liver post-pandemic. The Latin American countries had the highest search volume when using the search term "fatty liver disease" while predominantly North American and Middle Eastern countries used "NAFLD" as a search term. The NAFLD search volume index was positively correlated with obesity prevalence and GDP per capita while searches for fatty liver disease correlated with the NAFLD prevalence in these respective countries. Countries with high liver cirrhosis-related mortality also searched "fatty liver" the most. Although majority of countries had above average internet penetration rate, this did not approach statistical significance.

Conclusions: The study found that the global online interest in fatty liver disease is increasing especially in regions where NAFLD prevalence is high and the use of Google Trends™ can be utilized as an infodemiologic tool.

Abstract Submission No. 100820
O-0299

A COMPARISON OF THE KNOWLEDGE AND PRACTICES ON NON-ALCOHOLIC FATTY LIVER DISEASE AMONG PHYSICIANS

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Background: NAFLD affects 25% of the population worldwide and poses a significant economic burden. It is important that physicians are aware of the burden of NAFLD and its appropriate management. This study aims to assess the knowledge, attitude, and practices of physicians towards NAFLD in a tertiary hospital.

Methods A cross sectional study was done using an online questionnaire distributed to all specialists, fellows and residents in Internal and Family Medicine in Philippine General Hospital.

Results A total of 97 physicians participated in this online survey. Most of the respondents were from family medicine followed by internal medicine. In terms of knowledge, only half of participants correctly identified the true prevalence of NAFLD and just 20% were aware of the available tools to stage fibrosis in NAFLD. On multiple regression, only number of NAFLD patients seen per year seemed to correlate with knowledge but this did not reach statistical significance.

Despite most physicians agreeing that NAFLD may lead to cirrhosis, a third are not concerned about cirrhosis as a consequence of NAFLD and only half routinely screen for NAFLD in at-risk patients. Fibrosis risk assessment using predictive tools is almost never practiced and referral to specialists is only done occasionally. Majority however, routinely prescribe individualized diet and exercise regimens.

Conclusion: Despite the increasing burden of NAFLD, there is still a significant gap in the knowledge and practices among physicians. Reinforcement of guidelines should be shared to all physicians in order to improve diagnosis and management of this disease.

Abstract Submission No. 100830
O-0300

Lessons on Drug Development: A Literature Review of Challenges Faced in MASLD Clinical Trials

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Background: Metabolic-dysfunction associated Steatotic Liver Disease (MASLD) is a leading liver disorder worldwide, resulting in both hepatic and systemic complications, notably cardiovascular diseases. Notwithstanding its profound impact on healthcare, current therapeutic strategies for MASLD primarily hinge on weight management — a task often challenging for patients — with no pharmaceutical solutions approved by the FDA to date.

Methods: We conducted a review of MASLD-focused clinical trials for 22 drugs (Phase 2 and beyond) listed on ClinicalTrials.gov as of 24th August 2022. Data collected encompassed trial identifiers, titles/acronyms, duration, patient counts and diagnoses, trial outcomes, and associated side effects. Subsequently, drugs were grouped into five analytical categories: Hypoglycemic, Lipid-lowering, Bile-pathway, Anti-inflammatory, and a diverse set which included nutraceuticals.

Results: Challenges hampering progress in the MASLD drug landscape included limited data, challenging trial design and outcomes, and debilitating adverse events. These findings shed light on several key areas for improvement, including repurposing existing drugs, exploring drug combinations, adopting non-invasive outcome measures, advocating for standardization, addressing adverse reactions, and prioritizing precision medicine that duly accounts for the intricate heterogeneity of MASLD in clinical trials.

Conclusion: While every advancement in drug discovery invariably presents unique challenges, this study underscores the importance of drawing lessons from past experiences. Proposing strategic improvements based on prevailing data allow us to advance clinical trials towards uncovering effective therapeutic drugs for MASLD management.

Abstract Submission No. 100866
O-0301

OMENTIN-1: IMPLICATIONS ON ITS ROLE IN DIABETES AND METABOLIC- ASSOCIATED FATTY LIVER DISEASE

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Objectives: Obesity and diabetes are tightly linked to metabolic-associated fatty liver disease (MAFLD). Here, we explore the potential role of visceral adipose tissue (VAT) omentin-1, identified through *in silico* analysis, in the context of obesity-related MAFLD and diabetes.

Methods: Omentin-1 levels were measured in obese patients with biopsy-proven MAFLD and mice fed with high fat-diet (HFD). *In vitro* and/or *ex vivo* studies were conducted to investigate the effects of omentin-1 on MAFLD-related pathogenesis, including steatosis, inflammation, ER stress, oxidative stress, and glucose-insulin modulation. We also analyzed the levels of omentin-1 in diabetic patients before and after 1 year of bariatric surgery.

Results: VAT and plasma omentin-1 levels exhibit a significant step-wise reduction in MAFLD patients, depending on disease severity but independent of fibrosis status. Likewise, HFD-fed mice with histological signs of MASH exhibited significantly reduced omentin-1 levels compared to their control diet counterpart. *In vitro* and *ex vivo* experiments using fat-laden hepatocytes and VAT explants, respectively, showed that omentin-1 did not affect steatosis but significantly reduced TNF- α levels, ER stress, and oxidative stress. Furthermore, omentin-1 significantly decreased the mRNA expression of *NF- κ B* and mitogen-activated protein kinases. *Ex vivo* VAT explants showed that D-glucose and insulin significantly reduced omentin-1 mRNA expression and protein levels. Notably, diabetic patients exhibited a significant increase in plasma omentin-1 levels one year following bariatric surgery.

Conclusions: Our findings suggest that reduced omentin-1 levels contribute to the development of diabetes and MAFLD. Therefore, further research is warranted to explore its role as potential therapeutic target and/or biomarker.

Abstract Submission No. 100993
 O-0302

Non Alcoholic steatohepatitis examined by FAST score and colorectal carcinoma-A case-control study

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Background: FAST score has been recently suggested for non-invasive detection of Non alcoholic steatohepatitis(NASH). We evaluated the relationship between Colorectal carcinoma(CRC) and co-existence of NASH detected by FAST scoring, as a risk factor.

Methodology: Patients with biopsy proven CRC were enrolled for the study group (n=53) and those without liver diseases or malignancies as control (n=53). The quantitative values of steatosis and fibrosis were measured using FibroScan. FAST score was calculated using the equation as carried out by Newsome *et al.* The optimal rule-out (FAST: ≤ 0.55) and rule-in (FAST: ≥ 0.78) cut-offs were applied. CAP, LSM, AST and FAST score values were compared between the two groups.

Results: Mean age was 53.7 years and 50.8 years for the case and control groups, respectively. 77.3 % of CRC (41/53) and 71% of control (38/53) had steatosis, defined by CAP ≥ 238 dB/m ($p=0.23$). 68% of the case group (36/53) and 50% of the control (27/53) had fibrosis, defined by LSM ≥ 7.5 kPa ($p=0.002$). Median AST was 76 for the case and 60 for the control ($p=0.013$). With rule-in cut off value for FAST score as ≥ 0.78 , 63.4% of the case and 36.6% of the control had NASH with

statistically significant p-value of 0.045. Odd ratio for association of NASH in CRC patients was 3.12, 95%CI 1.27-7.58, $p=0.0015$.

Conclusion: From our study, NASH has an association in CRC development. Further studies may help us to identify the role of NASH in tumorigenesis. Also, validating FAST scoring as a screening tool may help in early detection of steatosis and preventing complications.

Abstract Submission No. 101228
 O-0303

Sphingomyelin synthase 2 deficiency attenuates liver inflammation and fibrosis

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Objective: Sphingomyelin, a vital component of the plasma membrane, plays an indispensable role in maintaining membrane stability, fluidity, and cellular signal transduction. Sphingomyelin synthase 2 (SMS2) facilitates the transformation of ceramide to sphingomyelin, thereby regulating the sphingomyelin concentration within the plasma membrane. However, the exact function and underlying mechanism of sphingomyelin in nonalcoholic steatohepatitis (NASH) remain to be elucidated.

Methods: Wild-type (WT) and SMS2-knockout (SMS2-KO) male mice, aged nine weeks, were subjected to a Western diet (WD) (comprising 21.1% fat, 41% sucrose, and 1.25% cholesterol) and a high-sugar solution (containing 23.1 g/L d-fructose and 18.9 g/L d-glucose). Carbon tetrachloride (CCl₄), diluted tenfold with corn oil, was administered intraperitoneally at a dosage of 2 μ l (0.32 μ g)/g of body weight once weekly for a duration of 12 weeks.

Results: Compared to WT mice, SMS2-KO mice exhibited a decrease in both plasma membrane sphingomyelin and total liver sphingomyelin. WD/CCl₄-treated SMS2-KO mice displayed mild hepatic steatosis without noticeable liver inflammation and fibrosis. Chemokine signaling was downregulated in the liver of SMS2-KO mice, accompanied by a reduction in the expression levels of proinflammatory and inflammatory cytokines, fibrogenic genes, and collagen accumulation. Furthermore, a significant downregulation of CARD11, CD14, TLR2, and TGF β 1 was observed in WD/CCl₄-treated SMS2-KO mice.

Conclusions: The depletion of SMS2 mitigates liver injury in WD/CCl₄-induced NASH mice due to a decrease in the inflammatory response and TGF β 1-mediated collagen accumulation. This suggests that SMS2 deficiency may exert a protective effect against the progression from simple steatosis to NASH.

Abstract Submission No. 101251
 O-0304

Intestinal IL-33 exacerbates NASH by increasing gut microbiota-derived TMAO synthesis

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Background: Gut microbiota and its metabolites play a critical role in the development of non-alcoholic steatohepatitis (NASH) through the gut-liver axis. IL-33 is highly expressed in the intestine and regulates intestinal and extraintestinal diseases. Herein, we investigated the role of intestinal IL-33 in NASH.

Methods: IL-33 knockout mice and their control mice were fed 60% high-fat diet (HFD) for 24 weeks to establish NASH models. 3,3-dimethyl-1-butanol (DMB), a kind of choline analogue, was administered to inhibit gut microbiota-derived trimethylamine N-oxide (TMAO) synthesis. Fecal microbiota transplantation was carried out to study the role of IL-33-related gut microbiota alterations in NASH. Feces and serum were analyzed by 16S rRNA sequencing and metabolomics. Human intestinal epithelial cell line, Caco-2, and spleen naïve CD4⁺ T cells were used for *in vitro* studies.

Results: The expression of intestinal IL-33 was increased in NASH. IL-33 knockout improved NASH progression by alleviating intestinal barrier leakage and gut microbiota dysbiosis, with the decrease level of TMAO. Inhibition of TMAO synthesis by DMB reduced hepatic injury in NASH. Intracellular IL-33 inhibited the expression of intestinal barrier related genes, directly damaging the intestinal barrier. Extracellular IL-33 promoted Th1 differentiation and function leading to the pro-inflammatory environment in the gut. Transplantation of gut microbiota reversed NASH phenotypes.

Conclusion: These findings suggest that intestinal IL-33 increases gut microbiota-derived TMAO synthesis and aggravates NASH progression. Targeting intestinal IL-33 and its related microbiota may provide a potential strategy for treating NASH.

Abstract Submission No. 101257
O-0305

Heme Oxygenase-1 Improve Mitochondrial Function and Apoptosis in Non-Alcoholic Steatohepatitis

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Background: We aimed to explore the significance of Heme oxygenase 1 (HO-1) in regulating mitochondrial function and apoptosis during NASH development in animal models, cultured hepatocytes and NASH patients.

Methods: The effects of HO-1 on mitochondrial function were evaluated by genetic knockout in mouse models and *in vitro*. Meanwhile, NASH patients and healthy controls were enrolled. The mitochondrial structure was observed by confocal microscopy. The expression of proteins related to mitochondrial function and apoptosis were detected by western blot and immunohistochemical staining. Hepatic levels of mitochondrial reactive oxygen species (ROS), DNA damage and ATP were examined. Cell apoptosis were assessed by tunnel staining.

Results: In mice, HFD and MCD caused lipid accumulation, steatohepatitis injury, and cell apoptosis, which were aggravated by HO-1^{HEPKO}. Meanwhile, mitochondrial function was impaired in HFD or MCD HO-1^{HEPKO} mice compared to WT HFD or MCD mice, evidenced by increased protein expression of dynamic-related protein-1 (DRP1) and decreased protein expression of mitofusin-2 (MFN2) and optic atrophy 1 (OPA1). In line with the results *in vivo*, HO-1 knock-down upregulated lipid accumulation, DNA damage, lipid peroxidation and cell apoptosis, while reduced the ATP level in AML12 and HepG2 cells, which were in contrast to HO-1 overexpression *in vitro*. Likewise, these findings were consistent with the results in liver histopathology of NASH patients.

Conclusion: HO-1 could alleviate the NASH progression by mediating mitochondrial function and suppressing apoptosis.

Keywords: Non-alcoholic steatohepatitis; Heme oxygenase-1; Mitochondrial function; Apoptosis; Oxidative stress

Abstract Submission No. 101335
O-0306

Intrafamilial presence of NAFLD : The Genetic-environment link for fibrogenesis

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Background and Aims: NAFLD has its roots in genetic and environmental risk factors. First-degree relatives (FDRs) of patients with NAFLD-related cirrhosis share genetic and environmental risk factors for NAFLD while spouses only share environmental risk factors.

Methods: Cross-sectional study including 300 family members (150 spouses and 150 FDRs) of 150 consecutive patients. Liver stiffness was measured using vibration-controlled transient-elastography (VCTE). Independent risk factors for advanced fibrosis (AF) were identified and the best cut-off points for predicting advanced fibrosis were determined.

Results: 82(54.6%) of the FDRs assessed had NAFLD, and 92(61.4%) of spouses(p=0.34). The mean age of spouses was 52.9±7.8years and FDRs was 31.9±11.08(p=0.00). Metabolic syndrome was present in 75(81.5%) spouses and 40(47.6%) of FDRs(p=0.00). AF(VCTE ≥9.7kPa) was significantly more in FDRs compared to spouses(p=0.017). FDRs have 2.86 times increased risk of fibrosis(CI=0.14-0.85). AF was higher in those FDRs with high BMI(p<0.001), diabetes mellitus(p=0.00), high HbA1c(p=0.00), high LDL(p=0.007) and low HDL(p<0.001), and in spouses with high BMI(p=0.00), high TGL(p<0.001) and low HDL(p<0.001). The cut-off values for predicting AF in FDRs were BMI ≥27.9 kg/m², LDL ≥128 mg/dl, HDL ≤39.5 mg/dl, AST ≥43.5 U/L, ALT ≥44.5 U/L and HbA1c ≥ 6.45% and in spouses were BMI ≥29.4 kg/m², TG ≥153 mg/dl and HDL ≤35.85 mg/dl

Conclusion: FDRs with NAFLD are more likely to develop advanced fibrosis than spouses irrespective of age. Those FDRs with metabolic risk factors have a higher risk to have advanced fibrosis. The role of genetic and environmental factors in fibrosis development needs to be further explored

Abstract Submission No. 101346
O-0307

Liquid-Biopsy Derived Exosome RNA-Content Based Diagnostic Signature for Fatty Liver Disease

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MAFLD is now the number one chronic liver diseases worldwide. So far diagnosis of the disease still depends on invasive liver biopsy or expensive imaging technologies, limiting the possibility of population wide screening and monitoring. Therefore, we went on to establish a liquid biopsy-based biomarker signature for MAFLD diagnostic purposes. Specifically, exosome-based signatures from blood serum, which would allow population wide screening, disease progression and treatment response monitoring.

To identify high-confidence diagnostic markers we isolated and analyzed the RNA content of exosomes from different MAFLD mouse models and human patients. For establishing disease stage specific mouse liquid biopsy-based exosome RNA content signatures we collected serum from mice being exposed for 1, 6 or 8 weeks CDHFD, 8, 14, 20 or 26 weeks to Western Diet or respective controls, exposed to normal chow for the indicated times. Exosomes were precipitated, RNA isolated and high quality NGS libraries for sequencing were prepared. The same approach was applied to human patient serum from patients with liver biopsy verified disease stage. Data was in depth analyzed with a focus on interspecies conserved high confidence biomarkers, which were validated by qPCR on independent patient samples.

Pathway analysis shows that the mRNA content of isolated exosomes reflects important gene expression changes associated with the metabolic syndrome. We can identify liver related, but also cardio-vascular and bacterial changes associated with this disease. We then pinpointed 16 specific and reliable mRNA biomarker, which we could validate in mice and man.

Abstract Submission No. 101369

O-0308

Hepcidin alleviates hepatic steatosis through inhibiting PERK signaling pathway

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Background: Hepcidin is a crucial protein regulating iron homeostasis, while hepatic steatosis was more severe in hepcidin knockout mice in our previous study. The aim of this study is to investigate the role and mechanism of hepcidin modulating lipid metabolism in metabolic-associated fatty liver disease (MAFLD).

Methods: A mouse model of fatty liver was established by high fat diet (HFD) or methionine choline deficiency diet (MCD) feeding. Mice were injected with recombinant adeno-associated virus carrying hepcidin (AAV-Hamp) or green fluorescence protein. AML12 cell line was used to investigate the mechanism of hepcidin in regulating lipid metabolism.

Results: Treatment with AAV-Hamp significantly improved hepatic steatosis in both HFD and MCD mice, accompanied by a decrease in triglyceride (TG) content, lipid droplet formation and changes in mRNA and protein related to lipid synthesis and lipolysis. However, hepcidin did not significantly improve liver inflammation and fibrosis in MCD mice. In an *in vitro* model of lipid deposition using AML12 cells stimulated with oleic acid, hepcidin administration reduced the expression of lipid synthesis-related mRNA and protein, consistent with the *in vivo* experiments. Specifically, hepcidin decreased the expression of fatty acid synthase (FASN) and protein kinase RNA-like ER kinase (PERK), one of the three endoplasmic reticulum stress sensors. Furthermore, intervention of the PERK signaling pathway with a PERK activator abolished the protective effect of hepcidin on lipid deposition by inhibiting FASN.

Conclusions: Hepcidin plays a protective effect in hepatic lipid metabolism by decreasing the expression of FASN through inhibiting PERK signaling pathway, thereby alleviating MAFLD.

Abstract Submission No. 101396

O-0309

C-reactive Protein and Nonalcoholic Fatty Liver Disease

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Background: C-reactive protein (CRP) was found to increase in patients with nonalcoholic fatty liver disease (NAFLD). However, the causal association between NAFLD and CRP need to be further assessed.

Methods: Baseline information of 202 subjects between were collected from Tongji Hospital. Univariable and multivariable binary logistic regression analyses were conducted to assess the association between CRP and NAFLD. Furthermore, summary-level data from GWAS was employed in MR analysis. Inverse variance weighted (IVW) method was the primary analytic approach to infer the causality. Then, the Cochran's Q test and MR-Egger regression analysis were performed to determine the heterogeneity and pleiotropy, and the leave-one-out analysis was conducted to assess the stability of MR result.

Results: The retrospective study showed that CRP significantly increased in patients with NAFLD compared to non-NAFLD controls (2.40 vs 0.70, $P < 0.001$). Multivariable logistic regression analysis revealed that elevated CRP was an independent risk factor for NAFLD (OR=1.141, 95%CI 1.007-1.294, $P=0.039$). Subsequently, a significant positive causality of CRP with NAFLD was observed by IVW method (OR=1.187, 95%CI 1.004-1.404, $P=0.045$). It was further confirmed by the results of weighted mode (OR=1.321, 95%CI 1.147-1.521, $P=0.000$), and weighted median (OR=1.341, 95%CI 1.132-1.589, $P=0.001$). Meantime, no causal effect of NAFLD on CRP. Horizontal pleiotropy was not found among instrument variables (IVs). Despite the presence of heterogeneity, the MR result was proved robust by leave-one-out sensitivity analysis.

Conclusion: CRP is significantly increased in patients with NAFLD and may serve as an independent predictor for the risk of NAFLD.

Abstract Submission No. 101423

O-0310

Assessment of Liver Fibrosis with Transient Elastography in NAFLD Patients

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Background: Transient elastography is a non-invasive technique for estimating liver fibrosis. There is limited data about the performance of TE in Pakistani patients with non-alcoholic fatty liver disease (NAFLD). The overall prevalence of NAFLD in Pakistan is 47%.

Method: A Cross-sectional study was undertaken at the Department of Gastroenterology, Jinnah Postgraduate Medical Centre, Pakistan. After obtaining ethical approval, all patients above the age of 18 years, with the diagnosis of NAFLD based on abnormal liver-function tests and ultrasound abdomen consistent with fatty liver were included in the study. All patients with hepatitis, hepatic malignancies, hepatobiliary infections, and biliary tract disease were excluded from the study. Fibrosis score was calculated through Elastography as F0-F1 (5.3-7.1 kPa, Normal); F2 (7.5-8.5 kPa, Mild/Grade-I); F3 (9.5-13.0 kPa, Moderate/Grade-II); and F4 (13.1-18.8 kPa, Severe/Grade-III).

Results: A total of 171 patients were enrolled in the study, from which 69 (40.35%) were male and 102 (59.64%) were female, with a mean age of 37.50 ± 9.74 years. Of these, 112 (65.49%) belonged to the lower socioeconomic class. One hundred and twenty-two (71.34%) patients had fatty liver on ultrasound and 49 (28.65%) had hepatomegaly

with fatty changes. TE revealed that 69 (40.35%) patients had a score of F0-F1, 62 (36.25%) F2, 29 (16.95%) F3, and only 11 (6.43%) had a score of F4.

Conclusion: Detecting liver fibrosis at its early stages is crucial in preventing its progression to cirrhosis. Reversal of fibrosis is only possible if it is diagnosed as early as possible and managed with appropriate treatment.

Abstract Submission No. 101592

O-0311

Exploring the Interplay of Hepatic Steatosis, Body Fat Ratio, and Hepatic Fibrosis in MAFLD

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Background: Hepatic fibrosis is a significant pathological condition with far-reaching implications for public health, often associated with hepatic steatosis and the overall distribution of body fat. This study encapsulates a comprehensive investigation aimed at elucidating the intricate relationship between hepatic steatosis, body fat ratio, and the development of hepatic fibrosis in patients with MAFLD.

Methods: Data from hospital-based records of a tertiary liver specialty centre was collected for the period from April 2021 to August 2023. Transient elastography provided Liver Stiffness Measurement values, and cut-off for liver fibrosis was kept at 7.9 kPa. Continued Attenuation Parameter (CAP) value of more than or equal to 248 Db/m was defined as hepatic steatosis. Body composition analysis was performed using InBody 770 machine.

Results: A total of 586 MAFLD patients were studied of which 288 (49.1%) had some degree of liver fibrosis. Mean age was 46.6±13.1 years and 71.6% were males. Percent Body Fat was significantly higher in those with no liver fibrosis (33.8±9.5% vs 32.5±9.6%; p=0.031). When study subjects were stratified according to liver steatosis and total body fat percentage, it was observed that median liver fibrosis was 7.6kPa [IQR 5.1-20.6] in those with liver steatosis present & body fat percentage more than normal upper limit. In those with liver steatosis present but normal body fat percentage, liver fibrosis was 13.7kPa [IQR 8.8-62.9]. Liver fibrosis was significantly correlated to liver steatosis (-0.125; p<0.001), body fat percentage (-0.101; p=0.001), liver steatosis/body fat mass ratio (-0.108; p=0.001), BMI (0.113; p<0.001) and obesity degree (0.082; p=0.01).

Conclusions: MAFLD patients having central obesity (having higher visceral fat content) had higher tendency to develop hepatic fibrosis. Such patients may be more predisposed to having other metabolic ailments and strategies to decrease hepatic fat may benefit both liver and help prevent other metabolic diseases.

Abstract Submission No. 101621

O-0312

IMPACT OF RENAMING NAFLD TO METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD)

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Background: The second-most recent change in steatosis nomenclature required 2/3 weight-metabolic criteria to be met and may lead to missed diagnosis in patients who develop weight-metabolic abnormalities later on. The metabolic-dysfunction-associated steatotic liver disease (MASLD) criteria requires only one criterion and may mitigate this. We aimed to characterize our steatotic patients into: 1.) nonalcoholic fatty liver disease (NAFLD) only; 2.) MASLD only; 3.) NAFLD-MASLD; 4.) not NAFLD-MASLD.

MATERIALS AND METHODS: Consecutive patients with steatotic liver on ultrasound in a Hepatology clinic database from August 2007-July 2017 were included. Demographic, laboratories, AST/Platelet ratio (APRI), FIB4, and NAFLD fibrosis score (NFS) were compared between the groups.

Results: The 663 steatotic patients were categorized into: 6(0.9%) NAFLD, 326(49.2%) MASLD, 325(49%) NAFLD-MASLD, and 6(0.9%) not NAFLD-MASLD. Among patients meeting MASLD criteria, majority (80%) met >2 cardiometabolic criteria while only a minority (8.3%) satisfied only 1 criterion, of which overweight/obesity (79.6%) was most common. NAFLD-MASLD and MASLD patients had higher ALT, AST and platelet levels as compared to NAFLD and not NAFLD-MASLD patients (p<0.05). A higher probability of advanced fibrosis was seen in MASLD only compared to the other groups using APRI. There was a trend for more no/minimal fibrosis patients in the NAFLD and not NAFLD-MASLD groups compared to the MASLD and NAFLD-MASLD groups using non-invasive liver fibrosis tests.

Conclusions: Majority (82%) of patients with steatosis on ultrasound meet MASLD criteria. Serial follow-up is needed to determine if patients who do not meet MASLD criteria now will meet it in the future.

Abstract Submission No. 101655

O-0313

The Hedgehog signal factors and FGFs regulate endothelial cells in non-alcoholic fatty liver disease

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Background: The Hedgehog signaling pathway is a crucial developmental pathway that plays a fundamental role in embryonic development, as well as in tissue regeneration and stem cell maintenance in adults. However, few researches reveal the relationship between Hedgehog signaling and FGFs in NAFLD progression, in which liver fibrosis is often complicated. In this study, we discover the crosstalk of FGFs and Hedgehog signaling pathway in NAFLD.

Methods: In this study, liver tissue was obtained from obese patients with/without diabetes and steatosis. We used transcriptome analysis to discover the underlying pathway signals networks of NAFLD and prove it by Western blotting, Immunohistochemistry, Immunofluorescence staining, etc. R language and packages were used to explore bioinformatic parts and data statistics.

Results: Firstly we found the differential expression genes between the two groups in the threshold of logFC value exceeding 1 and the P value less than 0.05. Totally 126 up-expressed genes and 127 down-expressed genes were found. The Gene Set Enrichment Analysis using Gene Ontology shows an obvious enrichment in Positive Regulation Of Endothelial Cell Chemotaxis (GO:2001028) and Regulation Of Endothelial Cell Chemotaxis To Fibroblast Growth Factor (GO:2000544). Furthermore, we adopted the Gene Set Variation Analysis to evaluate the pathways' activities and noticed that the Hedgehog signaling pathway is the most important molecular pathway in regulation pathways.

Western blotting, Immunohistochemistry, and Immunofluorescence staining exhibited the same trend.

Conclusion: In the NAFLD microenvironment, Cell-cell communication via FGFs is hopefully a promising therapeutic target. The Hedgehog signaling pathway may be the essential mechanism that plays a counterpart role.

Abstract Submission No. 101825

O-0314

CD36-mediated uptake of oxidized LDL induces ferroptosis and dysfunction in DNTregs in NAFLD

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Background: Inflammation plays a pivotal role in the development of NAFLD. CD3⁺TCR^β⁺CD4⁺CD8⁻ double negative immune-regulatory T cells (DNTregs) are important for maintaining liver immune homeostasis. However, during NAFLD progression, intrahepatic DNTregs have decreased cell survival and immunosuppressive function, which lead to aggravated liver proinflammation. However, the reasons and underlying mechanisms that cause the changes of DNTregs during NAFLD progression are still unknown.

Methods and results: We analyzed DNTregs in PBMCs from NAFLD patients and in NAFLD mouse models with serum biochemical test index. Correlation analysis showed a significant negative correlation between serum oxLDL levels and both the survival and functional molecule expression levels of DNTregs. Moreover, stimulating DNTregs with oxLDL, we noticed decreased cell survival and immunosuppressive function of DNTregs accompanied by an increased DNTreg ferroptosis. Ferroptosis inhibitors were able to regain the immunosuppressive function of DNTregs. Further investigation revealed that CD36 is the primary regulator of oxLDL-mediated ferroptosis in DNTregs. CD36 knockout significantly rescued oxLDL-induced ferroptosis in DNTregs. Meanwhile, CD36 predominantly enhanced ferroptosis in DNTregs by upregulating ACSL4 expression. CUT&TAG experiments confirmed the oxLDL-induced upregulation of Hif-1 α , which bound to the ACSL4 promoter region, thereby induced CD36-mediated ferroptosis. Finally, transferring CD36^{-/-} DNTregs into NAFLD mice, we observed a significantly reduced ferroptosis, enhanced survival and immune regulation of CD36^{-/-} DNTregs compared with those of WT DNTregs. This improvement of DNTregs resulted in a notable enhancement of the therapeutic efficacy against NAFLD.

Conclusions: Specifically targeting CD36 to prevent ferroptosis of DNTregs may provides a novel therapeutic approach for NAFLD.

Abstract Submission No. 200012

O-0315

Effects of Individual Bile Acid on MASH Development in Low Bile Acid Mouse Model

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Bile acids (BA) function as signaling molecules that regulate lipid and glucose homeostasis, as well as liver and gastrointestinal functions. Individual BAs selectively activate the farnesoid X receptor (FXR) to induce target genes including fibroblast growth factor 15/19. BA dysregulation is a key pathophysiology of liver diseases, such as metabolic dysfunction associated steatohepatitis (MASH). Currently, there are no FDA-approved drugs for the treatment of NASH. We showed short-term exposure to individual BA leads to deferential effects on lipid, inflammation and oxidative stress pathways in a low-BA mouse model-Cyp7a1/Cyp27a1 double knockout (DKO) mice-than in wild type (WT) mice. The current study determines effects of individual BAs at physiological concentrations (CA, DCA, or UDCA) in the DKO mice during MASH development. DKO mice on MASH diet were found to be insulin sensitive compared to WT mice. By 16 weeks, DKO mice were resistant to weight gain compared to WT mice, which is not worsened by BAs. CA, DCA and UDCA varied in activating hepatic and intestinal FXR to induce target genes. In addition, there were individual effects in disrupting lipid homeostasis. CA or DCA but not UDCA could differentially induce inflammation and fibrosis. Finally, our findings support UDCA as an intestinal FXR agonist under low BA conditions. Significant alterations in lipid uptake and metabolism following BA feeding indicated differences in cholesterol and lipid handling without BAs. Overall, DKO mice were susceptible to inflammation and fibrosis on CA and DCA supplement, while WT mice were more vulnerable to CA-induced fibrosis on control diet.

Abstract Submission No. 200029

O-0316

Therapeutic target identification of MAFLD through patient transcriptomic-based in vivo RNAi screen

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Backgrounds: Metabolic dysfunction-associated fatty liver disease (MAFLD) has become a significant global health concern, yet it remains underrepresented with limited identified effective therapeutic targets. Although analyzing patient transcriptomics provides insights into dysregulated genes with therapeutic potential, MAFLD is a complex condition involving intricate interactions among multiple organs. Consequently, the identification of effective therapeutic targets necessitates an innovative approach. To meet this challenge, we have devised a novel approach utilizing patient transcriptome-based in vivo RNAi screening to identify potential therapeutic targets for MAFLD.

Method: Dysregulated genes in patient liver tissues were identified through RNA sequencing. A pooled-shRNA library was constructed to target these genes and hydrodynamically introduced into mouse hepatocytes. Mice were divided into treated (high-fat diet) and control (normal diet) groups. Genomic DNA was collected from liver samples post-diet for quantifying shRNA abundance. Therapeutic target candidates were determined by identifying enriched shRNA in treated group mice.

Results: We identified four primary candidates as the most promising targets following a screening process, warranting further validation assays. Silencing these target genes resulted in a notable reduction in disease progression, specifically in fibrosis formation. One of the four targets underwent additional validation to elucidate its mechanism of

action, revealing that the knockdown of this target significantly enhances lipid metabolism.

Conclusion: Our findings highlight the efficacy of our approach in identifying novel targets for MAFLD therapeutics. Suppression of the identified target gene expression significantly alleviated disease progression. This study contributes valuable insights to the discovery of novel MAFLD therapeutics.

Abstract Submission No. 200098
O-0317

MicroRNA-411-5p targets the EIF4G2 / FOXO3 axis to alleviate lipid deposition in MAFLD

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Background: Abnormal lipid deposition is an important driver of metabolic dysfunction-associated fatty liver disease (MAFLD) progression. MicroRNA-411-5p (miR-411-5p) and eukaryotic translation initiation factor 4γ2 (EIF4G2) are related to abnormal lipid deposition, but the mechanism is unknown.

Methods: A high-fat and high-cholesterol diet (HFHCD) or a choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD) was used to construct the MAFLD rat or mouse models. Adeno-associated virus type 8 carrying EIF4G2 shRNA were injected into the tail vein to downregulate EIF4G2. MiR-411-5p mimic was used to upregulate the expression of miR-411-5p.

Results: The miR-411-5p level was decreased in both MAFLD rats and mice, and was negatively correlated with the liver triglycerides and the degree of liver injury. Up-regulation of miR-411-5p reduced fatty acid synthesis to alleviate lipid deposition. Moreover, EIF4G2 was confirmed to be a target gene of miR-411-5p, and miR-411-5p downregulated the expression of EIF4G2. Down-regulation of EIF4G2 expression reduced fatty acid synthesis and alleviated lipid deposition in palmitic acid-induced steatosis hepatocytes. Importantly, down-regulation of EIF4G2 in the liver alleviated liver damage and abnormal lipid deposition in MAFLD mice. Besides, EIF4G2 regulated the expression of forkhead box class O 3 (FOXO3), and up-regulation of miR-411-5p or down-regulation of EIF4G2 both lead to reduced expression of FOXO3.

Conclusions: Up-regulation of miR-411-5p inhibits EIF4G2 to reduce the expression of FOXO3, thereby inhibiting fatty acid synthesis and alleviating abnormal lipid deposition in MAFLD. MiR-411-5p is beneficial for improving MAFLD and EIF4G2 is expected to become a therapeutic target for MAFLD.

Abstract Submission No. 200146
O-0318

FTZ inhibits the hepatic lipid deposition by TFF3/PPAR α/AMPK signaling pathway in diabetes mice

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Background: Trefoil Factor 3 (TFF3) TFF3 is a novel liver glycolipid metabolism regulatory factor that can maintain the homeostasis in the

body by PPARα/AMPK signaling pathway. FTZ as a representative formula of the “Tiao Gan Qi Shu Hua Zhuo” method in prevention and treatment of glycolipid metabolism diseases, the inner mechanism is unknown.

Methods: 1. Animals: db/db and C57BL/6J mice (induced by 40mg/kg STZ and HFD) were used in our study. FTZ (1-2 g/kg) and Atorvastatin (5mg/kg) were used for 12 weeks treatment. 2. L02 cells: Palmitic acid (0.25 mmol/L) and Glucose (6 mmol/L) were used to stimulate the L02 cells, followed by FTZ intervention for 24h. And the indicators including TC, TG, LDL-C, HDL-C, ALT and AST were detected by biochemical test kits. H&E and Oil Red staining methods were used to evaluate the histopathological changes and lipid accumulation in liver. IHC and WB methods were used to detect the TFF3, PPARα, p-AMPK/AMPK, p-ACC/ACC and CPT-1α levels.

Results: FTZ can significantly reduce the TC and TG content, and improve the liver function, inhibit liver lipid deposition, and significantly increase the protein levels of TFF3, PPARα, p-AMPK, p-ACC and CPT-1α in the liver and L02 cells.

Conclusion: FTZ can inhibit the hepatic lipid deposition, which could be related with TFF3/PPARα/AMPK signaling pathway, and further accelerate fatty acids β oxidation to decrease lipid accumulation. The study provides a new perspective and experiment basis for the prevention and treatment of metabolic diseases.

Abstract Submission No. 200168
O-0319

Enhancing liver health in type 2 diabetes: CD26 inhibitors & Glycine max antioxidants synergy

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Aims: Non-alcoholic fatty liver disease (NAFLD) is the predominant chronic liver ailment globally, afflicting over half of type 2 diabetes mellitus (T2DM) patients due to exacerbated insulin resistance, oxidative stress, and inflammatory disruptions. A promising avenue for T2DM treatment involves leveraging the incretin hormone GLP-1. Di-peptidyl peptidase-IV (DPP-IV/CD26) inhibitors, sourced from *Glycine max*'s phenolic-rich fraction, may exhibit pleiotropic effects via the presence of incretin hormone receptors in diverse tissues, including the liver. Our study explores the potential impact of DPP-IV inhibitors with antioxidant capabilities on NAFLD in a T2DM rat model.

Methods: Wistar rats underwent T2DM induction via a high-sucrose diet and dexamethasone. Biochemical, toxicological, and histological parameters were assessed. Evaluations encompassed serum DPP-IV inhibition, glycosylated hemoglobin, HOMA-IR, hepatic lipid peroxidation, SGOT, SGPT, and tissue antioxidants. Serum lipid profiles were examined to correlate with the antiperoxidative effects of *Glycine max*'s phenolic-rich fraction.

Results: Diabetes induction via corticosteroid and high sucrose diet was confirmed by HOMA-IR (2.5%), HOMA-β (36.3%), and HOMA sensitivity (44.3%). In-vitro DPP-IV inhibition assay demonstrated 63.1±2.8%, while serum activity was 41.9±1.3%. The DPP-IV inhibitors lowered aminotransferases (SGOT & SGPT) and alkaline phosphatase, elevated insulin, and reduced HbA1c. Triglyceride and cholesterol levels normalized. *Glycine max* extract exhibited superior antioxidant capacity, safeguarding against lipid peroxidation, and preserving liver histoarchitecture, emphasizing positive outcomes post-DPP-IV inhibitor treatment.

Conclusions: DPP-IV inhibitors along with antioxidant properties improve insulin sensitivity, reduce oxidative stress and toxicity which lead to improve liver dysfunction in T2DM. These findings also suggest that GLP-1 in liver has beneficial effects on NAFLD.

Abstract Submission No. 200201
O-0320

The potential mechanism of methotrexate induced liver injury in MAFLD: *in silico* analysis

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Background: The putative liver toxicity of methotrexate should be evaluated in the pathogenesis and natural history of liver disease, especially metabolic associated fatty liver disease (MAFLD). We initially identify the potential effects of methotrexate in MAFLD based on network toxicology and molecular docking technology.

Methods: The drug toxicity information was obtained from ProTox-II and ADMETlab 2.0. The potential targets related to methotrexate and MAFLD were identified through ChEMBL, STITCH, GeneCards and OMIM databases. The core genes were analyzed using STRING and Cytoscape, gene ontology (GO) analysis, and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment. The interactions between methotrexate and these core genes were confirmed by AutoDock Vina.

Results: ProTox-II and ADMETlab 2.0 confirmed the hepatotoxicity of methotrexate, and 22510 disease target genes and 541 drug target genes were identified from the database. Venn diagram showed 189 common related potential target genes between Methotrexate and MAFLD. Among these genes, 20 core targets were identified by STRING and Cytoscape. Further analysis of GO and KEGG pathway showed that genes related to methotrexate induced MAFLD mainly distributed in cancer and proteoglycans in cancer pathway and estrogen signaling pathway. AutoDock Vina confirmed the intensity of binding between methotrexate and the core target genes. The binding ability was relatively higher in ACLY, LDHA, HMGCR, ITGB3, MMP2, BCL2, and CASP3, than other target genes.

Conclusion: The core genes identified here maybe can serve as targets for the prevention and treatment of MAFLD in patients taking methotrexate.

Abstract Submission No. 100082
O-0321

Vitamin E versus Placebo in the Treatment of NASH: a Multicenter, Randomized, Double-blind Study

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Background: Despite the proven efficacy of long-term high-dose vitamin E (800IU) for the treatment of nondiabetic patients with non-alcoholic steatohepatitis (NASH), potential risks hinder its application. The efficacy and safety of a lower dose of vitamin E for NASH treatment is unclear.

Methods This was a multicenter, randomized, double-blind, placebo-controlled study of nondiabetic patients with biopsy-proven NASH. Patients were randomly assigned to receive oral vitamin E (300mg about 450 IU) or placebo. The primary outcome was an improvement in hepatic histology. The exploratory secondary endpoint was improvement in liver fibrosis by at least one stage and no worsening of NASH.

Results A total of 124 patients were randomly assigned to receive vitamin E (58 patients) or placebo (66 patients). In the modified ITT population, 29.3% of those who received vitamin E demonstrated an improvement in histology (43.6% in PPS) compared with 14.1% (17.7% in PPS) in the placebo group ($p = 0.040$ in modified ITT, $p = 0.0071$ in PPS). An improvement in the exploratory secondary endpoint was observed in 25.9% (38.5% in PPS) of the vitamin E group and 15.6% (19.6% in PPS) of the placebo group ($p = 0.16$ in modified ITT, $p = 0.048$ in PPS). Serious adverse events were reported in a similar proportion of patients across groups but were not considered to be related to treatment.

Conclusions Oral vitamin E administered at a dose of 300mg daily resulted in a significantly higher histologic improvement in nondiabetic NASH patients and was safe and well tolerated for NASH treatment.

Abstract Submission No. 100099
O-0322

The greater impact of *PNPLA3* polymorphism on liver-related events in Japanese NAFLD

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BACKGROUND & AIMS: *PNPLA3* rs738409 has been associated with an increased risk of liver-related events in patients with non-alcoholic fatty liver disease (NAFLD). In this study, we investigated the epidemiology of NAFLD and the impact of *PNPLA3* on prognosis in Japan.

Methods: A longitudinal multicenter cohort study, the JAGUAR study, includes 1550 patients with biopsy-proven NAFLD in Japan. We performed genetic testing and evaluated outcomes from this cohort. Liver-related events were defined as hepatocellular carcinoma (HCC) and decompensated liver cirrhosis events.

Results: During follow-up (median [range], 7.1 [1.0-24.0] years), 80 patients developed HCC, 104 developed liver-related events, and 59 died of any cause. The 5-year rate of liver-related events for each single-nucleotide polymorphism was 0.5% for CC, 3.8% for CG, and 5.8% for GG. Liver-related deaths were most common ($n=28$); only 3 deaths were due to cardiovascular disease. Multivariate analysis identified carriage of *PNPLA3* CG/GG (hazard ratio [HR] 16.04, $p=0.006$) and FIB-4 index >2.67 (HR 10.70, $p<0.01$) as predictors of liver-related event development. No HCC or liver-related death was found among patients with *PNPLA3* CC. There was a significantly increased risk of HCC, liver-related events, and mortality for CG/GG versus CC, but no difference between the CG and GG genotypes.

Conclusions: In Japanese individuals, the main cause of death from NAFLD is liver-related death. The greater risk of liver-related events incurred by *PNPLA3* G allele was shown in Japan. Risk stratification for NAFLD in Japan is best accomplished by integrating *PNPLA3* with the FIB-4 index.

Abstract Submission No. 100116
O-0323

Dissecting the Impact of Sex and Menopause on Steatotic Liver Disease: A Population-Based Study

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Background: Steatotic liver disease (SLD) is affecting approximately 20-30% of the general population. However, data regarding sex differences are limited.

Methods: Therefore, we conducted a population-based study using the UK Biobank. Participants who underwent liver magnetic resonance imaging (MRI) and provided information on their sex/menopausal status were included. Logistic regression models were used to assess the association between sex differences (18,135 men, 6159 premenopausal women, and 11,069 postmenopausal women) and steatosis on MRI, adjusting for age and BMI.

Results: Our results revealed that men had a higher prevalence of steatosis than women (34.5%), regardless of menopausal status. Postmenopausal women exhibited a higher prevalence of steatosis than premenopausal women (17.4% premenopausal women 20.9% in postmenopausal women), suggesting that menopause may increase the risk of steatosis. Additionally, we observed distinct clinical and laboratory profiles in male and female patients with simple steatosis. FIB4 levels were elevated in 8.4% of premenopausal women, 33.7% of postmenopausal women, and 35.9% of men. Homozygous carriers of *TM6SF2* rs58542926 or *PNPLA3* rs738409 were at increased risk of steatosis on MRI across all three groups. Shorter sleep duration increased the risk of steatosis in pre-menopausal women, while alcohol intake increased the risk in men only.

Conclusion: Our findings indicate that sex and menopausal status are important factors to be considered when studying hepatic steatosis. These results emphasize the need for personalized, sex-specific approaches to prevent steatosis. Further research is needed to elucidate the mechanisms underlying sex differences in, identify therapeutic targets, and develop sex-specific strategies for medical interventions.

Abstract Submission No. 100134
O-0324

Comparison of NAFLD, MAFLD, MASLD and pure-MASLD characteristics and mortality outcomes in US adults

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Background & Aims: After metabolic dysfunction-associated fatty liver disease (MAFLD), non-alcoholic fatty liver disease (NAFLD) has recently been redefined again as metabolic dysfunction-associated steatotic liver disease (MASLD). However, the distinctions in characteristics and mortality outcomes between NAFLD, MAFLD, MASLD, and pure-MASLD are still unclear.

Methods: We analyzed data from 6,708 participants in the third National Health and Nutrition Examination Surveys of United States (US) and their linked mortality through 2019. Survey-weight adjusted multivariable Cox proportional model was used to study the mortality of the four terms.

Results: The overall prevalence of NAFLD, MAFLD, MASLD and pure-MASLD was 28.9%, 26.1%, 29.0%, and 26.0%, respectively. For NAFLD, 81.3%, 89.9% and 89.9% fulfilled the criteria for MAFLD, MASLD and pure MASLD. For MAFLD, all were classified into the MASLD, and 89.8% were met the criteria of pure-MASLD. During a median follow-up of 27 years, both individuals with MAFLD and MASLD had higher risk of all-cause mortality (adjusted hazard ratio [aHR]: 1.21, 95% CI 1.09-1.352; and 1.11, 1.00-1.23, respectively). NAFLD and pure-MASLD were not associated with all-cause mortality. All the four terms were associated with increased all-cause mortality in individuals with advanced fibrosis (aHR: 1.66-1.83). Subgroup analyses showed that higher risk of all-cause mortality of NAFLD, MAFLD, MASLD and pure-MASLD were observed in female, age 41-55 years, non-Hispanic white, and never smoking subgroups when focused on moderate-severe hepatic steatosis.

Conclusions: MASLD could identify more individuals with all-cause mortality risk than MAFLD, especially in female, age 41-55 years, non-Hispanic white, and never smoking subgroups.

Abstract Submission No. 100204
O-0325

The correlation between LDL level and the development of NAFLD

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Background and Aims: NAFLD is a type of liver pathology that is associated with obesity, high cholesterol, Diabetes Mellitus, hypertension and genetics. The end result of NAFLD is liver cirrhosis and hepatocellular carcinoma(HCC). The aim of this study is to examine the correlation between LDL levels with the development of NAFLD.

Method: This is a retrospective study where a total of 1000 NAFLD patients were included. Variables such as age, sex, ethnicity, BMI, comorbidities, smoking status, liver function test and fasting serum lipid were recorded. Data from the years 2015 to 2020 were analyzed using the software empower stats version 5.0. Multivariate non-parametric analysis of the mean data was studied using the MANOVA test with a confidence interval (CI) of 95%. Receiver operating characteristic (ROC) curves were plotted to study the correlation between LDL and NAFLD. The area under the curve (AUC) was calculated and the DeLong test was used to determine the significance of the data. NAFLD was defined using liver ultrasound criteria such as liver brightness, vascular blurring, deep attenuation, and hepatorenal echo contrast. The scans were performed by the trained ultra-sonographer to reduce the operator bias.

Results: The level of LDL in both men and women was statistically significant in the development of NAFLD. ROC analysis for both sexes was performed and AUC for LDL was significantly higher in the NAFLD patients.

Conclusion: The level of LDL is significantly higher in NAFLD patients of both sexes and can be utilized as an early biomarker for the development of NAFLD.

Abstract Submission No. 100413
O-0326

Liver Fibrosis Tests and Outcomes of Bariatric Surgery in Morbidly Obese Patients with MASLD

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Background: MASLD is common among morbidly obese patients, but data on NITs for liver fibrosis assessment is limited. We aimed to validate NITs for predicting liver fibrosis and post-bariatric surgery outcomes.

Methods: In a single-tertiary-center retrospective cohort, we studied morbidly obese adults with biopsy-proven MASLD undergoing bariatric surgery between 2011 and 2022 (LRYGB/LSG). Follow-up exceeded 1 year. The primary outcome was NITs' performance in predicting liver fibrosis, including LSM, FIB-4, NFS, APRI, and BARD scores. Secondary outcomes included biochemical and anthropometric changes.

Results: Among 193 patients, 103(53.4%) were female, mean age 36.3±10.9 years. Mean BMI was 47.7±14.4 kg/m², and 78(40.4%) had diabetes. Of these, 58(30.1%) had liver fibrosis(≥F1), and 9(4.7%) had significant fibrosis(≥F2). NITs showed low diagnostic accuracy for liver fibrosis (AUROCs: LSM 0.38, FIB-4 0.59, NFS 0.53, APRI 0.50, BARD 0.51). After a median 1.9-year follow-up, LSM significantly decreased post-surgery (7.8 to 5.5 kPa, p<0.001). APRI and NFS improved (0.21 to 0.18, -0.773 to -1.395, p<0.001), while FIB-4 and BARD scores increased (0.52 to 0.60, 2 to 3, p<0.001) over a median 2.9-year follow-up (**Figure**). Anthropometrically, %TWL and BMI decreased significantly (30.8% to 28.5%, p=0.04, and 47.7 to 35.1, p<0.001). LRYGB had higher %TWL than LSG (30.8% vs. 28.5%, p=0.040). Biochemical parameters (AST, ALT, albumin, platelets, LDL-cholesterol, and triglycerides) improved significantly post-surgery. Subgroup analysis(n=27) showed LSM improvement>20% from baseline correlated with %TWL>30%(p=0.041).

Conclusion: Bariatric surgery improved long-term clinical/biological outcomes, though NITs demonstrated limited diagnostic accuracy for baseline liver fibrosis. Further research is needed to assess new NITs for monitoring liver fibrosis in morbidly obese patients.

Abstract Submission No. 100468
O-0327

Effect of empagliflozin on non-diabetic metabolic-dysfunction associated steatotic liver disease

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Background: We investigated whether empagliflozin can reduce hepatic steatosis in metabolic-dysfunction associated steatotic liver disease (MASLD) patients without diabetes mellitus (DM).

Methods: This was an investigator-initiated, double-blind, randomized, placebo-controlled trial recruiting adult subjects from the community. Eligible subjects had magnetic resonance imaging-proton density fat fraction [MRI-PDFF] ≥5% but without DM (fasting plasma glucose <7mmol/L and HbA1c <6.5%). They were randomly allocated to receive empagliflozin 10mg daily or placebo (1:1 ratio) for 52 weeks (end of treatment, EOT). MRI-PDFF was conducted at baseline and EOT. The primary outcome was the difference in changes of MRI-PDFF between two groups at EOT. Secondary outcomes were resolution of hepatic steatosis (MRI-PDFF <5%) and changes of anthropometric and laboratory parameters at EOT. All outcomes were based on intention-to-treat analysis.

Results: Of 98 recruited subjects (median age 55.7years [IQR:49.5-63.4]; male:54 [55.1%]), 97 (empagliflozin:49; placebo:48) had MRI-PDFF repeated at EOT. The median MRI-PDFF at baseline was 9.7% and 9.0%, respectively. At EOT, empagliflozin group had a greater drop in median MRI-PDFF than placebo group (-2.49% vs -1.43%; p=0.025), with a non-significant trend of resolution of hepatic steatosis (44.9% vs 28.6%; p=0.094). Empagliflozin group had a greater drop in body weight (-2.7 vs -0.2kg), waist circumference (-2.0 vs -0.4cm), fasting glucose (-0.3 vs 0mmol/L) and ferritin (-126 vs -22pmol/L) compared with placebo group (all p<0.05).

Conclusions: Treatment with empagliflozin for 52 weeks reduces hepatic fat in MASLD subjects without DM.

Abstract Submission No. 100501
O-0328

Intelligent Diagnosis of Non-alcoholic Fatty Liver Disease Based on Multi-modal Ultrasound Features

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Background: Non-alcoholic fatty liver disease (NAFLD) is a prevalent chronic liver disease worldwide. The gold standard for NAFLD and at-risk non-alcoholic steatohepatitis (NASH) diagnosis is invasive liver biopsy. Therefore, there is an urgent need to develop non-invasive techniques for diagnosing key histological components of NAFLD and at-risk NASH.

Methods: Ninety-four patients with biopsy-proven NAFLD were included. A total of 262 features were extracted from an iLivTouch

system, ultrasound (US) images, and medical records by quantitative US techniques and US radiomics. A logistic regression model was developed for feature selection, and support vector machine (SVM) was used as the classifier for NAFLD diagnosis. Five-fold cross-validation was used to evaluate the classification performance.

Results: Multi-modal US features can accurately diagnose key histological components of NAFLD and at-risk NASH. The AUC values are 0.91 (95% CI, 0.75-1.00) for steatosis S2-S3 ($\geq$ S2), 0.85 (95% CI, 0.74-0.99) for steatosis S3, 0.80 (95% CI, 0.71-0.88) for ballooning grade 2, 0.73 (95% CI, 0.57-0.81) for lobular inflammation grade 2-3 ($\geq$ I2), 0.82 (95% CI, 0.28-0.85) for fibrosis grade 1-4 ($\geq$ F1), 0.73 (95% CI, 0.59-0.78) for fibrosis grade 2-4 ($\geq$ F2), 0.76 (95% CI, 0.58-0.88) for fibrosis grade 3-4 ($\geq$ F3), and 0.81 (95% CI, 0.62-0.91) for at-risk NASH, respectively.

Conclusions: Multi-modal US features can accurately diagnose key components of NAFLD and at-risk NASH. With continued validation, they may be promising for evaluating the severity of NAFLD, diagnosing at-risk NASH, and dynamically assessing NASH resolution.

Abstract Submission No. 100558
O-0329

Prevalence of Fatty liver disease in the Middle East and North Africa: A Systematic Review

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Background: Nonalcoholic fatty liver disease (NAFLD) is part of the spectrum of fatty liver disease which is closely associated with type 2 diabetes (T2D) and other metabolic abnormalities. We assessed the prevalence of NAFLD among the general population and diabetics in the Middle East and North Africa (MENA) region using systematic review.

Method: We searched PubMed and Embase for articles published between 1990-2023 according to PRISMA. Each country's NAFLD prevalence in the general population and in T2D patients was predicted by using multivariable meta regression model (global burden of disease-GBD 2019). Input data were extracted from our systematic review, GBD and NCD Risk Factor Collaboration. Confidence intervals were constructed by using prediction intervals with the Delta method.

Results: Meta-analytic pooling estimated NAFLD prevalence is 39.43% in the general population and 68.71% in T2D patients. NAFLD prevalence has increased from 35.42% (2008-2016) to 46.20% (2017-2020). Using GBD-2019, 141.51 million NAFLD prevalent cases were expected in the MENA region. The highest number of NAFLD cases were expected in Egypt (25.71 million), Türkiye (23.33 million), Iran (19.85 million), with the lowest cases from Bahrain (0.33 million). Estimated NAFLD prevalence exceeded 40% in 10 of 21 countries with the top countries being Kuwait (45.37%), Egypt (45.0%), Qatar (44.4%), and Jordan (43.3%). Furthermore, 24.96 million cases of NAFLD with T2D were expected in the MENA region.

Conclusion: Prevalence of NAFLD in the general population and among T2D is very high and growing necessitating urgent need to develop public policy to deal with this growing burden.

Abstract Submission No. 100598
O-0330

Riding the Wave of Name-Change: Prevalence, Clinical Profile and Outcomes of NAFLD, MAFLD, and MASLD

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Background: The evolving renamed Non-Alcoholic Fatty Liver Disease (NAFLD) to Metabolic-Associated Fatty Liver Disease (MAFLD) and, subsequently, to Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) has prompted a comparative investigation into these diagnostic criteria. This study aimed to identify its prevalence, clinical profile, and their outcomes.

Methods: Employing a five-year cross-sectional design, we collected data from our Liver Bank, including individuals diagnosed with hepatic steatosis Ultrasound, CT Scan, or MRI. We collected demographic data, metabolic and liver profiles, fibrosis scores, liver-related complications, and all-cause mortality.

RESULTS: A total of 201 patients (57.2% male) were included. Most patients were NAFLD-MAFLD-MASLD-overlap (50.25%). Alcohol ingestion was seen predominantly in the MAFLD only group (95%). Overall, triglycerides levels have a median of 139 mg/dL (29-375 mg/dL) with a significant difference across groups ($p = .007$). Cirrhosis was present (22.61%), which varied significantly across patient categories ($p = .030$), where 44.4% of these, seen in MAFLD-only group. Cirrhosis outcomes had density rate of 3.45, while HCC stands at 4.15, where this was highest in the MAFLD+MASLD overlap group at 14.7%. The Kaplan Meier survival curve, at day 49, MAFLD-only had higher survival probability (76%, 95% CI 0.565-1.00) compared to NAFLD+MAFLD+MASLD (69%, 95% CI 0.461-1.00). All three and their overlaps were associated with increased all-cause mortality in individuals with Liver cirrhosis and HCC.

CONCLUSION: Patients excluded under the NAFLD definition, yet encompassed by MAFLD and MASLD, demonstrated an increased susceptibility to adverse liver-related outcomes. The nomenclature change appeared to enhance the clinical utility of these definitions.

Abstract Submission No. 100618
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EUS-guided assessment of metabolic liver disease in patients with morbid obesity

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Background: Bariatric surgery patients have a higher prevalence of metabolic associated- steatotic liver disease (MASLD). Percutaneous liver biopsy has technical difficulties and non-invasive markers are not very accurate in this population.

Aims: Evaluate the efficacy and safety of EUS-guided bilobar liver biopsy plus EUS-guided portal pressure gradient measurement in diagnosing MASLD and its correlation with non-invasive test.

Methods: Suspected MASLD by liver ultrasound or fatty liver index (FLI) score > 60.

Demographic, anthropometrics, blood test, non-invasive serological markers (FLI, NAFLD, HEPAMET, APRI, FIB-4) and transient elastography (TE) with XL probe variables were evaluated.

Results: The prevalence of MASLD was 69%, metabolic dysfunction-associated steatohepatitis (MASH) 54.5%, and fibrosis (F1-F2) 12.6%. EUS-guided portal pressure gradient median was 4 mmHg., 9/33 (28%) patients had a gradient > 6 mmHg.

MASLD patients showed higher levels of fibrosis determined by transient elastography (TE), of steatosis evaluated by coefficient attenuated parameter (CAP) and portal vein pressure, although they were not statistically significant. No differences were detected in FIB-4, NAFLD and HEPAMET scores according to MASLD.

The quality of liver biopsies was deemed adequate with a median of 7 portal spaces.

There were observed 2 mild adverse events in 2 patients, one mild abdominal pain and one atrial fibrillation, successfully treated by medical therapy.

Conclusions: The prevalence of MASLD and MASH was high in morbid obesity patients.

EUS-guided portal pressure gradient and EUS-guided liver biopsies seem safe and accurately evaluate the presence of portal hypertension and the underlying metabolic liver disease.

Abstract Submission No. 100619

O-0332

Variability of Knowledge About Fatty Liver Disease: A Survey of Physicians from Asia

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Background: Despite the growing burden of fatty liver disease (FLD), there is low awareness and knowledge about the disease across different regions of the world. Our aim was to assess knowledge about FLD physicians in Asian countries.

Methods: Two specifically designed knowledge surveys containing 54-59 items were developed by the Global NASH Council members, one for GI/Liver specialists (hepatologists and gastroenterologists) and one for non-specialists (endocrinologists, primary care providers (PCPs), others). The surveys focused on terms such as FLD, NAFLD, NASH, and other related terms. Physicians from the Asian region completed the surveys using an approved electronic data collection form.

Results: There were 1482 physicians from 15 Asian countries who completed the survey: 180 hepatologists, 469 gastroenterologists, 115 endocrinologists, and 718 PCPs/other specialties. Their median practice duration was 12 years (IQR 4-24 years), 81% were hospital-based and 10% clinic-based physicians. Availability of diagnostic methods for fatty liver (imaging, liver biopsy) was the highest among hepatologists (39%-93%) and the lowest among PCPs (18%-80%) (all p<0.05). Practice guidelines were the most common primary source of latest knowledge about the disease for all the specialties (mean 43%) followed by national or international conferences (mean 16%) although Internet was the second most common source for PCPs (30%). Disease knowledge related to epidemiology, pathogenesis, diagnostic

tests, treatment, and understanding the causes of death was higher among hepatologists than GIs (mean 68% vs. 61% correct answers) and higher among endocrinologists than PCPs (mean 73% vs. 63% correct) (both p<0.01). In multivariate analysis, the hepatology specialty (vs. GI), a hospital-based practice, seeing a greater number of affected patients per year, and using medical conferences or journals as a primary source of knowledge about the disease were independently predictive of a greater proportion of correct answers among specialists from Asian countries (all p<0.05). Similarly, the endocrinology specialty (vs. PCP) and a greater number of affected patients in the practice were associated with higher knowledge scores while using Internet as a primary source of knowledge about the disease was associated with lower knowledge scores (p<0.05) among non-specialists from Asia. Although 39%-73% survey completers believed that very few (<10%) patients have symptoms, the vast majority (78%-89%) believed that patients suffered from impaired quality of life.

Conclusions: Despite growing burden of FLD in Asia, a gap remains about disease knowledge and awareness. Better implementation of guidelines via conferences at society meetings in Asia may improve this knowledge gap.

Abstract Submission No. 100622

O-0333

Fatty Liver Disease and Stigma- Patients' and Providers' Perspectives from Asian Countries

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Background: NAFLD may be associated with stigma in Asia.

Method: The Global NASH Council created two stigma surveys: 68-item patient, 41-item provider about NAFLD experiences/attitudes and related terms.

Results: NAFLD patients (n=1239) from 10 Asian countries (70% male), providers (n=483) from 9 Asian countries (65% gastroenterologists or hepatologists) completed surveys. Among patients, 31% ever disclosed having NAFLD to family/friends; most common discussion words were "fatty liver" (83% used at least sometimes, 65% frequently/always); "metabolic disease" or "MAFLD" were rarely used (never by >75%); 12% experienced stigma/discrimination from obesity/overweight vs. 4% from NAFLD. The reported greatest social-emotional burdens were: "being identified as a person with liver disease" (18% agree, 12% male vs. 34% female) and "others believing that they do not eat properly" (19% agree, male/female similar). Providers believed lack of patient motivation (86%) and training in effective communication (69%) were biggest obstacles to weight loss discussions. Provider discomfort was related to perceived patients' lack of willpower for lifestyle changes and taking care of their diabetes (53-57% providers agree). For diagnostic terms by patient perception, no substantial differences noted between "NAFLD", "fatty liver disease (FLD)", "NASH", or "MAFLD"-most popular response was being neither comfortable nor uncomfortable with either term (69%-82%). Among providers, 35% believed "fatty" and 35% believed "non-alcoholic" in NAFLD was stigmatizing; 27% reported "FLD" stigmatizing; 39% believed a name change may reduce stigma (similar between specialists)

Conclusions: Perception of NAFLD stigma varies among patients and providers in Asia. NAFLD patients reported obesity to be more stigmatizing than NAFLD.

Abstract Submission No. 100689
O-0334

Diagnostic Performance in Detecting MASH with Fibrosis Stage 1 or Higher Using Machine Learning

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MASH, evolving from MASLD, is linked to liver cirrhosis and hepatocellular carcinoma. Early detection of early-stage fibrosis MASH is pivotal for timely intervention. This study sought to design a supervised machine learning (ML) model for predicting mild fibrosis MASH using routine blood data and to evaluate its diagnostic capabilities.

From 2003 to 2022, we analyzed 436 MASLD patients who had liver biopsies at our center. We characterized early stage MASH as Fibrosis ≥ 1 . Supervised ML models, including Logistic Regression; LR, Support Vector Machine; SVC, Random Forest; RF, XGBoost, LightGBM, were trained on clinical and blood test data at biopsy. The cohort was split into a Training group (n=370) and a Test group (n=93). ML was employed on the Training set, and its diagnostic efficacy was gauged in the Test set through AUROC, Sensitivity, and Specificity.

The average age was 56, with 44% males. We observed 353 early-stage fibrosis MASH instances (F0: 83, F1: 198, F2: 55, F3: 99, F4: 28). Among 32 clinical and blood markers at biopsy, the RF model showcased the best prediction (AUROC=0.81). After implementing feature engineering, the RF model, using BMI, HbA1c, ALT, fasting glucose, and age+AST, outperformed others in the Test set (AUROC=0.84, Sensitivity=0.76, Specificity=0.86), exceeding APRI (AUROC 0.75) and FIB-4 (AUROC 0.72).

In conclusion, the RF model, with five clinical parameters, showed notable accuracy in identifying early-stage MASH.

Abstract Submission No. 100706
O-0335

Genetic Variants of Metabolic Dysfunction Associated Fatty Liver Disease from Taiwan Biobank

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Background and Aims: The large-scale study aimed to investigate the risk factors and genetic variants associated with metabolic dysfunction-associated fatty liver disease (MASLD).

Methods: The study included 101,450 participants who underwent whole-genome genotyping throughout the Taiwan Biobank. All participants were non-drinkers and tested seronegative for HBsAg and anti-HCV antibodies. MASLD was defined by a fatty liver index of ≥ 30 and the presence of at least one cardiometabolic risk factor. Participants with a fatty liver index < 30 were categorized as non-steatotic liver disease. Logistic regression models were utilized to estimate the odds ratios (ORs) with 95% confidence intervals (CIs).

Results: Among the total population, 31389 (30.9%) had MASLD, while 70061 (69.1%) were individuals without steatotic liver disease. Individuals with MASLD showed significant positive associations

with increased triglyceride levels, metabolic syndrome, central obesity, and cardiovascular disease ($p < 0.001$). In addition, variants in the PNPL3, TM6SF2, and GCKR genes were found to be associated with MASLD, with the adjusted ORs (95% CI) of 1.73 (1.64-1.84), 1.22 (1.14-1.29), and 1.06 (1.02-1.11), respectively. Individuals with a higher number of risk alleles had an increased likelihood of having MASLD compared to non-steatotic liver disease. Participants with 4 risk alleles and 5 to 6 SNP risk alleles exhibited adjusted ORs of 1.19 (1.13-1.25) and 1.46 (1.39-1.54), respectively, when compared to those with 0 to 3 risk alleles.

Conclusions: Individuals with a greater number of risk alleles were more likely to have MASLD, emphasizing the importance of risk consultations for obesity-related comorbidities.

Abstract Submission No. 100720
O-0336

Results of triple therapy for NAFLD in Mongolia

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Background: Although it is well noted that hepatitis caused by viruses have recently decreased in Mongolia, it is expected that liver steatosis and cirrhosis related to unhealthy lifestyles will increase. Therefore, we conducted a study to determine the results of the triple therapy of NAFLD for the first time in our country.

Methods: Before treatment, the degree of steatosis was determined using the Fibrotouch/transient elastography/ device and patients with higher than normal values of steatosis were included, and then a triple medical therapy and lifestyle modifications were recommended for 1 month, and a second measurement was performed after treatment. The treatment was performed at the outpatient clinic of Happy Veritas Hospital. Treatment consisted of atorvastatin 20-40 mg once a day, ursodeoxycholic acid 250 mg 2-3 times a day, vitamin E 400 IU, 2 capsules per day after meals.

Results: 64 patients showed a decrease in fatty liver of 98.4%, and decrease in CAP values varied between 2 and 168 db/m respectively. Steatosis decreased in n=60 (93.7%) patients by at least one stage, 3% or 4.6% decreased by few db/m within the steatosis stage, and only in one patient (1.6%) steatosis did not decrease at all. There were 10 patients (20.4%) whose steatosis reduced but the liver stiffness increased after treatment.

Conclusion: Triple therapy that consisted of lifestyle modifications plus statins, vitamin E and ursodeoxycholic acid was highly effective in Mongolian NAFLD patients.

Abstract Submission No. 100732
O-0337

Genetic Architecture of Lean NAFLD and Paradoxical Obesity-Hepatic Steatosis Phenotypes

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Background: Patients with “paradoxical” metabolic phenotypes—eg, “lean NAFLD”, or conversely, severely-obese patients with uncannily ‘pristine’ livers—represent clinical enigmas. However, they also hold clues to new disease biology and therapeutic targets.

Methods: We recruited participants who had liver biopsy for suspected NASH or opportunistically during bariatric surgery. Histology was graded using CRN NAS. GWAS was performed using IPW based on disease risk scores, which assigned greater statistical-weight to patients with “extreme” and “paradoxical” phenotypes. Associations were adjusted for baseline demographics, comorbidities, medications, caffeine, alcohol consumption, ethnicity and genomic PCs.

Results: n=232 patients were analyzed at time of writing (M:F=110:122, Chinese/Malay/Indian/Others:54.4%/27.0%/14.1%/4.4%, BMI median[IQR] 32.2[27.2-38.8]). We identified novel polymorphisms enriched in loci that regulate energy-sensing and lipid/sterol metabolism (*LEPR* [encodes leptin receptor involved in fatty-acid β -oxidation], *PPP1R3G* [glycogenesis], *DHCR7* [vitamin D/cholesterol metabolic switch], *LDLRAD4* [LDL metabolism]) that appeared to be exquisitely-protective against development of hepatic steatosis in high-BMI individuals. Other genetic loci containing variants associated with lean NAFLD or the extreme opposite phenotype include: *REEP5* (whose overexpression of its protein interaction partner RTN3 is reportedly associated with liver steatosis and hypertriglyceridemia), *ZBTB16* (reported as a pleiotropic node for metabolic syndrome and overexpressed in experimentally-induced hepatic steatosis), and *SMOC1* (glucose-sensitive hepatokine).

Conclusions: This GWAS study utilized a novel bioinformatics framework prioritizing candidates associated with “paradoxical” NAFLD phenotypes, and identified several genetic loci with strong biological plausibility for regulating hepatic fat accumulation. GWAS of additional n=227 patients (total: n=459) patients is underway, and complete results including fine-mapping will be presented at the meeting.

Abstract Submission No. 100756
O-0338

Prevalence and characteristics of lean MAFLD in patients with diabetes: a multicenter study

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Background: Metabolic associated fatty liver disease (MAFLD) is associated with obesity and type 2 diabetes (T2DM). Little is known

about the prevalence and characteristics of MAFLD patients with normal body mass index and T2DM.

Methods: Inpatients from 13 clinics in China were screened for MAFLD from January to October of 2023 in the study. Participants completed laboratory tests and underwent elastography for steatosis and fibrosis by controlled attenuation parameter and liver stiffness measurement.

Results: In total, 1257 patients were included, of whom 28.8% were lean. The prevalence of lean MAFLD and liver fibrosis patients in the whole cohort was 13.6% and 7.4%. In lean patients, 47.2% were affected by MAFLD and 25.9% by liver fibrosis. The proportion of mild steatosis (S1) was more in lean patients compared to non-lean (31.3% vs 21.0%, $P < 0.05$) and the proportions of all-stage fibrosis (F2 to F4) were lower in lean patients. Among lean patients with MAFLD, the prevalence of macrovascular and microvascular T2DM complications were 69% and 56.6%, respectively. After adjusting for sex and age, BMI [aOR (95% CI) = 1.614 (1.336-1.951), $p < 0.001$] and triglyceride [aOR (95% CI) = 1.365 (1.046-1.781), $p = 0.022$] were risk factors of lean MAFLD. Total bile acid [aOR (95% CI) = 1.304 (1.113-1.528), $p = 0.001$] was risk factor of fibrosis.

Conclusion: The prevalence of MAFLD and liver fibrosis were high in lean patients with T2DM. Screening for MAFLD was essential in patients with diabetes, even if normal weight.

Abstract Submission No. 100759
O-0339

Comparing 1.5T and 3.0T MRI for Assessing Hepatic Steatosis with Proton Density Fat Fraction

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Background: Magnetic resonance spectroscopy(MRS) serves as a non-invasive method for assessing hepatic steatosis. However it also presents shortcomings, including selection variability and spatial limitation. Proton density fat fraction (PDFF), a newly developed quantitative method for measuring liver fat across the entire liver, shows potential in replacing MRS.

There is no uniform protocol about PDFF, our study aims to compare the correlation between PDFF and MRS under the different magnetic fields, 1.5T and 3.0T.

Methods: 401 healthy liver donors of NTUH receiving pre-transplantation evaluation prospectively enrolled from August 2011 to September 2021. After 1:1 matching for age, gender and body mass index (BMI), 250 patients included in the study, evenly distributed in the two magnetic fields.

PDFF value measurements were taken from the six liver segments (S5, S6, S7, S8, medial and lateral). Correlations with MRS were separately analyzed, as well as the averages of 6 segments were also analyzed. Patients were categorized into high-fat and low-fat groups using a PDFF cutoff of 5%, and correlations were examined.

Results: The highest correlation was found in the average of the six segments in 3.0T (Spearman's r value: 0.8945, $p < 0.05$) and the lowest correlation in the lateral segment in 1.5T (Spearman's r value: 0.7725, $p < 0.05$). After grouping patients by fat content, the average of the six segments in 1.5T exhibited the highest correlation (Spearman's r value: 0.9336, $p < 0.05$), while the lateral segment in 1.5T displayed the lowest correlation (Spearman's r value: 0.5096, $p < 0.05$).

Conclusions: In our research, the average PDFF value of 6 segments has the highest correlation with MRS in both magnetic fields. And after after grouping patients by fat content, 1.5T is better for the high-fat group and 3.0T is better for the low-fat group.

Abstract Submission No. 100816
O-0340

Real-World Utility of ELF in a Two-step Strategy for Detecting Fibrosis in At-Risk NAFLD patients

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Aims: The proposed two-step strategy aims to differentiate fibrosis in patients with nonalcoholic fatty liver disease (NAFLD) by combining the Fibrosis-4 (FIB-4) Index and the Enhanced Liver Fibrosis (ELF) test. This study assesses the diagnostic performance of the ELF test when it is performed alone and when it is combined with FIB-4 as part of the two-step strategy, with the goal of evaluating the utility of the ELF test.

Methods: In this single-center retrospective study, a total of 152 high-risk patients were enrolled. Various non-invasive tests for assessing liver fibrosis, such as aspartate aminotransferase-to-platelet ratio index (APRI), FIB-4, NAFLD fibrosis score (NFS), and ELF, were employed, and the degree of fibrosis was determined based on the results of the liver biopsy.

Results: The AUROC of APRI, FIB-4, NFS, and ELF for advanced fibrosis ($\geq F3$) were 0.802, 0.732, 0.662, and 0.812, respectively. To reduce the unnecessary liver biopsies, ELF was additionally applied using the two-step diagnostic method presented in the American Association for the study of Liver Disease guidelines to patients with FIB-4 scores of 1.30 or higher ($n=56$, 36.8%). This approach allowed for the exclusion of 29 individuals (72.5%) from unnecessary liver biopsies. Sensitivity, specificity, accuracy, and negative predictive value, as analyzed by applying the proposed algorithm of the two-step strategy to actual clinical trials, were 0.459, 0.913, 0.802, and 0.989, respectively.

Conclusion: Results from this study demonstrate the potential to reduce unnecessary testing and referrals to tertiary healthcare centers when the two-step strategy is applied in actual clinical settings.

Abstract Submission No. 100832
O-0341

Metabolic dysfunction-associated steatotic liver disease and liver-related outcome

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Introduction: Compared to nonalcoholic fatty liver disease (NAFLD), the recently proposed metabolic dysfunction-associated steatotic liver disease (MASLD) has been suggested to better reflect the metabolic components of fatty liver disease (FLD). This study examines the occurrence of hepatocellular carcinoma (HCC) and liver cirrhosis-related complications in patients with and without MASLD, metabolic dysfunction, and alcohol-associated steatotic liver disease (MetALD.)

Materials and methods: Using the Korean National Health Insurance database, we identified participants who underwent a health-screening program in 2010 and 2011 and retrospectively analyzed their data until 2019. The main objective was to ascertain the rate of newly diagnosed HCC and liver cirrhosis-related complications during the observation period for each patient group.

Results: Out of the 310,724 individuals, 108,996 (35.1%) were part of the MASLD group, 13,960 (4.5%) belonged to the MetALD group, and 187,768 (60.4%) were in the neither FLD group. When using the neither FLD group as the reference, the multivariable-adjusted hazard ratio (95% confidence interval) for HCC events was 1.34 (1.26-1.42) in the MASLD group and 1.48 (1.31-1.67) in the MetALD group, while the hazard ratios for liver cirrhosis-related complications were 1.31 (1.24-1.38) in the MASLD group and 1.73 (1.56-1.92) in the MetALD group.

Conclusions: Individuals with MASLD exhibit higher rates of HCC and liver cirrhosis-related complications compared to those without the condition.

Abstract Submission No. 100850
O-0342

Impact of MASLD on patients with hepatocellular carcinoma undergoing liver resection

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Background: Non-B non-C (NBNC) hepatocellular carcinoma (HCC) caused by non-alcoholic fatty liver disease (NAFLD) or alcoholic liver disease (ALD) has been on the increase. Patients with NBNC HCC frequently have metabolic dysfunction-associated steatotic liver disease (MASLD). The impact of MASLD on the outcome of liver resection for HCC remain unclear.

Methods: We analyzed 1010 patients who underwent initial liver resection for HCC at our institution between 2000 and 2021.

Results: The underlying diseases were HBV ($N=186$ [18%]), HCV ($N=446$ [44%]), HBV-HCV overlap ($N=14$ [1%]), and NBNC ($N=364$ [36%]). NBNC etiologies included ALD ($N=110$ [31%]), NAFLD ($N=94$ [26%]), cryptogenic ($N=152$ [42%]), and other known etiologies (8[2%]). MASLD was found in 274 (27%) patients; 41 (22%) in HBV, 62 (14%) in HCV, 41 (37%) in ALD, 90 (96%) in NAFLD and 34 (22%) in cryptogenic. The prognosis of NAFLD patients was better than that of HCV patients. MASLD patients had a better prognosis than non-MASLD patients in OS (HR, 0.71; 95%CI, 0.59-0.86) and RFS (HR, 0.82; 95%CI, 0.70-0.96). Patients with SLD and without metabolic dysfunction had a better prognosis than patients with MASLD, while patients without SLD and with metabolic dysfunction had worse liver function and more advanced tumors than patients with MASLD. In NBNC patients, non-SLD, multiple tumors and AFP level contributed to poor prognosis. In MASLD patients, prothrombin activity, DCP level, and presence of cirrhosis were associated with OS and RFS.

Conclusions: MASLD is associated with the etiologies of NBNC HCC, and the prevalence of SLD and metabolic dysfunction impacted on the outcome after liver resection.

Abstract Submission No. 101071
O-0343

Effects of GLP-1-Agonist Liraglutide and Semaglutide on steatotic liver disease and obesity

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GLP-1 receptor agonists (RA) like liraglutide and semaglutide are approved antidiabetic drugs and have shown to reduce weight and cardiovascular risks in multiple studies. Real life data on the effect of these GLP-1RA in steatotic liver disease (SLD) are scarce.

Methods: Observational study examining liraglutide and semaglutide in SLD patients. Patients received therapy with liraglutide 0.6mg increased to 3.0mg daily or semaglutide 0.25mg weekly increased to 1mg subcutaneously for a period of at least 2 months. Elasticity using Fibroscan®, fat content using CAP (controlled attenuation parameter), weight and laboratory were recorded directly before, immediately after the end of therapy and after 6 months.

Results: 33 (17 female) patients were treated with GLP-1RA. 73% of patients were diagnosed with NAFLD, 16% with NASH and 11% with BASH. After 2 months of treatment with GLP-1RA, there was significant reduction in elasticity (median decrease 29.2% (± 1.9 kPa)) and significant decrease in CAP (median decrease 29.0% (± 82 dB/m)). Significant weight reduction was achieved (7.4% reduction after two, 6.3% reduction six months post treatment). In 12 patients with elevated ALAT, reduction was achieved in 9 patients after 2 months, stable after 6. The subgroup of women (10.7%, $p=0.8$) and those not suffering from diabetes showed a more pronounced weight reduction (10.2%, $p=0.09$) after 2 months. There was no significant difference between liraglutide (25) and semaglutide (8) patients. Both 1 patient with liraglutide and semaglutide stopped after 1 month due to mild pain and constipation. Severe side effects never occurred.

Conclusion: GLP-1RA feature promising drugs in the treatment of steatotic liver disease.

Abstract Submission No. 101106

O-0344

Effect of Empagliflozin for the Treatment of Nonalcoholic Steatohepatitis in Patients with Type 2 DM

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Background: Non-alcoholic fatty liver disease (NAFLD) encompasses a spectrum of liver conditions, ranging from benign hepatic steatosis to the more severe non-alcoholic steatohepatitis (NASH), often leading to liver fibrosis. This study aims to assess the effects of empagliflozin on liver fibrosis in patients with nonalcoholic steatohepatitis (NASH) and type 2 diabetes mellitus.

Methods: This prospective, randomized, controlled, open-label study was conducted at the Department of GHPD, BIRDEM General Hospital, Dhaka, over a six-month period. Ninety patients with Type 2 diabetes mellitus (DM) and NASH were enrolled from the department's outpatient population after obtaining informed written consent. They were randomly allocated into two groups: the empagliflozin group (Group A) and the control group (Group B) in a 1:1 ratio, with treatment allocation being open-label. Socio-demographic characteristics, clinical features, and laboratory investigations were assessed. Data was collected using a semi-structured questionnaire, and analysis was performed using Statistical Package for Social Science (SPSS) version 24.0.

Results: The mean age of respondents in the empagliflozin and control groups was 49.11 $\pm$ 7.90 and 46.98 $\pm$ 10.19 years, respectively, with a higher proportion of males in both groups (77.8% and 84.4%, respectively). There were no significant differences in age, sex, occupation,

or smoking history between the two groups. After treatment with empagliflozin, weight (76.91 $\pm$ 6.4 vs. 73.52 $\pm$ 6.8 kg, $p<0.001$), BMI (22.52 $\pm$ 4.6 vs. 21.47 $\pm$ 4.6 kg/m², $p<0.001$), HbA1C (7.65 $\pm$ 1.5 vs. 7.27 $\pm$ 1.47%, $p=0.012$), AST (43.25 $\pm$ 3.8 vs. 41.17 $\pm$ 4.1 IU/L, $p<0.001$), ALT (56.04 $\pm$ 7.7 vs. 52.53 $\pm$ 7.5 IU/L, $p<0.001$), GCT (67.4 $\pm$ 4.4 vs. 59.77 $\pm$ 5.1 IU/L, $p<0.001$), total cholesterol (177.4 $\pm$ 19.7 vs. 170.9 $\pm$ 18.1 mg/dl, $p<0.001$), triglycerides (138.4 $\pm$ 15.1 vs. 132.8 $\pm$ 14.2 mg/dl, $p<0.001$), and LDL (109.6 $\pm$ 16.7 vs. 103.7 $\pm$ 17.1 mg/dl, $p<0.001$) significantly decreased. Additionally, the mean liver stiffness significantly decreased from baseline in the empagliflozin group (3.28 $\pm$ 0.46 vs. 3.40 $\pm$ 0.40 kPa, $p=0.031$), with a notable improvement in stages of liver stiffness among respondents.

Conclusion: Empagliflozin had a significant impact on liver fibrosis, weight, and liver function tests when used in patients with NASH and type 2 diabetes mellitus.

Abstract Submission No. 101133

O-0345

Serum GDF15 is a novel predictive biomarker for liver cancer occurrence in patients with MASLD.

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Background & Aims: The number of patients with metabolic dysfunction-associated steatotic liver disease (MASLD) continues to increase, and it is necessary to identify the high-risk population who should receive follow-up surveillance. We previously found that serum GDF15 is a predictor of liver cancer in chronic hepatitis C patients; thus, in this study, we investigated the usefulness of this biomarker for stratifying MASLD patients based on their risk for liver cancer occurrence.

Methods: GDF15 levels were measured in stored serum samples from MASLD patients without a history of liver cancer. We examined 518 patients with biopsy-proven MASLD and validated our findings in a cohort of 216 MASLD patients from a separate institution.

Results: In the biopsy-proven cohort, during a median observation period of 63 months, 22 cases developed liver cancer. By multivariate analysis, both the Fib-4 index and serum GDF15 were identified as independent risk factors for liver cancer occurrence. The AUROC for predicting liver cancer occurrence within 5 years for GDF15 was 0.941. Using a GDF15 cutoff value of 1.75 ng/ml based on the Youden index, patients with high GDF15 had a significantly higher rate of liver cancer development and a worse prognosis.

In the validation cohort, during a median observation period of 48 months, 9 cases developed liver cancer. Patients with high GDF15 levels had significantly higher rates of liver cancer and poor prognosis.

Conclusions: High serum GDF15 level is a risk factor for liver cancer occurrence and poor prognosis in patients with MASLD.

Abstract Submission No. 101248

O-0346

Combination of LiverSTAT and Fibroscan outperforms FIB-4 and LSM, for MASLD advanced fibrosis, F3F4.

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Background: LiverSTAT (LST) is a new blood test for MASLD risk stratification based on common biochemistry biomarkers.

Aims: To retrospectively compare the efficacy of two combinations in one step approach with two biomarkers: LST&Fibroscan (LSM) versus FIB-4&LSM, for the identification of histological advanced fibrosis (F3F4) in a multicenter multiethnic meta-dataset of MASLD patients.

Methods: Retrospective data from 5 hepatology centers on MASLD patients that underwent biopsy along with LSM by Fibroscan, FIB-4 and LST blood biomarkers. Efficiency has been assessed using concordance rates against liver biopsy (LB), number needed to screen (NNS) and double false positive/negative rates (DFP/DFN) whenever both LST and LSM disagreed with LB staging.

Results: Data from 786 patients (22.1%US, 39.2%Asia, 38.7%EU) was analyzed [age 57.1years, female 54.5%, BMI 31.4kg/m², ALT 52U/L]. Prevalence of F3F4 was 32.8% based on LB.

In the overall cohort, LB confirmed F3F4 among concordant LST&LSM and FIB-4&LSM, respectively, in 107/142(75%) vs 54/64(84.4%) with a screening efficiency (NNS) of 1.8 vs 2.2; the combination LST&LSM correctly identified twice more F3F4 patients than FIB-4&LSM.

In the subgroup with LB≥20mm, LB confirmed F3F4 among concordant LST&LSM and FIB-4&LSM in 43/50(86%) vs 30/33(90%), NNS 1.6 and 1.8, respectively; the combination LST&LSM correctly identified 43% more F3F4 patients than FIB-4&LSM.

DFP rate was higher with FIB-4&LSM than with LST&LSM (11.3% vs. 7%).

Conclusion: The combination LST&LSM outperforms FIB-4&LSM for the identification of MASH advanced fibrosis F3F4.

Figure 1. Scatterplots of the combinations LiverSTAT and LSM and FIB-4 and LSM plotted against liver biopsy fibrosis staging (NASH-CRN).

Abstract Submission No. 101324

O-0347

Impact of single nucleotide polymorphisms on long-term prognosis in non-obese MASLD

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Purpose: Metabolic dysfunction-associated steatotic liver disease (MASLD) is recognized to occur not only in obese but also in non-obese individuals. There is no consensus on the long-term prognosis of non-obese MASLD patients. Since mutations in single nucleotide polymorphisms (SNPs) are known to be involved in the progression of

MASLD, we investigated the impact of SNPs on the long-term prognosis of non-obese MASLD patients.

Methods: This is a multicenter, retrospective cohort study. Patients diagnosed with MASLD by liver biopsy between November 1, 1997 and October 31, 2020 and examined for SNPs including PNPLA3, TM6SF2, and HSD17B13 were enrolled. Patients were followed until December 31, 2022, for death and clinical events.

Results: Of 1294 MASLD patients, 331 (25.6%) were non-obese. They also included 147 (44.4%) patients with PNPLA3 type GG, which was significantly higher than in the obese group (p=0.04). After a median follow-up of 7.6 years, 17 (5.1%) patients in the non-obese group and 33 (3.4%) in the obese group died, and the Kaplan-Meier method showed no significant difference in survival rates between the two groups.

Multivariate analysis identified PNPLA3 GG and FIB4-index as predictors of mortality in non-obese MASLD. The Kaplan-Meier method showed that PNPLA3 GG had a significantly higher mortality rate than CC/CG (p=0.01). In the obese group, however, there was no difference in mortality according to SNPs.

Conclusion: Non-obese MASLD is more susceptible to SNPs than obese MASLD.

Our results suggest that analysis of SNPs, especially PNPLA3, may be able to predict prognosis in non-obese MASLD patients.

Abstract Submission No. 101695

O-0348

AI diagnostic system accurately diagnoses hepatocellular carcinoma in nonalcoholic steatohepatitis

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Background & Aims: To develop a novel noninvasive test using an artificial intelligence neural network system (named HCC-Scope) that can diagnose early stage hepatocellular carcinoma (HCC) in nonalcoholic steatohepatitis (NASH).

Methods: 175 with histologically proven nonalcoholic fatty liver disease (NAFLD) and 55 NASH-HCC patients were enrolled. Of the 55 HCC patients 27 (49.1%) were very early stage HCC and 6 (10.9%) were early stage HCC. HCC-Scope was conducted using 15 items: age, sex, height, weight, body mass index, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, cholesterol, triglyceride, platelet count, diabetes, alpha-fetoprotein (AFP), des-gamma carboxy prothrombin (DCP), and IgM-free apoptosis inhibitor of macrophage (fAIM). The FMVWG2U47 (Fujitsu Co. Ltd) hardware and the originally developed software were used.

Results: Differential diagnosis between not HCC and HCC using the HCC-Scope revealed 100.0% sensitivity, 100.0% specificity, 100.0% positive predictive value, and 100.0% negative predictive value in a training study with gray-zone analysis, and which was also effective in the analysis in the explorative study. It was also excellent in the validation study (95.0% sensitivity, 100.0% specificity, 100.0% PPV, and 97.1% NPV with gray zone analysis, and it was 95.2%, 100.0%, 100.0% and 97.1% without gray zone analysis. HCC-Scope showed significantly better sensitivity and specificity than AFP, AFP-L3, DCP and even than GALAD (gender, age, AFP-L3, AFP, DCP) score (its sensitivity: 85.3%, specificity: 85.1%).

Conclusions: The newly developed artificial intelligence neural network system algorithms termed HCC-Scope are easy to use and can

accurately differentially diagnose between NASH without HCC and NASH-HCC including early stage HCC.

Abstract Submission No. 101715
O-0349

Comprehensive Analysis of Specific MicroRNAs Related to Therapeutic Efficacy of Pemafibrate in MASLD

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Background: MASLD has become a major social problem in recent years. Pemafibrate binds to PPAR α and regulates the expression of its target gene, thereby decreasing plasma triglyceride levels and increasing HDL-cholesterol.

Aim: The aim of this study was to comprehensively analyze the efficacy of pemafibrate in patients with hyperlipidemia complicated with MASLD and the specific microRNAs involved in its therapeutic effect.

Methods: Thirty hyperlipidemia complicated patients with a confirmed diagnosis of NAFLD were treated with pemafibrate, a hyperlipidemic drug, as usual medical treatment. In parallel, clinical data (T-Bil, ALB, AST, ALT, platelets, type IV collagen 7S, M2BPGi, Autotaxin, FIB-4 index), efficacy (liver function, changes in the degree of liver fibrosis, etc.), and safety in MAFLD treated with exercise and diet, Fobrosan data and microRNA were comprehensively analyzed.

Results: Comparing clinical data before, one month after, and three months after Pemafibrate administration, significant changes were observed in AST, ALT, and Autotaxin, and correlated with the FAST score. Comprehensive analysis of microRNA expression in serum before and 3 months after treatment showed that they formed different clusters. The number of microRNAs that were significantly up-regulated and down-regulated was 15 and 10 molecules, respectively.

Discussion: Pemafibrate treatment significantly altered microRNAs, consistent with the improvement in clinical data and FAST score. These microRNAs may be involved in the therapeutic effect of Pemafibrate.

Conclusion: Pemafibrate is effective in improving liver function in MASLD patients with hyperlipidemia, and the specific microRNAs involved in the therapeutic effect may help to elucidate the mechanism of this effect.

Abstract Submission No. 101751
O-0350

Study to compare the efficacies of vitamin E and Saroglitazar in non diabetic NAFLD patients

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Introduction: NAFLD (Nonalcoholic fatty liver disease) is a major cause of chronic liver disease globally. The spectrum of NAFLD ranges from simple steatosis to non-alcoholic steatohepatitis which can progress to cirrhosis and hepatocellular carcinoma. There is no study comparing Vitamin E and Saroglitazar in non diabetic NAFLD patients.

Methods: It is a retrospective observational study conducted in Gastrocare hospital over a period of 4 years. The subjects having CAP score 215 or more (E score < 12.5kPa) were labeled as NAFLD. Total subjects included in the study were 306, 158 in Vitamin E group and 148 in Saroglitazar group. Subjects received capsule Vitamin E 400mg twice daily while Saroglitazar 4mg once daily along with standard treatment.

Results: After completion of 6 months treatment, mean baseline values of CAP scores showed statistically significant reduction from (310 $\pm$ 26.4 & 312 $\pm$ 31.2) to (268 $\pm$ 18.6 & 238.8 $\pm$ 18.5) in Vitamin E and Saroglitazar group respectively. After treatment mean E score was 7.1 3.1 and 7.2 3.2 respectively in Vitamin E and Saroglitazar groups. Both groups showed statistically Significant improvement in CAP score after therapy (p value <0.001 for Vitamin E group v/s < 0.001 for Saroglitazar group). On intergroup analysis, there was 13.5% improvement in the CAP score in Vitamin E group where as in Saroglitazar group it was 23.7%. It was found to be statistically significant (P value <0.03).

Conclusion: Both Vitamin E and Saroglitazar showed significant improvement in CAP score but Saroglitazar was significantly more effective than Vitamin E.

Abstract Submission No. 101838
O-0351

Molecular MASLD subtype to inform disease progression and therapeutic decision making

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) has marked molecular and clinical heterogeneity, yet there is no tool to inform disease progression and therapeutic decision making.

Methods: To identify molecular subtypes of MASLD associated with functional status of the liver, we performed an integrative hepatic transcriptome meta-analysis of multi-regional cohorts, including 1,232 mild- to advanced-stage MASLD patients. The MASLD subtypes were characterized according to clinico-histological features, fibrosis progression, HCC development, and estimated therapeutic effects.

Results: We identified and validated three reproducible subtypes across the cohorts, subtypes 1 to 3. Subtype 1 was associated with advanced histological fibrosis compared to the two other subtypes. Despite the indistinguishable clinico-histological features, the likelihood of histological fibrosis progression for subtype 2 was higher compared to subtype 3 (adjusted odds ratio, 1.43; 95% confidence interval [CI], 1.12-1.84). While subtype 3 was HCC-free up to 15 years, incident HCC rates in subtypes 2 and 3 were comparable (adjusted hazard ratio for subtype 1 compared to subtype 2, 0.75; 95% CI, 0.11-5.27). Based on the findings, we named subtypes 1, 2, and 3 as advanced-MASLD (a-MASLD), progressive-MASLD (p-MASLD), and indolent-MASLD (i-MASLD) subtypes, respectively. Transcriptomic analysis suggests that some of the existing and candidate MASLD therapies may yield subtype-specific benefit. Consistent with the transcriptome-based drug response assessment, cenicriviroc, an oral CCR2/5 antagonist, was more effective in reducing histological fibrosis in p- and a-MASLD in the phase 2b CENTAUR trial.

Conclusion: Molecular MASLD subtypes can serve as a tool to inform disease progression and therapeutic decision making.

Abstract Submission No. 101866

O-0352

Diagnostic Performance of CT/MRI LI-RADS v2018 in Non-Cirrhotic Steatotic Liver Disease

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Background: Our objective was to assess the performance of LI-RADS among patients with non-cirrhotic steatotic liver disease (SLD). **Methods:** This IRB-approved, retrospective study included 119 observations from 77 adult patients (36 women, 41 men; median age 64 years) who received liver protocol CT or MRI from 2010-2023. All patients had SLD by histopathology without cirrhosis. Three board-certified abdominal radiologists blinded to final tissue diagnosis and imaging follow-up assessed each observation per LI-RADS and assigned a final category. Inter-reader agreement with weighted kappa was calculated for major features and final category. The positive predictive value, sensitivity, specificity, and accuracy in identifying hepatocellular carcinoma (HCC) and overall malignancy was calculated. **Results:** 75 observations (63%) were benign and 44 (37%) were malignant. Positive predictive value for HCC was 0-0% for LR-1, 0-0% for LR-2, 0-7% for LR-3, 11-20% for LR-4, 75-88% for LR-5, 0-8% for LR-M, and 50-75% for LR-TIV. For overall malignancy, positive predictive value was 0-0% for LR-1, 0-11% for LR-2, 3-9% for LR-3, 16-31% for LR-4, 78-88% for LR-5, 65-100% for LR-M, and 100-100% for LR-TIV. For LR-5 in identifying HCC, sensitivity was 79-83%, specificity was 91-97%, and accuracy was 89-92%. For composite categories of LR-5, LR-M, or LR-TIV in identifying overall malignancy, sensitivity was 86-89%, specificity was 85-96%, and accuracy was 86-93%. Most common false positives for LR-5 were hepatocellular adenomas. Inter-reader agreement for final category was 0.766.

Conclusion: LI-RADS 5 still most commonly represents HCC, but its specificity is slightly lowered due to misclassification of hepatocellular adenomas.

Abstract Submission No. 101883

O-0353

Causespecific mortality in Japanese patients with biopsy-confirmed nonalcoholic fatty liver diseases

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Objectives: The main cause of death in NAFLD patients is considered to be CVD in the West. We examined mortality and causes of death in Japanese NAFLD patients.

Methods: Histologically diagnosed NAFLD patients at Saiseikai Suita Hospital, between 2004 and 2023 were included. As a prospective cohort study, mortality using the Kaplan-Meier method and causes of death were verified, compared for NAFL versus NASH and mild versus advanced fibrosis.

Results: The study included 1085 subjects (a mean age 57.2, a mean observation period 6.65 years). During the period, 76 patients died, with a mortality of 72/747 in the NASH, higher than in the NAFL 4/338 ($p<0.0001$). After adjustment for age and sex, NASH (HR 7.35), men (HR 2.05) and older age (HR 1.09) were risks of death.

Mortality was higher ($p<0.0001$) in the advanced fibrosis group (41/218) than in the mild (35/867). After adjustment, advanced fibrosis (HR 3.64), men (HR 1.93) and older age (HR 1.08) were risks of death. Causes of death in NAFLD patients included 17 HCC, 16 cirrhosis, 18 extrahepatic malignancies, 3 CVD, 8 other and 13 unknown causes. Mortality from liver-related diseases was higher in the NASH/advanced fibrosis than in the NAFL/mild fibrosis, while mortality from extrahepatic malignancies did not differ.

Conclusion: NASH and advanced fibrosis were independent risks of death. The main causes of death in Japanese NAFLD outpatients were liver-related diseases or extrahepatic malignancies, with less CVD, which may differ from those in the West.

Abstract Submission No. 101908

O-0354

Unveiling NAFLD: The Interplay of SCFA, Elastography, and CAP

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Background: Non-alcoholic Fatty Liver Disease (NAFLD), a growing global health concern, is believed to be influenced by multiple factors, including gut microbiota. A key metabolite of gut microbiota, Short Chain Fatty Acid (SCFA), is hypothesized to play a significant role in NAFLD progression.

Objective: This study aims to explore the relationship between SCFA levels and the severity of fibrosis and steatosis in NAFLD, utilizing transient elastography and controlled attenuation parameter (CAP) as assessment tools.

Method: A cross-sectional analysis was conducted on 38 NAFLD patients at Cipto Mangunkusumo Hospital from January to August 2023. The study involved comprehensive patient assessments, including anamnesis, physical examination, laboratory tests, CAP-TE (Transient Elastography), and SCFA analysis via GC-MS (Gas Chromatography-Mass Spectrometry).

Results: Notably, propionate levels were significantly higher in patients with significant fibrosis than in those with less severe fibrosis ($p=0.019$ for absolute propionate; $p=0.035$ for propionate level). However, no significant correlation was found between SCFA levels and CAP or transient elastography values ($p>0.05$).

Conclusion: This study highlights a significant increase in propionate levels in NAFLD patients with pronounced fibrosis, suggesting a potential link between gut metabolites and liver fibrosis. However, SCFA levels did not correlate with CAP and transient elastography values, indicating the complexity of NAFLD pathogenesis.

Keywords: Short Chain Fatty Acid, NAFLD, Transient Elastography, Controlled Attenuation Parameter

Abstract Submission No. 101972

O-0355

SOCS1, MIOX, HNF4A: Novel ferroptosis genes in NAFLD pathogenesis and fibrosis

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Background: NAFLD is a chronic liver disorder linked to metabolic syndrome and inflammation. Ferroptosis is a cell death process that depends on iron and lipid oxidation. How ferroptosis affects NAFLD and liver fibrosis is unclear. We used public transcriptomic data to find ferroptosis genes and pathways in NAFLD.

Methodology: We analysed microarray gene expression and clinical data from a cohort of 40 NAFLD human liver samples and 18 healthy controls. We performed differential expression analysis to identify ferroptosis-related genes and putative pathways that may be associated with NAFLD. We harnessed machine-learning approaches, like SVM-RFE and LASSO to identify genes associated with a fibrotic phenotype. We evaluated the prediction accuracy of these genes as biomarkers of NASH using multivariate regression and correlation analysis.

Results: We identified IL17, TNF signalling, JAK-STAT signalling pathways were found to be related to NAFLD progression with FADS2, ZFP36, HNF4A being upregulated and SOCS1, JUN, IL6, SLC2A3, ATF3, MIOX, PTGS2, CDKN1A being down-regulated. Our machine learning models identified novel genes like SOCS1, HNF4A, MIOX as potential biomarkers with ROC values of 0.92, 0.64 and 0.74.

Conclusion: We explored the role of ferroptosis pathway in NAFLD progression. We found that SOCS1 can modulate HSC activation and fibrosis. We also found that HNF4A can regulate the expression of genes that maintain the epithelial characteristics of hepatocytes and HSCs. We discovered some new genes that may be useful as biomarkers for early detection of NASH.

Abstract Submission No. 101979

O-0356

Semaglutide for Metabolic-Associated Fatty Liver Disease A Meta Analysis and Systematic Review

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Background: Semaglutide is a once-weekly glucagon-like peptide-1 receptor agonist with a smaller molecular weight that is approved for the treatment of type 2 diabetes mellitus and obesity. It is associated with dose dependent reduction in HbA1c and body weight among diabetic patients. However, its potential role in the treatment of non-alcoholic steatohepatitis remains unclear. The objective of this study is to determine the effectiveness of semaglutide in decreasing steatosis and fibrosis among patients with metabolic associated fatty liver disease.

Methods: Eligible studies were identified by a systematic literature search of Pubmed, Cochrane, Google scholar databases until September 2023. **Randomized control trials were included and the quality of the studies was assessed using the Cochrane handbook. Statistical analyses were conducted using RevMan 5.4 software.**

Results: A total of 458 patients from three randomised control trials were included. Histologically, semaglutide increased the likelihood of resolution of steatohepatitis (OR: 3.18, CI: 1.70, 5.95; $P < 0.001$). Radiologically, semaglutide caused a reduction in liver stiffness as measured by magnetic resonance elastography and fibroscan (SMD: -0.45, CI: -0.84, -0.09; $P = 0.02$). It also caused a reduction in the degree of steatosis measured by MRI proton density fat fraction (MD: -4.96%, CI: -9.92, 0.01; $P = 0.05$).

Conclusion: Semaglutide is effective for the histologic resolution of steatohepatitis and the radiologic improvement of both steatosis and fibrosis.

Abstract Submission No. 102055

O-0357

Pilot randomized controlled trial of effects of dapagliflozin and vit E on MASLD with type 2 DM

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Aim: We investigated the effects of dapagliflozin and vitamin E on metabolic dysfunction-associated steatotic liver disease (MASLD) with type 2 diabetes by randomized, open-label, controlled study.

Methods: Total 24 patients with an HbA1c $\geq 6.5\%$, hepatic steatosis on ultrasonography, and ethanol consumption of < 30 g/day for men and < 20 g/day for women were randomly assigned to treatment with dapagliflozin 5 mg (DAPA group, $n=13$) and tocopherol 150 mg (VE group, $n=11$), and the clinical course was monitored during the 24 week-treatment period (JRCT1031180386).

Results: Three patients in DAPA group complained of frequent urination or dry mouth, and 1 of them discontinued treatment due to frequent urination. There was no significant difference between clinical courses of the two groups by repeated measures analysis of variance. Comparing before and after 24 weeks of the start of treatment in each group, both AST and ALT values significantly decreased in DAPA group whereas only AST levels significantly decreased in VE group. In addition, BMI, body fat percentage and HbA1c levels decreased significantly in DAPA group. No significant decrease in fibrosis markers or liver stiffness was observed before and after treatment in either group.

Conclusion: Tocopherol reduced only serum AST levels, whereas dapagliflozin significantly lowered both serum AST and ALT levels in MASLD with type 2 diabetes; however, there was no significant difference between the two groups in a group comparison. These findings revealed the benefits and risks of treating MASLD with type 2 diabetes using SGLT2 inhibitor or vitamin E.

Abstract Submission No. 200040

O-0358

Meta-analysis of Luseogliflozin on Hepatic Steatosis/Fibrosis Indexes in Diabetic Patients in Japan

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Backgrounds: Luseogliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor, is known to decrease serum ALT levels in patients with diabetes mellitus. We aimed to investigate the effects of luseogliflozin on hepatic steatosis/fibrosis indexes and BMI in Japanese patients with diabetes mellitus by a meta-analysis.

Methods: In this pooled meta-analysis, we included 5 phase III clinical trials conducted in Japan. The primary outcomes were fatty liver index (FLI) and aspartate aminotransferase to platelet ratio index (APRI) after 24 weeks. The secondary outcome was BMI after 24 weeks. Statistical analysis was performed using propensity scoring analysis by the inverse probability of treatment weighting (IPTW) method.

Results: Patients' characteristics were adjusted by 20 covariates including age, sex, BMI, FLLI, and APRI using IPTW. A total of 493 participants (luseogliflozin group n=302, placebo group n=191) were enrolled in this meta-analysis. *Primary outcomes:* Luseogliflozin significantly decreased FLI compared to placebo after 24 weeks (adjusted coefficient -5.423, 95%CI -8.760 to -2.086, P=0.0016). Luseogliflozin also significantly decreased APRI compared to placebo after 24 weeks (adjusted coefficient -0.024, 95%CI -0.042 to -0.007, P=0.0066). *Secondary outcome:* Luseogliflozin significantly decreased BMI (adjusted coefficient -0.416, 95%CI -0.657 to -0.536, P<0.0001) compared to placebo after 24 weeks in patients with diabetes mellitus.

Conclusions: This pooled meta-analysis demonstrated that luseogliflozin improved non-invasive indexes for hepatic steatosis and fibrosis in patients with diabetes mellitus. We also revealed that luseogliflozin decreased BMI. Thus, luseogliflozin may be beneficial for improving hepatic steatosis and fibrosis with a reduction of body weight in Japanese patients with diabetes mellitus.

Abstract Submission No. 200076

O-0359

Effects of Biejia-Ruangan compound on patients with non-alcoholic fatty liver disease

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Background: Non-alcoholic fatty liver disease (NAFLD) is the main form of chronic liver disease, inducing nonalcoholic steatohepatitis (NASH), liver fibrosis and even liver cancer.

Methods: In this retrospective study, patients with NAFLD were included based on the EASL-EASD-EASO NAFLD Guidelines. The data, including laboratory parameters and liver stiffness measurement (LSM) at baseline and after six months treatment, were collected to evaluate the effectiveness of Biejia-Ruangan compound (BRC). These patients were grouped in BRC plus lifestyle intervention (BRC group) or lifestyle intervention (control group) by patients' wishes. Propensity score matching (PSM) was performed to reduce the effect from selection bias. The primary endpoint was the aminotransferase (ALT) normalization rate and the other endpoints were aspartate aminotransferase (AST) normalization rate, liver stiffness measurement (LSM) and Fibrosis-4 (FIB-4).

Results: 255 patients were enrolled in this retrospective study. After PSM, 96 patients in BRC were matched with 96 patients in control group ultimately. The ALT and AST normalization rates in the BRC group were higher than in the control group (87.5% vs. 7.3%, P<0.001; 84.4% vs. 4.2%, P<0.001). A reduction of LSM and FIB-4 score was observed in BRC group while an increase was observed in control group (-1.1 vs. 1.9, P<0.001; -0.8 vs. 0.3, P<0.001). Subgroup analysis showed that the effect of BRC group was superior to the control group and did not associate with gender, age, body mass index (BMI), diabetes mellitus (DM), LSM and cirrhosis (no vs. yes).

Conclusion: BRC have great therapeutic effect for NAFLD patients.

Abstract Submission No. 200123

O-0360

Long-term mass surveys by FibroScan have shown that the "burnout phenomenon" is extremely rare.

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Purpose: We examined the relationship between liver stiffness and liver fat content distribution and liver cancer by FibroScan.

Methods: We used 4214 FibroScan data (1163 individuals) (VCTE: Vibration-controlled transient elastography /CAP: Controlled Attenuation Parameter) and 73634 HBV, HCV data extracted from data warehouse, and 983 HCC data from 26783 cancer registry data of prefectural cancer center hospitals.

Results: The number of patients in each of the following zones (Zone 1: LSM≥12.0&CAP≥260, Zone 2: LSM≥12.0&CAP<260, Zone 3: LSM<12.0&CAP≥260, Zone 4: LSM<12.0&CAP<260) at the time of the first examination were 664 cases (5.7%), 155 (24.7%), 285 (11.7%), and 59 (58.3%), respectively.

Of the 1163 patients, 93 liver cancers occurred (8.5%), and the incidence in each zone was

27/664(4.1%), 4/155(2.6%), 58/285(20.3%), 4/59(6.8%), respectively.

However, looking at the FS transition from initial to final, only 6 of the 626 patients (1%) who could be followed moved from zone 2 (low stiffness high fat) to zone 3 (high stiffness low fat).

The above trends were also observed in HCV-positive patients, HCV-DAA-treated patients, and non-B non-C patients.

Conclusion: Crosssectional analysis of FibroScan shows that the "burnout phenomenon" is extremely rare.

Abstract Submission No. 200167

O-0361

HSK31679 (a thyroid hormone receptor β agonist) in Asian NAFLD with hypercholesterolemia

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Background: HSK31679 is a thyroid hormone receptor (THR)-β agonist. This study evaluated the efficacy and safety of HSK31679 in non-alcoholic fatty liver disease (NAFLD) with hypercholesterolemia.

Methods: This was a multicentre, randomised, double-blind, placebo-controlled, phase 2a study. Liver fat content (LFC) was assessed by MRI-PDFF. Subjects with an LFC of ≥8% and low-density lipoprotein cholesterol (LDL-C) ≥3.44mmol/L were eligible. Subjects were randomised 1:1:1:1 to oral HSK31679 doses of 40mg QD, 80mg QD, 160mg QD, placebo, or Ezetimibe 10mg QD. The two primary endpoints were relative reduction from baseline in LFC (%) and the reduction of LDL-C after 12 weeks of treatment.

Results: 784 participants were screened and 210 were randomly assigned to the five groups at 26 sites in China. At baseline, the mean

age of the participants was 41.87 years, 64.76% were male, 10.00% had 2 diabetes mellitus, 26.19% had hypertension, mean BMI was 29.05kg/m², mean LFC was 17.54% and mean LDL-C was 4.37mmol/L. By December 25, 2023, of 140 subjects who had already completed the treatment, 70.71% had LFC reductions and the mean relative change from baseline in LFC was -14.37%. The mean relative change from baseline in LDL-C and TG was -10.05% and -4.35%, respectively. Adverse events were reported in 116 subjects. One participant discontinuation due to a skin rash. No severe adverse events occurred. The final data analysis for this study will be completed in February 2024.

Conclusion: This study will show the safety and efficacy of THR- β agonist in the Asian NAFLD population.

Abstract Submission No. 200206

O-0362

The Effects of GLP-1 Receptor Agonists in Histological Improvement of NASH: A Meta-analysis of RCT

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Background: No pharmacotherapy has been approved for nonalcoholic steatohepatitis (NASH). Meanwhile, GLP-1 receptor agonists (GLP-1RAs) have demonstrated beneficial effects on diabetes and obesity, both of which are linked to NASH. This study aims to investigate the impact of GLP-1RAs on the histological features of NASH, a critical target indicating disease progression.

Method: Literature searching was conducted following the PRISMA guidelines on Cochrane, PubMed, Embase, Scopus, and ClinicalKey. Histological improvement was defined as the resolution of steatohepatitis or a decrease in fibrosis stage. All eligible studies were included and analyzed using Revman 5.4 software.

Result: A total of 3 randomized controlled trials (RCTs) involving 462 subjects, with 242 in the GLP-1RAs arm and 220 in placebo arms, who underwent pre- and post-treatment biopsies were included. The resolution of NASH was statistically significant in the GLP-1RAs arm (OR 3.66; 95% CI; $p < 0.00001$, $I^2 = 5\%$), while improvement in fibrosis stage was not statistically significant between the two arms (OR 1.27; 95% CI; $p = 0.24$, $I^2 = 48\%$). Upon excluding the study involving cirrhosis subjects, both NASH resolution and fibrosis stage improvement were not significantly different.

Conclusion: Treatment with GLP-1RAs in NASH subjects showed significant NASH resolution, but did not improve the fibrosis stage.

Keyword: GLP-1RA, NASH, fibrosis stage, NASH resolution

Abstract Submission No. 100092

O-0363

MISOPROSTOL FOR NON-ALCOHOLIC STEATOHEPATITIS-A RANDOMIZED CONTROL TRIAL

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Background: The management of non-alcoholic steatohepatitis (NASH) is an unmet clinical need. Misoprostol, a structural analogue of naturally occurring prostaglandin E1 (PGE1), has been reported to

decrease pro-inflammatory cytokine production and may have a potential role to treat NASH. We aimed to evaluate the efficacy and safety of misoprostol in treating patients with NASH.

Methods: In this phase 2, double-blind, randomized, placebo-controlled trial, patients with NASH were randomly assigned in a 1:1 ratio to receive 200 mcg of misoprostol or placebo thrice daily for 2 months. The primary endpoint was an improvement in liver function tests, interleukin-6 (IL-6), and endotoxin levels. The secondary endpoint was improvement in insulin resistance, dyslipidemia, hepatic fibrosis, and hepatic steatosis.

Results: A total of 50 patients underwent randomization, of whom forty-four (88%) were males. The age range was 25-64 years (mean 38.1 $\pm$ SEM1.4). 19 (38%) patients had concomitant type 2 diabetes mellitus. 32 (64%) patients were either overweight or obese. At the end of 2 months treatment, a reduction in total leucocyte count (TLC) ($p=0.005$), alanine aminotransferase (ALT) ($p<0.001$), aspartate aminotransferase (AST) ($p=0.002$), and controlled attenuation parameter (CAP) ($p=0.003$) was observed in the misoprostol group, whereas placebo ensued a decline in ALT ($p<0.001$), AST ($p=0.018$), gamma glutamyl transferase (GGT) ($p=0.003$), CAP ($p=0.010$) and triglycerides ($p=0.048$). There was no diminution in insulin resistance, hepatic fibrosis, and dyslipidemia in both groups. However, misoprostol resulted in a significant reduction in CAP as compared with the placebo group ($p=0.039$). Moreover, in the misoprostol group pre and post treatment IL-6 and endotoxin levels remained stable, while in the placebo group, an increase in the IL-6 levels was noted ($p=0.049$). In the misoprostol group six (12%) patients had at least one adverse event in the misoprostol group, as did five (10%) in the placebo group. The most common adverse event in the misoprostol group was diarrhoea. No life-threatening events or treatment-related deaths occurred in each group.

Conclusions: Improvement in biochemical profile was seen both in misoprostol and placebo groups without any statistically significant difference. However, there was more improvement in steatosis, as depicted by CAP, in the misoprostol group and worsening of IL-6 levels in the placebo group.

Abstract Submission No. 100184

O-0364

Association of sex and baseline ALT levels with response to pioglitazone for SLD patients

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Background/Aim: The response rate and factors for pioglitazone to improve liver biochemistry of steatotic liver diseases (SLD) patients remained elusive in Taiwan.

Methods: A 3-year prospective cohort study of 126 Taiwanese SLD patients treated with pioglitazone (15-30 mg/day) was conducted. The genetics including phospholipase domain-containing protein 3 I148M-rs738409, methylenetetrahydrofolate reductase-rs1801133 and aldehyde dehydrogenase 2 (ALDH2)-rs671 were assessed.

Results: Of 126, 78 (61.9%) were males, with a mean and median ages of 54.3 and 56.5 years, respectively; 105 (83.3%) were pioglitazone responders (decreased alanine aminotransferase (ALT) levels at 6 months after treatment). Compared with non-responders, the responders were more frequently female, had higher baseline ALT but lower uric acid levels and lower ALDH2-rs671 GG genotype rates (38.6% vs. 66.6%, $p=0.027$). Sex [female sex: odds ratio (OR): 4.514, $p=0.023$] and baseline ALT levels (OR:1.015, $p=0.046$) were

associated with pioglitazone response. The cut-off level for baseline ALT to predict pioglitazone response is 82 U/L. Among responders, liver biochemistry and HOMA-IR were improved from 6 months to 24 months after treatment. Total cholesterol levels reduced in the first 6 months, while HDL-C increment, triglycerides and fibrosis-4 index reductions were noted only at 24 months after treatment.

Conclusions: For liver biochemistry, over 80% of SLD Taiwanese had pioglitazone response, which was positively associated with female sex and baseline ALT levels. Insuline resistance improved as early as 6 months after treatment, while liver fibrosis improvement was not evident until 24 months after treatment. The link between pioglitazone response and ALDH2 genotype demands further investigation.

Abstract Submission No. 100207

O-0365

AI-based digital pathology offers newer insights into lifestyle-induced fibrosis regression in MAFLD

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Background & Aims: Lifestyle intervention is the mainstay of therapy for metabolic-associated steatohepatitis (MASH), and liver fibrosis is a key consequence of MASH that predicts adverse clinical outcomes. The placebo response plays a pivotal role in the MASH clinical trials. Second harmonic generation/two-photon excitation fluorescence (SHG/TPEF) microscopy with artificial intelligence analyses provides an automated quantitative assessment of fibrosis on a continuous scale, called qFibrosis. We used this approach to gain insight into lifestyle intervention-induced fibrosis changes in MASH.

Methods: We examined unstained sections from paired liver biopsies (baseline and end-of-intervention) from MASH patients who had received either routine lifestyle intervention (RLI) (n=35) or strengthened lifestyle intervention (SLI) (n=17). We quantified liver fibrosis with qFibrosis in the portal tract, periportal, transitional, pericentral, and central vein regions.

Results: 20% (7/35) and 65% (11/17) of patients had fibrosis regression in the RLI and SLI groups, respectively. Liver fibrosis tended toward no change or regression after each lifestyle intervention, and this phenomenon was more prominent in the SLI group. SLI-induced fibrosis regression was mainly concentrated in the periportal region.

Conclusions: Using digital pathology, we could detect more pronounced fibrosis regression in the periportal region, with SLI. The patients with RLI were regarded as placebo patients with awareness of MASH conditions. With fibrosis regression in the periportal region, we could potentially differentiate RLI and SLI patients in the placebo group in the MASH clinical trial. Digital pathology provides new insight into lifestyle-induced fibrosis regression and placebo response, which is not captured by conventional histological staging.

Abstract Submission No. 100222

O-0366

Risk factors for extrahepatic cancer in people with non-alcoholic fatty liver disease

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Background: Although cancer is the second leading cause of death in people with non-alcoholic fatty liver disease (NAFLD), the magnitude of risk and relationship with disease severity and metabolic comorbidity remains unclear. We compared incidence of cancers in people hospitalised with NAFLD or non-alcoholic steatohepatitis (NASH) during 2007-2019 in Queensland, Australia, and investigated the association between cirrhosis, type 2 diabetes (T2D) and cancer risk.

Methods: In this retrospective state-wide data-linkage cohort study, we identified all cancers after the first hospitalisation with NAFLD/NASH to December-2019, estimated age-standardized incidence (ASI) of cancers, compared that to the ASI in the Queensland population (incidence rate-ratios [IRR]), and examined the association between cirrhosis, T2D and cancer risk (Cox regression).

Results: 11,483 patients age ≥ 20 years with NAFLD/NASH followed for a median of 3.8 years (interquartile range 1.5-7.4 years; 54,204 person-years) were diagnosed with 1,104 primary cancers. The ASI of any cancer in NAFLD/NASH patients (1,460/100,000 person-years, 95%CI 1,368-1,557) was double the ASI in the Queensland population for men (IRR=1.94, 95%CI 1.75-2.16)* and women (IRR=1.99, 95%CI 1.78-2.22)*. The ASI of extrahepatic cancers was 1,326/100,000 person-years (95%CI 1,238-1,419), and was 1.5-fold higher (95%CI 1.13-2.00)* in patients with cirrhosis vs not, but did not vary by T2D status (IRR=1.08, 95%CI 0.84-1.38). In multivariable analysis, age, T2D and cirrhosis were associated with increased extrahepatic cancer risk (Table).

Conclusions: NAFLD is associated with a significantly increased risk of extrahepatic cancer. Demonstrating a higher risk in people with cirrhosis, T2D, men, and age ≥ 40 years provides an opportunity for targeted vigilance.

Abstract Submission No. 100235

O-0367

Exhaled nitric oxide for the non-invasive identification of patients with fibrotic MASH

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Background: Fibrotic metabolic dysfunction-associated steatohepatitis (MASH) is a condition at risk of progressing to advanced liver disease. We examined whether an innovative exhaled nitric oxide (eNO) breath test (BT) can accurately diagnose fibrotic MASH without requiring blood tests.

Methods: 147 patients with MASH were recruited, and all tests were undertaken within one week of recruitment. With fibrotic MASH (NAS $\geq$ 4 and fibrosis stage $\geq$ 2) as the main outcome indicator, the diagnostic efficacy of eNO in identifying fibrotic MASH was compared to other validated models for advanced fibrosis requiring venesection, namely FAST, Agile 3⁺ and FIB-4 scores.

Results: The mean age was 40.36 $\pm$ 12.28 years, 73.5% were men. Mean body mass index (BMI) was 28.83 $\pm$ 4.31 kg/m². The proportion of fibrotic MASH was 29.25%. The AUROC for eNO in diagnosing fibrotic MASH was 0.737 [95% CI 0.650-0.823], which was comparable to FAST (0.751 [0.656-0.846]), Agile 3⁺ (0.764 [0.670-0.858]), and FIB-4 (0.721 [0.620-0.821]) (all DeLong test $p > 0.05$). A cut-off of eNO <8.5 ppb gave a sensitivity of 86.0% and a negative predictive value of 88.5% for ruling-out fibrotic MASH. A cut-off of eNO >13.5 ppb provided a specificity of 91.3% and a positive predictive value of 65.4% for ruling-in fibrotic MASH. Sensitivity analyses demonstrated that the diagnostic efficacy of eNO was similar across characteristics such as age. Moreover, adding VCTE-LSM (liver stiffness measurement) reduced the uncertainty interval from 46.9% to 39.5%.

Conclusions: The eNO-BT is a promising simple test for non-invasively identifying fibrotic MASH and its performance is further improved by adding LSM measurement.

Abstract Submission No. 100259
O-0368

Antifibrotic effect of Polyene phosphatidylcholine in chinese MAFLD patients: a real-world study.

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Background: Polyene phosphatidylcholine is considered one of the most promising therapeutic agents for the treatment of steatosis because of its antioxidant, anti-inflammatory, and anti-fibrotic actions by liver cell regeneration. We aimed to conduct an observational study based on retrospective real-world data to analyze the antifibrotic effect

of Polyene phosphatidylcholine (Essentiale® Capsule, Ess) in MAFLD patients.

Methods: This is a multicenter, retrospective study. Patients with MAFLD (aged $\geq$ 18) were identified from the tertiary public hospital electronic database between January 1st, 2020 and December 31st, 2022 following APASL 2020 guideline. Propensity score matching (PSM) was used to match Ess monotherapy group and control (non-hepato-protective-treated) group at a 1:1 ratio. The primary endpoint was the change of fibrosis-4 index (FIB-4) after 24 weeks treatment with Ess. **Results:** The median age of enrolled 82,908 MAFLD patients from 11 hospitals was 53 (IQR, 43-63) years old and 64.3% were male. The median FIB-4 was 1.22 (IQR, 0.83-1.85). Among the FIB-4-based fibrosis risk stratification, 33.4% were at intermediate-risk (1.3-2.67), and 12.3% were at high-risk (>2.67). Of the 291 MAFLD patients treated with Ess only for 24 weeks, 42 patients have FIB-4 data. After PSM analysis matching for age, sex, T2DM, CVD, hypertension, and hyperlipidemia, the FIB-4 index adjusted for covariates was significantly reduced in the Ess-treated group than control group by using ANCOVA (-0.12 $\pm$ 0.62 for Ess vs. 0.11 $\pm$ 0.50 for control, $P = 0.034$).

Conclusions: Our study found that Ess treatment for 24 weeks can significantly reduce the FIB-4 index in MAFLD patients. Funding by Sanofi.

Abstract Submission No. 100277
O-0369

The Impact of Statotoc Liver Disease on Liver-Related Events in Patients Cured of Hepatitis C Virus

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Background and Aims: The new fatty liver nomenclature statotoc liver disease (SLD) was proposed in June 2023. The prevalence and impact of different subclass SLDs on liver-related events (LREs) in patients with chronic hepatitis C (CHC) and achieving a sustained virologic response (SVR) to direct-acting antiviral agents (DAAs) is unknown.

Methods: 1185 patients with cured CHC with body mass index or lipid profile data were enrolled. The cardiometabolic criteria (CMC) and alcohol consumption were defined accordingly. Variables at 12 or 24 weeks after DAA therapy (PW12) were used to identify predictors of LREs.

Results: The median age of the 1185 patients was 57 (47-65) years. Of the participants, 557 (47.0%) were men, and the median BMI was 24.13 (21.87-26.83) kg/m². There were 562 (47.4%), 96 (8.1%), 14 (1.2%), 78 (6.6%), and 435 (36.7%) patients who had metabolic dysfunction-associated (MASLD), MetALD (MASLD and increased alcohol intake), alcohol-related liver disease (ALD), specific-etiology or cryptogenic SLD, and no SLD, respectively. The multivariable Cox regression analysis indicated that age, alcohol consumption, per CMC (hazard ratio 1.307, 95% confidence interval: 1.070-1.596, $P = 0.009$), post-therapeutic albumin, alpha-fetoprotein, and fibrosis-4 were independent predictors of LREs. Kaplan-Meier analysis showed that patients with 3-5 CMCs had a higher cumulative incidence of LRE than those with 0-2 CMCs.

Conclusions: The new fatty liver nomenclature SLD could stratify CHC patients with viral eradication by DAA therapy. The risk of LREs increased by about 30% per CMC in this group of patients.

Abstract Submission No. 100429

O-0370

Association between Skeletal Muscle Strength and Chronic Kidney Disease in Patients with MAFLD

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Background: A decline in skeletal muscle strength is closely associated with metabolic diseases, but whether skeletal muscle strength declines with chronic kidney disease (CKD) in people with metabolic dysfunction-associated fatty liver disease (MAFLD) is uncertain. This study investigated the association between skeletal muscle strength and metabolic dysfunction-associated fatty liver disease with chronic kidney disease (MLKD).

Method: We performed cross-sectional investigations within a hospital-based Chinese liver biopsy cohort (the PERSONS cohort; n=460) and a United States population-based cohort (NHANES 2011-2014 cohort; n=1,414), respectively. A handgrip dynamometer measured handgrip strength as a proxy for overall skeletal muscle strength. Subjects were stratified according to the absence [non-CKD (stage 0) or presence of CKD (stages 1-5)].

Results: In the PERSONS cohort, the CKD group had a significantly lower handgrip strength than the non-CKD group (27.02±9.27 vs. 33.59±11.90 kg, p<0.05). In a generalized additive logistic regression model, there was an inverse association between handgrip strength and the risk of abnormal albuminuria or CKD and higher handgrip strength was associated with lower odds of albuminuria or CKD (OR: 0.95, 95%CI: 0.92-0.99, p=0.018; OR: 0.95, 95%CI: 0.91-0.99, p=0.009) after adjustment for potential confounders. The highest handgrip strength tertile was associated with the lowest risk of abnormal albuminuria or CKD (compared with the lowest or the middle tertile). The results were validated using the NHANES 2011-2014 cohort. Combining handgrip strength, age, sex, BMI, hypertension and diabetes status to discriminate between MLKD and non-MLKD groups had an AUROC of 0.74 (95% CI: 0.67-0.81) in the PERSONS cohort and 0.72 (95% CI: 0.68-0.75) in the NHANES 2011-2014 cohort.

Conclusion: Lower handgrip/muscle strength is closely associated with a higher risk of abnormal albuminuria or CKD in people with MAFLD.

Abstract Submission No. 100442

O-0371

Metabolic Dysfunction-Associated Steatotic Liver Disease in People Living with HIV

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Background: The high prevalence of MASLD is driven by factors related to HIV-infection, comorbidities, and antiretroviral therapy. We aimed to study the characteristics of MASLD in PLWH.

Method: We conducted a retrospective cohort study of PLWH with CD4 counts≥200, enrolled between April and October 2023 at two tertiary hospitals. The primary outcome was MASLD prevalence, defined by CAP≥238dB/m and meeting cardiometabolic criteria. Secondary outcomes exploring MASLD characteristics and significant fibrosis (F≥2).

Results: Of 96 PLWH, 52(54.2%) had MASLD, with a mean age of 49.7±8.0 years and 63.5% were male. The mean BMI was 25.8±4.1 kg/m², 17.3% had obesity, 19.2% had diabetes, and 46.2% had dyslipidemia. The mean CAP was 285±36 dB/m, median TE was 6.1 (5.2,8.8) kPa. Significant fibrosis (F≥2) was present in 46.2%. Those with significant fibrosis had higher BMI (27.1vs24.7 kg/m², p=0.016), waist and hip circumference, rates of dyslipidemia (62.5%vs32.1%, p=0.029), AST (53.5vs28.2 U/L, p<0.001), ALT (72.1vs37.9 U/L, p=0.002), and globulin, but lower platelet count, and HDL-cholesterol compared to those with F0-1. Scoring systems (FIB4, APRI, NFS) were also significantly higher in F≥2 patients. AUROCs for FIB-4, APRI, and NFS scores were 0.84, 0.85, and 0.76, respectively (**Figure**). Multivariate analysis identified predictors of significant fibrosis: higher BMI (aOR 1.24, p=0.042), presence of dyslipidemia (aOR 3.96, p=0.038), and higher AST (aOR 1.19, p=0.011) (**Table**).

Conclusion: MASLD is highly prevalent in PLWH, with about half experiencing significant fibrosis. Predictors of significant fibrosis include dyslipidemia, higher BMI, and elevated AST/ALT levels. Furthermore, fibrosis scoring systems exhibit good accuracy for fibrosis prediction.

Abstract Submission No. 100445

O-0372

Alfaamylase treatment and prophylaxis of NAFLD in experimental animals

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Non alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in the world. It includes wide spectrum of pathological and histopathological features ranging from simple steatosis, steatohepatitis, (NASH) with ballooning and inflammation and fibrosis driven for liver cirrhosis and hepatocellular carcinoma.

Salivary amylase is a glucose polymer cleavage enzyme produced mainly by pancreas, salivary glands and is expressed in many body organs as liver, brain, kidneys, intestine, lacrimal glands. Recent several researches proved positive correlations between low copy numbers of amylase and type 1, type 11 diabetes, obesity, metabolic syndrome and NAFLD. Other studies show inverse correlation of amylase copy numbers with total visceral fat volume. Also positive correlation with HDL cholesterol, serum adiponectin. Subjects with high copy number of amylase has gut microbiota able of degradation of resistant starch so produce higher level of short chain fatty acids. Upon these background of data we suggest that it may be effective in treating and/or prophylactic NAFLD in experimental animals.

Abstract Submission No. 100471

O-0373

Ectopic liver fat is associated with diabetes and adverse cardiac remodeling

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Background: We aim to characterize fat composition in the liver and abdominal depots by magnetic resonance imaging (MRI), in relation to diabetes and cardiac remodeling.

Methods: A cohort of 149 adults (57±13 years, 65% males, 38% type 2 diabetes) from the National Heart Centre Singapore Biobank underwent multiparametric MRI for quantification of liver proton-density-fat-fraction (PDFF) and abdominal subcutaneous and visceral adipose tissue (SAT, VAT), analyzed by trained operators blinded to clinical data (Perspectum, Oxford, UK). PDFF>5.6% was considered as abnormal liver fat accumulation. Adverse features of cardiac functions and remodeling were evaluated by cardiac MRI. Multivariate linear and logistic regressions were performed to assess independent associations of PDFF as a continuous and categorical variable, respectively, with other parameters. Analyses were adjusted for potential confounders including age, sex, systolic blood pressure, BMI, diabetes and hyperlipidemia.

Results: Increased PDFF was associated with VAT ($\beta=0.49$, $P<0.001$) but not with SAT. Diabetic individuals had significantly higher PDFF [9.6 (5.2-17.7) versus 5.5 (2.8-8.9) %, $P<0.001$] and diabetes status was independently associated with elevated PDFF ($\beta=0.24$, $P=0.007$). Stratifying by PDFF 5.6% threshold, those with excessive liver fat were associated with diabetes (OR=3.82, 95% CI=1.54-9.46, $P=0.004$), reduced stroke volume ($\beta=-0.18$, $P=0.031$) and increased global myocardial wall stress denoted by a lower remodeling index ($\beta=-0.19$, $P=0.012$). Findings remained consistent with PDFF as a continuous variable, whereby increased PDFF was associated with reduced stroke volume ($\beta=-0.27$, $P=0.002$) and worse remodeling index ($\beta=-0.15$, $P=0.049$).

Conclusion: Ectopic liver fat accumulation was associated with visceral adiposity, diabetes and adverse cardiac remodeling.

Abstract Submission No. 100500

O-0374

A phase I DDI study to evaluate the effect of ASC42 on the pharmacokinetics of atorvastatin

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Background and Aims: Farnesoid X receptor (FXR) agonist, ASC42, is a potential drug candidate for nonalcoholic fatty liver disease (NAFLD) and primary biliary cholangitis (PBC). ASC42 is an inhibitor of organic anion transporter polypeptide 1B1 and 1B3 (OATP1 B1/OATP1B3). This study (NCT05464628) aimed to evaluate the effects of ASC42 on the pharmacokinetics (PK) of atorvastatin and its metabolite (2-hydroxy-atorvastatin), and safety of atorvastatin in the presence of ASC42 in healthy subjects.

Method: Twelve healthy subjects were dosed orally with a single dose of 20mg atorvastatin on Day 1 followed by a daily dose of 15mg ASC42 on Day 6 through Day 15. On Day 11, subjects received both 15mg ASC42 and 20mg atorvastatin. Samples for PK were collected on Days 1 and 11.

Results: Atorvastatin C_{max} was 15% lower, while AUC_{inf} , AUC_{0-24} , and AUC_{last} were similar when atorvastatin was co-administered with ASC42. There was little/no change of 2-hydroxy-atorvastatin PK parameters when atorvastatin was co-administered with ASC42. As for ASC42, following multiple dose administration of ASC42 in combination with a single dose of atorvastatin, the inter-subject variability for C_{max} and AUCs were moderate, ranging from 38% to 47%. Six adverse events (AEs) were reported in 5 subjects (41.7%), and all were mild (grade 1) in severity and only 1 AE (8.3%) was considered probably related to study drug.

Conclusion: ASC42 has no effect on the overall exposure of atorvastatin or its metabolite, 2-hydroxy-atorvastatin, and co-administration of atorvastatin 20mg and ASC42 15mg was safe and well tolerated in healthy subjects.

Abstract Submission No. 100547

O-0375

Non-Alcoholic Fatty Liver Disease (NAFLD) burden among Filipino People Living with HIV (PLHIV)

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Background: Non-Alcoholic Fatty Liver Disease (NAFLD) is a significant concern for people living with HIV (PLHIV) due to its impact on non-HIV-related mortality.

Methods:

A total of 35 Filipino male patients with HIV were screened which included 27 patients divided into two groups: 15 with NAFLD and 12 without, resulting in a 55% NAFLD prevalence.

Results: The average age of patients was 38 years, with an HIV duration of 7 years and a mean CD4 count of approximately 600 cells/mm³. Antiretroviral regimens included Lamivudine + Tenofovir with Dolutegravir (44%), Efavirenz (52%), and one patient on Lamivudine + Zidovudine + Efavirenz (4%).

Both groups experienced dyslipidemia, with 73% of NAFLD patients and 67% of those without NAFLD affected. Among NAFLD patients, 53% were overweight, often associated with Type 2 Diabetes and Hypertension (26%). In contrast, 83% of those without NAFLD had a normal BMI and a higher rate of opportunistic co-infections (50%). Liver-related measurements, including mean transaminase levels (AST: 77, ALT: 144), liver stiffness (8.3 kPa), and CAP scores (330 dB/m), were higher in the NAFLD group compared to those without NAFLD. Although mean FIB4 scores indicated mild fibrosis in all patients, mean APRI scores revealed evidence of fibrosis (0.76) in the

NAFLD group, while those without NAFLD showed an absence of fibrosis (0.46).

Conclusion: Risk factors of metabolic syndrome (overweight, hypertension, diabetes) are strongly linked to NAFLD in PLHIV. There is no significant relationship between ARV regimen, CD4 count, HIV duration and presence of opportunistic co-infections in development of NAFLD.

Abstract Submission No. 100645
O-0376

Long-term impact of metabolic dysfunction-associated fatty liver disease on cardiovascular diseases

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Background & Aims: The prospective study aimed to investigate the potential influence of metabolic dysfunction-associated steatotic liver disease (MASLD) on the associated risk of cardiovascular disease (CVD).

Methods: We enrolled 329,528 adults aged ≥ 30 years who participated in a health screening program from 1997 through 2013. MASLD was defined by abdominal ultrasound-observed hepatic steatosis, limited alcohol consumption (<20 g/d for men and <10 g/d for women), and cardiometabolic risk factors. Participants were categorized into non-steatotic liver disease and the MASLD groups. We linked data to the Taiwan National Health Insurance Database (1997-2020) to identify CVD incidence and subtypes using ICD codes. Cox's proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for MASLD's impact on each CVD subtype.

Results: Among all participants, 106,926 were classified as having MASLD, while 222,602 were classified as having non-steatotic liver disease, resulting in a MASLD prevalence of 32.4%. Individuals with MASLD were more likely to be older, male, having a higher body mass index, diabetes, and more cardiometabolic risk factors ($p < 0.05$). There were a total of 125,053 CVD cases, including 6,033 myocardial infarction, 10,955 atrial fibrillation, and 21,585 heart failure cases. Using the non-SLD as a reference, the multivariate-adjusted HRs (95% CIs) for MASLD were: 1.21 (1.19-1.23) for all CVD, 1.80 (1.71-1.90) for myocardial infarction, 1.12 (1.08-1.17) for atrial fibrillation, and 1.23 (1.24-1.31) for heart failure.

Conclusion: MASLD was linked to an increased risk of CVD and its subsets, highlighting the need for behavior modifications and risk consultations.

Abstract Submission No. 100676
O-0377

Survey of stigmatization among Thai NAFLD patients, a preliminary result

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Background: Stigmata has been evaluated in patients with viral hepatitis, including hepatitis B and hepatitis C infection. However, the data about stigmata in patients with non-alcoholic fatty liver disease

(NAFLD), especially the Asian population, is lacking. Our study aims to evaluate NAFLD patients' perception using previously validated self-stigma short form (SSS-S) and Hepatic stigmata (HS) questionnaires.

Methods: We included Thai patients with NAFLD diagnosed with CAP ≥ 238 dB/m. SSS-S and HS questionnaire were translated into the Thai language. Answers to questions of SSS-S and HS are rated on a 4-point Likert scale. Higher scores indicate a high burden of stigmatization.

Results: In the preliminary analysis of 71 Thai patients with NAFLD, most were male (56.3%), aged above 45 (78.8%), and had other comorbidities (71.7%). The mean BMI was 26.77 ± 5.02 kg/m². SSS-S HS significantly correlated with HS with Spearman's r 0.73, $p < 0.001$. 11.3% and 25.4% reported discrimination from healthcare personnel due to NAFLD and obesity, respectively. The mean unweighted average SSS-S and HS scores were 1.90 ± 0.49 and 1.76 ± 0.45 , respectively. The cognitive questions of SSS-S and questions noted eating habits and obesity in HS had a mean score above two. (Tables 1 and 2) None of the factors, including age, gender, education level, comorbidities, and BMI, was significantly correlated with SSS-S or HS.

Conclusion: Perceived stigmatization in Thai patients with NAFLD is uncommon. Nevertheless, certain factors, including dietary habits and obesity, appear to be of greater concern among this NAFLD patients.

Abstract Submission No. 100704
O-0378

Patients with Diabetes Mellitus and Liver Diseases in Azerbaijan: Epidemiological Studies

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Introduction: Diabetes mellitus - a metabolic disorder, which is expected to affect 300-400 million worldwide by 2030. Multiple studies with subsequent meta-analyses from Europe, Asia, and North America support the idea that DM and insulin resistance are independent risk factors for liver diseases and HCC. According to official data, there are about 300,000 patients with type 2 diabetes mellitus in Azerbaijan. There are not any epidemiological studies about Diabetes Mellitus and its relationship with liver diseases.

Methods: We have collected data for 3110 patients with Diabetes Mellitus admitted between January 2008 and June 2023 to Baku Health Center.

Results: There were 2425 patients with MAFLD/NAFLD (78%), 544 patients (17.5%) with liver cirrhosis and 139 patients (4.5%) with HCC. Among patients with MAFLD/NAFLD males accounted for 43.5% (mean age- 52 y), and 56.5%-females (mean age- 57 y).

Among patients with liver cirrhosis 50% were males (mean age - 60 y), females -50% (mean age-69 y).

Among patients with HCC -62% were males (mean age-64 y), and 38%-females (mean age-67y).

Conclusion: Liver involvement in type 2 diabetes has been found in a large number of cases in the form of non-alcoholic fatty liver disease associated fatty liver disease (NAFLD/MAFLD), which can range from simple steatosis to non-alcoholic steatohepatitis (NASH), cirrhosis and HCC. The mean age of patients increases in correlation with the severity of liver pathology, which confirms the importance of the duration of diabetes mellitus as a pathognomonic factor. Follow-up examination of the liver are recommended in patients with diabetes mellitus.

Abstract Submission No. 100726
O-0379

The Role of Vitamin D Supplementation in Metabolic-Associated Fatty Liver Disease: Systematic Review

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The prevalence of metabolic-associated fatty liver disease (MAFLD), which was previously known as non-alcoholic fatty liver disease (NAFLD) in Asia was increased to 29.62%. The considered causes are the socio-economic changes and the overnutrition condition in Asia. Serum vitamin D level is considered to increase the risk of fatty liver. However, the study that reports the efficacy of vitamin D supplementation for patients with MAFLD or NAFLD is limited. This systematic review reports the selected articles from five sources with the searching keywords: "(Metabolic associated fatty liver disease OR MAFLD) OR (Non-Alcoholic Fatty Liver Disease OR NAFLD) AND (Vitamin D OR Vitamin D Supplementation) AND (Controlled Attenuation Parameter OR CAP) AND (liver stiffness measurement OR LSM)". Two trials (the first study used oral vitamin D supplementation [1000 IU] every day for 360 days compared with placebo, and the second study used intramuscular vitamin D supplementation [200,000 IU] every month for 180 days compared with placebo) report that vitamin D supplementation can significantly decrease ($p < 0.05$) the controlled attenuation parameter or CAP (22.8-39.1 dB/m) and liver stiffness measurement or LSM (0.07-0.52 kPa) compared to control group. The mechanism of its efficacy is achieved by inhibiting the progression of liver fibrosis induced by stellate cells after its binding to the hepatocyte. In conclusion, the efficacy of vitamin D in decreasing liver steatosis and fibrosis in MAFLD has been proven. However, the limitations of these studies should be followed by further research to state the recommendation of vitamin D supplementation in MAFLD.

Abstract Submission No. 100751
O-0380

The Impact of Fatty Liver Index on HCC among non-viral hepatitis subjects in an HBV Endemic Region

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The first two authors contribute equally to this work.

Background and Aims: MAFLD, a major liver disease cause, is tied to HCC risk. FLI, assessing BMI, waist circumference, triglycerides, and GGT, is a hepatic steatosis indicator. This study delves into high FLI's link to HCC in non-viral hepatitis in an HBV-endemic region.

Method: We enrolled Taiwan Biobank participants without HBsAg and anti-HCV, validated HCC diagnoses through the Taiwan National Cancer Registry. Type 2 diabetes was determined via ICD codes (E10-E14) in the National Health Insurance database. Cox regression analysis was used to identified HCC predictors.

Results: In this study of 116,269 HBsAg and anti-HCV seronegative subjects with an average age of 49.6 (11.1), 35.6% male, and 59.1% anti-HBc Ab positive, 80 were diagnosed with HCC during a 4.4-year follow-up. HCC incidence was higher for FLI > 20 (0.03%) compared to FLI < 20 (0.006%). Multivariate Cox regression revealed older age [aHR: 1.096, $P < 0.0001$], male gender [aHR: 2.002, $P = 0.0048$], and FLI > 20 [aHR: 3.376, $P < 0.0001$] as significant HCC risk factors. When stratified by anti-HBc positivity, FLI > 20 remained a significant HCC risk factor (Anti-HBc (+) aHR: 4.496, $P = 0.0235$; Anti-HBc (-) aHR: 3.153, $P = 0.0003$). After adjusting for age, gender, alcohol, smoking, and anti-HBc status, individuals with FLI > 20 and diabetes had the highest HCC risk (aHR: 4.1, $P < 0.05$).

Conclusion: FLI >20 increased the risk for individuals regardless of anti-HBc seropositivity, especially when combined with diabetes mellitus.

Abstract Submission No. 100800
O-0381

Lifestyle modification programme for HIV-infected patients with NAFLD: A randomized controlled trial

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Background: Lifestyle modification directing at weight loss is currently the cornerstone of treatment for fatty liver disease in the general population. No studies have been performed to specifically evaluate the efficacy of lifestyle modification programmes targeting non-alcoholic fatty liver disease (NAFLD) in people living with human immunodeficiency virus (HIV) (PLWH).

Objectives: To assess lifestyle modification programme in inducing resolution of NAFLD in PLWH.

Methods: This is a single-blinded randomized controlled trial. 84 PLWH with NAFLD in Hong Kong were randomly assigned to either receive a lifestyle modification programme or standard care for 12 months. The primary outcome is the resolution of NAFLD as determined by proton magnetic resonance spectroscopy (¹H-MRS) at month 12. Resolution of NAFLD is defined as intrahepatic triglyceride (IHTG) content less than 5%.

Results: 43 patients were randomized to the intervention group and 41 patients to the control group. 77 patients completed all assessments during 12-month intervention. In the intention-to-treat analysis, 12 (27.9%) patients in the intervention group and 4 (9.8%) in the control group achieved the resolution of NAFLD ($p = 0.034$). The mean reduction of IHTG was significantly higher in the intervention group ($5.1 \pm 7.1\%$) compared to the control group ($0.2 \pm 6.9\%$) ($P = 0.004$). The mean change of total body fat was significantly higher in the intervention group (-1.81 ± 2.97 Kg) compared to the control group ($+0.10 \pm 1.78$ Kg) ($P = 0.001$). (Figure)

Conclusion: Lifestyle modification programme has efficacy in inducing resolution of NAFLD in PLWH.

Abstract Submission No. 100814
O-0382

The effects of lifestyle modification interventions on self-efficacy among NAFLD patients: SR

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Background: Patients with NAFLD reported low self-efficacy, poor illness perception and self-management behaviours which would affect the disease progression. Lifestyle modification has been regarded as the first-line therapies to NAFLD. However, no studies have been conducted to investigate the effects of lifestyle modification interventions on these outcomes, and there is no consistent design of such intervention for the patients.

Methods: A systematic literature search was conducted in nine electronic databases. Meta-analysis was conducted to pool the quantitative results from comparable studies.

Results: The review included 16 randomised controlled trials. The meta-analysis results indicated that the lifestyle modification interventions significantly improve general self-efficacy (standardised mean difference [SMD] = 0.82, 95% confidence interval [CI] [0.27, 1.38], $p = .0004$, $I^2 = 71\%$), self-management behaviours (SMD = 7.91, 95% CI [5.74, 10.07], $p < .00001$, $I^2 = 96\%$), dietary behaviours (SMD = 2.33, 95% CI [1.15, 3.51], $p = .0001$, $I^2 = 97\%$), total physical activity (SMD = 1.36, 95% CI [0.57, 2.14], $p = .0007$, $I^2 = 96\%$), and steatosis grade (SMD = -0.56, 95% CI [-0.80, -0.31], $p < .00001$, $I^2 = 0\%$). Individual studies suggested significant improvement in illness perception ($p < .001$). The overall methodological quality of the included studies was average.

Conclusion: Lifestyle modification interventions were found to be effective in improving self-efficacy, illness perception, self-management behaviours and steatosis grade among patients with NAFLD. Suggested design of the intervention has also been identified but more rigorous trials should be conducted to evaluate the effects of the interventions.

Abstract Submission No. 100837
O-0383

Fibrosis-Associated Genetic Variants in Metabolic Dysfunction-Associated Steatotic Liver Disease.

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Abstract

Background and aim: The study aimed to investigate genetic variants associated with liver fibrosis among individuals with metabolic dysfunction-associated steatotic liver disease (MASLD).

Method: The study included 31,389 individuals with MASLD from Taiwan Biobank, defined by a fatty liver index ≥ 30 and the presence of any cardiometabolic risk factor. Fibrosis was assessed using the fibrosis index-4 (FIB-4), categorizing participants with FIB-4 ≥ 1.45 as

having mild fibrosis and FIB-4 < 1.45 as non-fibrosis. Logistic regressions were used to estimate the odds ratios (ORs) with 95% confidence intervals (CIs) on potential risk factors and fibrosis-associated genetic variants among the individuals with MASLD.

Result: Among individuals with MASLD, 6711 (21.4%) had FIB-4 > 1.45 . Advanced age, male, and comorbidities were positively associated with mild fibrosis ($p < 0.05$). Variants in PNPLA3 and GCKR genes showed significant associations with fibrosis in MASLD individuals ($p < 0.001$). Variants on PNPLA3, GCKR and TM6SF2 genes were examined, and the numbers of risk alleles were calculated. Individuals with more risk alleles were more likely to have fibrosis. Categorizing the number of alleles as 0-1, 2, and ≥ 3 , the adjusted OR (95% CI) was 1.23 (1.15, 1.31) for risk alleles ≥ 3 and 1.14 (1.07-1.22) for 2 risk alleles. The trend remained significant in individuals with MASLD and obese (BMI ≥ 24 kg/m²), the findings were consistent, with an adjusted OR of 1.14 (1.06-1.22) for 2 risk alleles, and 1.22 (1.13-1.31) for risk alleles ≥ 3 .

Conclusion: Individuals with MASLD, carried a higher number of risk alleles were at increased risk of mild fibrosis, highlighting the importance of intensive care and monitoring.

Abstract Submission No. 100859
O-0384

Change in Fibrosis-4 Index (FIB4) over time is associated with subsequent risk of liver events

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Background: Tools assessing morbidity/mortality risk of non-alcoholic steatohepatitis (NASH) are lacking. We evaluated associations between changes in fibrosis-4 index (Δ FIB4) and subsequent liver events.

Methods: This longitudinal study included adults with obesity and/or type 2 diabetes (T2D); ≥ 2 FIB4 measurements; no alcohol-related and/or chronic liver diseases (except non-alcoholic fatty liver disease/NASH). Δ FIB4 was calculated using baseline and 12-month scores. Follow-up included time from second measurement until first liver event, first cardiovascular event, all-cause mortality, 10 years' follow-up; or 1/1/2020.

Results: Among 20,443 patients, there were 466 liver events. After 10 years, patients with high baseline FIB4 (> 2.67) had a 12.8% risk of a liver event; the risk was 18.5% or 10.1% when FIB4 increased or decreased after 12 months, respectively. In patients with indeterminate (1.30-2.67) or low (< 1.30) FIB4, increasing FIB4 was associated with increased risk. Δ FIB4 was directly associated with risk of liver event, dependent on baseline FIB4 (Cox models). Compared with low baseline FIB4 and no change in FIB4 (reference), the hazard ratio (95% confidence interval) in patients with high baseline FIB4 was 24.27 (16.98; 34.68) with 1-unit FIB4 increase; and 10.90 (7.90; 15.05) with 1-unit decrease. Patients with indeterminate/low FIB4 and 1-unit increase/decrease had significantly higher/lower risk compared with the reference group. Similar results were seen for cardiovascular events/mortality.

Conclusion: In patients with obesity and/or T2D, a 12-month increase/decrease in FIB4 was associated with higher/lower risk of

NASH-related liver events across FIB4 groups, highlighting FIB4's potential to identify patients at risk of severe events.

Abstract Submission No. 100865
O-0385

Effect of metabolic dysfunction-associated steatotic liver disease on BNT162b2 immunogenicity

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Background: We aimed to investigate effect of metabolic dysfunction-associated steatotic liver disease (MASLD) on COVID-19 vaccine immunogenicity to *omicron* variant.

Methods: Adult recipients of three doses of BNT162b2 were prospectively recruited from vaccination centers between May and December 2021. Serology of neutralising antibody by live virus microneutralization (vMN) to *omicron* variant was measured at baseline, day180 and day360 after first dose (**Figure 1**). Study outcome was seroconversion (vMN titer ≥ 10) at day360 after first dose. Exposure of interest was MASLD. Hepatic steatosis was defined by controlled attenuation parameter (CAP) ≥ 248 dB/M on transient elastography. Subjects with infection prior to one-year follow-up were excluded. Multivariable logistic regression model was used to derive adjusted odds ratio (aOR) of seroconversion with MASLD by adjusting for age, sex, antibiotic and proton pump inhibitor use.

Results: 148 BNT162b2 recipients (male:48 [32.4%]; median age:51.0years [IQR:44.5-57.3]) were recruited. The median time from first dose to third dose was 8.5 months (IQR:7.9-8.9). Only 4 [2.7%] subjects were seropositive at day180. MASLD subjects had lower seroconversion rate than non-MASLD ones (89.6% vs 99.0%; $p=0.007$) (**Table 1; Figure 2a**). MASLD was the only independent risk factor associated with lower odds of seroconversion (aOR:0.05, 95% CI:0.002-0.44). Subgroup analysis shows MASLD subjects had lower vMN titer (13.06 [IQR:7.69-22.20] vs 33.49 [IQR:24.05-46.53]; $p=0.004$) and seroconversion rate (76.9% vs 97.4%; $p=0.016$) than non-MASLD subjects after 4 months from third dose but not within 4 months (**Table 1; Figure 2b**).

Conclusions: MASLD was associated with lower vaccine immunogenicity to *omicron* variant after three doses of BNT162b2.

Abstract Submission No. 100874
O-0386

Insulin resistance in MASLD and liver-related outcomes: a nationwide, population-based study

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Aims: Insulin resistance is a well-known factor in patients with metabolic syndrome or steatotic liver disease. Surrogate markers such as the triglyceride-glucose (TyG) index and triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) ratio assess insulin resistance (IR). In this study, our aim was to investigate the relationship between insulin resistance and factors in patients with metabolic associated steatotic liver disease (MASLD).

Methods: Using data from participants who underwent health screening in 2009 and 2010, we divided them into quartiles (Q1, Q2, Q3, Q4) for each marker and compared the incidence rates of liver-related diseases during the observation period.

Results: Among a total of 362,285 patients, 67,908 patients deemed suitable for this study were enrolled and followed-up for an average of 9.4 years. During this period, liver-related diseases occurred in 2,621 cases of decompensated cirrhosis and 2,056 cases of liver cancer. Participants were divided into 4 quartiles according to TyG and TG/HDL-C ratio, and the incidence rate of liver-related diseases was analyzed. As a result of the analysis, it was confirmed that TyG and TG/HDL-ratio all had an inverse proportional relationship in which the incidence of liver-related diseases decreased as IR increased.

Conclusion: Our study showed that TyG and TG/HDL ratio are inversely related to liver-related diseases in MASLD patients, which indirectly suggests nutritional imbalance and decreased function of liver mediators during liver fibrosis progression. Improvement in metabolic parameters in MASLD patients suggests that liver-related diseases should be reassessed.

Abstract Submission No. 100897
O-0387

NFTE- A Prediction rule for fibrosis in Metabolic-dysfunction associated steatotic liver disease

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Background: Accurate evaluation of liver fibrosis in Metabolic-dysfunction Associated Steatotic-Liver-Disease(MASLD) serves as a surrogate to predict liver-related outcomes. We evaluated the diagnostic performance of non-invasive tests(NITs) in detecting advanced fibrosis(AF) and tried to optimize diagnostic strategies for improved outcomes and reduce the need for liver biopsies.

Materials and Methods: Consecutive patients with biopsy-proven MASLD from September 2021 to March 2023 were enrolled. NITs were compared with histological grade of fibrosis(NASH-CRN) for diagnostic accuracy. Biomarkers were assessed individually and in paired combinations. Liver stiffness(LSM) was measured using 2D-Shear-Wave-Elastography(SWE) and Vibration-Controlled-Transient-Elastography (VCTE).

Results: 92 patients (53 male(57%)), median age 41 years were included. 64(69%) had biopsy-proven AF. T2DM present in 55(59%).Advanced age, male sex, lower platelet counts, and high triglyceride were significantly associated with advanced fibrosis($p<0.001$). NITs were moderately accurate in predicting advanced fibrosis while using previously published cut-offs. Newly derived cut-offs demonstrated a high positive predictive value(93%) to ruling in advanced fibrosis. The AUROCs of NAFLD Fibrosis Score(NFS), SWE, Aspartate-Aminotransferase-Platelet-Ratio-Index(APRI), VCTE, Fibrosis-index-4-Factors(FIB-4) and BARD were 0.94, 0.93, 0.93, 0.91, 0.90 and 0.88 respectively at newer cut-off. A New score derived by combining NITs- NFS and VCTE, namely the NF-TE demonstrated significant diagnostic accuracy(AUROC0.98) and discriminative power ($p<0.05$) when compared with individual NITs.

Conclusion: NITs are point-of-care strategies to assess hepatic fibrosis in MASLD. FIB-4 and NFS may require age-dependent novel cut-off points for adequate estimation of fibrosis. Combination NIT serves as an important adjunct to rule in advanced fibrosis, thereby alleviating the need for liver biopsy.

Abstract Submission No. 100972

O-0388

Development of a novel supervised machine learning algorithm predicting MASLD in research volunteers

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Background and Aims: Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD) affects approximately one in four of the global adult population. MASLD has important implications for clinical trial volunteers as an occult co-morbid condition - there is evidence that MASLD modulates drug metabolism, with studies suggesting that Grade 3-4 liver reactions are four times more common in healthy volunteers with probable MASLD.

This research aims to develop a non-invasive, low-cost tool, utilising supervised machine learning techniques, to predict MASLD in a healthy volunteer population, enabling the stratification of this sub-population in early phase trials.

Method: This is an observational cross-sectional study, with a total of 1500 subjects. Assessments include bioimpedance vector analysis, BMI, waist circumference, and laboratory bloods (including HbA1c, liver enzymes and White cell count). FibroScan is performed as a pragmatic 'outcome' for MASLD.

In this interim analysis of 1243 volunteers, a logistic regression model was trained using 70% of data for the ability to predict the outcome of the FibroScan from a data subset containing: Age, Sex, Ethnicity/Race, Height, Weight, BMI, Waist Circumference, and Body Fat Percentage. The programming language R was used to build the model.

Results: Demographics of the included volunteers were assessed as representative of a typical early-phase population. On fitting a full model, BMI and Waist Circumference were ultimately included.

The model achieved an 88.4% predictive accuracy when tested against 30% volunteer test dataset

Conclusion: This preliminary model shows promising results as an early-stage clinical tool to accurately predict steatosis amongst trial volunteers.

Abstract Submission No. 100981

O-0389

IMPACT OF RENAMING (NAFLD) TO METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD)

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Background: The second-most recent change in steatosis nomenclature required 2/3 weight-metabolic criteria to be met and may lead to missed diagnosis in patients who develop weight-metabolic abnormalities later on. The metabolic-dysfunction-associated steatotic liver disease (MASLD) criteria requires only one criterion and may mitigate

this. We aimed to characterize our steatotic patients into: 1.) nonalcoholic fatty liver disease (NAFLD) only; 2.) MASLD only; 3.) NAFLD-MASLD; 4.) not NAFLD-MASLD.

MATERIALS AND METHODS: Consecutive patients with steatotic liver on ultrasound in a Hepatology clinic database from August 2007-July 2017 were included. Demographic, laboratories, AST/Platelet ratio (APRI), FIB4, and NAFLD fibrosis score (NFS) were compared between the groups.

Results: The 663 steatotic patients were categorized into: 6(0.9%) NAFLD, 326(49.2%) MASLD, 325(49%) NAFLD-MASLD, and 6(0.9%) not NAFLD-MASLD. Among patients meeting MASLD criteria, majority (80%) met >2 cardiometabolic criteria while only a minority (8.3%) satisfied only 1 criterion, of which overweight/obesity (79.6%) was most common. NAFLD-MASLD and MASLD patients had higher ALT, AST and platelet levels as compared to NAFLD and not NAFLD-MASLD patients ($p<0.05$). A higher probability of advanced fibrosis was seen in MASLD only compared to the other groups using APRI. There was a trend for more no/minimal fibrosis patients in the NAFLD and not NAFLD-MASLD groups compared to the MASLD and NAFLD-MASLD groups using non-invasive liver fibrosis tests.

Conclusions: Majority (98.2%) of patients with steatosis on ultrasound meet MASLD criteria. Serial follow-up is needed to determine if patients who do not meet MASLD criteria now will meet it in the future.

Abstract Submission No. 101011

O-0390

Effect of Lifestyle Measures in Normal Body Mass Index NonAlcoholic Fatty Liver Disease Patients

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Background and Aims: Lean nonalcoholic fatty liver disease (NAFLD) is a distinct entity shaped by the dynamic interaction of genetic predisposition, metabolic dysregulation, gut microbiota and enterohepatic circulation. There is paucity of data on effects of lifestyle measures in lean NAFLD patients. Our aim was to study the effects of lifestyle measures in normal body mass index (BMI) patients with NAFLD.

Methods: This prospective interventional study was conducted on patients of NAFLD patients with normal BMI, who were divided in to cases who received healthy lifestyle measures in the form of diet [low fat, low carbohydrates, high fiber and high protein (1-1.5gm/kg body weight) with total 15-20kcal/kg/day] and exercise (150-200 minutes/week moderate intensity over 3-5 sessions) along with standard medical therapy and controls who received standard medical therapy only, for 6 months.

Results: A total of 120 patients, 60 cases (31 males, age 37.41 ± 17.4 years) and 60 controls (27 males, age 41.81 ± 16.8 years) were enrolled. Baseline parameters, co-morbid conditions and grade of fatty liver were similar in both the groups. Improvement in SGOT (Δ SGOT - 16.6 ± 6.8 vs -1.2 ± 1.1 , $p=0.001$), SGPT (Δ SGPT - 23.24 ± 8.8 vs -4.3 ± 2.8 , $P=0.001$), controlled attenuation parameter (CAP) score (Δ CAP - 36.6 ± 13.8 vs -6.9 ± 5.2 , $p=0.001$), was observed in cases compared to controls at the end of study. However, the improvement in liver stiffness measurement (LSM) (Δ LSM - 0.8 ± 0.6 vs -0.6 ± 0.4 , $p=0.45$) was comparable in both cases and controls.

Conclusion: Lifestyle modifications and dietary intervention is effective for lean NAFLD patients.

Abstract Submission No. 101024
O-0391

Low Accuracy of Noninvasive Tests for Screening for advanced Fibrosis Among Chinese Adults With MAFLD

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Background: Fibrosis-4 (FIB-4), the nonalcoholic fatty liver disease fibrosis score (NFS) and aspartate aminotransferase to platelet ratio index (APRI) are popular non-invasive tests (NITs) for fibrosis screening. In this study, we aimed to evaluate the accuracy of these simple NITs for advanced fibrosis in MAFLD.

Method: We conducted a multicentered, cross-sectional study comprising 980 adult inpatients with MAFLD. Hepatic steatosis and fibrosis were assessed by transient elastography to measure CAP and LSM, respectively. We evaluated the correlation between NITs and LSM. The diagnostic performance of NITs was assessed.

Result: The mean [SD] age was 57.5 [13.9] years and 58.7% were male. There was a significant but weak correlation between LSM values and APRI (Spearman's rho = 0.261, $p < 0.001$) and FIB-4 (Spearman's rho = 0.174, $p < 0.001$), rather than NFS (Spearman's rho = 0.044, $p = 0.207$). APRI had a significantly higher AUROC compared with FIB-4 and NFS for advanced fibrosis (AUROC: APRI 0.68, FIB-4 0.64, NFS 0.55, $p < 0.05$) in MAFLD. However, APRI had the lowest sensitivity based on its cutoff values (APRI > 0.5 Se 0.25; APRI > 2.0 Se 0.02; $p < 0.05$) for advanced fibrosis. We also found low cutoff values of NITs outperformed high cutoff values: FIB-4 > 1.3 Se 0.56, FIB-4 > 2.67 Se 0.17; NFS > 1.45 Se 0.78, NFS > 0.675 Se 0.22; all $p < 0.01$. In addition, 16.2%, 9.5% and 4.4% false-negatives were observed in APRI, FIB-4 and NFS based on their low cutoff values for advanced fibrosis, respectively. And false-negatives accounted for higher proportion when using high cutoff values (APRI: 21.2%, FIB-4: 17.7%, NFS: 15.7%).

Conclusion: In our research, NITs had poor correlation with liver stiffness and unsatisfactory performance in AUROC (all < 0.7) for advanced fibrosis. Therefore, these NITs seems inadequate to be screening tools for advanced fibrosis in patients with MAFLD from China and more appropriate cutoff points should be set.

Abstract Submission No. 101033
O-0392

Reducing Metabolic Syndrome Risk in Liver Transplantation: The Impact of Donor Selection

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We conducted a study to assess the prevalence of clinical diagnoses associated with risk factors for metabolic syndrome and cardiovascular complications in liver transplant recipients, comparing recipients of deceased donors (DDLT) to those of living donors (LDLT).

Methods: 1277 patients were transplanted (1183 DDLT, 94 LDLT) between 2010 and 2020 at one institution. Clinical diagnoses following transplant were identified from the electronic medical record and assessed by multivariate logistic regression.

Results: The median recipient age at the time of transplantation was similar in both groups (58.9 years for DDLT and 58 years for LDLT,

$p = 0.11$). 70% of DDLT recipients were male, while 53.2% of LDLT recipients were male ($p = 0.0007$). Hyper/mixed-lipidemia was observed in 32.8% of DDLT recipients and 22.3% of LDLT recipients ($p = 0.036$). Hypertension was more common among DDLT (75.7%) compared to LDLT (58.5%) recipients ($p = 0.0002$). 51.8% of DDLT recipients had diabetes, while 39.4% of LDLT recipients were diabetic ($p = 0.02$). Overweight/obesity was more prevalent in the DDLT group (21.7%) compared to the LDLT group (11.7%), ($p = 0.02$). Metabolic syndrome was more common among DDLT recipients (27.6%), compared to 17% of LDLT recipients ($p = 0.03$). Coronary artery disease (CAD) was significantly more prevalent among DDLT recipients, (37.4%) of them having CAD, whereas only 18.1% of LDLT recipients had the condition ($p = 0.0002$). Myocardial infarction was observed in 12% of DDLT vs 5.3% of LDLT recipients ($p = 0.05$).

These findings underscore the potential benefits of living donor liver transplantation in mitigating the development of metabolic syndrome and its associated health risks.

Abstract Submission No. 101051
O-0393

Prevalence and risk factors of MASLD and liver fibrosis in an urban Chinese population

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Backgrounds: With societal development and lifestyle changes, metabolic associated fatty liver disease (MAFLD) becomes the most common chronic liver disease worldwide, affecting almost a quarter of the global population. This study aimed to investigate the prevalence and characteristics of MAFLD and liver fibrosis in China, and identify the risk factors for liver fibrosis in MAFLD patients.

Methods: Participants were enrolled from a physical examination center of The Third Hospital of Hebei Medical University from May 2019 to March 2023. General data, laboratory biochemical parameters and abdominal ultrasonography were explored. MAFLD diagnosis followed clinical practice guidelines. Hepatic fibrosis was assessed by the fibrosis-4 index score (FIB-4, significant fibrosis was defined as FIB-4 ≥ 1.3 . Binary logistic regression was used to determine the risk factors for significant fibrosis of MAFLD.

Results: A total of 22970 participants were included in the final analysis. The overall prevalence of MAFLD was 28.77%, of which 16.87% of MAFLD patients had significant fibrosis. Moreover, lean MAFLD patients had higher proportion of significant fibrosis than overweight participants. Multivariate logistic regression revealed male, overweight, hypertension, elevated liver enzymes, lipid and glucose indexes, and hypoalbuminemia were significantly associated with MAFLD, and the independent risk factors for significant fibrosis in MAFLD patients were male (OR=0.676, 95%CI 0.558-0.821; $P < 0.001$), HBsAg positivity (OR=2.611, 95%CI 1.557-4.379; $P < 0.001$), BMI $\geq 23\text{kg/m}^2$ (OR=0.632, 95%CI 0.470-0.851; $P = 0.002$), BP $\geq 130/85\text{ mmHg}$ (OR=1.885, 95%CI 1.564-2.272; $P < 0.001$).

Conclusions: Approximately 16% of MAFLD patients has significant liver fibrosis, and varies among BMI, ages, genders, and metabolic status.

Abstract Submission No. 101076
O-0394

Validation of AGILE scores in Indian patients with NAFLD: interim analysis of the ICON-D study

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Background: AGILE-3+ and AGILE-4 are novel non-invasive tests for ruling-in advanced fibrosis and cirrhosis, respectively, with reduced grey-zone. They incorporate age, gender, AST, ALT, platelet count, diabetic status and liver stiffness measurement (LSM) on transient elastography.

Methods: In an on-going real-life study of ICON-D, interim data across 42 centres over 4 years (n=8043), data of all patients with liver-biopsy (n=381, 63.2% males, age:42(33-50)) were analysed to explore the diagnostic performance of AGILE-3+ and AGILE-4.

Results: Advanced fibrosis (F $\geq$ 3) and cirrhosis (F4) were present in 70 (18.3%) and 39 (9.97%) patients, respectively. AGILE-3+ showed good calibration (p=0.474 on Hosmer-Lemeshow test, 95 % CI of slope: 0.82-1.218, 95% CI of x-intercept: -0.05 to 0.04) with an AU-ROC of [(0.78(95% CI:0.74-0.82))] for F $\geq$ 3 which was significantly better than APRI, NFS and FIB-4 but not LSM. The proportion of patients falling in the grey zone with AGILE3+ (12.07%) was significantly less than APRI, FIB-4, NFS and LSM.

AGILE-4 showed good calibration (p=0.147 on Hosmer-Lemeshow test, 95 % CI of slope: 0.79 to 1.166, 95% CI of x-intercept: -0.041 to 0.028) with an AUROC of [0.81(95% CI:0.77 to 0.85)] for cirrhosis which was significantly better than APRI and NFS but not from FIB-4 or LSM. The proportion of patients falling in the grey zone with AGILE 4 (13.9%) was significantly less than with APRI, FIB-4, NFS and LSM.

Conclusion: The AGILE-3+ and AGILE 4 score showed AUROC for detecting advanced fibrosis and cirrhosis, and may help to decrease the grey zone.

Abstract Submission No. 101140
O-0395

Gut microflora composition in patients with non-alcoholic fatty liver disease

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Background and Aims: Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver and affects 25-30% of the population. Number of studies have indicated relationship between dysbiosis and NAFLD. Hence, the aim of this study was to analyze gut microbiota composition in NAFLD patients with possible examination of aggressive and protective factors, including small intestinal bacterial overgrowth existence and biochemical markers

Method: Study included 93 subjects diagnosed with NASH/NAFLD based on a fibro scan of the liver, ultrasound and biochemical tests. Stool sample examination was performed using Real time-PCR. Hydrogen breath test was performed to all patients

Results: The study's findings were as follows: A 55.1% correlation was found between NAFLD and SIBO in the gut microbiome.

The following bacteria were present: Firmicutes (46.3 $\pm$ 1.99), Actinobacteria (26.1 $\pm$ 18). Bacteroidetes and Firmicutes had a markedly negative connection (r = -0.89), as did the Bacteroidetes and Firmicutes/Bacteroidetes index (r = -0.74) and Bacteroidetes and Actinobacteria (r = -0.90). There was a significant association between the F/B index and ALT (r = 0.5) and triglycerides (r = 0.52). Also, middle-strong connection (r = 0.43) between the presence of SIBO and the growth of Firmicutes in NAFLD patients.

Conclusion: Increased Firmicutes and Actinobacteria are caused by decreased levels of Bacteroidetes, which raises triglycerides and ALTs in patients with NAFLD and is associated with SIBO. The F/B index may be a marker for the presence of NAFLD, while Bacteroidetes may act as potential inhibitors of NAFLD progression. Patients with NAFLD should be tested for SIBO.

Abstract Submission No. 101212
O-0396

COMPARISON OF FATTY LIVER INDEX WITH FIBROSCAN IN NON ALCOHOLIC FATTY LIVER DISEASE

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Background: Non-alcoholic fatty liver disease (NAFLD), is a global health issue. This study is to compare Fatty Liver index (FLI) values with Fibroscan in NAFLD.

METHODOLOGY: A cross-sectional study was done at gastroenterology clinics of Liaquat National Hospital, Karachi, Pakistan. Participants underwent laboratory assessments, abdominal ultrasound and Fibroscan. Those with history of alcohol intake and positive for hepatitis B and C were excluded.

RESULTS: Total 225 participants were studied (52.9%) were males. Median BMI and Waist Circumference were 29.8 kg/m² (IQR=26.9-34.2 kg/m²) and 103 cm (IQR=95-110 cm), respectively. Metabolic syndrome (MetS) was present in 139(61.8%). Mild Steatosis were not found among 11(4.9%) patients whereas severe steatosis was seen among 115 (51.1%) patients. Significant variations in BMI, Waist Circumference, GGT levels, and Triglyceride TG levels were identified when comparing individuals with Fatty Liver Index (FLI) scores below 30 and those exceeding 60. Similar variations were observed in relation to the frequency of MetS as FLI scores increased. The agreement between FLI and ultrasound observations was found to be (k=0.077, p=0.027), and the Spearman correlation analysis indicated a statistically significant but weak positive correlation (r=0.384, p<0.001). On the multivariable regression model, participants having diabetes, elevated SGPT levels and mild disease on ultrasound were associated with increased odds of severe steatosis.

CONCLUSION: FLI is a good predictor of frequency of MetS & NAFLD and correlates well with increasing steatosis score (CAP) on fibro scan which can be utilized as an effective screening tool at primary care level for early detecting of NAFLD.

Abstract Submission No. 101361
O-0397

CVI-2742 is a potential best-in-class second generation oral liver-targeted THR- β selective agonist

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Selective activation of thyroid hormone receptor-beta (THR- β) in liver tissue ameliorates MASH symptoms without causing cardiac abnormalities mediated by THR- α activation. We have discovered and developed CVI-2742 as an oral liver-targeted THR- β selective second generation agonist for MASH treatment. Our biochemical THR- β or THR- α /RXR heterodimeric assays demonstrate that CVI-2742 activates THR- β with an EC₅₀ of 8.4 nM and activates THR- α with an EC₅₀ of 507 nM, representing a β -selectivity of 65-fold. In vivo tissue partition studies in mouse and rat indicate that CVI-2742 is rapidly localized in the liver after oral administration with undetectable or neglectable levels in other tissues. In rat, CVI-2742 AUC₀₋₁ in liver is 68.2-fold of that in plasma. Importantly, CVI-2742 has demonstrated strong anti-steatosis and anti-fibrosis effects at an maximal effective dose of 0.5 mg/kg, translating into an predicted effective dose of 2 mg/day in MASH patients. Multiple dosing toxicity studies in rat demonstrate that CVI-2742 has a wide-safety window of 60-fold of efficacy dose. Therefore, combined all important features of this PCC compound including strong efficacy, high THR- β selectivity and ideal tissue partition we believe that CVI-2742 has a potential to be the best-in-class second generation THR- β agonist for MASH treatment.

Abstract Submission No. 101362
O-0398

Liver Stiffness with Magnetic Resonance Elastography in Indonesia and Metabolic Dysfunction

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Background: Metabolic Associated Fatty Liver Disease (MAFLD) is a problem in many countries around the world including Indonesia. Magnetic Resonance Elastography (MRE) is used to assess people with MAFLD particularly regarding fat accumulation and fibrosis. However, the data in Indonesia is still limited. We aim to describe the correlation between the baseline characteristics and liver stiffness of fatty liver patients in Indonesia.

Methods: This is a cross sectional retrospective study that included 46 patients with clinically diagnosed fatty liver who underwent MRE from 2021-2022. Data were collected from medical record and analyzed using Spearman's test and Mann-Whitney U test.

Results: The liver stiffness ranged from 1.45-7.80 kPa with a geometric mean and coefficient of variation of 3.26 and 40.6%, respectively. There was correlation between mean liver stiffness with age ($p = 0.047$, $r = 0.295$), fibrosis marker FIB-4 ($p < 0.001$, $r = 0.720$), and platelets ($p < 0.001$, $r = -0.559$). Hepatocellular damage is also correlated with liver stiffness (SGOT, $p < 0.001$, $r = 0.615$; GGT, $p = 0.002$, $r = 0.533$; ALP, $p = 0.002$, $r = 0.573$). Likewise, metabolic marker particularly regarding glucose control (HbA1c, $p = 0.015$, $r = 0.501$), and fat metabolism (total cholesterol levels, $p = 0.011$, $r = -0.519$) correlate with liver stiffness.

Conclusions: The liver stiffness in Indonesian fatty liver patients was correlated with age, liver fibrosis marker (FIB-4 score, platelets),

hepatocellular damage (SGOT, GGT, ALP) and metabolic dysfunction (HbA1c and total cholesterol). This may explain the relationship between liver damage and metabolic dysfunction.

Keywords: Liver Stiffness, Fatty Liver, Magnetic Resonance Elastography, Liver Fibrosis, Indonesia

Abstract Submission No. 101460
O-0399

Saga of an Outlier: Lean MASLD in Urban, Population of Karachi, Pakistan

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Background: Lean steatotic liver disease (MASLD) is unique where in the absence of obesity and unrecognized traditional risk factors, diagnosis is either delayed or even overlooked; hence resulting in compromised effectiveness or complete absence of required treatment. We aim to investigate the prevalence of lean-MASLD and to compare the clinical, and metabolic characteristics of lean and obese MASLD in an urban, adult population of Karachi, Pakistan.

Methods: This was a population-based cross-sectional study piggy-backed with a large community-based trial "Pakistan Diabetes Prevention Programme" conducted in collaboration with the University of Helsinki in "Karachi", Pakistan. Approximately 20,000 residents of Karachi were screened for diabetes using systematic sampling. Individuals aged 35-75 years, having Indian Diabetes Risk Score (IDRs) score ≥ 60 were enrolled. Ultrasound liver was performed by an experienced sonologist to identify hepatic steatosis. Anthropometric measurements and laboratory investigations were carried out. Lean-MASLD was defined if BMI was $< 25 \text{ Kg/m}^2$ and obese was defined if BMI is $\geq 25 \text{ Kg/m}^2$. The study was funded by IDF and URC, AKUH, Pakistan.

Result: Out of 1225 individuals 741 (60.5%) had MASLD. Lean-MASLD was found in 128 (17.2%). Comparing lean with obese MASLD higher proportion of males, smaller waist circumferences, and lower ranges of metabolic factors were found in a lean group (table 1). The risk estimates for lean-MASLD were higher among smokers, subjects having larger waist circumference, HTN, elevated LDL, and ALT (Table 2).

Conclusion: Lean MASLD is common in the South Asian urban community of Pakistan. In the absence of significant metabolic derangements, early detection of lean-MASLD is challenging.

Abstract Submission No. 101465
O-0400

Sequential use of LSM and AGILE 3+ for assessing cACLD: Indian Consortium on NAFLD (ICON-D) study

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Background: Despite high sensitivity, LSM has relatively lower specificity and is more suited to ruling-out cALD ($F \geq 3$). AGILE 3+ is a novel LSM-based score, specifically designed to have high specificity for detecting $F \geq 3$ with a reduced grey-zone. We compared the diagnostic performance of combination of sequential LSM followed by AGILE 3+ with either of the methods alone.

Methods: In this on-going real-life study, covering 42 centres over 4 years ($n=8043$), data of all patients with liver-biopsy ($n=381$, 63.2% males, age:42(33-50) were analysed. LSM cut-offs of <8 kPa and >12 kPa were used for ruling-out and ruling-in $F \geq 3$, respectively. Corresponding cut-offs for AGILE 3+ were <0.45 and >0.68 . Similar cut-offs were used in the combined sequential approach where AGILE 3+ was applied when $F \geq 3$ was not ruled-out on LSM.

Results: $F \geq 3$ was present in 70 (18.3%) patients. AUROCs of AGILE-3+ and LSM were comparable (0.787 vs 0.782, $p=0.788$). Specificity of rule-in cut-offs of LSM (87.4%) and AGILE 3+ (88.4%), and sensitivity of rule-out cut-off of LSM (84%) were acceptable. However, sensitivity of rule-out cut-off of AGILE 3+ was suboptimal (70%). Proportion of patients in the grey-zone with LSM (29.9%) was significantly higher than with AGILE3+ (12.07%, $p<0.001$). The combined sequential approach had a sensitivity of 80% for rule-out zone and a specificity of 89.4% for rule-in zone. The grey-zone (9.1%) was comparable to AGILE 3+ alone ($p=0.196$) and significantly lower than LSM ($p<0.001$).

Conclusion: Sequential use of LSM followed by AGILE 3+ optimizes use of VCTE as a point-of-care tool for assessing cACLD.

Abstract Submission No. 101475
O-0401

Sequential use of LSM and AGILE 4 for assessing cirrhosis: Indian Consortium on NAFLD (ICON-D) study

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Background: Despite high sensitivity, LSM has relatively lower specificity and is more suited to ruling out cirrhosis. AGILE 4 is a novel LSM-based score, specifically designed to have high specificity for detecting cirrhosis with a reduced grey zone. We compared the diagnostic performance of combination of sequential LSM followed by AGILE 4 with either of the methods alone.

Methods: In this ongoing real-life study, covering 42 centers over 4 years ($n=8043$), data of all patients with liver-biopsy ($n=381$, 63.2% males, age:42(33-50) were analysed. LSM cut-offs of <8.3 kPa and >16.1 kPa were used for ruling-out and ruling-in cirrhosis, respectively. Corresponding cut-offs for AGILE 4 were <0.251 and >0.565 . Similar cut-offs were used in the combined sequential approach where AGILE 4 was applied when cirrhosis was not ruled-out on LSM.

Results: F4 was present in 39 (9.97%) patients. AUROCs of AGILE-4 and LSM were comparable [0.82 vs 0.80, $p=0.51$]. Specificity of rule-in cut-offs of LSM (91.4%) and AGILE 4 (94.7%), and sensitivity

of rule-out cut-off of LSM (84%) were acceptable. However, sensitivity of rule-out cut-off of AGILE 4 was suboptimal (69.2%). Proportion of patients in the grey-zone with LSM (34.9%) was significantly higher than with AGILE4 (14.2%, $p<0.001$). The combined sequential approach had a sensitivity of 81.8% for rule-out zone and a specificity of 95% for rule-in zone. The grey-zone (12.5%) was comparable to AGILE 4 alone ($p=0.52$) and significantly lower than LSM ($p<0.001$). **Conclusion:** Sequential use of LSM followed by AGILE 4 optimizes use of VCTE as a point-of-care tool for assessing cirrhosis

Abstract Submission No. 101492
O-0402

Point-of-Care Non-invasive Prediction Model for Steatotic Liver Disease: Using Bioimpedance Analysis

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Background/Aim: A simple and non-invasive screening method is needed to detect hidden SLD patients, especially among young adults and those with limited healthcare access due to socioeconomic factors. In this study, we aim to provide a more accessible and convenient SLD prediction model without conventional hospital laboratory infrastructure, facilitating early detection and timely intervention.

Methods: We retrospectively analyzed 28,506 adults at healthcare center in South Korea for a routine check-up. Participants' alcohol intake was assessed via a health questionnaire and their body composition measured using bioimpedance analysis. To analyze the data and make predictions, a logistic regression model was developed using machine learning algorithms.

Results: A total of 20,094 subjects were categorized into non-SLD and SLD groups based on the presence of fatty liver. SLD model 1 was based on age and BMI, SLD model 2 was derived from age, BMI, and body fat mass per muscle mass, and SLD model 3 consisted of age, BMI, and visceral fat mass per muscle mass. In the derivation cohort, the AUROC was 0.817 in the SLD model 1, 0.821 in the SLD model 2, and 0.820 in the SLD model 3. In the validation cohort, at the optimal upper and lower cutoff values, 86.8%, 86.9%, and 87.1% of subjects were correctly classified in SLD model 1, SLD model 2, and SLD model 3, respectively.

Conclusion: The three derived SLD models could be novel, validated clinical tools for mass screening of SLD.

Abstract Submission No. 101493
O-0403

Frequency of MASLD and cACLD among Adults with Steatotic Liver Disease

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Background and Objectives: Diagnostic criteria for metabolic steatotic liver disease (MASLD) have been proposed but not validated. We investigated the clinical application of the MASLD definition by

assessing the characteristics of its subclassifications and the associated risk of compensated advanced chronic liver disease (cACLD).

Methods: A total of 1319 outpatients with imaging or biopsy-proven hepatic steatosis, systematically screened for cardiometabolic criteria, underwent transient hepatic elastography (TE) and were enrolled. Liver stiffness ≥ 10 kPa was considered suggestive of cACLD.

Results: In the present investigation, 96.6% of SLD individuals in the current research had at least one cardiometabolic risk factor, of which 36.9% had MASLD, 46.2% VSLD (MASLD + viral hepatitis), 4.02% MetALD (MASLD + significant alcohol consumption), 2.05% ALD, and 0.76% cryptogenic SLD. 97.99% of patients with NAFLD met MASLD criteria. The possible presence of cACLD was detected in 11.7% (57/487), 25.89% (80/309) and 35.8% (19/53) of those with MASLD, VSLD with SVR and MetALD, respectively. Most importantly, metabolic dysfunction was found in over 97% (229/235) of these SLD adults with cACLD. Type 2 diabetes, older age, having a higher BMI and AST were all revealed to be independent risk factors for cACLD in MASLD patients. Patients with VSLD (with SVR) who had lower PLT counts and higher AST levels were more likely to have cACLD.

Conclusions: Metabolic dysfunction was observed in most of SLD patients in China. More than half of them had viral hepatitis with viral suppression and a significant percentage of cACLD.

Abstract Submission No. 101501

O-0404

Different minimal alcohol consumption in male and female individuals with MAFLD

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Background & aims: The relationship between moderate alcohol intake and health outcomes among individuals with Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD) is complex. Our aim was to investigate the association of minimal alcohol consumption with all-cause and cause-specific mortality among MAFLD individuals of different genders.

Methods: Our study included 2630 MAFLD individuals from the Third National Health and Nutrition Examination Survey (NHANES III). Cox regression analysis was performed to assess the association between alcohol use measures and all-cause and cause-specific mortality. Restricted cubic spline curves were used to evaluate the relationship between alcohol consumption per week and all-cause mortality.

Results: In the entire MAFLD cohort, we observed significant disparities in clinical characteristics between male and female individuals with MAFLD. Higher weekly alcohol consumption was significantly associated with all-cause and cause-specific mortality (male, HRs: 1.009, 95% CIs: 1.004-1.014; female, HRs: 1.032, 95% CIs: 1.022-1.042). In males with MAFLD, a linear association with all-cause mortality was observed for weekly alcohol consumption (P for Non-linearity = 0.21). Conversely, in females with MAFLD, the risk of all-cause mortality remained relatively stable until 2 drinks per week, after

which it rapidly increased with each additional drink consumed, and the increase in mortality risk was higher than that observed in males (P for Non-linearity <0.05).

Conclusions: Our findings indicate that any increase in weekly alcohol consumption was associated with increased all-cause mortality in men with MAFLD. Conversely, consuming less than 2 drinks per week had minimal impact on the risk of mortality among female.

Abstract Submission No. 101501

O-0405

Anomogram to predict severity of hepaticfibrosis by noninvasive-markers&treatment allocation inMAFLD

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Background&Aims: Obesity&associated comorbidities are reaching pandemic proportions worldwide.NonAlcoholic liver disease is hepatic component of this metabolic syndrome&has been recognized as leading etiology for HCC&a large societal&health problem.Aim of this study is to evaluate hepatic fibrosis stage in MAFLD by non-invasive markers as well as outcomes of patients undergoing treatment respectively,focusing on improvement of fibrosis stage of liver

Method: Patients were pooled prospectively on a Questionnaire.Demographic data like age,sex,comorbidities like HTN,DM,ischemic heart disease,PCOs disease in females.Laboratory findings were included like Complete blood picture, LFTs, HbA1c, TSH, Cr, serum albumin, &fasting lipid profile.Baseline Ultrasonography of abdomen&Fibroscan were part of scanning records.This nomogram map predicts the predicted probability of severity of hepatic fibrosis in MAFLD patients.For each covariate,record the value& notedown corresponding points.This is repeated for each covariate ending total score that corresponds to the severity of hepatic fibrosis.For females total score can count upto 31&for male 30 respectively.New MAFLD diagnostic pathways with use of this nomogram were modelled to diagnose&treat respectively.

Results: 100 patients were enrolled with suspected MAFLD.By using non invasive markers available in different studies to predict fibrosis stage it can be concluded that treatment can be allocated to patients depending on these scores safely so Prediction in these patients was optimised by stratifying patients into three categories based on scores(≤ 7 ,7-24& ≥ 25). Multivariable logistic regression analyses revealed that DM,central obesity,&increased cholesterol levels were independent risk factors for mortality after liver transplant.The receiver operating characteristic curve of nomogram prediction model was0.896(96%CI,0.803-0.989),&mean absolute error of internal validation by bootstrap (1000replications) was0.019 (n=184).These results showed that nomogram model had an excellent prediction accuracy.

Conclusion: A nomogram model can provide clinicians to accurately predict severity of hepatic fibrosis by noninvasive markers&treatment allocation in MAFLD patients

Abstract Submission No. 101512

O-0406

Vitamin intake and the progression of metabolic dysfunction-associated fatty liver disease

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Introduction: Few studies explored the association between vitamin intake and metabolic dysfunction-associated fatty liver disease (MAFLD). Moreover, the existing results were contradictory. We aimed to investigate the association between dietary vitamins and all-cause mortality as well as fibrosis risk in patients with MAFLD in US.

Methods: We extracted data from the third National Health and Nutrition Examination Surveys 1988-1994. Dietary vitamins was assessed using a 24 h diet recall, including vitamin A, vitamin B6, vitamin B12, vitamin C, vitamin D, thiamin, riboflavin, folic acid and α -tocopherol. The non-alcoholic fatty liver disease fibrosis score (NFS) <1.455 is considered as non-advanced fibrosis, while NFS ≥ 1.455 is considered as advanced fibrosis.

Results: A total of 3844 MAFLD participants were included in this study. The median time of follow-up was 310 months. 1739 participants (45.3%) were deceased during the follow-up. The intake of thiamin, riboflavin, α -tocopherol, VB6, and VB12 were significantly higher in patients with NFS-determined non-advanced fibrosis ($P<0.05$). After adjusting, a significantly lower risk of fibrosis was found in patients with the highest quartile ($>11.5\text{mg/d}$) of α -tocopherol intake compared to the lowest intake group ($P<0.05$). Compared to the lowest quartile group, the risk of mortality was reduced by 0.34 folds in the group consuming the highest quartile amount ($>130\text{ mg/d}$) of VC (HRs: 0.66, 95% CIs: 0.51-0.85, $P=0.002$).

Conclusions: More α -tocopherol intake reduced fibrosis grade in MAFLD patients. VC intake may reduce all-cause mortality in patients with MAFLD in US.

Abstract Submission No. 101513
O-0407

Daily water intake is protective against liver fibrosis in MAFLD

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Background and objectives: Metabolic dysfunction-associated fatty liver disease (MAFLD) refers to liver steatosis caused by metabolic abnormalities. Water is involved in many metabolic processes. This study aimed to explore whether total daily water intake affected the liver fibrosis in MAFLD.

Patients and Methods: We extracted data from the database of the third National Health and Nutrition Examination Surveys 1988-1994 (NHANES III). The amount of water intake was assessed using a 24 h diet recall by trained interviewers. Fibrosis-4 (FIB-4) score was calculated to evaluate liver fibrosis. Multivariate analysis was performed to explore the relationship between water intake and liver fibrosis.

Results: A total of 2863 MAFLD patients with FIB-4 scores were included in this study. There were 2744 cases in the FIB-4 <1.3 group, including 1323 males and 1451 females, and 89 cases in the FIB-4 >2.67 group, including 59 males and 30 females. Those in the FIB-4 >2.67 group had significantly lower daily water intake compared to the FIB-4 <1.3 group [2586 (1849, 3307) mL vs 3063 (2257, 4071) mL, $p<0.001$]. Further subgroup analysis revealed that when total water intake reached the third (3004-4019 mL) and fourth (>4020 mL) quartile, it became a significant protective factor against liver fibrosis in those without diabetes [T3 vs. T1, 0.207 (0.085, 0.501), $p<0.001$; T4 vs. T1, 0.085 (0.028, 0.262), $p<0.001$] and those BMI ≥ 25 [T3 vs. T1,

0.286 (0.121, 0.677), $p=0.004$; T4 vs. T1, 0.424 (0.203, 0.886), $p=0.023$].

Conclusions: Daily total water intake of 3000 ml or more was a protective factor for liver fibrosis in MAFLD patients, especially for those in non-diabetic populations and BMI ≥ 25 .

Abstract Submission No. 101558
O-0408

Impact of dietary intervention in reversal of fibrosis in Metabolic Associated Fatty Liver Disease

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Background-obesity, diet and MAFLD are closely associated. However, Impact of diet in reversal of fibrosis needs validation. This study aims to study dietary treatment as a therapy in management of reversal of fibrosis in MAFLD.

Method- Out of 768 elastography performed from June 2022 to June 2023, Fifty Metabolic Associated Fatty Liver Disease (MAFLD) patients with Severe steatosis and F3 or F4 fibrosis, were enrolled in the study. Age group was in range of 18 to 70 years with 25 Males and 25 Females. No patient had transaminitis. Dietary intervention in form of 6 feeds per day, low calorie diet; approximately 1500 Kilocalories per day was advised. No medication was prescribed to these patients.

Results- At the end of 3 months 47 patients were non-compliant to this dietary change. Only 3 patients followed this dietary advise. Weight loss of 5 kg or more was noted in all these 3 patients. Repeat elastography at end of 3 months demonstrated F0 fibrosis and no steatosis in all these 3 male patients.

Conclusion- Dietary intervention can completely reverse fibrosis and steatosis in patient with MAFLD; however, patient compliance to change the dietary pattern is very poor (6%). So, drugs like saroglitazone to be considered in all patients with MAFLD and F3/F4 fibrosis.

Abstract Submission No. 101637
O-0409

Metabolic-associated fatty liver disease (MAFLD) and its metrics for contributions to liver research

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Background: The international consensus to rename non-alcoholic fatty liver disease to metabolic (dysfunction)-associated fatty liver disease (MAFLD) in 2020 has been gained significant worldwide attention. The impact of the term MAFLD on the research community however has not been objectively assessed. We conducted a comprehensive survey of literature on MAFLD to understand the current trends in the research topic and country-level contributions.

Methods: We used PubMed, Scopus, and Web of Science to collect publications (articles, reviews, and editorials) written in English, published from 2020 to 10/10/2023 containing MAFLD or its fully spelled term in the titles or abstracts. Publication metrics, including numbers, publishing journals, author countries, author keywords, and cited times were analysed.

Results: 1470 MAFLD-related publications were published in 435 journals, with a steady increase in the numbers since 2020. Among the 97 countries and territories authoring the publications, China, followed

by Italy, USA, and Australia produced the greatest numbers of MAFLD publications. Country co-occurrence network analysis of 328 publications from multiple countries showed global and regional cross-country collaborations between 96 countries. Common topics from the highly cited publications were the MAFLD definition and the consequences resulting from the change in nomenclature. Apart from the terms describing fatty liver disease and its complications, top author keywords were enriched in those related to metabolic dysfunction, including obesity, metabolic syndrome, diabetes mellitus, and cardiovascular disease.

Conclusion: This survey provides a quantitative measure of the considerable international contribution of MAFLD to research with a focus on its relationship to metabolic dysfunction.

Abstract Submission No. 101649

O-0410

Factors predicting the future incidence of fatty liver: A single-center study

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Background: Identifying a population that requires special attention to prevent the development of fatty liver may contribute to the control of future complications.

Methods: We enrolled health-checkup participants without fatty liver on their first visit and performed logistic regression analyses to determine the association between various items and the incidence of fatty liver on their second visit.

Results: After a median follow-up period of 367 days, 278 out of 3,343 individuals (8.3%) had newly developed fatty liver. Body mass index (BMI; odds ratio, 1.196 per 1 increase; 95% confidence interval, 1.098-1.303), triglycerides (1.004 per 1 mg/dl increase, 1.001-1.007), γ -glutamyltransferase (GGT; 1.003 per 1 U/l increase, 1.001-1.007), low-density lipoprotein cholesterol (LDL-C; 1.023 per 1 mg/dl increase, 1.002-1.044), albumin (2.140 per 1 g/dl increase, 1.243-3.694), and platelet count (1.028 per 10,000/ μ l increase, 1.002-1.055) were independently associated with the incidence of fatty liver. ROC analysis revealed cutoffs of 22.1 for BMI (area under the curve, 0.726), 102 mg/dl for triglycerides (0.666), 19 U/l for GGT (0.648), 112 mg/dl for LDL-C (0.579), 4.5 g/dl for albumin (0.559), and 217,000/ μ l (0.555) for platelet count, with high values for any of these items indicating a risk of fatty liver. When 1 point was given for each item exceeding the cutoff value, the incidence of fatty liver exceeded 20% in those with a total score of 5-6, whereas it was less than 1% in those with 0-1 point.

Conclusions: Elevated BMI, triglycerides, GGT, LDL-C, albumin, and platelet counts may predict fatty liver development at one year.

Abstract Submission No. 101651

O-0411

The Association between Non-Alcoholic Fatty Liver Disease and Risk of Chronic Kidney Disease.

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is a spectrum of disorders ranging from hepatic steatosis to nonalcoholic steatohepatitis (NASH), NASH related cirrhosis and hepatocellular carcinoma (HCC). There is sparse data on the prevalence CKD in Egyptian patients with (NAFLD). Aim of the work: To estimate the prevalence of CKD in individuals with and without NAFLD. Patients and methods: a cross-sectional study was conducted on 430 patients from the Internal Medicine Department, Menoufia University Hospitals, including 215 patients with NAFLD, and 215 patients without NAFLD. NAFLD was diagnosed by abdominal ultrasonography. The liver fibrosis was assessed by NAFLD fibrosis score (NFS) and fibrosis-4 index (FIB-4). CKD was defined as an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m² and/or abnormal albuminuria (urinary albumin-to-creatinine ratio $\geq$ 30 mg/gm). The logistic regression analysis was performed to examine the association between NAFLD and risk of CKD.

Results: The prevalence of CKD was higher in individuals with NAFLD than in those without NAFLD (38.1 % vs 7.4 %, $p < 0.001$). Logistic regression analysis demonstrated that both NAFLD and CKD were risk factors of each other. The presence of hypertension, and the high levels of BMI and waist circumference were the other independent risk factors of NAFLD. While the presence of DM, and the high level of BMI were the other significant risk factors of CKD in the NAFLD group.

Conclusion: The presence and severity of NAFLD are associated with an increased risk and severity of CKD.

Abstract Submission No. 101654

O-0412

NASH complicating with T2DM can be well controlled by hepcidin inducer Laennec derived from Placenta

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Background: Recently it was elucidated that hepcidin, the principal regulator of iron metabolism, could express in pancreatic β -cells, of which level could be regulated by iron. This fact means that the pancreas also may contribute to the iron metabolism. In the cases of NASH complicating with T2DM, remarkable declines of serum ferritin and HbA1c were observed after treating with Laennec[®] ('hepcidin inducer' derived from placenta). Then, we examined whether Laennec[®] could restore the pathological background of NASH through regulating iron metabolism.

Methods: We divided 114 NASH cases (all complicating with T2DM, liver biopsied) into two groups retrospectively. Laennec[®]-treated 83 cases were treated with the infusion of 2 ampoules (224mg) of Laennec[®] 1-2 times/W, in addition to the ordinary liver supporting. Serum ferritin, ALT and HbA1c were measured, and liver re-biopsy was carried out to evaluate changes of iron deposition in 21 cases of NASH patients.

Results: By infusing Laennec[®], serum ferritin level declined from 282.3 $\pm$ 216.5 ng/ml (before medication) to 62.6 $\pm$ 51.8 (after) (Wilcoxon $P < 0.01$) in NASH patients. Serum ALT also declined from 61.4 $\pm$ 24.2 U/L to 29.6 $\pm$ 16.3 ($P < 0.001$). HbA1c level improved from 6.6 $\pm$ 1.1% to 5.7 $\pm$ 0.8 ($P < 0.01$). When compared these results in two groups, the changes observed in Laennec[®]-treated group were significantly larger than non-treated group (Mann-Whitney $P < 0.05$). In multiplex-logistic analysis, the improvement of iron deposition in the liver correlate significantly with the decline of serum ferritin ($P < 0.01$).

Conclusions: The improvement of NASH complicating with T2DM by the administration with Laennec® suggests the importance of iron regulation on refractory T2DM which shows the presence of hyperferritinemia.

Abstract Submission No. 101666
O-0413

The Role of Multiparametric US in Evaluating Advanced Fibrosis in Patients with MASLD

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Purpose: Liver fibrosis is a major prognostic factor in metabolic dysfunction-associated steatotic liver disease (MASLD), and there is a need for a non-invasive and highly accurate tool to assess advanced fibrosis. In this study, we aimed to develop a highly accurate model for identifying MASLD patients with advanced fibrosis using multiparametric ultrasound (US).

Materials and Methods: This prospective global multicenter study collected data from seven sites, including 65 biopsy-proven MASLD patients. Five US markers (shear-wave speed [SWS] in m/s, dispersion slope [DS] in (m/sec)/kHz, attenuation coefficient [AC] in dB/cm/MHz, normalized local variance [NLV], and the echo intensity ratio of liver to kidney [L/K ratio]) were measured using a 2D SWE system immediately before biopsy. The biopsy specimens were scored by expert pathologists from one site. Diagnostic performance was assessed using the area under the receiver operating characteristic curve (AUC) for identifying advanced fibrosis (fibrosis stage $\geq$ F3), and the best-fit multivariable logistic regression model for identifying patients with advanced fibrosis was determined.

Results: Sixty-five adults (mean age: 53 years $\pm$ 16 [standard deviation], 32 men) underwent a US examination. Among the five US markers, SWS and NLV enabled the appropriate identification of advanced fibrosis, with an AUC of 0.89 (95% CI: 0.80, 0.99) and 0.81 (95% CI: 0.67, 0.95), respectively. Performance of the combination of SWS and NLV was satisfactory, with an AUC of 0.91 (95% CI: 0.81, 1.00).

Conclusion: The combination of SWS and NLV improved the diagnostic performance of identifying MASLD patients with advanced fibrosis compared to SWS alone.

Abstract Submission No. 101676
O-0414

"Cryptogenic liver cirrhosis: the key role of metabolic-associated fatty disease NAFLD."

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is currently the leading cause of chronic liver disease worldwide and is projected to become the main cause of cirrhosis requiring liver transplantation in the next decade.

Case Description: Patient S., 56 years old, complains of aching pains in the epigastrium and right hypochondrium, bloating, unstable stool and increased fatigue. In the anamnesis there are no indications of

alcohol abuse, the use of hepatotoxic drugs, burdened heredity. On examination - a patient of the correct physique, BMI - 41 kg / m², waist circumference - 120 cm. On palpation - the abdomen is enlarged due to ascites, moderate soreness in the right hypochondrium and epigastric region, the lower edge of the liver is 3 cm lower than the right costal edge, the liver is dense and sensitive on palpation. Laboratory examination: hemoglobin - 140 g / l, leukocytes - 8.4 · 10⁹ / l, platelets - 179 · 10⁹ / l, SOE - 12 mm/hour. Biochemical blood test: total bilirubin - 22 mmol/L, thymol sample - 7.5 units, ALT - 80 units/l, AST - 60 units/l, GGTP - 48 IU/L, alkaline phosphatase - 70 IU/l, total cholesterol - 7.08 mmol/l, triglycerides - 2.85 mmol/l, HDL - 1.07 mmol/l, LDL - 5.89 mmol/l, VLDL - 1.31 mmol/l, glucose - 5.2 mmol/L. Serum cancer markers: AFP, CA 19-9 - within normal limits. According to ultrasound: Moderate ascites. Hepatomegaly. Diffuse changes in the pancreatic parenchyma. Echo signs of pronounced diffuse changes in liver parenchyma by type of fatty infiltration and cirrhotic changes.

Abstract Submission No. 101703
O-0415

Higher Incidence of DM in Healthy Fatty Liver Patient of Bangladesh: Prompt Intervention Can Avert Complication

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Background: Lifestyle changes and urbanization is progressively increasing the number of diabetic patients globally & in South-Asian countries. DM associated health complications threaten to reduce economic gains in third world country like Bangladesh.

Methods: This cross-sectional study was conducted in Sheikh Hasina medical college, Tangail, Bangladesh from August 2022 to February 2023. A total of 92 patients with ultrasonological evidence of grade II fatty change in liver were included and evaluated. Known DM, Hypothyroidism, Alcohol abuse, HBV, HCV, Wilsons Diseases, autoimmune liver disease, hemochromatosis and any other chronic liver disease patients were excluded. Then patients were assessed for presence and absence of DM using OGTT or HbA1c as diagnostic criteria.

Results: Out of 92 patients, male was 48 and female 44. A total of 50 patients (54.3%) were newly diagnosed as DM. No significant differences were evident in DM group and non-DM group in respect to Mean age (41 years versus 38), ALT values (58.9 IU versus 60.23), AST (50.33 IU versus 36.53), TG (270 mg/dl versus 189), BMI (28.85 versus 29.29).

Conclusions: Recent study states, more than 54% of patients with grade II fatty liver were newly diagnosed with DM. If not evaluated early, they will come later with more advanced DM and related complications. Although a larger study is needed, physicians and healthcare workers in Bangladesh should be more concerned about treating such metabolic dysfunction-associated steatotic liver disease (MASLD) patients with early diagnosis of DM, prompt lifestyle interventions, and prescribing drugs if needed.

Keywords: Diabetes, Fatty liver, Intervention, MASLD.

Abstract Submission No. 101735
O-0416

Modeling Disease Burden of Adolescent NAFLD and NASH Based on Body Mass Index

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Background: Currently, there is a lack of global or even country/regional level data on adolescent non-alcoholic fatty liver disease (NAFLD) prevalence. However, evidenced dose-dependent relationship exists between body mass index (BMI) and the risk of NAFLD. We aim to estimate the global and regional prevalence of adolescent NAFLD and related non-alcoholic steatohepatitis (NASH) based on BMI.

Methods: Sigmoidal fitting curves were generated between BMI and the risk of NAFLD/NASH using the data extracted from the NHANES database. With the aid of global and regional BMI data from the NCD-RisC database, adolescent NAFLD/NASH prevalence was estimated at the global, regional, and country levels from 1975 to 2016. The prevalence of adolescent NAFLD/NASH from 2017 to 2030 was also forecasted.

Results: The average NAFLD prevalence was 15.31%, and 12.68%, while the average NASH prevalence was 2.50%, and 2.47%, in boys, and girls aged 12-18, respectively. For both boys and girls, NAFLD/NASH prevalence increased with increasing BMI, and age. The global prevalence of adolescent NAFLD/NASH has gradually increased in the period from 1975 to 2016 and would maintain a similar trend between 2017 and 2030. High-income Western Countries had higher adolescent NAFLD/NASH whereas South Asia, and Sub-Saharan Africa exhibited relatively lower adolescent NAFLD/NASH prevalence.

Conclusion: The adolescent NAFLD/NASH prevalence increase year by year, and its burden varies significantly among different countries and regions. BMI is a precise predictor of NAFLD/NASH prevalence.

Abstract Submission No. 101765

O-0417

Correlation Between CAP Value and SYNTAX Score in Patient with Coronary Artery Disease (CAD)

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Background: Hepatic steatosis is an established risk factor for chronic liver disease (CLD), with cardiac-related mortality especially CAD serves as major cause of death. We aim to determine the correlation between hepatic steatosis and CAD burden.

Methods: Patients who underwent coronary angiography at Cipto Mangunkusumo Hospital catheterization laboratory from August 2022 to October 2023 with proven significant coronary occlusion were included in the study. Subsequent SYNTAX score was calculated. Liver elastography was used to assess hepatic steatosis and obtain CAP values. Patients with significant alcohol intake, viral hepatitis, HIV, other liver disease, ascites, pregnancy, and steatosis-inducing medication were excluded. All patients were subjected to clinical assessment and serum metabolic examinations.

Results: A total of 124 patients were enrolled, comprising 83.9% males, 55.6% smokers, 94.4% hypertensive, 55.6% diabetics, and 54.8% obese patients. Mean age was 59.8 years ($\sigma = 11.1$). Mean HDL-C was 38.8 mg/dL ($\sigma = 10.8$), median LDL-C and TG were 109.5 and 118.5 mg/dL respectively. 84.7% patients had multiple-vessel CAD, with median SYNTAX score 22. 52.5% patients had significant steatosis, with mean CAP 256.5 dB/m ($\sigma = 47.3$). Adjusted for confounders, a significant positive correlation between CAP and SYNTAX score was observed ($r = 0.372$, $p < 0.0001$).

Conclusions: This study suggests that hepatic steatosis correlates significantly with CAD burden. Early hepatic steatosis assessment is paramount to diminish the risk of developing CLD and its cardiac-related mortality.

Abstract Submission No. 101777

O-0418

Correlations of liver steatosis and fibrosis with metabolic parameters in young-onset diabetes

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Background: Liver steatosis and fibrosis are markers used to evaluate Metabolic Associated Fatty Liver Disease (MAFLD) in diabetes. The aim of this study was to investigate the correlations between several metabolic parameters (including obesity, insulin resistance, dyslipidaemia, and hypertension) and liver steatosis and fibrosis.

Methods: A cross-sectional study was conducted on outpatients with young-onset diabetes at Cipto Mangunkusumo Hospital, Jakarta, Indonesia, during November-December 2022. Liver steatosis, estimated through Controlled Attenuation Parameters (CAP) score (dB/m), and liver fibrosis, evaluated through Liver Stiffness Measurement (LSM) / E - score (kPa), were assessed using Vibration-Controlled Transient Elastography (Echosens (R), France). The metabolic parameters, including Body Mass Index (BMI), glycated haemoglobin, lipid profile (HDL, LDL, and triglyceride), and blood pressure, were assessed using physical examination, anthropometric measurements, and laboratory tests. Pearson or Spearman rank correlation test was performed.

Results: Sixty-two patients were included, 69.4% of which were female, and the mean age was 33.63 years (95% CI : 31.88 - 35.38 years). The CAP score showed a moderate correlation with BMI ($R = 0.54$; $p < 0.01$), triglycerides ($R = 0.58$; $p < 0.01$), HDL ($R = -0.46$; $p < 0.01$). Concurrently, the LSM / E - score exhibited a moderate correlation with BMI ($R = 0.40$; $p < 0.01$) and HDL ($R = -0.41$; $p < 0.01$).

Conclusions: The degree of liver steatosis correlates moderately with an increase in BMI, elevated triglycerides, and decrease in HDL. Meanwhile, the degree of fibrosis correlates moderately with an increase in BMI and a decrease in HDL.

Abstract Submission No. 101784

O-0419

Efficacy of Saroglitazar in MASLD at 6 months, a single center observational study**Rajdeep Singh¹, Gunjan Baweja¹**¹J P Medical Centre Chandigarh India**Introduction:** Saroglitazar is the first ever drug approved in Non- Cirrhotic MASLD.**Methods:** A retrospective analysis was conducted at a North Indian single setting. A total 50 patients with documented ultrasonographic fatty liver changes and dyslipidemia who were prescribed Saroglitazar 4 mg once daily for at least 6 months from May 2022 to November 2022 were retrospectively included in this data analysis. Change in CAP, LSM, AST, ALT, TG, TC, LDL, HbA1c, from baseline to 6 months was analyzed using paired t- test.**Results:** The mean age of patients analyzed was 49.45 ±11.76. 58.0 % were males and mean body weight 80.07 ±10.66. The baseline and follow up of CAP, LSM, AST, ALT, TG, TC, LDL and HbA1c values are given in Table 1. A significant and consistent reduction on CAP, LSM, AST, ALT, TG, TC, LDL and HbA1c was observed. No new safety signals were observed.**Conclusion:** Saroglitazar 4 mg per day for 6 months has high efficacy in treating MASLD.**Table 1: Baseline and 6 months follow up for various parameters****HbA1c (%)LDL-C (mg/dl)TC (mg/dl)TG (mg/dl)AST (IU/dl)ALT (IU/dl)CAP (dB/m)LSM (Kpa)**

Baseline6.77156.50235.83273.0961.4467.222947.70

6 months6.35144.50203.33235.2740.1143.67269.936.54

Absolute reduction at 6

months0.4312.0032.5037.8221.3323.5624.071.17

p value0.0010.260.0090.0010.0020.0030.0010.001

Percentage reduction at the end of 6

months6.317.6713.7813.8534.7235.048.1915.14

* Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Body mass index (BMI), Controlled attenuation parameter (CAP), Liver Stiffness Measurement (LSM), Low-density lipoprotein (LDL), Total Cholesterol (TC), Triglycerides (TG)

Abstract Submission No. 101805

O-0420

Fibroscan compared to non-invasive scores in patients with non-alcoholic fatty liver disease**Priyansh Bhayani¹, Sarojini Parameswaran¹, Natarajan Murugan¹, Kallipatti Palaniswamy¹, Paramasivan Piramanayagam¹**¹Apollo Hospitals Chennai India**Background:** Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease of the twenty-first century, and is one of the leading indications for liver transplantation. In India, the prevalence of NAFLD in the general population varies from 9% to 53%. Liver biopsy is the gold standard for assessing the severity of liver fibrosis. However due to various difficulties involved with liver biopsy, it is imperative to identify different non-invasive tools that can replace liver biopsy.**Methods:** A prospective observational study of 130 patients meeting the inclusion criteria for NAFLD was done for a period of 18 months. The aim was to compare different non-invasive scores (FIB-4, NFS

and APRI) to Fibroscan and determine cut-offs to rule out advanced fibrosis.

Results: In the study, 76.9% of patients were males. Advanced fibrosis was seen in 12.3% of the patients. Majority of the patients with advanced fibrosis had metabolic syndrome and an abnormal glycemic status (p value <0.05). Based on the AUROC, the new cut-off for ruling out advanced fibrosis for FIB-4, NFS and APRI were 1.18, -0.9, 0.65. APRI had the best AUROC (0.768).**Conclusion:** Abnormal glycemic status and metabolic syndrome were risk factors for advanced fibrosis. The newly derived cut-offs for FIB-4 score, NFS score and APRI score had a better Negative predictive value compared to original cut-offs. The newly derived cut-offs should be evaluated in larger cohort to exclude patients with advanced fibrosis in the absence of Fibroscan in a resource limited setting in India.

Abstract Submission No. 101839

O-0421

Diagnostic accuracy of using Anthropometric indices as predictors of Patients with MAFLD**Bernard Johannes A. Jimeno¹, Harold P. Iturralde¹, Diana A. Payawal¹**¹FATIMA UNIVERSITY MEDICAL CENTER VALENZUELA Philippines**Background:** MAFLD is associated with cirrhosis and hepatocellular carcinoma. Waist-to-height Ratio (WHtR), Waist Circumference (WC), Waist-to-Hip Ratio (WHR), and Body Mass Index (BMI) are predictors of MAFLD. However, lack of consensus and ethnic heterogeneity has challenged their accuracy. Therefore, the need to validate the diagnostic capacity of these indices is needed. The objective is to determine the most accurate predictor in diagnosing MAFLD.**Methods:** This is a prospective cross-sectional study involving anthropometric measurement using Asian standards cutoffs, Asian Pacific Association for the Study of the Liver (APASL) MAFLD criteria. STATA 13.1 was used for data analysis.**Results:** Of the 459 patients, 221(48%) had MAFLD, while 238 (52%) had no MAFLD. Comparing them, WHtR identified 201 (91%) versus 199 (84%) (OR = 7.50, CI = 3.33-16.92, p=0.0001), WC identified 188 (85%) versus 158 (66%) (OR = 5.53, CI = 3.27-9.38, p=0.0045), WHR identified 130 (59%) versus 165 (69%) (OR = 0.87, CI = 0.59-1.27, p=0.1550), and Asian BMI identified 193 (87%) versus 133 (56%) (OR = 11.42, CI = 6.39-20.41, p=0.0004) MAFLD patients, respectively. Sensitivity and specificity analysis were: WHtR: 96.63%, 20.72%; WC: 90.38%, 37.05%; WHR: 62.5%, 34.26%; BMI: 92.79%, 47.01%. AUROC in predicting MAFLD showed WHtR (AUC=0.64, CI=0.59-0.69), WC (AUC=0.66, CI=0.59-0.69), WHR (AUC=0.49, CI=0.44-0.54), Asian BMI (AUC=0.71, CI=0.67-0.76).**Conclusion:** Among adults with MAFLD, WHtR is the most sensitive but non-specific predictor of MAFLD compared to WC, WHR, and BMI. However, AUROC shows the inability to discriminate the accuracy among diagnostic indices probably indicating different cutoff values for Asian standards.

Abstract Submission No. 101846

O-0422

Role of Anthropometric Indices in the Predicting of NAFLD in Rural Population of Bangladesh**Mohammad Hoque¹, Forhad Abedin², Mohammad Belelul Islam³, Mustafa Kamal Azad⁴**

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Background: Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide. The screening of general population for the presence of NAFLD with abdominal ultrasound is not a cost-effective approach. Alternative non-invasive methods for prediction of NAFLD are needed. We conducted this study to assess whether the anthropometric indices like BMI, weight circumference, weight - height ratio are useful for predicting NAFLD.

Method: This cross-sectional study was performed in a village of Cumilla District, Bangladesh during a period of 6-months. 219 subjects with NAFLD detected on ultrasonography and 100 healthy controls were included. Those who were agreed to participate in this study was made an appointment with the study team for history and physical examination - including anthropometric measurement and laboratory testing.

Result: Mean BMI 26.6 ± 5.53 and 22.28 ± 4.12 , waist circumference 94.1 ± 8.3 and 80.2 ± 10.3 , waist hip ratio 94.1 ± 8.3 and 88 ± 0.07 , waist height ratio 0.59 ± 0.07 and 0.48 ± 0.06 were in NAFLD and control group respectively. The AUROC values were 0.832 for BMI, 0.763 for waist circumference, 0.771 for waist/height ratio, and 0.772 for waist/hip ratio. The Cut-off values were 24.4 for BMI, 75.40 for waist circumference, 0.54 for the waist/height ratio and 0.93 waist/hip ratio. Sensitivity was 80.24% for BMI, 82.34% for waist circumference, 79.56% for the waist/height ratio and 72.3% for waist/hip ratio. Specificity was 79.12% for BMI, 80.45% for waist circumference, 78.98% for the waist/height ratio and 74.4% for the waist/hip ratio.

Conclusion: The simple anthropometric parameters, such as BMI, waist circumference, waist height ratio is useful for predicting NAFLD.

Abstract Submission No. 101863

O-0423

Addition of Resveratrol to Orlistat Improves Elastography Parameters in Overweight

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Objectives: Weight reduction improves hepatic steatosis and fibrosis. Orlistat, an approved therapy for weight management. Resveratrol, an antioxidant, may aid weight loss by enhancing energy expenditure through SIRT-1 activation.

Materials & Methods: 298 subjects aged >18 years with (BMI $\geq 25 \text{ kg/m}^2$) were randomized into two groups: The control arm (O) received orlistat 120 mg thrice daily, and the test arm (O-R) received orlistat 120 mg + resveratrol 100 mg thrice daily for 12 weeks. Patients were followed up for 12 weeks.

Results: 247 subjects with a mean body weight $\sim 80 \text{ kg}$ completed the study with more than 80% patients achieving > 5% weight loss and accompanied by improvement in elastography parameters in 12 weeks. As compared to baseline, the O-R group exhibited a higher weight loss of -3.31 kg ($p < 0.001$) compared to -2.92 kg ($p = 0.001$) in the O group. The mean CAP score at 12 weeks was significantly lower in the O-R group as compared to the O group (253.16 dB/m vs 276.82 dB/m , $P < 0.05$).

The fibrosis score was not found to be statistically significant (7.04 KPa vs 7.47 KPa).

Subgroup analysis revealed that obese patients with a steatosis stage between S1-S3 or fibrosis stage between F2-F4, exhibited significant weight loss with O-R as compared to O.

Overall, the AEs were low with diarrhea only reported in the O group (7 patients).

Conclusion: Addition of resveratrol to orlistat provides synergistic benefits to weight loss. Subgroup with steatosis &/or fibrosis exhibited superior weight loss with the addition of resveratrol.

Abstract Submission No. 101920

O-0424

Histological disparity Pertaining to Insulin Resistance in Nonalcoholic Fatty Liver Disease Patients

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Background & aim: Non-alcoholic fatty liver disease (NAFLD) describes a spectrum of clinicopathological changes in liver extending from simple steatosis through non-alcoholic steatohepatitis (NASH) to fibrosis which can progress to cirrhosis and hepatocellular carcinoma. It is thought to be hepatic manifestation of metabolic syndrome (MS) or insulin resistance (IR). The aim of the study was to compare the histological profile of Non-alcoholic fatty liver disease patients with and without IR.

Methods: 100 NAFLD patients who attended OPD of Hepatology, BSMMU, with USG findings of fatty liver and elevated ALT of $>30 \text{ U/L}$ in male and $>19 \text{ U/L}$ in female were enrolled. IR was calculated using the homeostatic model assessment (HOMA) method. They were divided into two groups based on IR (50 patients in HOMA IR > 2 , and 50 patients in HOMA IR ≤ 2). After thorough evaluation, liver biopsy was performed and comparison of the histological profile of NAFLD patients between both groups was done.

Results: Female was predominated (70.0%) in IR group. Histopathology revealed that lobular inflammation, ballooning and fibrosis were equally severe in two groups, only steatosis score was higher in IR group [2.0 ± 0.7 vs. 1.8 ± 0.8 ; $P = 0.007$]. Despite the absence of IR, proportion of patients with high grades of fibrosis (fibrosis score ≥ 2) were almost similar with patients with IR.

Conclusion: Histologically NAFLD without IR were equally severe with NAFLD with IR regarding ballooning, lobular inflammation and hepatic fibrosis except hepatic steatosis which was much more in patients of NAFLD with IR.

Abstract Submission No. 101931

O-0425

Metabolic-Associated Fatty Liver Disease (MAFLD) as a Risk Factor of Developing Malignant Arrhythmia

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Background: Metabolic-associated fatty liver disease (MAFLD) is an emerging driver of cardiac arrhythmias and recent studies have

investigated the relationship between MAFLD and several types of arrhythmia. However, there has been no meta-analysis to summarize the existing studies of the relationship between MAFLD and malignant arrhythmia yet. This study is aimed to determine whether MAFLD is a risk factor of malignant arrhythmia.

Methods: According to PRISMA guidelines, we systematically searched the PUBMED and EMBASE database through October 2023 to identify all studies reporting the incidence of ventricular arrhythmia, malignant PVC, and prolonged QTc among patients with and without MAFLD. Random-effect models were used to estimate pooled odds ratio (OR), and 95% confidence intervals (CI); subgroup analyses, meta-regressions, and sensitivity analyses were additionally performed.

Results: A total of 9 studies with 38,813 Individuals met the eligibility criteria and were included in the meta-analysis. MAFLD was associated with an increased risk of ventricular arrhythmia (OR: 2.09, 95% CI: 1.52-2.88), Prolonged-QTc (OR: 1.84, 95% CI: 1.57-2.15), malignant PVC (OR: 2.5, 95% CI: 1.67-3.73) and overall pooled odds ratio of 1.94 (95% confidence interval, 1.70—2.22). We identified significant subgroup differences according to geographical location, study design, and risk of bias. Meta-regressions identified mean age and study-level characteristics as potential moderators of the risk of malignant arrhythmia.

Conclusions: MAFLD is an independent risk factor for developing malignant arrhythmias in the future. Further studies are required to confirm this finding and to evaluate specific arrhythmia prevention strategies in patients with MAFLD.

Abstract Submission No. 101945

O-0426

Comparison between 2D-US DL steatosis algorithm with Fibroscan in histology proven patients

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Background: 2D-ultrasound is widely used in screening of liver diseases. A deep learning algorithm to quantify liver steatosis from 2D-ultrasound images may change a subjective steatosis diagnosis to an objective quantification. We evaluate a deep learning (DL) algorithm established in our previous work in patients receiving liver histology study.

Methods: Patients who received liver histology and Fibroscan studies between 2015 and 2023 were enrolled. 2D-ultrasound images and Fibroscan studies examined within one month of histology study were retrospectively collected. We classified images into four scanning views and applied the algorithm. Mean values from 3-5 images in each group were used for the results and correlated with histology steatosis grades.

Results: Totally 403 patients were included. Images from the right intercostal view (G2) were available in 370 patients. A cut-off system (0.58, 0.43 and 0.22) was established with histology grades as gold standard. This system was then applied to images from the left hepatic lobe (G1 view, N=272) and subcostal view (G4, N=191). The accuracy was between 0.824 to 0.878 from different views and steatosis grades. The area under receiver operating characteristic curve (AUROC) were between 0.910 and 0.945 among different histology steatosis grades. By multinomial logistic regression on histology steatosis grades, the

DL steatosis algorithm was significantly associated with steatosis grades and better performance than continue attenuation parameter, especially in higher steatosis grades.

Conclusion: The DL algorithm objectively quantified liver steatosis from retrospectively collected 2D-ultrasound images. The high AU-ROC and accuracy warrant clinical applications.

Abstract Submission No. 102000

O-0427

Metabolic dysfunction associated steatotic liver disease in a Cohort in Trivandrum India

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Introduction: Non alcoholic fatty liver has a major public health issue in Trivandrum. We are reporting the prevalence of metabolic dysfunction associated steatotic liver disease (MASLD) in the cohort

Methods: Between May 2022 to September 2023, a total of 2846 participants (aged 25 or more) were recruited to this cohort through multistage cluster sampling across the whole population of Trivandrum district within the

state of Kerala, South India. Using the recent criteria for MASLD, we analysed the data. Metabolic syndrome, demographic profiles, anthropometric measures and biochemical profile and ultrasound assessment of the liver and liver stiffness were evaluated

Results: MASLD prevalence was 65.8% (95% CI 64-67.52%). There were 874 males and 998 females. Mean age was 51.71 years. Median Stiffness of liver >10.2 was seen in 20.5% in MASLD compared to those without MASLD (13.2 : p<0.001). MASLD Odds ratios after adjusting for age, sex, domicile, BMI category (with normal weight as

baseline), diabetes and metabolic syndrome are :

Age (Ref- <50 years) Adj OR (95% CI) 1.23(1.1 - 1.46)

Gender (Ref- Female) Adj OR (95% CI) 2.14(1.63 - 2.47)

Domicile (Ref- Rural) Adj OR (95% CI) 1.2(0.99 - 1.45)

BMI- Normal

Under weight- Normal Adj OR (95% CI) 0.16(0.05 - 0.48)

Over weight Adj OR (95% CI) 2.2(1.56 - 2.77)

Obese Adj OR (95% CI) 3.76(2.93 - 4.89)

Diabetes Adj OR (95% CI) 1.77(1.41 - 2.19)

Metabolic syndrome Adj OR (95% CI) 1.57(1.23 - 1.98)

Conclusion: MASLD is prevalent in 66% of general population and the main risk factors are obesity, diabetes and metabolic syndrome. Proactive population based life style interventions are needed

Abstract Submission No. 102073

O-0428

Triglycerid-Glucose (TyG) Index as Novel Predictor of New Onset Atrial Fibrillation in MAFLD Patient

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Background: Metabolic-associated fatty liver disease (MAFLD) is related with atrial fibrillation (AF). The main cause of the high prevalence of AF in MAFLD patients is Insulin resistance (IR). The triglyceride-glucose index (TyG) is a novel IR surrogate marker to predict incidence and severity of MAFLD. However, the role of TyG in determining the risk for AF in MAFLD patients remains unclear.

Methods: According to PRISMA guidelines, we systematically searched the Pubmed and EMBASE through October 2023. Published observational studies evaluating the association between TyG-index and AF among MAFLD patients and reported the hazard ratio (HR) or odds ratio (OR) for this association after multivariate analysis were included. The primary outcome was AF incidence in MAFLD patients, correlated to TyG-index level. We pooled ORs and HRs with the corresponding 95% confidence intervals (CI) from random-effect models; subgroup analyses, meta-regressions, and sensitivity analyses were additionally performed.

Results: Total of 17 observational studies including 121,975 participants, were included. For studies analyzing the TyG-index as a categorical variable, both pooled OR (6.00, CI:4.12-8.74) and HR (1.70, CI:1.28-2.27) were significant for the association between TyG-index and incident AF. For studies analyzing the TyG-index as a continuous variable, pooled OR (2.25, CI:1.66-3.04) showed similar results. Consistent results were obtained in subgroup analyses according to the study design, sample size, ethnicity, and diabetic status.

Conclusions: TyG-index is an independent predictive tool to screen risk of AF in MAFLD patients. Therefore, patients with a high TyG-index should check for electrocardiogram and start intense lifestyle modifications.

Abstract Submission No. 200068
 O-0429

EFFICACY AND SAFETY OF A STANDARDIZED EXTRACT OF PRUNUS MUME IN PATIENTS WITH MAFLD

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Background and Aims: Extract of *Prunus mume* is a herbal variant and choline; a content of cell membrane have been reported to exert potentially therapeutic effect on various body conditions. Recently these two have been used in the treatment of Metabolic-associated fatty liver disease (MAFLD) but data is lacking in this regard in our region.

Patients and Methods: This was a prospective observational hospital-based study carried out on 200 patients diagnosed with Metabolic-associated fatty liver disease (MAFLD). Both males and females, aged ≥ 18 years, were included in this study. 100 patients were kept on lifestyle modification and 100 patients were administered a tablet Revolic® (*Prunus mume* 150mg and choline 82.5mg) per day and the levels of ALT, AST, Triglycerides, Gamma GT, and total cholesterol were measured at the start of the treatment and then after 12 and 24 weeks. SPSS version 26.0 was used for data entry and analysis.

Results: Our study participants, the majority were females (83%) then males (17%) with a mean and SD of age was 40.49 ± 10.59 years. At the end of treatment, a significant mean reduction of serum AST (5.21 ± 0.9), ALT (3.21 ± 1.42), GGT (3.88 ± 0.2), total bilirubin (0.6 ± 0.1), and weight (4.27 ± 2.34) was observed in patients receiving *Prunus Mume* and Choline as compare to patients put on lifestyle modification, p-value < 0.05 . The most common side effects were the

presence of gastrointestinal symptoms (12.74%) followed by headache (6.2%), anorexia (3.2%), and body aches (1.8%).

Conclusion: This study proves that *Prunus Mume* and Choline have beneficial effects on liver function tests in patients with MAFLD. Furthermore, this drug has a beneficial effect on better glycemic control and weight loss. The observed side effects in this study are minor, and this drug was observed to be safe in patients with MAFLD.

Keywords: *Prunus Mume* and Choline, MAFLD, Pakistan, lifestyle medication, side effects.

Abstract Submission No. 200071
 O-0430

Validation of non-invasive tools for an assessment of liver fibrosis in MAFLD patients with obesity

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Introduction: The role of non-invasive tests in the detection of liver fibrosis in obesity is controversial. We aimed to validate the performance of non-invasive tools evaluating liver fibrosis in obese MAFLD patients.

Methods: We retrospectively included 314 liver biopsy-proven MAFLD patients from the obesity clinic. Patients with BMI between 23-40 kg/m² and ≥ 40 kg/m² were classified as mild/moderate (n=159) and morbid obesity (n=155), respectively. Significant liver fibrosis was defined by METAVIR stage $\geq F2$ and correlated with each non-invasive score.

Results: There were 61 (38.4%) and 17 (11%) patients with mild/moderate and morbid obesity had advanced liver fibrosis. FIB-4 score and APRI score had good performance in detecting significant liver fibrosis with AUROC of 0.702 and 0.708 for mild/moderate obesity and 0.710 and 0.738 for morbid obesity, respectively. For mild/moderate obesity, APRI ≥ 1.5 and FIB-4 ≥ 2.67 had high positive predictive value (PPV) (83.3% and 75.0%) to rule in and APRI ≥ 0.3 and FIB-4 > 1.3 had high negative predictive value (NPV) (87.5% and 72.1%) to exclude significant liver fibrosis. For morbid obesity, none of the scores was sufficient to rule in significant fibrosis (PPV 9.3%-66.7%), oppositely all scores (FIB-4 > 1.3 , APRI ≥ 0.3 , NFS > -1.455 , BARD ≥ 2) had high NPV to exclude significant fibrosis (NPV 85.1%-93.3%). Regarding the new score, SAFE (steatosis-associated fibrosis estimator) score > 100 had unsatisfactory performance in detecting significant fibrosis but SAFE score < 0 was useful to rule out significant fibrosis.

Conclusions: FIB-4 and APRI scores were valid for liver fibrosis assessment in mild/moderate obesity, whereas current non-invasive scores had limited ability to detect liver fibrosis in morbid obesity. Further studies with a larger number of morbid obesity patients may be required.

Abstract Submission No. 200110
 O-0431

Clinical characteristics of non-obese patients with nonalcoholic fatty liver disease

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Background: We aimed to elucidate the clinical characteristics of non-obese patients with nonalcoholic fatty liver disease (NAFLD).

Methods: Fifty-seven NAFLD patients were enrolled in this study. Biochemical factors, body components and dietary nutrients were compared between obese and non-obese NAFLD patients at entry.

Results: Ten of the 34 (29%) males and eleven of the 23 (48%) females fulfilled the criteria of non-obesity, and six male patients and nine female patients were diagnosed as "hidden obesity". Serum uremic acid levels and skeletal muscle indexes (SMIs) were significantly lower, and LDL-cholesterol levels tended to be lower in non-obese male patients than those in obese males. Ages at entry were significantly higher, and SMIs and bone mineral density were significantly lower in female non-obese patients compared to those in obese females. Carbohydrate intake tended to be higher in female non-obese patients than that in obese females. However, there were no significant differences in serum ALT levels and FIB4-indexes between obese and non-obese patients in both male and female.

Conclusion: These results suggest that non-obese NAFLD patients have a common characteristic of lower skeletal muscle mass in both male and female, and most of them fulfill the criteria of "hidden obesity". However, the pathogenesis of NAFLD may be slightly different between male and female non-obese patients.

Abstract Submission No. 200182
O-0432

Baseline fat deposition as no relation HCC occurrence but closely correlation non-HCC malignancy.

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Objective: The purpose of this study was to investigate whether fat deposition in the liver contributes to the development of hepatocellular carcinoma (HCC) and malignant tumors other than HCC (non-HCC malignancy).

Methods: We are prospectively studying hepatitis C patients treated with DAA for the period 2013-2023. The primary endpoint was the occurrence of all malignancies. Patients were divided into 4 groups based on liver stiffness and fat deposition by Fibro-scan (FS) before treatment (Group A: low stiffness and low fat, Group B: low stiffness and high fat, Group C: high stiffness and low fat, Group D: high stiffness and high fat). The incidence of HCC and non-HCC malignancy in each group was compared.

Results: All 689 patients were prospectively observed from the start date of DAA treatment until November 30, 2023. The median observation period was 6.0 years. During the observation period, 141 malignancies occurred in 128 patients. All patients were divided into groups A 334 (51%) / B 186 (27%) / C 96 (14%) / D 55 (8%) according to FS before DAA treatment. When comparing 5-year cancer-free survival rates for the low-fat group (A+C) to the high-fat group (B+D), HCC 90.6% vs 90.2% p=0.646, non-HCC malignancy 98.8% vs

87.2% p<0.001. On the other hand, when comparing the low hardness group (A+B) and the high hardness group (C+D) in terms of 5-year cancer-free survival, HCC 94.0% vs 77.5% p<0.001, non-HCC malignancy 95.6% vs 92.4% p=0.08.

Conclusion: Baseline fat deposition as no relation HCC occurrence but closely correlation non-HCC malignancy.

Abstract Submission No. 200207
O-0433

MASLD and the Risk of Mortality in Diabetic Patients: A Systematic Review and Meta-analysis

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The systematic review aimed to assess the risks of metabolic dysfunction-associated steatotic liver disease (MASLD) on all-cause and cause-specific mortality in patients with type 2 diabetes mellitus (T2DM). EMBASE and MEDLINE were searched from inception to June 2022 for observational studies examining the relationship between MASLD and the risk of mortality among T2DM patients. Meta-analysis was conducted using random-effects models with hazard ratios (HRs) to quantify the risk of mortality. A total of 5,877 articles were screened, and ultimately, 12 eligible studies encompassing 368,528 T2DM patients, with a median follow-up of 8.9 years (interquartile range, 4.7-14.5), were included. Our analysis revealed a significant association between MASLD and an increased risk of all-cause mortality in T2DM patients (HR 1.28; 95% CI, 1.05-1.58; I² = 90%). Meta-regression analyses did not show significant effects of mean age, mean body mass index, and percentage of smokers, hypertension, and hyperlipidemia on the association between MASLD and the risk of all-cause mortality. However, we found that MASLD was not significantly associated with mortality related to cardiovascular diseases (HR 1.05; 95% CI, 0.82- 1.35; I² = 0%) or cancer (HR 1.21; 95% CI, 0.41-3.51; I² = 79%) among patients with T2DM. No publication bias was observed. This comprehensive meta-analysis provides substantial evidence supporting a significant association between MASLD and an increased risk of all-cause mortality among the T2DM population. These findings underscore the benefits of screening for MASLD in T2DM patients, aiding in the early identification of high-risk individuals and enabling risk modification strategies to improve survival.

Abstract Submission No. 200264
O-0434

Ferritin as a biomarker on weight reduction

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Metabolic dysfunction-associated steatotic liver disease (MASLD) is associated with metabolic syndrome, weight loss showed an improvement in steatosis in obese patients, the main goal of MASLD treatment is to prevent hepatic fibrosis. Although the gold standard for hepatic fibrosis is biopsy, some non-invasive tools as MR elastography are used. The FIB4 index did not work to follow the fibrosis changes in time dependent after weight reduction therapy; also, CAP measure is useful to determinate steatosis; serum ferritin has been studied to assist with disease diagnosis and progression since it is an acute-phase reactant and a pro-inflammatory cytokine. The main goal of the study was to evaluate the changes on ferritin after the bariatric surgery and the correlation to CAP.

Thirty-three women elected to bariatric surgery was included on the study, they do not have any other hepatic diagnosis, it was registered the FIB4, CAP and serum ferritin before bariatric surgery and 6 months later. We analysed changes using T-student or Wilcoxon test, and the correlation using Spearman test.

After 6 months all women reduce weight, serum ferritin, CAP, FIB4. Ferritin reduces from 89 ng/ml (57.5, 106.5) to 89 ng/ml (48.5, 100), and CAP from 278 dB/m (242.5, 326) to 229 dB/m (205, 303), but there is not a correlation between CAP and ferritin before surgery or at 6 months.

Ferritin as a reactant to follow changes induced by weight reduction could be useful, at 6 months but it is necessary to corroborate histological changes, suggested by CAP measure.

Abstract Submission No. 100475

O-0439

Short-Term LMWH for The Prevention of Early TIPS Dysfunction: A Randomised Controlled Trial

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Backgrounds: Transjugular intrahepatic portosystemic shunt (TIPS) dysfunction is secondary to occlusion or stenosis of the shunt. Whether post-TIPS low molecular weight heparin (LMWH) was necessary when the polytetrafluoroethylene-covered stent was used during TIPS creation was not answered. The present study evaluated the effect of short-term use of LMWH on early TIPS dysfunction.

Methods: Between September 2015 and October 2017, consecutive eligible patients with cirrhosis and portal hypertension were randomly assigned to receive LMWH for three days after the TIPS procedure (n = 62) or not (n = 62), respectively. All patients were followed up over twelve months. The primary endpoint was the TIPS patency rate at one year. Secondary endpoints were overall survival and LMWH-related complications. This trial was registered in ClinicalTrials.gov (NCT03171727).

Results: During a median follow-up of 54.6 months, the TIPS patency rate at one year was 91.7% in the LMWH group and 93.5% in the control group (HR 1.52, 95% CI 0.78-2.99, P = 0.22). In multivariable logistic regression, stent shortening in the hepatic vein (HR 4.54; 95% CI 1.02-21.42; P=0.041) was demonstrated as an independent significant risk factor for shunt dysfunction. There were no statistically significant differences in survival (93.5% vs. 95.1% at 1 year; HR = 1.05, 95% CI 0.48-2.31, P = 0.90) or adverse events between the two groups.

Conclusion: Short-term use of LMWH after TIPS creation may not be necessary as it does not result in a distinct patency and survival benefit in covered TIPS.

Abstract Submission No. 100561

O-0440

Gradual High Power Radiofrequency Ablation with Multi-electrodes for Small HCC: A Prospective Study

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Background: Utilizing a separable clustered (SC) electrode and a two-channel 400W generator for gradual, stepwise high-power radiofrequency (RF) energy delivery significantly reduces electrode charring, enhancing targeted energy delivery to hepatocellular carcinoma (HCC), and potentially enhancing the efficacy and safety of radiofrequency ablation (RFA) for HCC.

Purpose: This study prospectively assesses the local tumor progression (LTP) and intrahepatic remote recurrence (IRR) rates of gradual, stepwise, high-power RFA in treating HCCs (≤ 4 cm).

Materials and Methods: Patients with single HCCs (≤ 4 cm) scheduled for treatment with RFA, were prospectively enrolled. The ablation procedure targeted the index tumor, guided by real-time US-CT/MR fusion imaging. A gradual, stepwise, high RF energy (~ 400 W) alternately delivered to two of the three clustered electrodes. Technical success, complications, and cumulative incidences of LTP and IRR, along with RFS, were assessed and estimated using the Kaplan-Meier method.

Results: Among 110 participants (83 men and 27 women, mean age: 66.4 ± 7.6 years), 116 HCCs (mean size: 1.65 ± 0.59 cm) were treated with no major complications. LTP and IRR were observed in 4 and 29 patients, respectively. At a median follow-up of 41.0 months (range: 35.4-46.6 months), the estimated 1-year, 2-year, and 3-year cumulative incidences were as follows: LTP (0.9%, 3.6%, 7.0%) and IRR (13.9%, 20.5%, 31.4%). The corresponding RFS rates were: LTP (99.1%, 96.4%, 93.0%) and IRR (86.1%, 79.5%, 68.6%).

Conclusions: A gradual, incremental high-power RFA using an SC electrode demonstrates a promising, effective, and safe method for the management of small HCCs.

Abstract Submission No. 101292

O-0441

Three-dimensional Ultrasound Fusion Imaging in Precise Ablation of Hepatocellular Carcinoma

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Purpose: To investigate the value of three-dimensional ultrasound fusion imaging (3DUS FI) technique in thermal ablation of hepatocellular carcinoma (HCC).

Methods: A total of 57 patients with 60 HCCs with 3DUS FI-guided thermal ablation were retrospectively included in the study. 3DUS volume data of liver were acquired preoperatively by freehand scanning with the tumor and predetermined 5 mm ablative margin automatically segmented. Plan of needle placement was made through a predetermined simulated ablation zone to ensure a 5 mm ablative margin with the coverage rate towards tumor and ablative margin. With real-time ultrasound and 3DUS fusion imaging, ablation needles were placed according to the plan. After ablation, the ablation margin was immediately evaluated by the contrast-enhanced ultrasound and 3DUS fusion imaging. The rate of intraoperative supplementary ablation, [gh1] adequate ablative margin, complete response (CR), local tumor progression (LTP), recurrence-free survival (RFS) and overall survival (OS) was evaluated.

Results: According to postoperative contrast-enhanced CT or MR imaging, the complete response rate was 100% (60/60), and 83% of tumors (30/36) achieved adequate ablative margin (> 5 mm) three-dimensionally. During follow-up period of 6.0-42.6 months, LTP occurred in 5 lesions, with 1-and 2-year LTP rates to be 7.0% and 9.4%. The 1-and 2-year RFS rates were 76.1% and 65.6%, and 1-and 2-year OS rates were 98.1% and 94.0%. No severe complications or ablation-related deaths were observed in any patients.

Conclusions: 3DUS FI technique may improve the needle placement of thermal ablation for HCC and reduce the rate of LTP.

Abstract Submission No. 101355

O-0442

Evaluation of RFA Therapeutic Effect Using Workstation

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It is important to have a larger area of ablation than the tumor and to determine the therapeutic effect of RFA in an objective and reproducible manner. In general, a comparison of CT or MRI before treatment and CT or MRI after treatment is often used to determine the therapeutic effect of RFA. However, due to differences in breath-hold, modalities, etc., it is difficult to accurately determine the treatment effect.

The workstation used in this study was a VINCENT, called SYNAPSE 3D internationally. Workstation SYNAPSE 3D is commonly used in many hospitals all over Japan.

With Synapse 3D, the tumor and post-treatment ablation area can be easily extracted. The region can be extracted automatically by dragging the diameter of the tumor and the whole tumor to be extracted in either the axial, sagittal, or coronal plane.

It is very important to tightly adjust the position of images of CECT or MRI before and after RFA to evaluate RFA response including safety margin. To evaluate current RFA response, you can just click on three corresponding points in the images of CECT or MRI before and after RFA.

And then, push the execute 2D registration, Synapse 3D automatically adjusts instantly and easily. So, we can estimate the correct treatment response of RFA without being distracted by the difference in position between the two images.

Abstract Submission No. 101590

O-0443

Analysis of infectious complications after ablation of HCC and the impact on long-term survival

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Purpose: This study aims to complete and detailed record of the clinical characteristics and treatment of HCC patients with post-ablation infection and evaluate the infections on recurrence-free survival (RFS) and overall survival (OS).

Methods: 3117 patients with liver tumors receiving thermal ablation from January 2010 to December 2021 were analyzed. A total of 49 patients with infectious complications after thermal ablation were selected as the infection group. 49 patients without postoperative infection were randomly selected among those who underwent ablation

within three days as the control group. Clinical characteristics of both were analyzed by independent sample T-test and chi-square test. The recurrence-free survival and overall survival were compared between patients with and without infection complications by Kaplan-Meier method and COX survival analysis. Subgroup analyses of mild and severe infections were conducted to further explore the infection-related situation.

Results: Between mild and severe infection groups, there were statistically significant differences in infection position ($P=0.043$), positive rate of body fluid culture ($P=0.002$), the proportion of catheter drainage ($P=0.017$), use of advanced antibiotics ($P=0.006$) and outcome ($P=0.00$). Kaplan-Meier survival analysis revealed that postoperative infection was significantly correlated with tumor recurrence ($P=0.028$) and severe infection was significantly associated with overall survival ($P=0.049$). The cox model showed that postoperative infection was an independent variable of RFS deterioration ($HR=1.745$; 95% $CI=1.054-2.891$; $P=0.031$).

Conclusion: Postoperative infection among patients receiving thermal ablation adversely affected tumor progression. Empirical antibiotics and catheterization to reduce pressure inside the lesion should be utilized to minimize symptoms in patients with postoperative infection.

Abstract Submission No. 101625

O-0444

The facts of ablation for liver cancer in patients aged ninety and above in our hospital.

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Purpose: In the context of Japan's super-aging society, characterized by a growing population of very elderly individuals, this study investigates the safety and challenges associated with liver cancer ablation in patients aged 90 and above.

Methods: The subjects were 28 patients aged 90 and above who underwent radiofrequency or microwave ablation for liver cancer at our hospital from 2017 to 2023. We evaluate the characteristics of them.

Results: The cohort consisted of 13 females and 15 males, median age 91 (90-96), 25 HCC and 3 metastatic liver cancer, mean number of treatments 1.8 times. Pretreatment performance status was 0-1; 23, 2; 5. Three patients had dementia. Prognosis was 11 survival, 6 death (liver-related death; 1, other diseases; 2, unknown; 3), 11 discontinuation. Because some patients received multiple ablations, total ablations were 51. Evaluation in 51 cases from here. The mean number of ablated tumors: 1.65, median diameter: 16mm, RFA/MWA: 21/30. All patients treated under sedation with midazolam (median 3mg). Poor awakening was observed in 9. Thirteen patients deviated clinical path (complications; 3, additional ablation; 2, decreased ADL; 2, develop other disease; 4). Three treatment-related complications occurred (hemothorax, liver abscess, portal vein thrombus).

Discussion: Patients aged over 90 who received ablation had good PS and liver function. A relatively large number of patients had poor arousal despite the use of low-dose sedatives, deviated from the clinical path due to decline in ADLs or development of other disease, or had difficulty attending the hospital. Complications were observed in 5.8%, but no serious complications were observed.

Conclusion: It became clear that ablation could be performed safely even in very elderly patients.

Abstract Submission No. 101832

O-0445

Combined percutaneous RFA and ethanol injection for HCC with portal vein tumor thrombus

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Purpose: To evaluate the feasibility and safety of radiofrequency ablation (RFA) combined with percutaneous ethanol injection (PEI) in the treatment of hepatocellular carcinoma (HCC) with portal vein tumor thrombus (PVTT).

Methods: From January 2010 to December 2020, a total of 25 HCC patients who underwent RFA for intrahepatic tumor combined with PEI for PVTT were enrolled. The treatment response, overall survival (OS), progression-free survival (PFS), and complication were assessed. Univariate and multivariate analyses were performed to identify the prognostic factors in predicting the OS and PFS.

Results: The overall response rate was 88.0%, including 12 (48%) patients achieving complete response (CR) and 10 (40.0%) patients achieving partial response (PR). Progressive disease (PD) was observed in 3 (12%) patients. The 1-, 3-, 6-, and 12- month PFS rates were 96.0%, 56%, 20.0%, and 4.0%, respectively. The OS rates at 6, 12, 24, 36, and 48 months were 96.0%, 52.0%, 28.0%, 8.0%, and 4.0%, respectively. The overall response was the only risk factor for the PFS in the univariate analysis ($P=0.026$), but not in the multivariate analysis ($P=0.288$). There was no independent prognostic factor of OS. No ablation-related mortality was observed. Major complication of liver abscess was observed in only 1 (4%) patient.

Conclusion: RFA combined with PEI is a feasible treatment for HCC patients with PVTT, which might reduce the tumor burden and create conditions for further adjuvant therapy.

Abstract Submission No. 101978

O-0446

MICROWAVE ABLATION COMPAIRED WITH RADIOFREQUENCY ABLATION FOR HEPATOCELLULAR CARCINOMA IN MONGOLIA

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In Mongolia, an estimated 6702 people were diagnosed new cancer, and liver cancer is the first rank or 33% of all cancer in 2022. The challenge in the treatment of primary liver cancer is to keep the no recurrence of HCC after surgery, liver resection, and liver transplantation. In worldwide, the most difficult problems in the treatment of HCC are that the curative resection rate is low and the recurrence rate is high. Microwave (MWA) and radiofrequency ablation (RFA) are the commonly used local ablation for hepatocellular carcinoma (HCC). We studied Thermal Ablation treatment of early HCC on 609 cases and 70.3% were RFA and 20.7% were MWA. Age range of the patient was from 23 to 92. Gender ratio was male 37.5% and female 62.5%. 52.9% of the patients had diagnosed history of HCV carriers and 33.4 of the patients were HBV carriers. 21.6% of the patients had not diagnosed any hepatic viral infection. Ablation duration and Watt were parallel to tumor size and location/ $p<0.05$. Three months after the treatment, 92% ($n=370$) of the RFA patients and 85% ($n=107$) of the MWA patients had no tumor recurrence noted. Complications were reported in 35 of 609 procedures (5.7%); In 2.9% of RFAs ($n=14$) and 16.6% of MWAs ($n=21$). Early complications were bleeding and liver failure.

Tumor sizes were decreased 1.52 times for RFA and 1.67 times for MWA.

According to the literature, overall survival, local recurrence, complication rates, disease-free survival, and mortality in patients with HCC treated with MWA (compared with RFA) vary between 6 months for non local recurrence 14% (vs.8%). One, three and five year overall survival rates from diagnosis of early hepatocellular carcinoma were 93.7%, 79.2% and 50.4% for RFA and 93.6%, 78.3% and 63.2% for MWA, respectively. Although no significant difference in long-term outcome was noted between the 2 treatments, a significantly increase in OS was observed in the MWA group. Thermal ablations have become an effective treatment with less trauma, positive effects, and low complications for liver tumor patients. MWA has similar efficacy compared with RFA for early stage HCC patients. MWA should be considered the technique of choice in selected patients, when the tumor is ≥ 3 cm in diameter or is close to large vessels, independent of its size. The benefits of MWA are an improved convection profile, higher constant intratumoral temperatures, faster ablation times, and the ability to use multiple probes to treat multiple lesions simultaneously.

Abstract Submission No. 200191

O-0447

A Novel Ultrasound Modality to Monitor and Visualize Ablation Area based on Real-time imaging

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Objective: Image-guided radiofrequency ablation is a well-established treatment for hepatocellular carcinoma. This study aimed to evaluate the predictive accuracy of BioTrace, a novel software utilizing B-mode ultrasound to classify the local changes in tissue viability in real-time, during liver ablation procedure.

Methods: The software provides an estimation of the ablation zone immediately post ablation (BioTrace Map) that correlates to the ablation zone as visualized in a 24-hour post-procedure (T=24) CECT scan. A comparison was carried out between the BioTrace Map based on B-mode ultrasound to that annotated by radiologists using contrast-enhanced CECT 24-hours after treatment, which is considered as the Gold Standard, for a total of 20 liver tumors. This comparison utilized the Dice Coefficient, Sensitivity, and Precision metrics

Results: The median Dice Coefficient, Sensitivity, and Precision between BioTrace Map and the ablation zone visualized on T=24 CECT reached $90.3\pm2.2\%$, $90.3\pm4.5\%$ and $90.1\pm4.4\%$, respectively. The intraclass correlation presented excellent agreement between the findings of BioTrace and the radiologists regarding the volume size (0.98). Bland-Altman plot showed no evidence of systematic or proportional biases.

Conclusion: BioTrace used to visualize the ablated area reproduced the true ablated area as effectively as that by radiologists using post-operative CT. This system could ensure safe and effective ablation procedures in the future. Meaning, the software can accurately predict the ablation zone as would be visualized on T=24 CECT, based on real-time ultrasound imaging, and provide physicians with adjunctive

information regarding the final ablation zone size and shape, as part of their overall clinical assessment.

Abstract Submission No. 101204
O-0448

Novel real-time ultrasound-based software for ablation zone prediction following liver MWA

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Objective: This study aimed to demonstrate the effectiveness of BioTrace, an algorithm-based imaging software, in estimating the ablation zone in liver MWA procedures using real-time ultrasound. The software provides an estimation of the ablation on the procedure day that shows a high level of agreement with the results of a CECT scan acquired 24 hours post-ablation.

Methods: We conducted a prospective single-arm trial on tumors undergoing ultrasound-monitored MWA with a single antenna. A CECT scan was obtained for each patient a day post-ablation (24h±4h, or T=24). The software produced a 2D BioTrace map (BTM) based on the ultrasound's field of view along the needle plane. The BTM results were then compared to the T=24 CECT segmented ablation zone in the oblique plane corresponding to the ultrasound plane. This comparison utilized the Dice Coefficient, Sensitivity, and Precision metrics.

Results: The average Dice Coefficient between the BTM and T=24 CECT ablation zone was 89.3% (STD 2.9%), indicating a strong correlation between the two areas. The averaged Sensitivity and Precision values were 85.5% (STD 6.6%) and 94.1% (STD 5.7%), respectively. These results underscore BTM's capability to accurately detect the ablation zone based on real-time ultrasound imaging during the procedure.

Conclusions: The BioTrace is effective in providing a close estimation of the ablation area as will be seen on the T=24 CECT, based on real-time ultrasound imaging thus can provide physicians with adjunctive information regarding the final ablation zone size and shape, allowing more accurate understanding of the ablation outcomes on procedure day.

Abstract Submission No. 101372
O-0449

Resection vs. RFA in Small and Large HCC: A Meta Analysis of Randomized Controlled Trial

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BACKGROUND: While Radiofrequency Ablation (RFA) is often applied for nodules under 3 cm, some studies have demonstrated a favorable tumor response for larger nodules. This study aims to compare the efficacy of RFA and resection in HCC patients, considering nodule size with a cutoff at 3 cm.

METHOD: Using the PRISMA guidelines, comprehensive search was performed on seven databases. Small nodule was defined as ≤ 3 cm and large nodule as > 3 cm. All eligible studies were assessed using Cochrane RoB 2 for RCT. The pooled effect sizes were calculated using DerSimonian-Laird random-effects model and heterogeneity was

investigated using Cochran's Q test. Fixed-effect model was used and meta analysis was conducted using RevMan 5.4 software.

RESULT: A total of 5 studies, including 1046 patients were eligible for analysis. Overall survival and recurrence free survival in RFA and resection group were not statistically significant with hazard ratio (HR): 0.99; 95% CI 0.83, 1.19; p=0.96; I²=0% and HR: 1.07; 95% CI 0.93, 1.23; p=0.34; I²=0%, respectively. Subgroup analysis by nodule size also yielded similar findings. RFA and resection group also had similar recurrence rate with odds ratio (OR): 1.13; 95% CI 0.85, 1.49; p=0.41; I²=0%. Analysis of extrahepatic and intrahepatic recurrence found no significant difference between RFA and resection group.

CONCLUSION: In small or large nodule HCC, the efficacy of RFA and resection is similar. Additional considerations may be taken into account when choosing between RFA or resection in such condition.

KEYWORD: RFA; resection, HCC; small nodule; large nodule

Abstract Submission No. 101677
O-0450

Introduction of a safe device "Gangi-HydroGuard" for artificial pleural effusion and ascites in RFA

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Recently, SURF trial from Japan showed the efficacy of radiofrequency ablation (RFA) for 3 or less hepatocellular carcinomas (HCC) under 3cm equivalent to surgery. For a safe and secure RFA, artificial pleural effusion and ascites are effective, when HCC is located in the surface of liver or is adjacent to other organs. We report the features of a coaxial needle with a spring loaded blunt tip stylet "Gangi-HydroGuard" and show our earlier HCC cases using this device.

We analyzed the success rate, adverse events, and recurrent rate in early 10 HCC cases from July 2021 when we introduced the procedure of artificial pleural effusion and ascites to Takatsuki Red Cross Hospital.

Six males and 4 female of median age 84 (48-87) were included. First, artificial pleural effusion was performed for 7 HCCs with average size 21.9mm (7-31) located in S8 or S5. Second, artificial ascites was performed for 3 HCCs with average size 23.7mm (16-35) located in S3 or S5. We succeeded the procedures in all cases, however in 1 case, the first puncture was difficult in penetrating peritoneum and the second puncture was succeeded. No adverse events were occurred except for 1 case with a temporary decrease of the oxygen concentration, after the artificial pleural effusion was performed. We experienced a recurrence of HCC in 1 case of size 35mm located in S3 with the artificial pleural effusion.

We could safely introduced the procedures of artificial pleural effusion and ascites in RFA with "Gangi-HydroGuard".

Abstract Submission No. 101730
O-0451

Percutaneous Liver Biopsy in the Era of Clinical sequence: Usefulness of Full-core Biopsy Needle

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Background: The advancement of cancer genomic medicine has emphasized the importance of liver tumor biopsy and clinical sequencing. Tissue collection devices are broadly classified into aspiration-biopsy and cutting type, and the cutting type is further divided into sidecut-biopsy needle and full-core biopsy needle. Recently, the usefulness of the full-core biopsy needle has been reported, but there have been few reports comparing the clinical sequence with each method. In the present study, we retrospectively evaluated the eligibility of various testing devices and the clinical sequence.

METHODS: We included 20 liver tumor biopsies submitted to clinical sequence among the liver tumor biopsies performed at our institution from 2019 to 2023. The clinical sequence eligibility of the specimens collected and the safety of the procedure were reviewed.

Results: The median age of patients was 68 years, with 55% being male. Biopsies were performed using aspiration-biopsy needles (Surecut®18G) in 4 cases, sidecut-biopsy needles (Monopty®18G) in 7 cases, and full-core biopsy needles (Corvocet®18G) in 9 cases. Ineligibility for clinical sequencing was observed in two cases using aspiration-needles and one with a sidecut-needle. In contrast, specimens from all full-core needle biopsies were eligible. No complications were reported in any of the biopsy procedures. Although the cutting type biopsy needles tended to require fewer biopsies for adequate tissue collection, this difference was not statistically significant. No needle type showed complications requiring treatment.

CONCLUSION: The full-core biopsy needle provided a clinical sequence-eligible tissue sample that was comparable to or better than existing methods for liver tumor biopsies.

Abstract Submission No. 101796

O-0452

Indocyanine green fluorescence-guided laparoscopic deroofing for giant hepatic cyst

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Background: Laparoscopic deroofing (LD) has recently been considered a standard procedure for giant liver cyst, although it has the risk of postoperative bile leakage. The line of resection is ambiguous and there is a risk of biliary fistula if it enters the liver parenchyma. To determine the line of resection, We performed Indocyanine green (ICG) fluorescence-guided LD.

Methods: This was a retrospective study including 29 patients who underwent LD between April 2013 and October 2023 at our institute. These enrolled patients were divided into an ICG group (n = 7) and a white light group (n = 22).

Results: There were no significant difference among age, gender, maximum tumor size, estimated blood loss and postoperative hospital stay. There was one case of postoperative bile leakage in ICG group, though there was no significant difference.

There was two cases to detect the bile leakage in real time at ICG group. Fluorescent bile juice was detected from the resection line intraoperatively and we could suture of the area and fix them. These cases were discharged without complications.

Conclusion: ICG fluorescence-guided LD may offer clinical benefits to avoid bile duct injury. It is useful in determining the line of dissection and can also avoid the bile leakage.

Abstract Submission No. 101870

O-0453

Percutaneous Radiofrequency Ablation for Recurrent HCC after Curative Surgery in Children

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Background: Hepatocellular carcinoma (HCC) is extremely rare in children. There is no consensus on the management of recurrent HCC (RHCC) after curative surgery in children. The purpose of the study was to summarize our single-center experience with percutaneous ultrasound (US)-guided radiofrequency ablation (RFA) for pediatric RHCC.

Materials and Methods: From September 2007 to September 2021, patients under 18 who underwent percutaneous US-guided RFA for RHCC were retrospectively enrolled in this study. Local effectiveness, complications, local tumor progression (LTP), progress free survival (PFS), and overall survival (OS) were evaluated.

Results: A total of 10 patients (9 male and 1 female; mean age, 11.7±4 years; age range, 6-17 years) with 15 intrahepatic RHCC lesions were enrolled in this study. Complete ablation (CA) was achieved in 14 out of 15 lesions (93.3%) after the first RFA. During the follow-up (mean, 63.1±18 months; range, 5.3-123.3 months), LTP was not observed. Five patients died including three with tumor progression and one with liver failure. The accumulative one- and three-year PFS rates were 30% and 10%, respectively. The accumulative one- and three-year OS rates were 77.8 % and 44.4%, respectively.

Conclusions: Our single-center experience suggests the safety and efficacy of percutaneous US-guided RFA for pediatric RHCC. Further investigation in large-scale randomized clinical trials is necessary to determine the role of RFA in pediatric RHCC.

Abstract Submission No. 200052

O-0454

Assessing and Predicting Liver Function by Elastography: 1-year Follow-up in HCC Ablation Patients

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Aim: The present study aims to investigate the changes in liver function and liver stiffness (LS) measured by two-dimensional shear wave elastography (2D-SWE) before and after ablation in patients with hepatocellular carcinoma (HCC), and to explore the feasibility of using LS before and after ablation as a means to assess and predict liver function, gaining a better understanding of the impact of ablation on liver function and LS's potential as a prognostic tool for HCC patients.

Material and Methods: From March 2022 to December 2023, 101 patients with treatment-naïve HCC and undergoing ablation were prospectively enrolled and followed-up for one year. Data including LS and indicators of liver function were collected at pre-operative period and post-operative 1month, 3 months, 6 months, and 12months, respectively. Statistical analysis was conducted to explore the correlation between LS and liver function during the follow-up.

Results: Among the enrolled patients, 69 (68.3%) underwent percutaneous radiofrequency ablation, 23 (22.8%) underwent percutaneous microwave ablation, and 9 (8.9%) cases underwent other methods of ablation (such as laparoscopic ablation). Using pre-operative LS as the baseline, paired *t*-test showed that LS slightly increased at 1 month post-operatively and then decreased (all $p < 0.050$). This trend was similar to the changes in liver function before and after ablation. There was a significant correlation between pre-operative LS and liver function (represented by Child-Pugh and ALBI scores) at pre-operative period and post-operative 1, 3, 6, and 12 months (all $p < 0.050$). Additionally, LS at 1, 3, and 6 months post-operatively was significantly correlated with the immediate post-operative liver function (all $p < 0.050$).
Conclusion: LS is expected to become a powerful tool for assessing and predicting liver function in HCC ablation patients, which could help alleviate the burden of follow-up examinations to some extent.

Abstract Submission No. 200064
O-0455

Safety and efficacy of MVA of multiple lesions in multiple Lung Metastasis of Colorectal Cancer

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Objective: This study aims to retrospectively analyze the safety and effectiveness of microwave ablation (MWA) in treating multiple lung metastases from colorectal cancer.

Approaches: A retrospective analysis was conducted on the clinical data of patients with colorectal cancer multiple lung metastases who underwent MWA treatment at Yunnan Cancer Hospital from January 2020 to December 2022. The main objective of the study was to determine the median overall survival (mOS), while additional objectives included assessing the median progression-free survival (mPFS), technical success rate, and complication rate. The statistical analysis involved the utilization of the log-rank test and the Cox proportional risk regression model.

Outcomes: There were 50 patients with numerous lung metastases from colorectal cancer who received MWA treatments. The overall mOS time for all patients was 26 months, with a 95% confidence interval (CI) ranging from 20.93 to 31.10 months. Similarly, the mPFS time was 23 months, with a 95% CI ranging from 16.76 to 29.24 months. Furthermore, the group that underwent single MWA showed a superior mOS compared to the group that underwent fractionated MWA. The hazard ratio (HR) was 4.756, with a 95% confidence interval (CI) of 1.076 to 21.033, and a *p*-value of 0.04.

Conclusion: MVA is a secure and efficient method for treating numerous metastases of colorectal cancer in the lungs. For one side of the lung, numerous metastases can be treated with a single, divided ablation procedure that targets many points. Further investigation is required to determine the efficacy of ablating numerous metastases in both lungs while ensuring safety.

Abstract Submission No. 200082
O-0456

THE ROLE OF CARTO IN PORTAL HYPERTENSION WITH RECURRENT UPPER GI BLEEDING FROM LARGE GASTRIC VARICES

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A 26-year-old, female with no co morbidities and unremarkable perinatal, personal, family, and OB Gyne history presented with melena associated with body weakness. She was hospitalized with a hemoglobin of 3 g/dL and was transfused with 7 units packed RBC. Emergency upper endoscopy revealed small esophageal varices and large gastroesophageal varices (GOV2) which was treated with injection of histoacryl glue to the gastric varices. After the bleeding was controlled, she was started on beta blockers and was advised further work up. Work up revealed non-reactive hepatitis B and C profile and a consideration of portal thrombosis and portal cavernoma on CT scan. Hematology service was on board to rule out hematologic causes of portal thrombosis. Work up were all unremarkable for ANA, anti-DsDNA, APAS panel, clotting factor II and V PCR, and JAK 2 mutation by PCR. On the following months, the patient had multiple recurrences of melena and hematochezia requiring massive blood transfusions and emergency endoscopic glue injections. A multi-disciplinary team meeting consisting of hepatology, interventional gastroenterology, hepatobiliary surgery, and interventional radiology was held to discuss the best acceptable management for the patient. The consensus of the meeting was to do a Coil-Assisted Retrograde Transvenous Obliteration (CARTO) to control the portal hypertension and subsequently the bleeding varices. The patient consented to the plan offered by the team and underwent CARTO successfully. On follow up; there was no longer recurrence of GI bleeding and laboratories are within normal. The patient was advised for surveillance endoscopy and liver function tests monitoring.

Abstract Submission No. 200117
O-0457

Efficacy of Emprint™ Ablation System for Perivascular Hepatocellular Carcinoma

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Background: Conventional microwave ablation encounters major challenges with unpredictable and inconsistent ablation zones, particularly in dynamic tissue environment near intrahepatic blood vessels. The Emprint™ system with thermosphere technology offers a potential solution to this issue. This retrospective study assesses the effectiveness of the Emprint™ ablation system in treating hepatocellular carcinoma (HCC), emphasizing outcome comparisons between perivascular and non-perivascular cases.

Methods: From January 2019 to September 2022, 135 HCC patients underwent Emprint™ microwave ablation were enrolled. Cases were categorized into perivascular (N=109) and non-perivascular (N=26) groups based on tumor proximity to intrahepatic vascular. Propensity score matching (PSM) was then applied to balance the baseline characteristics between two groups. The 1-year post-ablation intrahepatic tumor recurrence rates and major complications rates were subsequently analyzed.

Results: The 1-year post-ablation intrahepatic tumor recurrence rates were lower in the perivascular group compared to non-perivascular cases in the overall cohort (7.7% vs. 15.6%, $P=0.529$) and in the PSM cohorts (8.7% vs. 14.8%, $P=0.714$). The major complication rate in the non-perivascular group was [3.7% (4/109)] in the total cohort and [5.6% (3/54)] in the PSM cohort. No complications were observed in the perivascular group.

Conclusions: The Emprint™ microwave ablation system demonstrated compelling efficacy with reduced tumor recurrence and

complication rates in the management of the previously challenging perivascular HCC lesions. These encouraging results position the Emprint™ system as a promising and viable treatment option for patient with perivascular HCC.

Abstract Submission No. 200229

O-0458

AI Based Tumor Progression Prediction following Hepatocellular Carcinoma Ablation

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Materials & Methods: Single-center retrospective single-arm study. 216 patients underwent radiofrequency ablation to treat HCC. Tumor progression was defined as residual unablated tumor or local tumor progression (LTP), which was based on a CECT scan 24 hours post procedure. The study assessed a novel fully automatic 3D software for ablation outcome assessment and the LTP predictive power of a novel metric named weighted relative ablated target (WRAT). The LTP predictors were compared using the area under curve of the receiver operating characteristic curve.

Results: The area under curve of the receiver operating characteristic curve results for the evaluated LTP predictors: human expert MAM, fully automated MAM and fully automated WRAT are 70.9%, 78.4% and 81.7% respectively.

Conclusions: The study results indicate that our AI based fully automatic SW using deformable registration is more effective in predicting LTP than human expert assisted by semi-automatic segmentation and rigid registration tools. The improvement is most significant for sub capsular tumors. In addition, our novel weighted relative ablated target (WRAT) metric for LTP prediction is more accurate than the commonly used minimal ablation margin metric.

Abstract Submission No. 100350

O-0459

An AI model for steatosis segmentation in mouse models

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Background: Steatosis is an earliest histopathological feature in the pathogenesis of metabolic dysfunction associated steatotic liver disease (MASLD). Advancements in deep learning and image recognition enable the application of digital pathology, expected to provide more accurate quantitative assays for clinical diagnosis.

Methods: We propose a method designated as Curriculum Learning-based Fully-aware Steatosis Segmentation (CuFASS) algorithm that integrates a boundary-aware model with curriculum learning techniques, enabling the model to learn comprehensive steatosis shapes. Whole training dataset consisted of 1868 patches (512x512 pixels) was divided into three subsets by intricacy of the steatosis.

Results: The evaluation dataset consisted of 5120 patches which collected from 35 samples were categorized based on different fatty liver induction methods. The F1-score, precision, recall, and specificity values for the overall metrics, high-fat diet-induced fatty liver (HFD) group, STZ with high-fat diet-induced fatty liver (STZ+HFD) group and normal group were as follows: overall (F1-score: 0.91, Precision: 0.93, Recall: 0.90, Specificity: 0.99), HFD group (F1-score: 0.89, Precision: 0.90, Recall: 0.88, Specificity: 0.99), STZ+HFD group (F1-score: 0.93, Precision: 0.95, Recall: 0.91, Specificity: 0.97), and normal group (F1-score: 0.80, Precision: 0.94, Recall: 0.70, Specificity: 1.00). Furthermore, when compared to semi-quantitative scores computed by clinicians, the model achieved a strong correlation with an R-squared value of 0.834.

Conclusions: Our current model exhibits strong performance in terms of precision and sensitivity in the detection and quantification of vesicular steatosis in mouse MASLD.

Abstract Submission No. 100853

O-0460

IMPACT OF SAMPLE VARIABILITY OF LIVER NEEDLE BIOPSIES ON FIBROSIS ASSESSMENT

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Introduction: Variability in fibrosis assessment due to needle positioning in liver biopsy is currently under-evaluated. This study investigates the influence of positional and rotational variability on the accuracy of fibrosis assessment using Second Harmonic Generation/Two Photon Excitation (SHG/TPE) microscopy and artificial intelligence (AI)-based analysis.

Methods: 100 liver resection and explant samples, covering NASH-CRN stages F0-F4, were evaluated by SHG/TPE microscopy. The virtual needle biopsies (width 0.9mm and length 15mm) were taken from each sample. Rotational and positional variability introduced through rotation angles at 20° intervals and varying tissue positions within samples respectively. qFibrosis assessment was performed for all virtual needle biopsies and the whole tissues. The analysis employed linear weighted kappa (LWK), Obuchowski-index (multinomial version of AUROC), Spearman's correlation to evaluate accuracy and agreement of assessments.

Results: The Obuchowski-index of qFibrosis continuous value was 0.92-0.95 for rotation variability, 0.90-0.95 for position variability. There was substantial agreement between qFibrosis stage and pathologist readings (LWK=0.70-0.81 rotation variability,

LWK=0.68-0.79 position variability). Correlation of total fibrosis area between virtual biopsies and whole tissues was strong for rotation variability (r -value=0.85-0.89) and position variability (0.82-0.92). Fibrosis area in portal tract, peri-portal, and zone 2 regions exhibited higher correlation (mean r -value=0.87) compared to central vein and peri-central regions (mean r -value=0.55) between virtual biopsies and whole tissues.

Conclusions: Positional and rotational variabilities had no significant impact on liver fibrosis assessment using qFibrosis. The strong correlation between virtual biopsies and whole tissue fibrosis evaluation using SHG/TPE microscopy further support qFibrosis as a reliable method for quantitative fibrosis assessment.

Abstract Submission No. 100883

O-0461

Understanding early stage-fibrosis in KBI-NASH non-human primate model using AI digital pathology

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Background: Liver biopsy specimens contain abundant information on liver microenvironment, which may offer novel biological insights into disease progression/regression. Here, we investigated changes in liver microenvironment features during early development of NASH.

Methods: We evaluated 11 paired liver biopsies from NASH-NHP model developed by Kunming Biomed International (KBI), at >2 years after high-fat diet (baseline) and at the following 12 weeks, using HistoIndex AI digital pathology platform, which combines a novel imaging technique based on Second Harmonic Generation/Two-Photon Excitation Fluorescence and a proprietary image analysis to quantify zone-specific fibrosis and steatosis features.

Results: At baseline, most animals exhibited steatosis (median of 3 pathologist's grade S0: 1/11, S1: 3/11, S2: 4/11, S3: 3/11), without pathological fibrosis (F0: 10/11, F2: 1/11), which progressed at week 12 (F0 to F1: 3/11, F0 to F2: 6/11). The progression was characterized by a high PS steatosis activity, with increased macrosteatosis ($P=0.04$ vs. baseline) and PS fibrosis ($P<0.05$ for most features of aggregated fibrosis, vs. baseline). Increased steatosis-colocalized fibrosis was also observed ($P=0.03$ vs. baseline), which suggests a metabolic contribution to the early-stage fibrosis in this model. Unsupervised clustering revealed 3 patterns of disease progression: (1) worsened PS fibrosis with mildly increased PT, (2) mildly increased PS fibrosis, (3) markedly increased CV fibrosis.

Conclusion: Our study demonstrated the metabolic relevance of KBI-NASH-NHP model and the utility of AI digital pathology in studying changes during the early-stage fibrosis. Future work includes validation in a larger dataset to elucidate key differentiators for progression at early-stage and late-stage fibrosis.

Abstract Submission No. 100985

O-0462

Artificial intelligence to measure fibrosis change on liver biopsy in the MAESTRO-NASH phase 3 trial

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Background: MAESTRO-NASH, a phase 3 registrational non-cirrhotic NASH clinical trial achieved NASH resolution and fibrosis reduction endpoints on liver biopsy at 52 weeks. As an exploratory endpoint, artificial intelligence slide reading technologies were employed to measure the effect on fibrosis in serial liver biopsy using both continuous and quantitative scoring.

Method: Fibrosis was estimated as a continuous and categorical variable using second harmonic generation (SHG) (qFibrosis)/two-photon excited fluorescence of 768 paired biopsy samples from MAESTRO-NASH. A separate unstained slide was analyzed for qFibrosis [normalized by tissue area and then corrected for qSteatosis (tissue area-steatosis area)].

Results: Based on a continuous qSteatosis score, the % change from baseline in steatosis was 80 mg, -36%; 100 mg, -46%; placebo, -10%, $p<0.0001$ for both doses, the continuous change from baseline in corrected qFibrosis score was 80 mg, -22%; 100 mg, -20%; placebo, 3%, $p<0.0001$ for both. Based on categorical change in qFibrosis score, there was a significant improvement in fibrosis stage (1- or 2-stage improvement) at 80 and 100 mg relative to placebo, and less worsening of fibrosis in the resmetirom treatment groups compared with placebo (Table). The percentage showing improvement in qFibrosis (≥ 1 -stage) was higher than scored by pathologists and identified 90% of resmetirom responders.

Conclusion: Measurements of fibrosis change using qFibrosis on either a continuous or categorical scale demonstrated a clear improvement and less worsening in fibrosis in resmetirom treated NASH patients as compared with placebo after 52 weeks of treatment.

Abstract Submission No. 100989

O-0463

Assessment of resmetirom-mediated reductions in liver volume on fibrosis changes MAESTRO-NASH trial

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Background: MAESTRO-NASH, a phase 3 registrational non-cirrhotic NASH clinical trial achieved NASH resolution and fibrosis reduction endpoints on liver biopsy at 52 weeks, with resmetirom-treated patients achieving significant improvements in liver volume. In this analysis, we explored the effect of liver volume reduction on AI-based fibrosis assessment at the parameter-level.

Method: Quantified collagen parameters in the liver lobule regions were obtained from AI measurements of separate unstained slides using SHG/TPEF microscopy. Using liver volume from serial MRIs at baseline and week52 for 634 patients, a coefficient was applied to the AI-based collagen parameters to account for the liver volume reduction to analyse the impact on patients showing more than 10% relative reduction of collagen parameters.

Results: Both resmetirom doses revealed a larger percentage of patients showing more than 10% relative reduction of collagen parameters at the portal, peri-portal and zone 2 regions (Fig. A) (8 to 24%, $p<0.01$) compared to placebo. After applying the coefficient to account

for liver volume reduction with resmetirom treatment (Fig. B), the percentage of resmetirom-treated patients with more than 10% relative reduction of collagen parameters increased across all zones, notably at the portal, peri-portal and zone 2 regions (26 to 36%, $p < 0.01$), and at the peri-central region (11 to 14%, $p < 0.05$) in both resmetirom doses versus placebo.

Conclusion: Quantification of changes in NASH fibrosis are impacted by therapeutic interventions that alter liver volume. Correcting for liver volume reveals the greater impact of resmetirom with more pronounced regression patterns at the collagen parameter-level compared to placebo.

Abstract Submission No. 101079

O-0464

The Deep Learning of Ultrasonography in Automatic Detection and Diagnosis of Liver Tumors.

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Background: Ultrasound (US) is the most common screening tool for hepatocellular carcinoma (HCC). However, the diagnostic performance of ultrasound is highly operator-dependent. We aimed to develop deep-learning models to detect and diagnose hepatic lesions automatically.

Materials and methods: We enrolled patients diagnosed with hepatic tumors by the abdominal US from January 2002 to December 2020 in a retrospective cohort with the diagnosis of malignant (HCC, cholangiocarcinoma, and metastasis) and benign lesions (hepatic cysts, hemangiomas, focal fatty sparing, focal nodular hyperplasia, and other benign findings). 1,576 patients with 4,600 images, and 6,001 lesions were analyzed. Deep learning models included ResNet50, Xception, Inception Resnet V2, and EfficientNet-B5 for non-real-time classification and YOLO v4 for lesion automatic detection and diagnosis.

Results: A total of 1,576 patients separated into 1,061 in training, 373 in validation and 142 in testing set. The AUC for ResNet50, Xception, Inception Resnet V2, and EfficientNet-B5 were 0.88, 0.89, 0.88, and 0.90. After the optimal threshold was selected in the base model of EfficientNet-B5, the accuracy, recall (sensitivity), precision and F1 score for the validation and testing dataset were 0.836, 0.837, 0.626, 0.716 and 0.699, 0.699, 0.289, 0.408. The mean Average Precision score to differentiate between malignant and benign lesions for YOLO v4 was 0.5441.

Conclusion: Our study provides the deep learning model with high accuracy in ultrasound differentiation and diagnosis of benign and malignant lesions. Furthermore, the Yolo-v4 model also demonstrates high performance in real-time automatic detection and diagnosis.

Abstract Submission No. 101309

O-0465

Insights into Post-Hepatectomy Liver Failure Prediction with Interpretable Deep Learning Framework

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Purpose: To develop an interpretable framework for understanding the predictions of the deep learning model for Post-hepatectomy liver failure (PHLF).

Material and Methods: A total of 345 consecutive patients were enrolled. We employed a variational autoencoder (VAE) to transform two-dimensional shear wave elastography (2D-SWE) images into latent space encodings, which were then used to train a multi-layer perceptron (VAE_MLP_SWE) model. Clinical variables were incorporated into the latent space to train a VAE_MLP_SWE_clinical model. Counterfactual explanations were generated by latent space traversal of the VAE to observe the change in 2D-SWE images with predicted probability. Layerwise relevance propagation (LRP) was used for global and local explainability with respect to SWE image and clinical variables.

Results: The VAE-MLP_SWE model showed a higher AUC (0.759) than the Densenet121 (0.745) and Resnet18 (0.703) models during five-fold cross-validation. The VAE_MLP_SWE_clinical model demonstrated a significant improvement ($p < 0.05$) in AUC (0.828) compared to clinical indices such as Child-Pugh score, ALBI score, and MELD score (AUC 0.529-0.684) on the test set. Qualitative analysis of counterfactual explanations generated for both VAE_MLP_SWE and VAE_MLP_SWE_clinical revealed that clinically relevant semantic features were used for prediction. Quantitative evaluation of counterfactuals with different predicted probabilities revealed a consistent correlation with liver stiffness measurement. The global LRP analysis identified SWE image, future liver remnant volume (FLR), and albumin (ALB) as the most important features for PHLF prediction.

Conclusion: The proposed VAE-MLP framework offers insights into the decision-making mechanism of the deep learning model for prediction of PHLF with high accuracy.

Abstract Submission No. 101412

O-0466

Finding Undiagnosed Hepatitis C Using a Machine Learning Algorithm: An Australian Pilot

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Background: To validate an artificial intelligence (AI) algorithm capable of identifying patients in an Australian population who are undiagnosed with Hepatitis C Virus (HCV)

Methods: This study analyzed retrospective data from 371 Australian general practices' electronic medical records (EMR) between 2017 and 2022, comprising 19 million patients. A high-performance machine learning model (XGBoost) was trained on deidentified clinical data to find undiagnosed HCV cases by using clinical predictors associated with HCV infection, then validated on a separate dataset. Algorithm performance was evaluated based on recall and fold improvement compared to standard screening methods recommended by the World Health Organization (WHO).

Results: The dataset contained 9 million deidentified patients aged >18 years who exhibited evidence of attending healthcare within a 24-month period. Of these, 2,515 patients were identified as HCV-positive. Table 1 shows the model performance compared to universal screening

and birth cohort screening. At 5% recall (the population with the highest predicted risk), the algorithm demonstrated a 116.5-fold improvement over universal screening, which is comparable to the performance of a previous US-based algorithm. As a point of comparison, the birth cohort (i.e., WHO recommendation to screen patients born between 1946-64) demonstrated a 2.2-fold improvement over universal screening. AUROC of the model was 0.735. Top predictors used by the model included age, gender, chronic liver disease, anti-anxiety medications, analgesics, bilirubin, and alanine transaminase (ALT).

Conclusion: This study demonstrates that our validated machine learning algorithm can identify undiagnosed HCV patients in Australia, and can improve patient screening efficiency.

Abstract Submission No. 101552

O-0467

Predictive validation of GLIM criteria for mortality in patients with cirrhosis: a machine learning

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Background: Recently, a novel framework designated as GLIM criteria has been proposed to harmonize malnutrition diagnosis across distinct populations and disease settings. From the standpoints of predictive, preventive and personalized medicine, we sought to validate the prognostic performance and refine the best combinations of phenotypic and etiologic GLIM criteria associated with long-term mortality in patients with decompensated cirrhosis.

Methods: This retrospective observational study enrolled decompensated hospitalized patients with cirrhosis. The GLIM phenotypic criteria comprised unconscious weight loss, low BMI and low SMI, while etiologic criteria entailed reduced food intake or assimilation, disease burden indicative of high MELD-based scores, aggravating Child-Pugh classification and inflammation indicative of high NLR. Fifty GLIM combinations were examined according to the sensitivity, specificity, negative/positive predictive values along with a machine learning algorithm (Random forest).

Results: The sample consisted of 219 patients with decompensated cirrhosis; 50.7% females; a median age of 63 years. The prevalence of malnutrition varied from 3.7% to 45.7%. Cox regression indicated that 38 combinations were significantly associated with 1-year all-cause mortality with hazard ratios (HRs) ≥ 2 . Notably, the HRs of SMI.MELD, BMI.MELD, BMI.MELD3.0 were as high as 4.832, 4.497, 4.335, respectively. Random forest algorithm unraveled that SMI.MELD performed best for prediction.

Conclusions: The majority of GLIM combinations was linked to inferior outcomes in the context of decompensated cirrhosis. Our findings shed light on the predictive diagnostics, targeted preventive and individualized treatment to counteract distinctive malnourished features among hospitalized cirrhosis, which may improve outcomes, symptoms and quality of life and correct nutritional status.

Abstract Submission No. 101644

O-0468

Artificial intelligence assisted navigation surgery in laparoscopic liver resection.

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Background and Objective: Recently, the prediction of anatomical structures by artificial intelligence (AI) is expected to support surgeons as navigation tool. We reported AI system can recognize vascular structures during liver parenchymal transection. This preliminary study demonstrated whether AI technology become navigation tool in recognizing anatomical structures during LLR.

Method: We used Surgical AI Eureka® (Anaut Inc., Tokyo, Japan) to recognize anatomical structures during LLR. This AI system can recognize various anatomical structures and detect bleeding. We made AI recognize loose connective tissue during liver mobilization and vascular structures during liver transection, and we examined bleeding detection function.

Results: This AI model enabled to recognize these vascular structures of any size with high accuracy (IoU=0.33, Dice=0.44) and AI could distinguish glissons from hepatic veins. AI recognized loose connective tissue (IoU=0.56, Dice=0.60) during liver mobilization and dissection of hepatoduodenal ligament for safe dissection plane. Loose connective tissue was also recognized by AI in intractable cases of repeat liver resection and tumor invaded other organs. We could identify the bleeding point using bleeding detection function. AI exactly highlights anatomical structures without any visual disagreement in real time about 0.12 second.

Conclusion: This AI system is useful as navigation technology in laparoscopic liver surgery. Nobel navigation surgery using AI technology suggested the possibility to perform safer and more reliable liver surgery in near future.

Abstract Submission No. 100822

O-0469

Causal inference data analysis pipeline for identifying proteins within NAFLD/NASH sub-cohorts

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Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NAFLD/NASH) is a highly prevalent heterogenous disease with several sub-cohorts. Herein, we propose a data analysis pipeline for identifying proteins within these sub-cohorts to gain insights into NAFLD/NASH. The pipeline consists of two algorithms: 1) LIMMA (Linear Models for Microarray) differential expression analysis to identify proteins that differentiate between the various sub-cohorts of NAFLD/NASH; 2) Causal inference to determine the causality of differentiating proteins identified in the previous step to the biomarker. The analysis is conducted using data from the UK Biobank (UKB) with subjects having olink proteomics data. The proposed pipeline is applied on 4 sub-cohorts of group of individuals with fatty liver disease: proteins differentiating the interaction between (i) elevated cT1 and PNPLA3 (rs738409) + and - variants, (ii) PNPLA3 (rs738409)+ variant with high and low cT1, (iii) elevated cT1 and PNPLA3 (rs738409)+ variant, (iv) elevated cT1 and PNPLA3 (rs738409)- variant. The results of the analysis provided insights into NAFLD/NASH progression for these four sub-cohorts: 1) perturbed glucose metabolism appears to primarily drive immune regulation and pro-inflammatory signaling, 2) proteins associated with inflammation (IL-6), lipid metabolism and cardiovascular function are upregulated, 3) innate

immune response may play a role in the progression of NAFLD/NASH, 4) direct cytokine signaling and oxidative stress, which are likely associated with obesity (for example, visceral adipose tissue expansion), may contribute to the development of NAFLD/NASH. These insights help enhance our understanding of the underlying mechanisms of NAFLD/NASH progression.

Abstract Submission No. 101496

O-0470

Application of transformer model for capsule endoscopic gastric structure recognition

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Background: Gastric structure recognition systems have become increasingly necessary for the complete and accurate diagnosis of gastric lesions in capsule endoscopy. Deep learning, especially using transformer models, has shown great potential in the recognition of GI images according to self-attention. This study aims to establish a precise label library of capsule endoscopy gastric structures to improve the clinical applicability of deep learning to endoscopic image recognition.

Methods: A total of 2433 WCE videos collected at our center between 2011 and 2021 were used to train a transformer-based AI model, while 118 additional WCE videos were used for validation. Fifteen upper gastrointestinal structures were selected for quantifying the examination quality. We also conducted a comparison of the classification performance between the AI model and endoscopists by the accuracy, sensitivity, specificity, and positive and negative predictive values.

Results: The transformer-based AI model reached a relatively high level of diagnostic accuracy in gastric structure recognition. Regarding the performance of identifying 15 upper gastrointestinal structures, the AI model achieved a macroaverage accuracy of 99.6% (95% CI, 99.5-99.7), a macroaverage sensitivity of 96.4% (95% CI, 95.3-97.5), and a macroaverage specificity of 99.8% (95% CI, 99.7-99.9) and achieved a high level of interobserver agreement with the expert endoscopists.

Conclusion: The transformer-based AI model can accurately evaluate the gastric structure information of capsule endoscopy with the same performance as that of expert endoscopists, which will provide tremendous help for doctors in making a diagnosis from a large number of images and improve the efficiency of examination.

Abstract Submission No. 101504

O-0471

Practical Clinical Uses of Chat GPT: What Hepatologists Should Know

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Artificial Intelligence (AI), particularly through tools like Chat GPT, is transforming Clinical Hepatology by enhancing patient care and research. This integration is crucial as many hepatologists are unfamiliar with AI's practical applications in their field. AI focuses on improving diagnostic accuracy, tailoring treatment plans, and efficiently managing patient data. Its role extends to interpreting complex diagnostic images, forecasting disease progression, and guiding liver transplant

decisions. These advancements, however, come with ethical and practical challenges in implementation.

AI's impact in hepatology is profound, improving diagnostics, therapy, and research. Advanced algorithms refine imaging interpretation, aiding in early detection and management of liver diseases. AI also streamlines processing vast amounts of data in Electronic Health Records (EHR), enhancing both care and research precision.

AI contributes significantly to risk prediction models, enabling more accurate forecasts of disease progression and treatment outcomes. This leads to more personalized patient care. AI is also instrumental in formulating individualized treatment plans and in decision support systems, essential for informed clinical decision-making in hepatology.

Despite its benefits, AI integration in hepatology faces challenges like data privacy concerns, the need for diverse datasets, and algorithmic biases. Overcoming these challenges requires careful planning and training for effective AI integration into existing healthcare systems.

In summary, AI, especially Chat GPT, represents a major leap in Clinical Hepatology. Its current applications have already enhanced diagnostic precision and patient care, yet its full potential in hepatology is still unfolding, contingent on addressing ongoing ethical and practical issues.

Abstract Submission No. 101830

O-0472

Predicting Lymph Node Metastasis of Hilar Cholangiocarcinoma Based on Deep Learning Radiomics

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Purpose: To explore the potential deep learning radiomic(DLR) models based on B-mode ultrasound(BUS) and contrast-enhanced ultrasound(CEUS) images in predicting preoperative lymph node metastasis(LNM) of hilar cholangiocarcinoma(HCCA).

Methods: 110 HCCA patients from two different clinical center were included, and divided into a primary cohort(training group: n=75; internal validation group: n=25) and an external validation cohort(n=10). Pathologists confirmed the status of lymph node. The ResNet101 model was pre-trained on ImageNet and utilized for transfer learning. The ResNet101 was employed to extract deep learning features(DLFs) from BUS and CEUS images. Additionally, the Genetic Programming-based Symbolic Regression(GPSR) algorithm was used to combine the radiomic features(RadFs) and DLFs to generate deep learning radiomic features(DLRFs). Finally, the DLR models were constructed based on eXtreme Gradient Boosting algorithm.

Results: LNM occurred in 48 of 110(43.64%) HCCA patients. 847 RadFs and 4095 DLFs were extracted from the region of interest (ROI) of each tumor. After data cleaning and feature selection, 10 RadFs(BUS:4, CEUS:6) and 27 DLFs(BUS: 5, CEUS: 22) were obtained. After GPSR algorithm, 5 BUS-DLRFs, 10 CEUS-DLRFs, and 15 Combination-DLRFs were obtain and three corresponding DLR models are established, respectively. In the internal/external validation group, the AUC of BUS-DLR/CEUS-DLR/Combination-DLR models were 0.70 vs. 0.77 vs. 0.83(internal validation group) and 0.66 vs. 0.68 vs. 0.72(external validation group).

Conclusions: The DLR models based on DLRFs could better predict preoperative LNM in HCCA, and could further improve the detection rate of LNM to enhance clinical decision-making.

Abstract Submission No. 101935

O-0473

AI in Hepatitis B Screening: A Machine Learning Approach to Demographic Determinants

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Background: Hepatitis B Virus (HBV) affects nearly 300 million people globally, yet approximately 1/10 of these cases remain underdiagnosed. The primary objective is to assess the efficacy of AI (machine learning) and statistical models, particularly logistic regression for HBV screening using demographic factors.

Methods: Data from a HBV screening seroprevalence survey in Ho Chi Minh City (2019-2020) were analyzed, involving 17600 participants aged 18+ from an estimated 20000 sample using multi-stage cluster sampling. The dataset covered variables like HBsAg, demographics, and KAP questionnaire responses. MATLAB R2023b was used to process the data. SMOTE was used to fix imbalance data. Feature selection included Recursive Feature Elimination (RFE), Tree-Based Feature Importance (TBFI), minimum Redundancy Maximum Relevance (mRMR), and Pearson's correlation. Key features were interactively chosen. Classifiers used were Medium Tree (MT), Bilayered Neural Network (BNN), Logistic Regression (LR), Linear SVM, and Fine k-Nearest Neighbors (FKNN). Model performance was assessed via cross-validation, ROC curves, and confusion matrices.

Results: Of the initial 20,000 participants, 14,675 (73.4%) were included in the final analysis. Among them, 1,096 were HbsAg (+), and 6,086 were non-infected (negative for both HBsAg and anti-HBc), with a median birth year of 52 ± 14 . The feature selection by RFE and TBFI identified show best performance, finally seven significant features associated with HBsAg positive were found. Performance analysis showed Medium Tree = 92.6%, BNN = 92.5%, Linear SVM = 91.7%, LR = 91.7, FKNN = 87.8%.

Conclusion: Machine learning models demonstrate significant potential in screening for HBV infection using demographic data.

Abstract Submission No. 200056
O-0474

Deep Learning Algorithm Applied to Plain CT Images to Identify SMA Abnormalities

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Purpose: To develop a DL model for detecting SMA abnormalities on plain CT and evaluate its performance in comparison with a clinical model and radiologist assessment.

Materials and Methods: A total of 1048 patients comprised the internal (474 with SMA abnormalities, 474 controls) and external testing (50 with SMA abnormalities, 50 controls) cohorts. The internal cohort was divided into the training cohort ($n = 776$), validation cohort ($n = 86$), and internal testing cohort ($n = 86$). A total of 5 You Only Look Once version 8 (YOLOv8)-based DL submodels were developed.

Results: Of the submodels, YOLOv8x had the best performance. The area under the curve (AUC) of the YOLOv8x submodel was higher than that of the clinical model (internal test set: 0.990 vs 0.878, $P = .002$; external test set: 0.967 vs 0.912, $P = .140$) and that of all radiologists ($P < .001$). The YOLOv8x submodel, when compared with radiologist assessment, demonstrated higher sensitivity (internal test set: 100.0% vs 70.7%, $P = .002$; external test set: 96.0% vs 68.8%, $P < .001$) and specificity (internal test set: 90.7% vs 66.0%, $P = .025$; external test set: = 88.0% vs 66.0%, $P < .001$) and shorter inference time (internal test set: 1.04 min vs 94.80 min, $P < .001$; external test set: 1.24 min vs 104.80 min, $P < .001$).

Conclusion: Using plain CT images, YOLOv8x was able to efficiently identify cases of SMA abnormalities. This could potentially shorten the time to diagnosis and thus improve clinical outcomes.

Abstract Submission No. 200163
O-0475

Automated Abdomen CT Diagnostic Pipeline for Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC), a leading cause of global cancer-related deaths, lacks comprehensive characterization in previous abdominal CT screening studies. Our innovative AI pipeline utilizes advanced architectures for liver and lesion analysis, achieving a remarkable 97.5% dice score for liver segmentation and an 89.1% F1 score for lesion classification. With 86% sensitivity and 97% specificity, the pipeline holds promise for efficient and accurate HCC diagnosis. This study employs a significantly extensive dataset, which surpasses the size of previous works in this field by a factor of ten. This dataset comprises a comprehensive "golden ground truth" gathered from retrospective clinical reports and is the basis of the study's robust findings. Through the power of AI, our objective is to contribute to early detection, precise characterization, and improved patient outcomes in combating HCC

Abstract Submission No. 101555
O-0476

The role of the Retinoid X Receptor- α in liver regeneration in mice

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Background: Vitamin A is primarily stored in hepatic stellate cells (HSCs) as retinyl ester. HSCs are activated in response to external

stimulations, including hepatectomy, by conversion of stored retinyl ester into retinoic acid, and thereby associate with liver regeneration. Retinoid x receptor- α (RXR α), one of the retinoid nuclear receptors, forms heterodimer with the other nuclear receptors, and regulates downstream gene expressions. Thus, RXR α functions as a master regulator of retinoid signaling; however, the role of RXR α in liver regeneration remains unclear.

Methods: We used transgenic (TG) mice in which the expression of a dominant-negative form of RXR α is induced by doxycycline administration. Mice lacking the transgene were used as control. First, both TG and the control mice (Male, 10-12 weeks of age) were subjected to 70% partial hepatectomy (PH). Then, the liver/body weight ratio, serum alanine aminotransferase (ALT) levels, and liver histology on days 0, 1, 3, and 7 after PH were compared between the two groups.

Results: The liver/body weight ratios of TG mice at day 3 were significantly lower than that of the control. The infiltration of inflammatory cells and serum ALT levels were comparable between the two groups. The number of Ki67-positive liver cells in TG mice were significantly decreased on day 1, but increased significantly on day 3 compared to that of control.

Conclusions: RXR α plays a role in liver regeneration in mice by regulating the proliferation of liver cells at early time points after PH. Thus, targeting RXR α could be a therapeutic strategy for liver regeneration.

Abstract Submission No. 101810
O-0477

Exosomes trigger the production of inflammatory cytokine by hepatic macrophages via TLR-4 signaling

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Background: Exosomes (EXOs) were involved in acute lung injury (ALI) in hemorrhage shock. Therefore, this study aimed to investigate the role of EXOs in the activation of hepatic macrophage (Mfs) and ALI in a rat sepsis model.

Methods: In rats undergoing cecal ligation and puncture (CLP), EXOs were isolated by the centrifugal method from blood and administered intravenously to normal rats. Lung tissues and blood samples were harvested. Pathophysiological changes in the lung, the lung wet/dry weight ratio, and the lung microvascular permeability were assessed. Furthermore, plasma inflammatory cytokine levels were measured. In another set of experiments, the production of inflammatory cytokines by isolated hepatic macrophages (Mfs) was assessed *in vitro*. Moreover, the mechanism of a signaling cascade of activation of Mfs was investigated.

Results: Pulmonary interstitial edema, inflammatory cell infiltration, microhemorrhage, and microthrombosis were observed in lung tissues in normal animals administered with EXOs; however, the extent of these changes was not as severe as in animals undergoing CLP. These pathophysiological changes were blunted by the deletion of hepatic Mfs by clodronate-liposomes *in vivo*. Inflammatory cytokine production by hepatic Mfs also increased by EXOs and was inhibited in cells cocultured with toll-like receptor (TLR) 4 antibodies *in vitro*.

Conclusion: In conclusion, EXOs isolated from blood in sepsis are triggering the production of inflammatory cytokines by hepatic Mfs via TLR-4 signaling, and are partly involved in ALI

Abstract Submission No. 102042
O-0478

AFP-expressing hepatocytes function as hepatic stem cells that give rise to liver cancer

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While it is clinically evident that AFP is a crucial factor in liver regeneration and carcinogenesis, the significance of hepatocytes expressing AFP remains unclear. Here, we analyzed the biological significance of AFP-positive hepatocytes using the latest molecular biology technologies. AFP-CreERT mice were crossed with Rosa-LSL-Tomato reporter mice (AFP-Tom mice), and lineage tracing revealed that Tomato-positive cells did not proliferate significantly under homeostatic conditions. However, when crossed with the MUP-uPA mouse, a model of liver injury, or subjected to a choline-deficient high-fat diet (CDAHFD) for MASLD-HCC model, Tomato-positive cells proliferated over time, expanding to occupy a substantial portion of the liver. In the CDAHFD model, most developed HCCs were Tomato-positive, confirming that AFP-positive hepatocytes not only function as hepatic stem cells during liver injury but also have the potential to become cell of origin of HCC. To elucidate the characteristics of AFP-positive cells during liver injury, single-cell RNA-seq analysis in MUP-uPA mice identified eight distinct clusters of hepatocytes, with the Hep7 cluster exhibiting significantly higher AFP positivity. Hep7 cells displayed characteristics such as increased cell proliferation, activation of lipid synthesis, and downregulation of cell death pathway. Integrated analysis with spatial gene expression mapping of Hep7 cells on liver tissue sections revealed no anatomical zonation differences but a higher presence near dead cells, suggesting induction of AFP-positive cells through interactions with dying hepatocytes. Further functional analysis of AFP-expressing hepatocytes may lead to the development of novel therapies for liver regeneration and cancer prevention.

Abstract Submission No. 100300
O-0479

The effect of portal diversion model in dog for the liver function

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Portal blood consists of mesenteric and splenic venous blood. In order to determine which one is more important in maintaining liver functions, canine models of a splenocaval shunt (SC shunt) and small bowel autotransplantation (partial mesocaval shunt, MC shunt) which diverts small bowel venous outflow into the systemic circulation and leaves the gastric, duodenal, pancreatic and colonic venous outflow undisturbed was produced, and metabolic changes of the two models was compared. There was no difference in serum amino acid and ammonia leveled between the two models. But amount of hepatic ATP in the MC shunt model is lower compared to the control and the SC shunt model. These data suggest that venous blood supply from the small intestine may be more important in maintaining ATP amount in the liver. Therefore, portal drainage, which reestablishes the physiological route of venous outflow, may be more preferable in small bowel transplantation.

Abstract Submission No. 101159
O-0480

Glutamine Promotes Liver Regeneration by Portal Tract Collagen Synthesis After Extended Hepatectomy

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Background: Glutamine (Gln) is a vital amino acid for energy expenditure and extracellular matrix (ECM) formation in liver. Liver mass recovery post hepatectomy poses a regenerative challenge in both proliferative and metabolic demand. However, little is known about the role of Gln in liver regeneration process, notably the structural remodeling in a hepatic acinus.

Objectives: The study aimed to explore the role of Gln in liver regeneration and ECM remodeling after mass loss in a spatial-oriented manner.

Methods: Mice received partial hepatectomy and Gln supplementation and were compared for mass regrowth alterations. Second harmonic generation/two-photon excitation fluorescence microscopy (SHG/TPEF) was introduced to reveal the ECM collagen deposition according to functional hepatic zonation.

Results: Gln promotes liver mass regrowth by inducing hepatocytic proliferation through cell-cycle related genes after hepatectomy. Ornithine transaminase (OAT) is up-regulated and thereby facilitating Gln uptake and cellular proliferation. SHG/TPEF showed that Gln potentiated ECM collagen deposition predominantly in the near portal tract area in contrast to central vein area. In addition, the structural remodeling was also enriched in portal tract area during liver regeneration process after mass loss.

Conclusion: Gln promotes liver regeneration via cellular proliferation and metabolic reprogramming after mass loss. The ECM collagen deposition and remodeling are enriched in portal tract area in contrast to central vein area. Together the results highlight the spatial orientation and mechanistic clues of Gln in liver regeneration and provides research potentials into clinical studies.

Abstract Submission No. 101633
O-0481

PTEN/AKT signal promotes cholangiocyte fate in liver tumorigenesis via Notch/SOX9 signal

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Backgrounds: Cholangiocarcinoma (CCA) is the second most dominant primary liver malignancy next to hepatocellular carcinoma (HCC), and among the most mortal among human cancers. The PI3K/AKT signaling pathway was considered a permissive signal for the development of CCA.

Methods: To explore how PI3K/AKT signal contribute to CCA development, we deleted *Pten*, the lipid phosphatase that negatively regulates PI3K/AKT signal in various cell types in the liver. We explored

the mechanisms of tumor development in these mice as well as in vitro. We also generated mice carrying compound deletion of both *Pten* and *Akt*.

Results: The Lv-PTEN (*PtenloxP/loxP*; Alb-Cre⁺) mice developed a mixed HCC and CCA tumor phenotype with all mice developing CCA by 12-month-age. Deletion of *Akt2* in the Lv-PTEN mice (Lv-DM, *Akt2loxP/loxP*; *PtenloxP/loxP*; Alb-Cre⁺) significantly attenuates tumor development and significantly reduced the expression of SOX9, a cholangiocyte gene. SOX9 expression is also induced in the livers of mice where *Pten* deletion is targeted to the hepatocytes only. Notch signal is robustly induced in the tumors of the Lv-PTEN mice. Exposure to Jag1 ligand coated extracellular matrix or expression of NICD also induced the expression of SOX9 while DAPT time-dependently attenuated the expression of SOX9. Inhibiting the Notch pathway with DAPT attenuated ductal reaction and led to downregulation of SOX9 in the Lv-PTEN livers, suggesting a positive regulatory role of Notch on SOX9.

Conclusion: These data support that Notch activation regulates SOX9 and collaborate with PTEN loss to drive cholangiocyte fate and CCA development.

Abstract Submission No. 101822
O-0482

The histological findings with fluorescence microscopy for benign liver tumors

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Background: Currently, indocyanine green fluorescence imaging (ICG-FI) is considered an effective assistive technique in hepatobiliary-pancreatic surgery for tumor identification. In our previous study, we have reported that ICG-FI can detect hepatocellular cancer and colorectal liver metastasis via fluorescence visualization. However, we have detected not only malignant but also benign tumors are visualized intraoperatively and its mechanism has not been investigated. The aim of this study is to investigate fluorescence microscope findings in benign liver tumors.

Patients and Methods: 14 patients were included in this study from Sep. 2011 to Mar. 2023. We resected all the tumors with ICG-guided techniques to identify tumors and secure surgical margin, and all the cases were diagnosed with no malignant post-operatively. Following that we evaluated histological findings with fluorescent microscope (BZ-X800:Keyence corporation).

Results: In 14 cases, tumors were diagnosed with hepatic hemangioma (n=4), focal nodular hyperplasia (FNH; n=3), solitary hepatic cyst (n=1) representatively. 0.5mg/body of ICG was administered intravenously in 2-14 days before surgery, and we divided the fluorescence pattern into 3 types (total, partial, rim). In the case of hepatic hemangioma and FNH, we could detect strong fluorescence in the whole tumor (total fluorescent type). Otherwise, in the cases of solitary hepatic cyst, fluorescence was only observed in the liver parenchyma surrounding the tumor (rim fluorescent type).

Conclusion: This study showed that benign liver tumors such as hepatic hemangioma and FNH exhibit various fluorescence patterns under ICG fluorescence microscopy. We have to accumulate more cases and do further study to investigate its mechanism.

Abstract Submission No. 101987
O-0483

Herbs and the liver

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Bangladesh has a rich heritage of traditional medicine with coexistence of Hekimi or Muslim and Ayurveda or Hindu traditional medicines within the political boundary of today's Bangladesh. However today's unfortunate reality remains that in Bangladesh, we have not been able to retain our glory. When our neighboring India is doing so good with Ayurveda and even have a separate Ayush Ministry, we are trailing behind in this area despite having such rich heritage. It is now one of our principal research focus to revive our traditional herbal medicine. We have already demonstrated the beneficial effects of *Glycyrrhiza Glabra* (joshtimodhu) in end stage hepatocellular carcinoma. Recently during the COVID-19 pandemic our study revealed that hospital stay could be shortened with *Silybum Marianum* (dudhsor) in patients infected with mild to moderate Delta variant COVID-19. Currently we are focusing on non-alcoholic fatty liver disease. We are exploring the prospects of *Andrographis Paniculata* (kalomegh) and *Terminalia Arjuna* (arjun). We are collaborating with a galaxy of public-private universities in our humble effort to revive our glory. Our initial experience with Kalomegh in fatty liver is encouraging.

Abstract Submission No. 200081
O-0484

Upregulated WNT Signaling is Associated with Biliary Hyperproliferation in Biliary Cancer and Injury

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Background: Cholangiocyte hyperproliferation is a hallmark of incurable biliary cancer, cholangiocarcinoma, and cholangiopathies. To develop effective therapies, we need better understanding of the mechanisms regulating aberrant cholangiocyte proliferation. Developmental WNT signaling has been implicated in cell proliferation and stem cell regulation in the liver.

Aim: is to uncover the role of WNT signaling in cholangiocyte proliferation in the understudied extrahepatic bile ducts (EHBDs).

Methods: To examine gene expression and localization in human EHBDs, we performed bulk RNA-seq analysis of human biliary organoids, *in vitro* biliary progenitor cell models, and interrogated cholangiocarcinoma/normal EHBD samples from The Cancer Genome Atlas (TCGA) and our biobank. In mice, we conducted bulk and single-cell RNA-seq analysis of EHBDs at homeostasis and after injury with bile duct ligation (BDL). We used human and mouse biliary organoids and *in vivo* mouse models to examine WNT effects on cholangiocyte proliferation.

Results: Organoid analysis revealed *WNT7B* as the predominant ligand in human and mouse cholangiocytes. Human cholangiocarcinoma

samples (TCGA) demonstrated increased proliferation (*KI67*) and *WNT7B*. *Wnt7b* and WNT target genes (*Birc5*, *Cd44*, *Ccnd1*) were upregulated in mouse EHBDs post-BDL and localized primarily to cholangiocytes in human and mouse EHBDs. *In vitro*, cholangiocyte-secreted WNT ligands activated canonical WNT signaling to induce organoid growth. *In vivo*, inhibition of WNT ligand secretion resulted in decreased biliary proliferation post-BDL.

Conclusions: WNT signaling is upregulated in cholangiocarcinoma and post-EHBD injury. WNT signaling inhibition decreases EHBD cholangiocyte proliferation. Understanding of aberrant WNT-induced biliary proliferation can inform therapeutic strategies for cholangiocarcinoma and cholangiopathies in humans.

Abstract Submission No. 200124
O-0485

Tumor infiltrating immune cells in hepatocellular carcinoma differs according to the viral status

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Background: Tumor infiltrating immune cells play an important role in the prognosis of hepatocellular carcinoma (HCC). The HCC development has several aetiologies, which may lead to differences in the types of cells that constitute the tumour tissue. In this study, a comparison of the immune cells constituting the human tumour tissue was performed using single-cell RNA-seq analysis. Specifically, HCV-, HBV- and non-B-non-C (NBNC)-derived HCC were compared.

Methods: A total of 35 HCC patients were enrolled in this study, consisting of 9 HCV, 12 HBV and 14 NBNC-derived HCC. Fresh liver tissue obtained by hepatectomy was used for single cell RNA-seq analysis using a 10x genomics device. After NGS analysis, tumour-infiltrating immune cells were classified based on gene expression patterns.

Results: The tumour-infiltrating immune cells could be divided into 48 clusters based on gene expression patterns. The profile of clusters and cell types was similar between the NBNC and HBV-positive groups, but the HCV-positive group showed distinct profiles. In the HCV-positive group, the proportion of type 3 innate lymphoid cells (ILC3) and CD8-positive NKT cells were increased approximately 5.4-fold and 4.2-fold, respectively, compared to the other group. M2 macrophages were frequently observed in the HBV-positive and NBNC groups at 22.2-fold and 4.7-fold, respectively, compared to the HCV-positive group. Interestingly, a monocyte expressing S100A8/9/12 was frequently observed in the NBNC group at approximately 3.6-fold compared to the HCV- and HBV-positive groups.

Conclusions: This study has revealed significant differences in the infiltrating immune cells in different aetiologies.

Abstract Submission No. 100255
O-0486

Metabolite-Based, Weight-Independent Diagnostic Model for Non-Alcoholic Fatty Liver Disease (NAFLD)

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Background: NAFLD is a growing public health concern. Despite its commonly known association with obesity, NAFLD is also prevalent in individuals with a lean body mass ($18.5 \leq \text{body mass index [BMI]} < 23 \text{ kg/m}^2$). Consequently, there is an urgent need for a diagnostic method capable of identifying NAFLD regardless of body weight. This report describes the development of such a model.

Methods: This cross-sectional study involved 4555 participants who underwent annual health check-ups in 2015 and 2016 that collected clinical data, including anthropometric measurements, laboratory results, and abdominal ultrasounds. A gas chromatography-mass spectrometry-based metabolomics analysis of serum samples measured 40 metabolites. The diagnostic model was constructed using the least absolute shrinkage and selection operator (LASSO) method with 10-fold cross-validation. Quantitative model performance was assessed using the area under the curve (AUC) obtained through receiver operating characteristic analysis.

Results: The overall prevalence of NAFLD was 22.5% ($n=1026$) and was higher in males (62.6% vs 35.3% non-NAFLD), older individuals (mean age: 54.4 vs 51.5 years non-NAFLD), and those with high BMIs (mean BMI: 25.5 vs 21.2 kg/m^2 non-NAFLD). LASSO identified 13 key metabolites (alanine, 2-hydroxybutyric acid, isoleucine, proline, glycine, serine, decanoic acid, 2-oxoglutaric acid, glutamic acid, asparagine, glucose, tyrosine, and uric acid). The model exhibited robust diagnostic performance (test set: AUC=0.860; 95% CI, 0.843-0.878). Moreover, it demonstrated superior NAFLD diagnostic accuracy in lean individuals compared with BMI (test set AUC: LASSO=0.823, BMI=0.730).

Conclusion: This NAFLD metabolite-based diagnostic model can be universally applied for large-scale NAFLD screening, regardless of examinee's weight.

Abstract Submission No. 100355
O-0487

Deciphering the Dynamic Immune Landscape of Primary Liver Cancer to Predict Immunotherapy Response

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Combinatory immunotherapies employing PD-1/PD-L1 immune checkpoint inhibitors (ICIs) are vital for primary liver cancer (PLC) treatment, but response rates remain unsatisfying. It is urgent needed to explore novel non-invasive methods distinguishing responders from non-responders. Here, we used CyTOF analysis on sequential peripheral blood mononuclear cell (PBMC) samples from ICI-treated PLC patients, analyzing immune signatures, clinical traits, and therapeutic response. Tissue residence was assessed via multiplex immunohistochemistry, and a prospective model was developed using generalized linear model. In the discovery cohort ($n=24$), responders had lower baseline B cell and HLA-DR⁺CD8⁺ T cell percentages, with higher CD14⁺CD16⁺ classical monocyte (CM) proportions. CMs decreased more in responders' PBMCs post-ICI exposure, while HLA-DR⁺CD8⁺ T cells increased in both groups. Pre-therapy, responsive individuals displayed upregulated exhaustion and activation markers in peripheral immune lineages. In the expanded cohort of 77 patients, we observed

a positive correlation between the B cell percent and serum IL-6 levels, and re-confirmed the augment of the B cells in ICI non-responders. Responders demonstrated over two-fold higher enrichment of B cells or tertiary lymphoid structures in situ tumor compared to non-responders. We also identified response-specific immune signatures for PLC and developed a five-parameter-based predictive model that excelled in early discrimination of responders to treatment. In summary, our study unveils dynamic immune landscapes in unresectable PLC patients undergoing ICI-based therapy, and established a non-invasive and efficient model to predict clinical response before immunotherapy. This model could enhance clinical care, aiding in PLC patient stratification for ICI-based treatment and fostering new response monitoring strategies.

Abstract Submission No. 100831
O-0488

HBV virus-host chimera DNA serves as a personalized circulating biomarker for residual tumors of HCC

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Background: Timely detection of minimal residual tumor for hepatocellular carcinoma (HCC) is helpful in recurrence monitoring and evaluating treatment strategies. This study examined the feasibility of HBV virus-host chimera DNA (vh-DNA) as a personalized circulating biomarker for residual tumors after surgery.

Methods: The tumor-specific vh-DNA integration sites were determined in 148 HBV-related HCC patients by next-generation sequencing. For each individual HCC, vh-DNA was quantified using a customized droplet digital PCR (ddPCR) assay in plasma samples collected within 14 months after surgery, and the results were compared with the clinical outcomes.

Results: HBV integrations were identified in 132 out of 148 patients with HBV-related HCC (89.2%). Among the 116 patients who completed the postoperative follow-up, the positive predictive value (PPV) of vh-DNA for tumor recurrence was 68% (17/25), and the negative predictive value (NPV) was 92% (84/91). The mean leading time of vh-DNA detection was 140 days earlier than computed tomography scanning. A total of 78% (18/23) of recurrences originated from the same HCC clones sharing the same vh-DNA, suggesting that most of the early recurrence came from residual tumor cells. Moreover, multivariate cox regression analysis showed that vh-DNA was an independent risk factor for predicting early recurrence. When vh-DNA combined with serum AFP, the sensitivity and specificity of recurrent HCC were 92% and 88%, respectively.

Conclusion: This study demonstrates that utilizing vh-DNA to monitor the presence of residual tumors after surgery could be a promising solution for prognosis assessment, recurrence monitoring, and guiding adjuvant therapies in the future.

Abstract Submission No. 101176
O-0489

Chemoprotective mechanisms of skullcapflavone in aflatoxin-induced toxicity in THLE-3 hepatocytes

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The protective effect of skullcapflavone I (SKI) against aflatoxin B1 (AFB1)-induced cytotoxicity and genotoxicity in THLE-3 cells including possible mechanisms were investigated. SKI previously elucidated and isolated from *Andrographis paniculata* were tested to be biocompatible with THLE-3. THLE-3 were treated with or without SKI for 24 h before AFB1 exposure. Expressed *Akt*, *Bcl2*, and *CYP2E1* transcripts were detected by qRT-PCR. Immunoblotting was performed for translated CYP2E1 including Akt and ERK1/2 phosphorylation. GST activity and AFB1 genotoxic metabolite, aflatoxin B1-8,9 epoxide (AFBO), were quantified. Comet assay was performed to assess DNA damage. AFB1 significantly downregulated the gene and protein expression products of *Akt*, *Bcl-2* while upregulating *CYP2E1*. Akt phosphorylation was inhibited while increased ERK1/2 activation was observed. High percentages of comet tail length and moment connote DNA damage. Pre-treatment with SKI afforded cytoprotective effect in THLE-3 viability with half-maximal effective dose of 8.46 µg/mL. SKI pre-treatment reversed AFB1-induced activities through dynamic *Akt*, *Bcl-2* upregulation and *CYP2E1* downregulation. Moreover, Akt activation increased while ERK1/2 phosphorylation was inhibited. GST activity significantly increased accompanied by decreased AFBO. Comet tail length and moment were comparable with untreated controls. Remarkably, LYS294002, a specific inhibitor of PI3K, impaired SKI protective effect on THLE-3 suggesting the role of the pathway. This study is the first report describing the protective activities of SKI against AFB1-induced toxicity on human hepatocytes and may help contribute to the development of pharmaceutical leads targeting aflatoxin poisoning and carcinogenicity.

Abstract Submission No. 101226
O-0490

Urine Interleukin-18 (uIL-18) as a Prognostic Marker for Mortality Risk in Liver Cirrhotic

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Background: Urine interleukin-18 (uIL-18) has shown to provide prognostic value for several diseases. The release of uIL-18 may reflect the severity of inflammation and the ongoing pathological processes within the liver. Identifying additional biomarkers that can enhance prognostic accuracy in liver cirrhotic patients is essential. This study aimed to evaluate uIL-18 as prognostic indicator to determine higher mortality risk in liver cirrhotic patients.

Methods: This was an analytic cross-sectional study to determine the risk of high uIL-18 for higher risk of mortality according to MELD score. Subjects with MELD score ≥ 20 were considered had higher risk for mortality. The level of uIL-18 measured with ELISA method. Cut-off of high uIL-18 was determined with Youden Index.

Results: A total of 75 subjects involved in this study with mean age of 54.71 ± 11.06 years. Majority of the subjects were male (78.7%). A total of 33 subjects (44%) had higher risk of mortality. The median of uIL-18 was 79.49 (386.63) ng/mL. The cutoff for uIL-18 was 36.87 ng/mL to provide the best value (youden index = 0.29). By using the optimal cutoff, the sensitivity was 78.8%, specificity 50%, positive

predictive value 55.3%, negative predictive value 75%, accuracy 62.6%. High uIL-18 associated with higher risk for mortality by 6.55 times ($p = 0.011$).

Conclusion: uIL-18 provides good specificity and validity to determine higher risk for mortality in liver cirrhotic. uIL-18 could be used as a complementary prognostic indicator, facilitating more precise risk stratification and guiding therapeutic decisions for high-risk liver cirrhosis population.

Abstract Submission No. 101365
O-0491

Evaluation of Tumor Microenvironment in HCC by TCRA Gene and Transcriptome Deconvolution Analysis

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Introduction: The indications for immune checkpoint inhibitors (ICIs) are expanding and their efficacy is recognized, but the predictors of efficacy are not as simple as previously thought. Tumors have limitations in conventional approaches because they require consideration of not only the malignancy and tumor-infiltrating lymphocytes (TILs), but also the tumor microenvironment (TME), which consists of many stromal cells and their activation states. We analyzed the TCRA (Tcell receptor α chain) gene and transcriptome to determine the probability of the presence of various immunocompetent cells and stromal cells in relation to ICI treatment efficacy.

Methods: DNA was extracted from tumor tissue FFPE operated on at our hospital, and the probability of cell presence was calculated by machine learning using a generalized additive model (Cell Exome TREC Tool. Nature 2021) using the process of elimination of delta strand from TCRA ($n=522$).

Transcriptome analysis was performed from mRNA and cell composition was calculated using deconvolution method ($n=251$). 22 immune system cell types were identified in Cibersort (Nat Methods 2015) and 64 cell types (immune system cells, epithelial cells, stromal cells) were identified in xCell (Genome Biology 2017). cells, and stromal cells) were annotated to evaluate the efficacy of ICI treatment and irAE.

Results: Compared to other cancer types, hepatocellular carcinoma has a low ratio of immunocompetent cells. It is necessary to take into account the intra-tumor heterogeneity and differences in the algorithms used to evaluate the immune environment, and further analysis using an integrated machine learning framework will be required in the future.

Abstract Submission No. 101628
O-0492

Serum anti-PD-1 autoantibody predicts survival of HCC receiving atezolizumab/bevacizumab

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Abstract

Background & Aims: In patients with advanced hepatocellular carcinoma (HCC), atezolizumab (anti-programmed cell death-ligand 1 [PD-L1]) and with bevacizumab (anti-vascular endothelial growth factor) combination therapy (Atezo/Bev therapy) is a first-line treatment. However, no reliable biomarkers are currently available to predict its efficacy. Here, we examined serum anti-programmed cell death-1 (PD-1) autoantibody levels as candidate biomarkers.

Methods: Patients with advanced HCC from four institutions participating in the Okayama Liver Cancer Group were prospectively registered and underwent Atezo/Bev therapy. A total of 63 patients were enrolled between November 2020 to October 2022. Serum anti-PD-1 autoantibody levels were measured before treatment using an indirect enzyme-linked immunosorbent assay (ELISA). The correlation between the titers and response to therapy was statistically examined.

Results: Serum anti-PD-1 autoantibody levels were not significantly associated with the treatment response in any patient. However, when examining only patients who received the Atezo/Bev as their first-line therapy, higher anti-PD-1 autoantibody levels were significantly associated with worse overall survival (OS) rates. The titer was an independent risk factor for poor prognosis (odds ratio [OR], 7.8; 95% confidence interval [CI], 1.5-39; $p = 0.013$), in addition to a higher neutrophil-to-lymphocyte ratio (OR, 7.1; 95% CI, 1.6-31; $p = 0.009$) and lower albumin levels (OR, 14.2; 95% CI, 2.38-84.9; $p = 0.003$).

Conclusion: Serum anti-PD-1 autoantibody levels correlated with the OS rate in patients who received Atezo/Bev as first-line therapy. Serum anti-PD-1 autoantibody levels may serve as new biomarkers for predicting the efficacy of immune checkpoint inhibitors in patients with HCC.

Abstract Submission No. 200244

O-0493

Identification of LRG-1 in urine as potential marker for early diagnosis of hepatocellular carcinoma

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Aims: The early diagnosis of hepatocellular carcinoma (HCC) is very important for clinical treatment. The aim of this study is to identify the potential biomarkers in urine for early screening and diagnosis of HCC.

Methods: The urine samples of HCC patients and healthy controls were analyzed, and the protein profiling was detected by LC/MS proteomic method. The data were retrieved from mascot database (Science Matrix). The samples of 142 patients and 48 controls were examined by dot-blot and western-blot analyses. LRG1 monoclonal antibody was prepared and utilized to analyze of LRG1 expression in both HCC cell lines and urine samples of HCC patients. Moreover, in a 247-cohort study, LRG1 protein levels were evaluated by ELISA assays in urine samples of patients with different clinic stages of liver disease from chronic hepatitis B (CHB), liver cirrhosis (LC) and HCC.

Result: Interestingly, leucine-rich-2-glycoprotein-1 (LRG-1) was uniquely present in the urine of HCC patients, but not in the samples of the control. Dot-blot and western-blot analyses further verified the results, which showed that the secretion of LRG-1 in urine was remarkably increased in HCC patients compared with those of the healthy controls. In the cohort study, ELISA data demonstrated that LRG-1 had high accuracy in discriminating HCC from healthy control

when cutoff was 0.78 (AUC=0.937; 95% CI, 0.889 to 0.986; sensitivity = 89.3%, specificity = 89.5%).

Conclusions: Our results suggest that the level of LRG-1 in urine may have the potential to serve as an effective biomarker for the early diagnosis of HCC.

Abstract Submission No. 100298

O-0494

The significance of plasma xanthine oxidoreductase activities in a variety of liver diseases

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Background: Xanthine oxidoreductase (XOR) is highly expressed in the liver, but the number of the study regarding XOR activities in patients with hepatic diseases was few, and the several etiologies were analyzed combinatorially. Recently, high-sensitive and accurate assay for the measurement of XOR activity has been developed.

Methods: We performed a prospective multi-institutional cross-sectional study in which the enrolled numbers of patients and controls were 329 and 32, respectively. We measured plasma XOR activities and purine metabolism-associated markers in etiology-based comprehensive liver diseases by using the novel method. We also analyzed the relationship between the plasma XOR activities and parameters of liver tests, purine metabolism-associated markers, oxidative stress markers, and an inflammation marker.

Results: Plasma XOR activities were generally increased in various liver diseases compared with those in control subjects. The highest activities were observed in a patient with acute hepatitis B. The XOR activities were likely to be high in the active phase. For example, the XOR activities in chronic hepatitis C were significantly higher in patients with active infection than past infection and in those with uncured hepatocellular carcinoma patients than cured ones. Most importantly, the XOR activities were significantly associated with parameters of liver tests, especially serum ALT levels, regardless of etiology and plasma xanthine levels.

Conclusions: The plasma XOR activities might reflect the active phase in various liver diseases. The longitudinal studies such as the comparison of plasma XOR activities between acute phase and recovery phase in various liver disease are needed to verify our results.

Abstract Submission No. 100717

O-0495

Autophagy-Related Genes Promote Development of Pediatric Metabolic-associated Fatty Liver Disease

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Background: Metabolic-associated fatty liver disease (MAFLD) is the most common cause of chronic liver disease worldwide. With an increasing number of overweight or obese children, MAFLD has emerged as one of the most common comorbidities in the pediatric obese population. Currently, the precise pathophysiology of pediatric MAFLD is still not completely understood.

Methods: Pediatric MAFLD dataset and autophagy-related genes(ATGs) were selected for identifying differentially expressed genes(DEGs). Then, protein-protein interaction(PPI) network were integrated to identify the hub genes as gene signature. Next, receiver operating characteristic(ROC) curves were used to evaluate the performance of gene signature. Last, we analysed the the hub genes for expression levels and correlation with immune cells.

Result: We identified six autophagy-related genes(KDR, MYC, VEGFA, CXCR4, IFNG and CCL2) as hub genes, that may be closely related to the development of pediatric MAFLD. Furthermore, we constructed prognosis gene markers based on the hub genes. This gene signature has shown good diagnostic accuracy in both obese and MAFLD pediatric population(AUC>0.6). Compared with mild liver fibrosis, expression level of MYC, CXCR2 and CCL2 significantly increased in advanced liver fibrosis in pediatric MAFLD. In addition, according to the immune cells composition, macrophage M2 significantly increased in pediatric MAFLD which was the opposite of adult MAFLD.

Conclusion: The six hub genes may predict the risk of MAFLD development in pediatric population by mediating autophagy-related mechanism, which is hopeful to be biomarkers for predicting occurrence, diagnosis and treatment of MAFLD.

Abstract Submission No. 100778

O-0496

Exploration of the potential biomarker between COVID-19 and liver cirrhosis-hepatocellular carcinoma

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Background: Coronavirus disease 2019 (COVID-19) pandemic is attributed to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which has widespread impacts on the patients with underlying disease. It is well known that liver cirrhosis (LC) has been coined as a very strong risk factor for the development of hepatocellular carcinoma (HCC). This study aimed to explore the potential gene signature and regulatory network between COVID-19 and LC-HCC. **Methods:** The candidate gene signatures were identified by the common differentially expressed genes (DEGs) based on COVID-19 and LC-HCC utilizing the bioinformatics analysis. Subsequently, the gene functional enrichment analysis (KEGG and GO) and protein-protein interaction (PPI) network were performed, exploring the hub gene as the key biomarker. Finally, receiver operating characteristic (ROC), biological function and gene expression network analyses were systematically conducted. **Results:** The common 78 candidate gene signatures were successfully screened out between COVID-19 and LC-HCC. Then, KEGG and GO enrichment analyses discovered that these candidate genes were mainly involved in the cell cycle. Based on the construction of PPI network, the hub gene CDK1 was successfully identified by means of ten scoring methods. ROC analysis confirmed that CDK1 exhibited a high predictive efficacy in COVID-19 (AUC = 0.955) and LC-HCC (AUC = 0.946) cohorts. Additionally, HCC patients with high CDK1 expression had poor clinical prognosis.

Finally, the comprehensive gene regulatory networks were established. **Conclusions:** This study successfully determined the key biomarker and gene regulatory network between COVID-19 and LC-HCC, contributing to predicting patients' prognosis and therapeutic targets.

Abstract Submission No. 101553

O-0497

Diagnosis of HBV-associated liver cirrhosis and HCC based on Lipid and peptide fingerprints

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Background: In this study, biological changes will be explored during the development of HBV-related HCC based on serum lipidomics and peptidomics and a classifier will be constructed to identify patients at different stages in the HBV-infected population.

Methods: A total of 846 serum samples were collected from 219 healthy volunteers, 206 patients with chronic hepatitis B (CHB), 160 patients with HBV-related LC and 261 patients with HBV-related HCC, and the lipid and peptide fingerprints were acquired based on Nano-assisted laser desorption/ionization time of flight mass spectrometry. Then molecular landscape was analyzed and the stepwise prediction model was conducted.

Results: We found that serum lipid and peptide fingerprints were altered during the evolution from CHB to HCC. The stepwise prediction model was built, which could identify 80.0% HC, 80.9% CHB, 55.6% LC and 90.0% HCC in the external test set. And 95.5%-96.8% of AFP negative HCC patients could be identified by the multi-omics model. When combined with AFP, the sensitivity for identifying HCC patients could reach 97.9%-98.3%.

Conclusions: Platform of acquiring lipid fingerprints and peptide profiling based on NALDI-TOF-MS had clinical application potential in identifying different stages during the evolution of CHB to HCC, which may be a supplementary method of AFP for screening and diagnosis of HBV-related HCC. Chicttr.org.cn number, ChiCTR2300073462.

Abstract Submission No. 101865

O-0498

Identification of Alcoholic Hepatitis-related genes and Mesenchymal Stem Cell treatment Target Genes

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부熟 ju South Korea Alcoholic hepatitis (AH) is a life-threatening condition and widespread chronic liver condition that places patients at risk of short-term mortality if it is not properly managed. This study aimed to identify transcriptomic biomarkers and cell therapy targets for AH.

We conduct a systematic meta-analysis of published human gene expression studies on liver biopsies and blood derived gene data. First, three liver AH transcriptome datasets and a blood AH dataset were combined to discover a common phenotype. Second, two AH prognosis datasets were compiled, which are including gene phenotype reflecting prognosis. Using inverse weighted variance-based method mounted in METAL software, the candidate genes related to AH in liver and blood tissues and annotated them as the liver-blood AH meta genes. Third, three MSC datasets were curated for gene identification in stem cell response. Meta-analysis was implemented on the individual cohort-specific summary statistics obtained from differential expression methods to identify the AH-related biomarkers. To narrow down the candidate hub genes among stem cell treated data, TF database, protein-protein interaction network, disease-gene association database, and disease- and expression-related SNP database were used to analysis.

With previously identified alcoholic gene-related databases, external verification was performed and finally 47 upstream AH-related genes were presented.

We present key genes involved in the progression of AH and provide a meta-analysis of results in a objective, statistically-based format. And at the same time, we suggest this biomarkers that can predict the prognosis of AH and treatment response.

Abstract Submission No. 101347

O-0499

Disease Specific Awareness And Knowledge Of HBV And HCV among CLD patients: Experience From Pakistan

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Introduction: Chronic viral hepatitis is a serious health hazard in developing nations like Pakistan, with estimated prevalence of 7.5% for chronic Hepatitis B (HBV) and 11.5% for chronic Hepatitis C (HCV). These viruses causes cirrhosis and hepatocellular carcinoma leading to significant morbidity and mortality. Many socio-economic variables have been linked to a continuous rise in the frequency of HBV and HCV infections.

Aims: To investigate the determinants related to overall knowledge and awareness about HBV and HCV amongst chronic liver disease patients.

Methods: This was a prospective, cross-sectional study conducted at the GI clinics of largest public sector hospital of Karachi using a self-constructed questionnaire to investigate items related to illness knowledge and perceptions among patients regarding HBV and HCV.

Results: Mean age of respondents were 39± 11 years. Female respondents were 374(58%) and males were 263 (41%). Out of 617, 357(56%) believed HBV and HCV viruses to be an airborne illness with only 250(39%) knew about the viral etiology. There were many misconceptions regarding mode of spread assuming feco-oral route (62%) as the primary source of illness followed by mosquito bite (52%), spread via simple touch (52%) and sharing utensils (49%). Overall literacy level was low as majority of our respondents were uneducated 456 (72%). Methods of prevention including Vaccination against HBV was not known to majority that is 382(60%) and many were ignorant of the treatments that are available.

Conclusion: It is important to design comprehensive hepatitis education initiatives to address patient knowledge gaps since there are misconceptions surrounding HBV and HCV.

Abstract Submission No. 100758

O-0500

A community-centered surveillance program for disease severity map in an under-resourced region

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Background/Aim: Taitung, located in eastern Taiwan, has the lowest population density, the lowest life expectancy, and the lowest medical personnel compared with other prefectures in Taiwan. Liver-related mortality remains one of the major causes of death in Taiwan. The study aimed to elucidate the epidemiological characteristics and the disease severity of liver diseases in Taitung.

Methods: We conducted a mass screening program for those who carried a high-risk for advanced liver disease and did not receive regular liver disease surveillance. The eligible participants were selected from the healthcare database and were invited by email or phone calls via township-based primary care centers. They received FibroScan as the initial surveillance, followed by liver disease tests.

Results: A total of 4,531 residents (1,859 males; mean age= 54.2 ± 14.0 years) participated the program. The prevalence of diabetes, hypertension, and hyperlipidemia were 12.8%, 28.9%, and 12.1%, respectively. There were 302 (6.7%) residents with HBV infection, whereas 49 (1.1%) residents had anti-HCV+. There were 2,044 (45.1%) participants of indigenous background. The prevalence of advanced fibrosis, defined as FibroScan> 9.5 kPa, was 7.0% (316/4,531), ranging from 3.7% to 10.2%. There were 2,874 (63.4%) participants with steatotic liver disease (SLD), defined as Controlled Attenuation Parameter (CAP) value> 238 dB/m. Excessive alcohol use (23.1% vs 6.9%, P= 0.001) and SLD (11.6% vs 4.8%, P< 0.001) were the major factors contributing to advanced fibrosis.

Conclusion: The community-centered surveillance program provided information for disease severity mapping in the under-resourced prefecture.

Abstract Submission No. 100992

O-0501

The Prevalence of Hepatitis B and Hepatitis C Among Police Officers of Rawalpindi, Pakistan

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Background: Police officers play a vital role in law-and-order management and during their frontline duty, they often ignore their health. This article explores the prevalence of these infections among police officers and the importance of addressing this issue.

Aims: Assesses the prevalence and risks leading to infection of hepatitis B and C.

Methods: An integrated screening camp was arranged to screen the Rawalpindi police force against communicable diseases. 15705 officers were tested in a month for Hepatitis B and C with rapid testing kits. 98 positive for HCV, 5 with HBV and 4 with coinfection were interviewed to explore various risk factors that lead to the infection.

Results: 0.24%(37/15705) participants were found reactive for HBsAg antigen, 1.85%(209/15705) were reactive for Anti-HCV.

Out of 327 positive officers, 108 were interviewed for potential risk factors for acquiring the infection. 33.3%(36) had family member with Hepatitis, 32.4%(35) had dental treatment, 27.7%(30) got IV medications, 25%(27) availed roadside barber services, 13.8%(15) had blood transfusion, 8.3%(9) had multiple sex partners, 2.7%(3) had piercings, 1.8%(2) were transgender, 1.8%(2) had IV drugs, 0.9%(1) were men having sex with men and 0.9%(1) got tattoo.

Conclusion: These frontline officers face many challenges in the line of duty, communicable diseases are not to be neglected as 0.24%(37/15705) and 1.85%(209/15705) of officers tested positive for Hepatitis B and C respectively. Major risk factors were positive family members, dental treatments and frequent IV medications. A follow-up viral load testing was done, and those positive were linked to care.

Abstract Submission No. 101089

O-0502

Earlier liver cirrhosis onset in intrafamilial hepatitis Delta Virus transmission in Moldova

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Background: Hepatitis delta, sometimes considered as a vanishing disease in Western Europe, is still widespread in the Republic of Moldova.

Methods: In this comparative cross-sectional study, we described demographic features of 224 HDV-infected patients either affected from chronic hepatitis or liver cirrhosis attending care in three Moldovan centers that we compared with 100 hepatitis B virus-mono-infected subjects.

Results: All delta-infected patients were anti-HBe and HBV DNA was detectable much less frequently (28%) than in mono-infected ones (76-92%, $P < 1.0E-09$). Familial transmission of the virus was much more prevalent in HDV infection than in HBV infection (39% vs 23%, $P = 0.0036$). Amongst patients with hepatitis delta, those with familial contamination developed liver cirrhosis much earlier than others (40.5 ± 9.3 years vs 46.9 ± 8.7 years, $P = 0.053$) and presented more frequently detectable HDV RNA in their plasma (98.7% vs 89.2%, $P = 0.0094$).

Conclusion: Hepatitis delta is a significant health problem in Moldova. Familial transmission of hepatitis delta, especially prevalent South of the country, is responsible of anticipation of the complications.

Abstract Submission No. 101400

O-0503

Modelling the impact of vaccination on HBV transmission and progress to elimination in Punjab, India

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Background: India was estimated to have 32.7 million persons living with Hepatitis B virus (PLHBV) in 2016. The prevalence of chronic HBV infection (HBsAg-positive) in Punjab, India, was 1.4% in 2014 (~400,000 PLHBV). India has scaled up infant HBV vaccination to 91% coverage and timely birth dose vaccination to 56% coverage, but few receive HBV treatment. The World Health Organization (WHO) HBV elimination targets include decreasing new HBV infections by 95% over 2015-2030 and decreasing HBsAg prevalence among children under five to <0.1% by 2030. We used modelling to evaluate progress towards these targets in Punjab.

Methods: A dynamic HBV transmission model was developed, including disease progression, vertical and horizontal transmission, population growth and vaccination. The model was parameterised and calibrated in a Bayesian framework using regional estimates of chronic (HBsAg-positive) and past infection (HBcAb-positive) prevalence, Indian data on HBeAg-prevalence, demographic data, and yearly data on infant and birth dose vaccination coverage. The model was used to simulate trends in HBV transmission and evaluate the impact of ongoing vaccination.

Results: Projections suggest HBV incidence has decreased by 39.9% (95% credibility interval: 30.5-45.6) over 2015-2022, while HBV-related deaths have remained stable. In 2022, 4.5% (2.2-23.6) of new infections and 19.0% (10.8-54.0) of new chronic HBV infections (CHB) were acquired vertically, with 0.11% (0.07-0.19) of new-borns acquiring HBV infection. Model projections estimate that the annual number of new CHB infections have decreased by 31.8% (19.7-38.7) over 2015-2022 and will decrease by 50.0% (36.3-56.5) by 2030. For under-fives, we project that the HBsAg-prevalence will be 0.08% (0.05-0.15) by 2030; below WHO's target. Existing vaccinations have averted 16,200 (6,800-34,500) CHB infections over 2007-2022, resulting in 39.6% (31.6-46.3) fewer infections in 2022.

Conclusion: HBV vaccination scale-up in Punjab has had substantial impact but further strategies are needed to reach the WHO HBV elimination targets.

Abstract Submission No. 100342

O-0504

A 10-year assessment of a population-based prospective liver cancer screening project in Zhongshan

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Background: A comprehensive, long-term assessment of liver cancer screening programs, comparing populations participating in screening with those not participating, is notably lacking in the global research landscape.

Method: We conducted a community-based screening trial in Xiaolan town, Zhongshan City, Guangdong, China, recruiting residents aged 35-64 years in 2012. In total, 18,185 eligible residents were enrolled in the screening group, while 50,073 residents were included in the non-screening group. Participants in the screening group underwent

testing for hepatitis B virus surface antigen (HBsAg) in serum. Those who tested positive for HBsAg were subsequently invited for alpha-fetoprotein (AFP) testing, liver ultrasonography, and/or computerized tomography twice per year. Liver cancer occurrence, vital survival status, and causes of death were monitored until December 31, 2021, using medical records from hospitals, as well as data from the Zhongshan Cancer Registry, Population Registry, and Cause of Death Registry. We calculated the early detection rate and cumulative incidence of liver cancer among residents in both the screening (HBsAg positive (+) or negative (-)) and non-screening groups. Additionally, we assessed the disparities in overall and liver cancer-specific survival probabilities between individuals in these groups.

Results: With a median follow-up period of 10 years, 432 liver cancer cases occurred. Within the study cohort, comprising 50,073 non-screening residents, 15,295 screening residents with HBsAg (-), and 2,893 screening residents with HBsAg (+), the proportion of liver cancer was 0.6%, 0.2%, and 3.7%, respectively ($p<0.01$). The early detection rates for these groups were 13.9%, 31.6%, and 29.9%, respectively ($p=0.001$). The cumulative incidence of liver cancer was highest among screening residents with HBsAg (+) ($p<0.001$). Furthermore, the cumulative overall survival ($p=0.002$) and liver-cancer specific survival ($p=0.028$) probabilities among liver cancer cases from screening residents with HBsAg (+) were superior to those among cases from screening residents with HBsAg (-) and non-screening residents. Their 1-year overall survival probabilities since diagnosis among screening group *versus* non-screening group were 53.8% and 34.5%; 3-year overall survival probabilities were 29.4% and 11.3%; and 5-year overall survival probabilities were 27.7% and 6.9%, respectively (all $p<0.05$). These survival advantages were more pronounced five years after enrollment (Adjusted hazards ratio (aHR): 0.55, 95% confidence interval (CI): 0.41, 0.75) than that within five years since enrollment (aHR: 0.99, 95% CI: 0.71, 1.39).

Conclusion: This study underscores the importance of proactive liver cancer screening strategies in the early detection of liver cancer. Notably, it highlights the potential to extend the survival probabilities for liver cancer individuals, especially in the long-term perspective.

Abstract Submission No. 100492
O-0505

HEPATOCELLULAR CARCINOMA AT LIVER TUMOR DEPARTMENT, CHO RAY HOSPITAL: CANCER REGISTRY 2010-2022

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HCC is found to contribute significant health care burden in Vietnam, the number of cases has steadily increased from 2010 to 2022. Liver Tumor Department of Cho Ray Hospital, HoChiMinh City is the biggest center of HCC in Vietnam. Data from 46,602 HCC patients from 2010 to 2022 were extracted, comprising of 82.13% male patients. Male/female ratio is 4.60/1. Mean age is 58.9. 92.33% of patients were older than 40 years old, mainly from 50 to 70 years old. This patient sample derived from numerous provinces throughout Southern Vietnam and southern of Central Vietnam (50.2 millions people), including 42.01% from Mekong River Delta (19578 patients/17.3 millions people/13 provinces), 14.15% from HoChiMinh City (6595 patients/9 millions people), 16.82% from SouthEast region (7840 patients/8.8 millions people/5 provinces), 16.30% from South Central Coast region (7596 patients/9.2 millions people/8 provinces) and 8.96% from Central Highland region (4176 patients/5.8 millions people/5 provinces). HBV infection was found in 58.96% of cases, HCV infection was found in 22.55% of cases, while HBV and HCV co-infection was found in 2.61% of cases. 11.70% of patients have no virus infection.

28.48% HCC patients have AFP level<20ng/ml, 25.39% have AFP 20-<400ng/ml and 44.58% have AFP>400 ng/ml. Over this 13-year period, the number of HCC cases is still in high level, with a large proportion of cases (23740 patients / 50.94%) presenting initially in far advanced stage and only suitable for best supportive care.

Abstract Submission No. 100502
O-0506

Epidemiology of HCC in patients with viral Hepatitis

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Background: Hepatocellular carcinoma is the most common cancer in the worldwide, representing more than 5% of all cancers. Liver cirrhosis, age, sex, smoking and drinking, and metabolic risk factors will increase the risk of cancer in HBV/HCV/HDV patients. Viral load, FIB-4, and stiffness of the liver can predict the risk of HCC in patients with viral infection. Moreover, effective prevention strategies are needed to reduce the risk of HCC. Secondary prevention includes effective antiviral treatment for HBV / HCV / HDV to prevent disease progression to HCC

Methods: During period since January 2019 to October 2023, 6240 patients (57% males, 43% females, mean age 34 years±6.5) were included to our study , while 1996 (32%) with Hepatitis B , 4224 (67,7%) Hepatitis C and 249 (4%) with Viral Hepatitis B and D.

Results

Totally HCC was diagnosed in 199 patients (3,2%) , with Hepatitis C 97 (2,3%) , with Hepatitis B 55 (2,8%) and also with Hepatitis B+D - 9 (3,8%) patients.

Conclusion: Chronic Viral Hepatitis are most important causes of HCC. Among viral hepatitis HCC often determined in B+D viral hepatitis group. Eliminating the route of transmission and vaccination against Hepatitis B will lead to a decrease in the incidence of HCC.

Abstract Submission No. 100523
O-0507

Clinical and immune feature of anti-MDA5 dermatomyositis patients with COVID-19 during Omicron wave

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The clinical and immunological features of patients with anti-melanoma differentiation-associated gene 5 (anti-MDA5) dermatomyositis (DM) after COVID-19 infection were still unclear. In this study, 67 patients with anti-MDA5 DM were recruited from the Second Affiliated Hospital of Chongqing Medical University during the Omicron wave epidemic. Clinical data were collected by questionnaire survey and electronic medical record. Blood samples were used to determine the antibody responses, B and T cell responses. From 9 December, 2022 to 31 March, 2023, 68.7% (46/67) patients were infected. The most common symptoms of COVID-19 infection were upper respiratory symptoms, with 7 days median duration, and most of them were

mild or moderate (97.8%). Vaccination is not a protective factor against the Omicron infection. Meanwhile, six patients with worsening DM symptoms were observed after infection, mainly respiratory and skin symptoms, and four of them were judged as related to COVID-19 infection. The other clinical laboratory indexes were relatively stable in patients after infection. Both wild-type (WT) NAbs titer and BA.5-specific IgG titer were significantly enhanced after infection ($p < 0.01$), which was as high as healthy controls (HC). The memory B cell responses were similar between patients and HC group. But both the WT-specific CD8⁺ T cell and CD4⁺ T cell were reduced in anti-MDA5 DM patients. In conclusion, patients with anti-MDA5 DM will not deteriorate the COVID-19, in turn, COVID-19 infection will not increase risk of anti-MDA5 DM exacerbation. The humoral responses were robust but the cellular responses were weakened in anti-MDA5 DM patients after COVID-19 infection.

Abstract Submission No. 100650
O-0508

Trends of the mortality of cirrhosis in China: an analysis of the China Death Surveillance Database

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Background: China accounted for 14.9% of the total cirrhosis deaths in the world, a detailed and comprehensive understanding of contemporary status of cirrhosis mortality in China will be crucial to establish strategies for intervention and decrease the disease burden of cirrhosis in the world.

Methods: Mortality data from 2008 to 2020 were retrieved from the Disease Surveillance Point system of Chinese Center for Disease Control and Prevention. Crude mortality rate and age-standardized mortality of cirrhosis were exhibited by sexes, residential locations, and regions, respectively. The average annual percentage change (AAPC) of cirrhosis mortality rates from 2008 to 2020 was also calculated.

Results: The crude mortality rate of cirrhosis was 4.57 per 100,000 people in 2020. Compared with females and individuals lived in urban areas, females and people lived in rural areas had higher age-standardized mortality. The crude mortality rate and age-standardized mortality rate in provinces from southwest China (Guangxi, Yunnan, Guizhou, Qinghai) was higher than that in other provinces. Meanwhile, with the increase of ages, the age-specific mortality rate increased significantly. From 2008 to 2020, the mortality rates of cirrhosis showed a downward trend in China except for males aged 50-59 years, females aged 45-49 years and 80-84 years.

Conclusions: From 2008 to 2020, the mortality rate of cirrhosis showed a decreasing trend in China. In the future, interventions for cirrhosis mortality control need to pay more attention to all males and females aged 45-49 and 80-84 years, people lived in rural areas and provinces in southwest China.

Abstract Submission No. 100829
O-0509

The role of nurses and clinical engineers in percutaneous locoregional treatment for liver cancer

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Background: In the ultrasound-guided percutaneous locoregional treatment for patients with liver cancer, we have been using the next-generation microwave thermosphere ablation system (Emprint™; Covidien, Boulder, CO, USA) since December 2019. Collaboration among doctors, nurses, clinical engineers (CE), and other medical staffs in the perioperative period is essential to provide safe and smooth medical care. We introduce the roles of nurses and CEs in the percutaneous ablation therapy in our hospital.

Methods: We use a clinical path for percutaneous thermosphere ablation therapy. Each patient is briefed about the treatment outline by nurses in admission. The information of patient is shared among all the departments involved in the treatment in advance. The medical team for ablation therapy is composed of total five members including two hepatologists, two nurses, and one CE. At the beginning of the treatment, whole team perform a time-out. Nurse's duty during the treatment includes management of drugs and supplies, drug injection, monitoring of vital signs, nursing records, and so on. CE's duty includes not only management and maintenance of controlled medical devices requiring special maintenance, but also supports for nurses by checking the vital sign monitor and patient's condition to ensure safety. Although the operation of microwave generator is simple, attention needs to be paid to coolant overheating when ablation time is longer. After the ablation, ward nurses continue post-operative care based on the clinical path.

Conclusions: Good team care collaborating with multiple medical professionals makes it possible to provide safe and smooth ablation therapy.

Abstract Submission No. 100922
O-0510

Changes in the prevalence of hepatitis B and C viral infections in Sindh province, Pakistan:

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Background/Aims: Pakistan harbours a large burden of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection. We utilised repeat sero-surveys to assess progress achieved towards hepatitis elimination in Pakistan.

Methods: Multilevel logistic regression evaluated the change in HBV infection (HBV surface antigen (HBsAg)-positive) prevalence and

HCV exposure (HCV antibody (HCV-Ab)-positive) prevalence between two sero-surveys from 2007 and 2019 for Sindh province, and associated risk factors. Adjusted Odds Ratios (aOR) were estimated, and population-attributable fractions (PAF) for modifiable risk factors for HCV exposure.

Results: The 2007 and 2019 surveys included 8855 and 6672 individuals. HBsAg prevalence decreased from 2.6% (95% confidence intervals (95%CI):2.2-2.9%) in 2007 to 1.1% (95%CI:0.8-1.3%) in 2019, while HCV-Ab prevalence increased from 5.1% (95%CI:4.6-5.5%) to 6.2% (95%CI:5.6-6.8%). The age and gender-adjusted HBsAg prevalence decreased by 80% (aOR=0.2, 95%CI:0.1-0.4) among children and 60% (aOR=0.4, 95%CI:0.3-0.6) among adults over 2007-2019, while HCV-Ab prevalence decreased by 60% (aOR=0.4, 95%CI:0.2-0.7) in children and increased by 40% (aOR=1.4, 95%CI:1.2-1.7) in adults. HCV-Ab prevalence was lower in adults with secondary (aOR=0.6, 95%CI:0.5-0.8) and higher (aOR=0.5, 95%CI:0.3-0.8) education compared to illiterates, and higher among adults reporting blood transfusion (aOR=1.7, 95%CI:1.2-2.4), family history of hepatitis (aOR=2.5, 95%CI:1.9-3.3), past year medical injection (aOR=2.1, 95%CI:1.6-2.7), being tattooed (aOR=1.4, 95%CI:1.0-1.9) and shaved by traditional barber (aOR=1.2, 95%CI:1.0-1.5). Modifiable risk factors accounted for 45% of HCV exposure, with medical injection(s) accounting for 38% (95%CI:25.7-48.4%).

Conclusions: Overall HCV has increased over 2007-2019 in Sindh province, while HBV prevalence has decreased. Medical injections should be an important focus of prevention activities.

Abstract Submission No. 101030

O-0511

Prognostic impact of solitary large (≥ 5 cm) hepatocellular carcinoma treated with proton beam

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Background: While Barcelona Clinic Liver Cancer classification puts an emphasis on resectability for an indicator between early and intermediate hepatocellular carcinoma (HCC), controversies exist about solitary large size of HCC (SLHCC) and several reports have suggested a size of 5 cm as the cut-off value for staging. Although several studies have reported the outstanding outcomes of Proton beam therapy (PBT) for HCC, only a handful of outcomes were reported about SLHCC with short-term follow-up periods and a small sample size. The purpose of the current study was to evaluate prognostic outcomes of PBT for SLHCC without major vascular invasion.

Methods: 110 Patients who underwent definitive PBT for solitary HCC at our institution between January 2010 and August 2016 were retrospectively reviewed. All were re-classified by tumor size into Group A (≤ 5 cm, $n = 81$ (73.6 %)) and Group B (> 5 cm, $n = 29$ (26.4 %)). Survival and local control were evaluated according to Kaplan-Meier method and compared by the log-rank test.

Results: The 1- and 5-year overall survival rates (OS) for Group A and B were 96.3 and 67.0% versus 93.1 and 35.3%, respectively ($p = 0.0027$). The corresponding progression-free survival rates (PFS) and local control rates were 86.2 and 45.7% versus 60.6 and 23.7% ($p = 0.001$) and 98.7 and 86.9% versus 92.4 and 67.1% ($p = 0.078$), respectively.

Conclusions: Long-term OS and PFS of PBT for SLHCC were significantly inferior to that of smaller HCC. Further studies are warranted for the combination therapy.

Abstract Submission No. 101334

O-0512

Hepatitis A Among Adult Patients Presenting With Acute Hepatitis: A Changing Epidemiological Trend

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Background: For decades, Hepatitis A virus (HAV) had been a leading cause of acute hepatitis among children and was less prevalent among adults. However, recently a paradigm shift has been observed in the epidemiology of HAV evident by cases of acute hepatitis due to HAV among adults. Very limited data is available from Pakistan about the burden of hepatitis A among adults. The study is designed to estimate the frequency of HAV among adult patients with acute viral hepatitis at a tertiary care hospital in Karachi, Pakistan.

Methods: This is an ongoing prospective, cross-sectional study, being conducted at Gastroenterology Department Aga Khan University Hospital from January 2022 to November 2023. Patients aged ≥ 18 years who presented with acute hepatitis to emergency or outpatient department are reviewed. Demographic data, clinical and laboratory parameters were recorded and analyzed.

Results: A total of 117 patients were found to have Acute hepatitis caused by hepatotropic viruses. Most common age group is 18-30. Approximately 64% of cases of acute hepatitis were attributed to HAV followed by 35% of the cases due to HEV, 1 % by HBV. Higher levels of ALT and AST were observed among adults with HAV than HEV. Higher proportion of HEV was recorded among pregnant patients. Higher proportion of Acute hepatitis with coagulopathy and ALF were observed among HEV cases than HAV.

Conclusions: HAV seems to be the rising cause of acute hepatitis among adults. This signifies the need of improved sanitation, hygiene and a robust vaccination programme against Hepatitis A among adult population.

Abstract Submission No. 101407

O-0513

Genetic variation in *SLC39A8* and risk of hepatocellular carcinoma in the Danish general population

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Background: Manganese is an important co-factor for numerous biological processes. Multiple studies have linked a common variant in the manganese transporter *SLC39A8*, p.Ala391Thr to lower blood levels of manganese. The variant has further been linked to increases in alanine transaminase levels and MRI determined hepatic inflammation. We hypothesize that the *SLC39A8*, p.Ala391Thr variant associates with increased risk of liver disease mediated by manganese deficiency in the general population.

Methods: We included $n = 334,886$ white participants from the UK Biobank and $n = 117,074$ white participants from the Copenhagen City Heart Study and the Copenhagen General Population Study combined. We tested associations with biochemical and imaging markers of liver disease, risk of ICD-based liver disease, and risk of liver-related and all-cause mortality for carriers of the *SLC39A8*, p.Ala391Thr variant.

Results: There were 56,705 heterozygous and 2,079 homozygous carriers of the p.Ala391Thr variant in total. The variant associated with increased plasma alanine transaminase, aspartate transaminase, and triglycerides and with lower levels of albumin, total cholesterol, and HDL cholesterol. In the Copenhagen cohort, the variant associated with increased risk of hepatocellular carcinoma (odds ratio = 1.89, 95 % confidence interval (CI): 1.19-2.98, $P = 0.006$). Heterozygous carriers had an increased risk of liver related mortality with a hazard ratio of 1.68 (95 % CI: 1.13-2.48, $P = 0.007$).

Conclusion: *SLC39A8* p.Ala391Thr associated with increased liver enzymes and increased risk of developing and dying from liver cancer in the general population.

Abstract Submission No. 101408

O-0514

Telomere length and risk of cirrhosis and liver cancer in the Danish general population

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Background: Inherited short telomeres are associated with risk of liver disease, whereas longer telomeres predispose to cancer. The association between telomere length and risk of hepatocellular carcinoma and cholangiocarcinoma remains unknown.

Method and Results: We measured leukocyte telomere length using multiplex PCR in 63,272 individuals from the Danish general population. Telomere length and plasma alanine transaminase concentration were not associated ($\beta = 4 \times 10^{-5}$ kcal, P -value = 0.06) in a linear regression model. We tested the association between telomere length and risk of cirrhosis, hepatocellular carcinoma, and cholangiocarcinoma using Cox regression. During a median follow-up of 11 years, 241, 76, and 112 individuals developed cirrhosis, hepatocellular carcinoma, and cholangiocarcinoma, respectively. Telomere length and risk of cirrhosis were inversely and linearly associated (P -value = 0.004, P for nonlinearity = 0.27). Individuals with telomeres in the shortest vs. longest quartile had a 2.25-fold higher risk of cirrhosis. Telomere length and risk of hepatocellular carcinoma were nonlinearly associated (P -value = 0.009, P -value for nonlinearity = 0.01). This relationship resembled an inverted J-shape, with the highest risk observed in individuals with short telomeres. Individuals with telomeres in the shortest vs. longest quartile had a 2.29-fold higher risk of hepatocellular carcinoma. Telomere length was inversely and linearly associated with the risk of cholangiocarcinoma (P -value = 0.03, P for nonlinearity = 0.95). Individuals with telomeres in the shortest vs. longest quartile had a 1.86-fold higher risk of cholangiocarcinoma.

Conclusion: Shorter telomere length is associated with a higher risk of cirrhosis, hepatocellular carcinoma, and cholangiocarcinoma.

Abstract Submission No. 101439

O-0515

Global, regional, and country-level estimates of new HCV infections attributed to injection drug use

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Background: We estimated, at country/regional/global levels, HCV incidence in people who inject drugs (PWID) and the number of new annual HCV infections attributed to injection drug use using multiple methods and data.

Methods: We compiled previously published estimates of HCV incidence in PWID from our global systematic review and modelling studies with new estimates. We used four different methods to estimate HCV incidence: (i) longitudinal re-testing of people-at-risk or assays for recent infection (direct), (ii) dynamic modelling using HCV Ab prevalence in PWID (modelled(M1)), (iii) force-of-infection modelling using HCV Ab prevalence by injecting duration (modelled(M2)), and (iv) imputation based on HCV Ab prevalence (imputed). Country-specific HCV incidence in PWID was estimated by pooling direct, modelled M1 and M2 estimates, as available; alternatively, we used imputed estimates. Number of new annual HCV infections attributed to injection drug use was estimated by multiplying country-specific HCV incidence with number of RNA- PWID.

Results: We included 247 HCV incidence estimates from 105 countries, representing 88% of the global PWID population. 66, 79, 88 and 14 of these estimates were direct, modelled(M1), modelled(M2) and imputed, respectively. HCV incidence ranged as 0.5-40.5/100person-years. We estimated 1,193,660 (95%CI: 710,350-1,917,410) new HCV infections are due to injection drug use annually, with variation regionally (Table) and by country (Figure). The largest number of new infections were in the US (325,230; 95%CI: 170,980-561,120; 27%), China (299,780; 95%CI: 203,290-424,160; 25%) and Russia (95,570; 95%CI: 67,400-132,860; 8%).

Conclusion: Unsafe injecting practices among PWID contribute substantially to incident HCV infections globally

Abstract Submission No. 101632

O-0516

The creation of a hepatocellular cancer (HCC) registry in a low-to-middle income country (LMIC)

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Background: Hepatocellular cancer (HCC) usually develops on top of chronic liver disease from various etiologies. A registry gathers real-world data on the effects of underlying risk factors, viral serologies, diagnostic imaging, and treatment on patient outcomes and helps guide screening recommendations and public policy.

Methods: Patients with HCC from the "Early Cancer Detection in the Liver of Filipinos with Chronic Active Hepatitis B using AI-Driven Integration of Clinical and Genomic Biomarkers (CANDLE) Study" were included. Follow-up was done every 6 months for three years or until study-end in March 2023. De-identified data was entered into an electronic database which served as the HCC registry.

Results: From December 2019 to January 2023, the CANDLE Study included 87 patients with HCC, 72.4% were male and majority

belonged to the lowest strata of income. On underlying liver disease: 51.7% were HbsAg+, 24.1% were HBSAg- and AntiHBC+, and NAFLD was present in 62.1%. Cirrhosis was present in 71.3%. HCC was diagnosed at an unresectable stage (BCLC B-D) in 59 (67.8%) patients, 21 (24.6%) received curative intent hepatectomy and only 46.0% received specific cancer treatment. 34 deaths were documented within the study and of these 82.4% died within 6 months of follow up. **Conclusion:** HCC registries containing epidemiologic data such as disease etiology and host metabolic and socioeconomic factors can be interrogated by researchers for more understanding leading to better outcomes of this disease.

Abstract Submission No. 101755
O-0517

Global, regional, and country-level estimates of new HCV infections attributed to injection drug use

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Background: We estimated, at country/regional/global levels, HCV incidence in people who inject drugs (PWID) and the number of new annual HCV infections attributed to injection drug use using multiple methods and data.

Methods: We compiled previously published estimates of HCV incidence in PWID from our global systematic review and modelling studies with new estimates. We used four different methods to estimate HCV incidence: (i) longitudinal re-testing of people-at-risk or assays for recent infection (direct), (ii) dynamic modelling using HCV Ab prevalence in PWID (modelled(M1)), (iii) force-of-infection modelling using HCV Ab prevalence by injecting duration (modelled(M2)), and (iv) imputation based on HCV Ab prevalence (imputed). Country-specific HCV incidence in PWID was estimated by pooling direct, modelled M1 and M2 estimates, as available; alternatively, we used imputed estimates. Number of new annual HCV infections attributed to injection drug use was estimated by multiplying country-specific HCV incidence with number of RNA- PWID.

Results: We included 247 HCV incidence estimates from 105 countries, representing 88% of the global PWID population. 66, 79, 88 and 14 of these estimates were direct, modelled(M1), modelled(M2) and imputed, respectively. HCV incidence ranged as 0.5-40.5/100person-years. We estimated 1,193,660 (95%CI: 710,350-1,917,410) new HCV infections are due to injection drug use annually, with variation regionally (Table) and by country (Figure). The largest number of new infections were in the US (325,230; 95%CI: 170,980-561,120; 27%), China (299,780; 95%CI: 203,290-424,160; 25%) and Russia (95,570; 95%CI: 67,400-132,860; 8%).

Conclusion: Unsafe injecting practices among PWID contribute substantially to incident HCV infections globally. Findings emphasize the importance of scaling-up prevention and treatment strategies for PWID.

Abstract Submission No. 101768
O-0518

Risk factors for short outcomes after EGVB: a follow-up study of 243 elder cirrhotic patients

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Background: Evidence of short-term outcomes after esophagogastric variceal bleeding (EGVB) in the elder cirrhotic patients is scarce. The study aimed to evaluate the 6-week rebleeding rate and mortality and explore their risk factors in elder cirrhotic patients with acute variceal bleeding.

Methods: Two hundred and forty-three elder cirrhotic patients without hepatocellular carcinoma admitted to the department of emergency with EGVB were included.

Results: Twenty three patients (23/237, 9.7%) developed rebleeding and 17 (17/243, 7.0%) patients dead after admission. Compared to patients without rebleeding, patients with 6-week rebleeding had significantly lower diastolic blood pressure (DBP), higher troponin I (TnI) level, MELD score and Child-Pugh score. Compared to survival patients, the patients who died within 6 week had significantly lower systolic pressure, higher levels of myohemoglobin (MYO) and TnI, higher MELD and Child-Pugh scores, and higher shock index and 6-week rebleeding rate. After adjusting for MELD, DBP remained an independent risk factor for rebleeding [OR=0.951, p<0.05]. After adjusting for 6-week rebleeding and MELD and Child-Pugh scores separately, MYO [OR=30.654, p<0.05] remained an independent risk factor for mortality. After adjusting for MELD score, shock index remained an independent risk factor for mortality.

Conclusion: Physical signs, including blood pressure and heart rate, and myocardial injury often suggest poor short-term prognosis in elderly cirrhotic patients.

Abstract Submission No. 101772
O-0519

Shifting Trends in Indications and Diagnoses of Liver Biopsies Over Two-Decades

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Background: Liver biopsy is golden standart for differential diagnosis and fibrosis staging in liver diseases, although its role has been recently challenged by non-invasive tests.

Methods: The liver biopsies done for non-malignant etiologies at Hacettepe University between January 2000 and April 2022 were retrospectively evaluated for the biopsy indications and final diagnosis.

Results: Liver biopsies of 1533 patients (789 female, 744 male) were included. Mean age was 43 years, and was stable through years. Main indications for biopsy were elevated liver enzymes (51.0%), assessment of liver fibrosis (36.7%), evaluation of treatment response (2.9%) or cirrhosis etiology (2.9%). Repeated biopsies were done in 100 patients mainly for assesment of disease activity (61%), progresive elevation in liver enzymes (16%), and insufficient or non-specific sampling at initial biopsy (11%) (Figure1).

The most frequent diagnoses at initial biopsies were chronic hepatitis B (HBV) or C (HCV) (38.7% and 11.4%, respectively), followed by non-alcoholic fatty liver diseases (NAFLD) (8.3%), autoimmune

hepatitis (7.6%), primary biliary cholangitis (4.0%) and drug induced liver injury (1.2%). Percentage of liver biopsies for HBV remained stable and that of HCV has decreased, whereas NAFLD and autoimmune liver diseases had rising percentages through years (Figure2).

There was no initial clinical diagnosis in 10.9% of patients, in whom liver biopsy was also mostly nonspecific (72%). However, NAFLD and autoimmune liver diseases were diagnosed in respectively 9.5% and 8.9% of these patients after biopsy.

Conclusion: While chronic hepatitis B infection remains most common diagnosis after liver biopsies, there were gradually increasing trends for autoimmune liver diseases and NAFLD during last decade.

Abstract Submission No. 101842

O-0520

The phylogenetic and geospatial approach for Hepatitis B Virus genotypes distribution in Indonesia

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The genetic landscape of Hepatitis B Virus (HBV) is intricate and exhibits geographical variations, with clinical implications and treatment responses linked to specific HBV genotypes. Despite the identification of predominant genotypes in previous studies, a comprehensive geospatial assessment of hepatitis B genotypes in Indonesia is notably absent. This underscores the urgency for extensive investigations into the burden of hepatitis B categorized by genotype in various regions. We examined the regional molecular epidemiology of the HBV genotype using a combined phylogenetic and geospatial approach. A hundred and ninety-three HBV samples were isolated from chronic hepatitis B patients and their clinical data were obtained from two distant regions, DKI Jakarta and South Sulawesi, representing western and eastern parts of Indonesia, respectively. HBV genotype was determined from DNA sequences of the S gene of HBV DNA subjected to phylogenetic analysis using standard reference sequences. Patients' data were characterized according to demographics, genotype likelihood phylogeny, and geospatial hotspot analysis using Getis-Ord Gi* statistics. Demographic data showed that HBV isolates from DKI Jakarta were dominated by genotype B while South Sulawesi was genotype C ($p < 0.001$). Geospatial analyses revealed a more concentrated focus on genotype C in the northern part of DKI Jakarta compared to B. Meanwhile, the distribution of HBV genotypes B and C in South Sulawesi was largely distributed across the region. This early study indicates the distinct pattern in hepatitis B molecular epidemiology and the need for a comprehensive study on the geospatial distribution of HBV genotypes in Indonesia.

Abstract Submission No. 100166

O-0521

Targeting CDK5/PAK1 attenuates lipid overload-induced HCC via suppressing lysosomal stress

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Background: Immunotherapy has revolutionized cancer treatment. Unfortunately, most tumor types do not respond to immunotherapy due to a lack of enhancing inflammation in tumor microenvironment (TME), a contributing factor is lysosomal stress (LS). How LS impacts the TME remains understudy.

Methods: We investigated the role of the CDK5/PAK1 pathway in the regulation of lysosomal stress in hepatocellular carcinoma (HCC) development by conducting metabolomic analysis, gene expression profiling and immunohistochemistry analyses in RAW264.7 cells, onco-gene-induced HCC mouse models and human HCC samples.

Results: We show that ox-LDL activates cyclin-dependent kinase 5 (CDK5), and CDK5 phosphorylates P21 (RAC1) Activated Kinase 1 (PAK1), which leads to LS. Furthermore, we found targeting of the CDK5/PAK1 pathways is a novel and tolerable approach to significantly reverse M2 transition to inhibit tumor development in vitro experiment. This approach reduced IL-10 and TGF- β expression of macrophages and suppressed ox-LDL-induced LS, together with decreasing deposition of lipofuscin and increasing expression and nuclear localization of TFEB, an indicator of LS.

Conclusions: This study suggests that CDK5/PAK1 pathway inhibition is a potential approach to broaden immunity therapies by suppressing lipid overload-mediated, LS-dependent M2 transition and supports the translation of this novel approach to further improve response rates for proliferation and metastatic hepatocellular carcinoma.

Keywords: CDK5, lysosomal stress, macrophage polarization, tumor microenvironment, liver cancer

Abstract Submission No. 100245

O-0522

TERT upregulation promotes cell growth via degradation of p21 and enhances hepatocarcinogenesis

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Background: Telomerase reverse transcriptase (TERT) gene aberration is detectable in more than 80% of the cases with hepatocellular carcinoma (HCC). Although TERT reactivation is essential for cellular immortalization because it stabilizes telomere length, the role of TERT in hepatocarcinogenesis remains unelucidated. This study aimed to elucidate the significance of aberrant TERT expression in hepatocytes in inflammation-associated hepatocarcinogenesis.

Method: We generated a mouse model with hepatocyte-specific Tert overexpression (Alb-Cre;TertTg) and examined their phenotype under chronic inflammation. Based on the transcriptome data from the liver tissue of Alb-Cre;TertTg mice, we examined the role of TERT in hepatocarcinogenesis in vitro. We also evaluated the relationship between TERT and cell cycle-related molecules, including p21, in HCC samples.

Result: The liver tumor development rate was increased by Tert over-expression during chronic inflammation, especially in the absence of p53 function. Gene set enrichment analysis of liver tissues revealed that gene sets related to cell cycle and apoptosis were upregulated in Alb-Cre;TertTg liver. It was found that TERT formed protein complexes with p21, cyclin A2, and cyclin E, promoted ubiquitin-mediated degradation of p21, specifically in the G1 phase. In the clinical HCC samples, TERT was highly expressed but p21 was conversely down-regulated, and TERT expression was associated with the upregulation of molecules related to the cell cycle.

Conclusion: The aberrant upregulation of TERT promoted cell cycle progression via ubiquitin-mediated degradation of p21 and enhanced hepatocarcinogenesis.

Abstract Submission No. 100448

O-0523

Integrated multiomics reveal clinical correlation between circPTK2 and liver transplantation for HCC

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Background: Circular RNAs (circRNAs)-mediated post-translational modification of RNA-binding proteins (RBP) plays a pivotal role in recurrence and metastasis of liver transplantation (LT) for hepatocellular carcinoma (HCC). However, the specific mechanism and potential clinical significance remain vague.

Methods: Patient derived tumor xenograft, organoids and the multi-omics approaches combining of transcriptome sequencing, tandem mass tag-based proteome sequencing and high-throughput sequencing were performed to screen the potential circRNAs. Tissue microarrays of LT for HCC containing 269 patients were used to evaluate the prognostic capacity of circRNAs and nucleolin (NCL).

Results: CircPTK2 was evaluated in HCC and was found to prevent the interaction between nucleolin (NCL) and the E3 ligase tripartite motif-containing 21 to reduce the proteasome-mediated degradation of NCL via K48-linked polyubiquitylation, promoting metastasis. Higher expression of circPTK2 and NCL in tumor tissue portended worse overall survival (OS) and recurrence free survival (RFS) (RFS rat: 41.3% vs. 55.4%, $P=0.0081$, 37.4% vs. 63.1%, $P<0.0001$). CircPTK2 and NCL had satisfactory evaluation capabilities for OS in patients who beyond the Milan criteria ($p=0.0034$ and 0.0033). In patients who met Hangzhou's criteria, elevated circPTK2 and NCL expression was correlated to a worse OS and RFS (OS: $P=0.0048$ and 0.0013 , RFS: $P=0.0374$ and 0.0001). Notably, patients with negative AFP and low circPTK2 expression had a superior OS than those with negative AFP but high circPTK2 expression ($P=0.0386$).

Conclusion: CircRNA and NCL are closely related to the metastasis of HCC and are effective prognostic indicators to patients with LT for HCC.

Abstract Submission No. 100858

O-0524

Intra-tumoral Microbiome Promotes Hepatoma Cell Proliferation and Is Associated with Prognosis

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Background: Cancer specific intra-tumoral microbiome had been identified. We aimed to explore the role of intra-tumoral microbiome in the pathogenesis of HCC.

Methods: The method to harvest primary hepatoma cells had been reported previously. Microbiome infiltration in more than 20% of areas under HPF was defined as abundant. Fluorescence in situ hybridization (FISH) was performed with bacterial 16s rRNA sequences in fresh HCC surgical tissues. Taxonomic compositions were analyzed by 16s rRNA sequencing. Hepatoma cell lines (Huh7, HA22T and Hep3B) cell line were cultured with microbiome medium for cell proliferation experiments. Metabolomic study was done by liquid chromatography-tandem mass spectrometry.

Results: FISH confirmed the presence of intra-tumoral microbiome in HCC. The most dominant microbe at the phylum level was Proteobacteria, and Xanthomonas, and Acetobacter were the most dominant microbes at the genus level. It showed no significant differences in the taxonomic compositions in different HCC stages and etiologies. HCC patients with abundant microbiome demonstrated a larger tumor size and decreased survival. The cell proliferation experiments by WST1 assay showed hepatoma cells cultured with medium of microbiome showed a higher cell proliferation and the effect diminished after removal of microbiome. These cells exhibited higher expression levels of YAP1, and the YAP1 expression decreased after removal of microbiome. The untargeted metabolomic study demonstrated a significantly difference of metabolites before and after the removal of microbiome.

Conclusions: Intra-tumoral microbiome promotes hepatoma cell proliferation through Hippo/YAP pathway, and was associated with a poor survival. The results implicated a therapeutic target of HCC.

Abstract Submission No. 100943

O-0525

Whole-genome sequencing-based mutational analysis on hypovascular small hepatocellular carcinoma.

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Background: Whole-genome sequencing (WGS) is a powerful tool to unveil the genetic landscape of individual tumors. Although WGS has been revealed the mutational landscape of classical HCCs, genetic feature of hypovascular small liver nodules remains still unclear.

Methods: We conducted multi-regional WGS on a total of 41 samples including sixteen surgically resected hypovascular tumor tissues, eight hypervascular HCCs, two extrahepatic metastatic lesions, seven non-tumor liver tissues and eight lymphocytes from nine HCC patients. We comparatively analyzed the genetic alterations, including point mutations, genetic structural variations and copy number variations of hypovascular liver tumor tissues, with hypervascular HCC tissues and also fifteen Japanese patients with advanced HCC with portal vein

invasion in LIRI-JP cohort of International Cancer Genome Consortium project.

Results: All the hypovascular nodules were pathologically revealed well to mod differentiated HCCs, which harbored approximately 8000 mutations including single nucleotide variants and short indels along with several structural variations such as chromosomal translocations, inversions and arm-level amplifications or heterozygous alterations. Importantly, these genetic alterations included several well-known cancer driver genes as well as hypervascular HCCs. As for the structural variations, advanced HCC with portal invasion had significantly more numbers of genomic rearrangements than hypovascular HCC tissues, suggesting the genetic alterations should be formed more complicated during multistep hepatocarcinogenesis from hypovascular HCCs to invasive HCCs.

Conclusions: Small hypovascular HCCs already accumulate various genetic alterations including driver gene mutations of HCC. Genetic comparison with the earlier stage noncancerous liver nodules should be useful for the understanding of the initial step of hepatocarcinogenesis.

Abstract Submission No. 101137
O-0526

Low-speed regular exercise reduces HCC development by muscle PGC1 α -mediated kynurenine degradation

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Recently, the number of patients with steatohepatitis-associated hepatocellular carcinoma (HCC) has been steadily increasing. The beneficial effects of exercise on cancer prevention have been generally accepted; however, the mechanisms remain largely unclear. In this study, we subjected mice to chemical liver carcinogenesis protocol with a continuous high-fat diet feeding for 35 weeks and subsequent low-speed (10m/min), one-hour regular running everyday for the last 8 weeks in the protocol. Interestingly, the exercised mice developed significantly reduced number of HCC. The metabolome analysis using mouse serum revealed that kynurenine, a well-known onco-metabolite that can act on AhR nuclear receptor to suppress antitumor immunity, significantly decreased in the exercised mice. In the exercised group, the expression of genes encoding PGC-1 α and PGC-1 α -dependent kynurenine aminotransferases (KAT), which can degrade kynurenine, significantly upregulated in the skeletal muscles, coinciding with the HCC reduction. These results suggest that the upregulation of skeletal muscle-derived PGC-1 α and KAT by exercise could activate anti-tumor immunity by degrading kynurenine. To this end, using the liver tumor tissue, we performed mRNA-sequencing and WGCNA (Weighted Gene Correlation Network Analysis), and successfully identified a series of gene-set modules altered in parallel by exercise. Interestingly, certain gene-set modules were associated with the reduction of Treg cells and tumor vascularity by exercise, indicating that exercise ameliorated the tumor microenvironment. We confirmed these modules are also reduced by AhR inhibitor treatment in mice, suggesting that these alterations are kynurenine-AhR signaling-dependent. Our analysis shows that low-speed exercise has beneficial inter-organ effects for significant HCC prevention.

Abstract Submission No. 101473
O-0527

Development of precision-bioprinted patient-derived organoids for high-throughput drug screening.

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Background and Aims: Liver cancer, the third most common cause of cancer mortality globally, is inadequately addressed by current systemic treatments due to limited efficacy and high toxicity. New targeted therapies are essential. The development of such therapies is hindered by the lack of suitable *in vitro* models. This study explores the use of patient-derived organoids (PDOs), potentially superior to traditional models, employing Inventia Life Science's defined bio-inks in a RASTRUMTM bio-printer for better simulation of the tumour micro-environment.

Methods: We processed 50 liver cancer samples (47 HCC, 3 CCA) to create PDOs in Cultrex Basement Membrane Extract (BME2) and Inventia's defined bio-inks. The RASTRUMTM bio-printer was employed, utilising bio-inks with stiffnesses of 1.1 or 3 kPa, to identify the best substrate for PDO growth, assessed via imaging and assays. Drug reactions were analysed in PDOs compared to hepatocyte cell lines across matrices.

Results: Eighteen PDO lines were established. Pre-defined matrices enhanced PDO growth, and successful lines were bio-printed for drug assays. The 3 kPa bio-ink was optimal for PDO growth and suitable for 384-well high-throughput assays, revealing significant matrix-dependent drug responses.

Conclusion: A biobank for primary liver cancer PDOs was developed for drug screening. With Inventia Life Sciences, we introduced high-throughput, precision-bioprinted PDO models for primary liver cancer, enhancing drug screening and paving the way for innovative liver cancer treatment development.

Abstract Submission No. 200046
O-0528

Alpha-mangostin nanoparticles exerts hepatocellular carcinoma via alteration of PI3K/Akt pathway

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Background: Hepatocellular carcinoma (HCC) is the widely documented danger to the liver and 3rd most common reason for tumor death around the world. Identification of oncogene and its related possible pathway is crucial for understanding therapy resistance and effectual treatment. Researcher targeted the 5-bisphosphate 3-kinase/protein kinase B, phosphatidylinositol-4 and mitogen activated protein kinase's pathway to suppress the cell proliferation and expansion. We made attempt to fabrication the solid lipid nanoparticle (SLN) of alpha-mangostin and examine against the diethylnitrosamine (DEN) induced HCC and explore possible mechanism of action.

Material & method: Double emulsion solvent displacement model was used for the preparation of alpha-mangostin-SLN. Intraperitoneal injection of DEN (200 mg/kg) was used for induction the HCC and various parameters were scrutinized. The genetic effects HP-SLN on Pdk1, Akt1, Pik3r1, Map3k1, Erbb2, Pik3ca using semi-quantitative RT-PCR analysis were assessed. Morphological and histopathological component of hepatic tissue were estimated.

Result: Surface methodology suggests the 182.3 nm particle size and 0.230 polydispersity index for alpha-mangostin-SLN. alpha-mangostin-SLN significantly ($P<0.001$) reduced the hepatic nodules (84.5%) and hepatic nodules (93.4%). alpha-mangostin-SLN significantly ($P<0.001$) modulated the hepatic parameter viz., AFP (83.4%), CEA (50.4%), ALT (58.5%), ALP (68.4%), AST (65.8%), GGT (63.4%); non-hepatic parameter viz., BUN (56.4%), total protein (64.5%), albumin (63.4%), direct bilirubin (67.4%), bilirubin (63.4%); antioxidant parameter LPO (71.3%), SOD (60.3%), CAT (64.9%), GPx (58.3%), GST (63.4%) respectively. alpha-mangostin-SLN significantly ($P<0.001$) modulated the expression of Pik3r1 (58.4%), Akt1 (43.5%), Pik3ca (54.9%), Erbb2 (53.6%) and Map3k1 (43.6%). Morphological and histopathological studies advice and support the above result by alpha-mangostin-SLN.

Conclusion: Collectively, we can conclude that alpha-mangostin-SLN regulated the PI3K and Akt pathways, which involved in reduction of hepatic cancer expansion and proliferation and its chemo-protective effect.

Abstract Submission No. 100043
O-0529

MiR-29a Restrains the Development of Hepatocellular Carcinoma via Targeting MYBL2

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Aims: Primary liver cancer remains a global health challenge, specifically hepatocellular carcinoma (HCC). MicroRNA (miR), a small non-coding RNA molecule, performs crucial functions in several biological processes, such as cancer growth and advancement. In this study, we investigated whether miR-29a could mitigate the oncogenesis of HCC.

Methods and Materials: Serum of HCC patients and HCC tissues derived from the western diet (WD)/carbon tetrachloride (CCl₄)-induced HCC animal model were collected. Transgenic mice were used to study the role of miR-29.

Key Findings: Reduced miR-29a levels in the serum of HCC patients and the liver tissue of the wild type (WT) of a WD/CCl₄-induced HCC animal model were noted. Proteomics analysis identified the pathway-centric role of miR-29a in HCC by targeting MYBL2. Human bioinformatics survey from GTEx and TCGA revealed higher expression of MYBL2, DNMT3A, DNMT3B, HRAS, CD276, FAM111B, and RUVBL1 in the HCC tissues through their RNA-seq profiles. Furthermore, high expression of these genes indicated poor prognosis in HCC patients. In addition, the overexpression of miR-29a notably reduced tumor formation and Ki-67 expression in the ontogenetic liver of the WD/CCl₄-induced HCC animal model. Compared to WT mice, miR-29a transgenic mice presented reduced levels of critical oncogenic factors, including PI3K-p85, c-MYC, DNMT3b, and MYBL2 in the liver. Moreover, in vitro, study confirmed that the direct binding of miR-29a to the MYBL2 3'UTR inhibited the gene expression.

Conclusion: This study integrated multi-omics investigations and experimental verification to provide novel insight into a hepatoprotective pathway of miR-29a that inhibits MYBL2 from repressing HCC oncogenesis.

Abstract Submission No. 100084
O-0530

Epigenetic regulation of the ZNF384/NOL9 axis in hepatocellular carcinoma

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Background: Accumulating evidence shows that nucleolar protein is important regulator molecule involved in diverse biological processes, including cancer initiation, progression, and therapeutic failure. Meanwhile, nucleolar protein 9 (NOL9) is a polynucleotide 5'-kinase promoting the formation of the endonuclease-kinase complex and the abnormal expression of NOL9 can affect cell cycle. However, the biological function and clinical significance of NOL9 in HCC remain unclear.

Methods: Clinical significance was analyzed in HCC tissue and TCGA databases. Stably overexpressing and depleting NOL9 in HCC cells were established for evaluating proliferation, apoptosis, cell cycle, and antiproliferative effect of sorafenib. The regulatory mechanisms in the upstream of NOL9 in HCC cells were disclosed by bioinformatics analysis and validated by western blot, qRT-PCR, methylation PCR, dual-luciferase reporter assay, and CHIP-qPCR.

Results: High NOL9 expression was associated with poor patient survival in TCGA HCC. Moreover, NOL9 protein levels were significantly upregulated in sorafenib resistant samples compared to non-resistant. And further, we found that sorafenib upregulated NOL9 expression by decreasing the DNA methylation level of its promoter. NOL9 functioned as a tumor promoting agent. Importantly, NOL9 enhanced the tumorigenesis by promoting cell cycle in vitro. Mechanistically, DNA methylation perturbed the recognition of NOL9 promoter by transcription factor ZNF384. Rescue experiments confirmed that ZNF384 down-expression could rescue the gain-of-function of NOL9. **Conclusion:** Our collective data reveals that epigenetic regulation of the ZNF384/NOL9 axis in HCC and the suppression of NOL9 might constitute a strategy for increasing the effect of sorafenib to inhibit HCC cells.

Abstract Submission No. 100124
O-0531

Cabozantinib inhibits tumor growth of lenvatinib-resistant hepatoma cells *in vitro* and *in vivo*

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Background and aim: Cabozantinib is a newly developed tyrosine kinase inhibitor, which can be used to treat patients with hepatocellular carcinoma (HCC) unresponsive to conventional tyrosine kinase inhibitors, including lenvatinib. However, the efficacy of cabozantinib in lenvatinib-resistant cases has not been well established in clinical trials or basic studies. The present study aims to determine whether cabozantinib can suppress tumor growth of lenvatinib-resistant HCC cell lines *in vitro* and *in vivo*.

Methods: To establish lenvatinib-resistant hepatoma cells, Hep3B cells were cultured with different doses of lenvatinib ranging from 1 to 20 μ M for three months. Cell proliferation assays were conducted using WST-8. Flowcytometry was adopted to evaluate cell cycle phase arrest and apoptotic changes. Proteome analysis of xenografts was

performed to identify tumor suppressor genes which contributed to efficacy of cabozantinib.

Results: Lenvatinib-resistant Hep3B cells (Hep3B-LR) exhibited approximately 20 times greater IC50 for lenvatinib than the wild type. Compared with wild-type Hep3B, Hep3B-LR was characterized by enhanced mTOR phosphorylation with the downregulation of phosphorylated Akt. Cabozantinib suppressed tumor growth in Hep3B-LR in vitro by inducing cell cycle arrest at G2 phase and apoptosis. The animal experiments validated the antitumor effect of cabozantinib. Proteome analysis demonstrated an upregulation of FDCT, a tumor suppressor gene. Knockdown of FTCD enhanced tumor growth of Hep3B-LR.

Conclusion: Cabozantinib inhibited the growth of Hep3B-LR in vitro and in vivo. FDCT may be a novel therapeutic target of cabozantinib in case of lenvatinib treatment failure.

Abstract Submission No. 100156
O-0532

IRGM is a novel regulator of PD-L1 via promoting S6K1/YBX1 axis in hepatocellular carcinoma

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Background: Immunity-related GTPase M (IRGM), an Interferon-inducible protein, functions as a pivotal immunoregulator in multiple autoimmune diseases and infections. However, the role of IRGM in hepatocellular carcinoma (HCC) development remains unveiled.

Methods: Orthotopic patient-derived xenograft (PDX) model, xenograft tumor models, IRGM-conditional knockout mice, and in vitro experiments were utilized to investigate the role of IFN-induced IRGM in HCC progression. Single-cell sequencing and flow cytometry were employed to explore tumor immune environment changes. Whole gene sequencing, Immunoprecipitation-Mass spectrometry (IP-MS), and ChIP assays were performed to elucidate the underlying mechanism.

Results: IFN- γ robustly triggers the expression of Irgm1 in HCC. High IRGM expression in tumor samples indicated poor prognosis in HCC patients. In vivo and in vitro experiments demonstrated that Irgm facilitated the malignant phenotype of HCC. Furthermore, Inhibition of Irgm promoted the infiltration of CD8⁺ cytotoxic T lymphocytes (CTLs) in TME of HCC, which was ascribed to the reduction of PD-L1. Mechanistically, IRGM promotes the interaction between YBX1 and its phosphokinase p70S6K1, leading to phosphorylation of YBX1, resulting in transcription activation of PD-L1 mediated by p-YBX1. The combined application of Irgm inhibition and α -PD1 demonstrated a stronger anti-tumor immune response in HCC tumor-burden mice.

Conclusion: IFN- γ -induced IRGM is a novel regulator in tumor microenvironment and HCC progression. And IRGM suppresses CD8⁺ CTLs infiltration and function in HCC via regulating p70S6K1/YBX1/PD-L1 axis. This study may raise a novel therapeutic strategy combined with immune checkpoint inhibitors (ICIs) against HCC.

Abstract Submission No. 100179
O-0533

Novel biomolecule potentiates classic therapeutic protocol against hepatocellular carcinoma

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Background: Sorafenib (SB) is a multi-kinase inhibitor and is the first line of treatment for advanced hepatocellular carcinoma (HCC), but its clinical applications are limited due to severe side effects and drug resistance. To optimize its therapeutic effects, we used here saffronal (SF); a major bioactive component of saffron, to assess the development of HCC in animal model.

Methods: Therapeutic effect of SF alone or combined with SB was assessed in cirrhosis rat model of HCC using histopathological, biochemical, immunohistochemical and immunoblotting techniques. Transcriptome analyses were also employed to determine the therapeutic effects of SF and SB.

Results: Combined treatments significantly reduced the nodule multiplicity compared to a single therapy group of HCC. It also induced apoptosis, blocked proliferation, and arrested the cell cycle, in the HCC group. Combined therapy improved SB's anti-inflammatory, anti-fibrotic, and anti-metastatic activities. Using transcriptomic analysis, 45 genes were found to be associated with HCC suppression. Those genes were associated with cellular development, oxidative stress, wound healing, and apoptosis.

Conclusions: Downregulation of NF-B-p65, COX-2 and β -catenin are possible mechanisms to underly SF beneficial effects. SF represents a viable candidate for pharmacological target as new anti-liver cancer treatment, both in monotherapy and combined with SB as the current gold standard therapy. Further research is necessary as the clinical safety margin and dosage of the presented combination medication have yet to be determined.

Abstract Submission No. 100219
O-0534

A Novel Bile Acid-related lncRNA Signature for Predicting Prognosis and Treatment Response in HCC

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Bile acids and salts have been shown to play a role in liver carcinogenesis through DNA damage, inflammation, and tumor proliferation. However, the correlation between bile acid metabolism and hepatocellular carcinoma (HCC) prognosis remains unclear. This study aimed to identify a predictive signature of bile acid and bile salt metabolism-related long non-coding RNAs (lncRNAs) for HCC prognosis and treatment response. The study used HCC RNA-sequencing data and corresponding clinical and prognostic data from The Cancer Genome Atlas. A prognostic model consisting of five bile acid and bile salt metabolism-related lncRNAs was developed and evaluated in a training set, a validation set and an external set. The model demonstrated good performance in predicting HCC prognosis and was shown to be an independent biomarker for prognosis. Additionally, our study revealed a significant association between the signature and immune cell infiltration, as well as its predictive value for therapeutic responses to both immunotherapy and chemotherapy. Furthermore, three lncRNAs (LUCAT1, AL031985.3 and AC015908.3) expression levels in our

signature were validated through qRT-PCR in a cohort of 50 pairs of HCC patient tumor samples and corresponding adjacent non-tumor samples, along with 10 samples of normal liver tissue adjacent to benign lesions. These findings suggest that this novel bile acid and bile salt metabolism-related lncRNA signature can independently predict the prognosis of patients with HCC and may be utilized as a potential predictor of response to treatment in this setting.

Abstract Submission No. 100225
O-0535

Inhibition of CDK4/6 and XPO1 induces senescence with acquired vulnerability to CRBN-based PROTACs

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Background: Despite the increasing number of treatment options available for liver cancer, only a small proportion of patients achieve long-term clinical benefits. Herein, we aim to develop new therapeutic approaches for liver cancer.

Methods: Compound screen was conducted to identify inhibitors that could synergistically induce senescence when combined with CDK4/6 inhibitor. The combination effects of CDK4/6 inhibitor and XPO1 inhibitor on cellular senescence were investigated in a panel of human liver cancer cell lines, mouse models of liver cancer, patient-derived organoids, and patient-derived xenografts. A senolytic-drug screen was performed to identify drugs that selectively killed senescent liver cancer cells.

Results: The combination of CDK4/6 inhibitor and XPO1 inhibitor synergistically induces senescence of liver cancer cells *in vitro* and *in vivo*. The XPO1 inhibitor acts by causing accumulation of RB1 in the nucleus, leading to decreased E2F signaling and promoting senescence induction by the CDK4/6 inhibitor. Through a senolytic-drug screen, CRBN-based PROTAC ARV-825 was identified as an agent that can selectively kill senescent liver cancer cells. Upregulation of CRBN was a vulnerability of senescent liver cancer cells, making them highly sensitive to CRBN-based PROTAC drugs. Mechanistically, we find that USP2 directly interacts with CRBN, leading to the deubiquitination and stabilization of CRBN in senescent liver cancer cells.

Conclusions: Our study demonstrates a striking synergy in senescence induction of liver cancer cells through the combination of CDK4/6 inhibitor and XPO1 inhibitor. These findings also shed light on the molecular processes underlying the vulnerability of senescent liver cancer cells to CRBN-based PROTAC therapy.

Abstract Submission No. 100260
O-0536

Clinical significance of Cytokine Change in Hepatocellular Carcinoma after Radiotherapy

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Background/Aim: Radiotherapy (RT) can enhance tumor immunogenicity and increases production of cytokines. Prior studies have examined change of cytokine level in cancer patients after radiotherapy, but study on hepatocellular carcinoma (HCC) is lacking. This study investigated the effects of radiotherapy on serum levels of interleukin-

2 (IL-2), IL-10, IL-22 and tumor necrosis factor alpha (TNF-a) with HCC.

Methods: Data of HCC patients who underwent radiotherapy at one tertiary referral hospitals between March 2016 and December 2019 for the prospective study. This study included 20 hepatitis B virus (HBV) patients with HCC undergoing RT and 69 HBV controls. The control group was classified into three groups as follows: chronic hepatitis B (CHB) (n=20), liver cirrhosis (LC) (n=21), decompensated LC (DLC) (n=20). Cytokines were serially monitored at pre-RT, end of RT, 1 week and 4 weeks after RT.

Results: At baseline, serum mean levels of IL-6 and IL-22 were higher in patients with HCC than in controls. In control group, serum mean levels of IL-6 and IL-22 were highest in DLC group and lowest in CHB group. The mean levels of IL-6 and IL-22 were increasing early after RT. Levels of TNF-a and aminotransferase (AST) had a positive correlation over time after RT (1 week : $r = 0.622$ ($p=0.004$), 4 week : $r = 0.523$ ($p=0.022$)).

Conclusion: RT induces changes in levels of IL-6 and IL-22 in HCC patients. Expression of IL-6 and IL-22 level is correlated with liver disease severity.

Abstract Submission No. 100273
O-0537

SOCS1 tumor suppressor sensitizes hepatocellular carcinoma cells to oxidative stress

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Background: The *SOCS1* gene is frequently repressed in hepatocellular carcinoma (HCC). Studying the tumor suppression mechanisms of SOCS1, we have shown that SOCS1 regulates p21-dependent NRF2 activation. Here, we investigated SOCS1-mediated modulation of cellular antioxidant response in HCC cells.

Methods: Murine Hepa1-6 cells expressing SOCS1 (Hepa-SOCS1) or control vector (Hepa-vector) were exposed to tert-butyl hydroperoxide (*t*-BHP) or cisplatin to induce oxidative stress. CDKN1A and NRF2 expression was evaluated by western blot. Induction of NRF2 target genes and proteins was assessed by RT-qPCR and immunofluorescence microscopy. Reactive oxygen species and lipid peroxidation were estimated by microscopy. Proteomes of Hepa-SOCS1 and Hepa-vector cells treated with *t*-BHP or cisplatin were studied by mass spectrometry.

Results: *t*-BHP and cisplatin upregulated CDKN1A and NRF2 proteins, and induced NRF2 target genes *Nfe2l2*, *Gclc*, *Gstm1*, *Gpx2*, *Hmox1* and *Nqo1* and their protein products, which were markedly attenuated by SOCS1. *t*-BHP and cisplatin markedly reduced the survival of Hepa-SOCS1 cells, accompanied by a reduction in reactive oxygen species and lipid peroxidation, suggesting increased sensitivity of SOCS1 expressing cells to oxidative stress. Proteomic data revealed that SOCS1 modulated many proteins involved in diverse molecular pathways, including 'chemical carcinogenesis - reactive oxygen species' with downregulation of several proteins. *GCLC*, downregulated by SOCS1 at the transcript and protein levels, correlated positively with *NFE2L2* and negatively with *SOCS1* expression in the TCGA-LIHC dataset.

Conclusions: SOCS1 attenuates NRF2-mediated antioxidant response in HCC cells and this regulation is crucial to prevent their ability to withstand elevated oxidative stress.

Abstract Submission No. 100297
O-0538

RESEARCH ON IMAGE CHARACTERISTICS OF PRIMOVIST - MRI IN DIAGNOSIS HEPATOCELLULAR CARCINOMA

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Purposes: To research the imaging characteristics of magnetic resonance imaging (MRI) with primovist in the diagnosis of hepatocellular carcinoma (HCC).

Material and methods: The study was conducted on 35 patients regardless of gender, of all ages who came for examination at K Tan Trieu hospital, during the period from May 2021 to October 2022, with indication for primovist MRI and underwent a biopsy or surgery with pathologic findings.

Results: The rate of HCC in the study was 86%. Mean age 56.8 years old. Male/female ratio: 10,67. 77% of patients in the study had type 1 - enhanced HCC. The mean value of ADC in patients with HCC was 1.2. Most patients have a moderate differentiation of 60%. Patients with high-differentiation on histopathology mostly have type 3 enhancement. With moderate-differentiation, most have type 1 enhancement. With poorly-differentiation, all have type 1 enhancement. The ADC value in the group of patients with high-differentiation was higher than in the group of patients with moderately-differentiation and poorly-differentiation.

Conclusion: Primovist magnetic resonance imaging is highly valuable in the diagnosis of hepatocellular carcinoma with typical changes in ADC values.

KEY WORDS: Hepatocellular carcinoma (HCC), Apparent diffusion coefficient (ADC), Magnetic Resonance Imaging (MRI).

Abstract Submission No. 100302
O-0539

MicroRNA-885-5p as a Master Regulator in Cell Cycle Progression of HCC Cells

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Background: MicroRNAs (miRNAs) are a class of small non-coding RNAs that regulate specific messenger RNAs (mRNAs) by inhibiting mRNA translation and stability. Emerging studies have demonstrated dysregulation of various miRNAs in the development of hepatocellular carcinoma (HCC). In this study, we aim to identify a novel tumor suppressor miRNA and dissect its molecular functions in HCC cells.

Methods: Three microRNA gene profiles of HCC tissues from the TCGA and GEO databases were analyzed to identify putative tumor suppressor miRNAs. MiRNA-885-5p (miR-885-5p) was chosen for functional tests, including MTT assay, BrdU incorporation, and cell cycle analysis, in three HCC cell lines. Transcriptomic profiling of control and miR-885-5p-overexpressing HCC cells was performed to identify potential targets of miR-885-5p. Dual luciferase assays were conducted to confirm the direct interaction between miR-885-5p and its target mRNAs.

Results: Analysis of miRNA expression profiles from three normal and HCC tissue pairs identified nine miRNAs commonly downregulated in HCC tissues, including miR-885-5p. Overexpression of miR-885-5p significantly suppressed proliferation of HCC cells. Transcriptomic profiles of these HCC cells revealed that miR-885-5p induced downregulation of several key genes that promote the G1-to-S transition, including *CDK6*, *E2F2*, and *CCNA2*. Accordingly, miR-885-5p-overexpressing cells displayed reduced rates of BrdU incorporation and G1 phase arrest in the cell cycle. Finally, dual luciferase assays confirmed the direct interaction of miR-885-5p with 3' untranslated regions of *CDK6*, *E2F2*, and *CCNA2* transcripts.

Conclusions: MiR-885-5p inhibits G1-to-S progression in HCC cells and may represent a new target for HCC therapy

Abstract Submission No. 100343
O-0540

A peptide encoded lincRNA promotes hepatocellular carcinoma progression

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At present, a large proportion of advanced hepatocellular carcinoma (HCC) patients are unable to benefit from immune checkpoint inhibitors or targeted therapies, so developing novel therapeutic drugs for HCC is of great importance. Recently, there was number of peptide was identified that encoded by lincRNA and participate in the progression of cancer. Through multiomic screening and verification, we identified SMIM45 was encoded by LINC00634 and was a small endogenous peptide. Our results showed that SMIM45 protein level was high in HCC tissues compared to adjacent tissues and SMIM45 could promote HCC cell proliferation and cell migration. Moreover, we further confirmed that SMIM45 interacted with MTDH by immunoprecipitation, and found that the protein level of MTDH was increased with SMIM45 overexpression, but not vice versa. The literatures indicated that MTDH could be degraded by ubiquitination though interacting with ubiquitin E3, and molecular docking showed that ubiquitinated MTDH affected by interaction with SMIM45. Therefore, we hypothesized that SMIM45 could interact with MTDH to promote HCC progression by inhibiting ubiquitination of MTDH. Finally, we conclude that SMIM45 binds MTDH, causing reduced ubiquitination of MTDH and promoted HCC progression. The work will provide a new biomarker for HCC and a new target for HCC cancer therapy.

Abstract Submission No. 100406
O-0541

Peripheral T cell subsets as a potential biomarker for immunotherapy in hepatocellular carcinoma

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Background: The efficacy of the combination immunotherapy of atezolizumab and bevacizumab (Atezo+Bev), the first-line systemic therapy for unresectable hepatocellular carcinoma (uHCC), varies from patient to patient. Therapeutic biomarkers might help improve patient outcomes of Atezo+Bev therapy for uHCC. This study aimed to evaluate the status and dynamics of peripheral T cell subpopulations in uHCC patients receiving Atezo+Bev treatment and to explore biomarkers predictive of therapeutic response.

Methods: 83 uHCC patients who initiated Atezo+Bev treatment at our hospital between October 2020 and June 2022 were enrolled. Peripheral T cell subpopulations in peripheral blood mononuclear cells (PBMCs) at baseline and at 3 weeks post-treatment were investigated using flow cytometry. The association between peripheral T cell subpopulation profiles and clinical outcomes was analyzed.

Results: Baseline peripheral T cell subpopulations could be profiled in 70 patients with sufficient cell counts, among which 3-week subpopulations could be evaluated in 51 patients. Multivariate analysis revealed that a high baseline proportion of CD8⁺ central memory T (TCM) cells was independently associated with longer progression-free survival (PFS). Further, overall survival (OS) was significantly prolonged in patients with increased CD8⁺ effector memory T (TEM) cell proportions after the initiation of Atezo+Bev treatment.

Conclusions: TCM proportion at baseline might be a good indicator of the efficacy of Atezo+Bev therapy. In addition, observation of increasing TEM cell proportions might be an early predictor of the potential clinical benefits of treatment.

Abstract Submission No. 100408

O-0542

Molecular Changes of Circulating Tumor Cells in HCC Patients Receiving Atezolizumab plus Bevacizumab

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Background: Mechanisms leading to cancer progression of Hepatocellular Carcinoma (HCC) during immunotherapies remain unclear. Circulating tumor cells (CTCs) are non-invasive and real-time biomarkers that provide information about metastatic processes. CTC analysis could reveal molecular mechanisms of cancer progression. We investigated changes in CTC counts and gene expression related to cancer progression in HCC patients treated by Atezolizumab plus Bevacizumab (Atezo/Bev).

Methods: We obtained peripheral blood from 19 HCC patients treated by Atezo/Bev at baseline and response evaluation. Treatment response was assessed by modified RECIST. CTCs were isolated with RosetteSepTM and stained with antibodies targeting CD45 and PanCK. CD45 negative and PanCK positive cells by flow cytometry were defined as CTCs. The expression of 373 genes in CTCs were investigated by next-generation sequencing (NGS) and qRT-PCR.

Results: CTC counts of PR/SD group decreased at response evaluation, compared with baseline (192 vs.94, $p < 0.01$). In NGS analysis, 99 genes showed significant expression changes in clinical course. Unsupervised hierarchical clustering of 99 genes classified into two clusters A and B. Patients in cluster A were responder and showed 100.0% survival rate at 1-year, which was better than 50.0% in cluster B. Apoptosis pathway was upregulated in responder (cluster A). Furthermore, TGF-beta pathway-related genes such as AKT1, CDKN1B and IKBKB were upregulated in non-responder (cluster B) ($p < 0.05$).

Conclusion: The change of CTC counts correlated with therapeutic effect and TGF-beta pathway may play an important role in resistance

to Atezo/Bev. CTC analysis in HCC patients during immunotherapy could reveal molecular mechanisms of cancer progression.

Abstract Submission No. 100449

O-0543

Multiple omics revealed the clinical correlation between circPTK2 and liver transplantation for HCC

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Background: Circular RNAs (circRNAs)-mediated post-translational modification of RNA-binding proteins (RBP) plays a pivotal role in recurrence and metastasis of liver transplantation (LT) for hepatocellular carcinoma (HCC). However, the specific mechanism and potential clinical significance remain vague.

Methods: Patient derived tumor xenograft, organoids and the multi-omics approaches combining of transcriptome sequencing, tandem mass tag-based proteome sequencing and high-throughput sequencing were performed to screen the potential circRNAs. Tissue microarrays of LT for HCC containing 269 patients were used to evaluate the prognostic capacity of circRNAs and nucleolin (NCL).

Results: CircPTK2 was evaluated in HCC and was found to prevent the interaction between nucleolin (NCL) and the E3 ligase tripartite motif-containing 21 to reduce the proteasome-mediated degradation of NCL via K48-linked polyubiquitylation, promoting metastasis. Higher expression of circPTK2 and NCL in tumor tissue portended worse overall survival (OS) and recurrence free survival (RFS) (RFS rat: 41.3% vs. 55.4%, $P=0.0081$, 37.4% vs. 63.1%, $P < 0.0001$). CircPTK2 and NCL had satisfactory evaluation capabilities for OS in patients who beyond the Milan criteria ($p=0.0034$ and 0.0033). In patients who met Hangzhou's criteria, elevated circPTK2 and NCL expression was correlated to a worse OS and RFS (OS: $P=0.0048$ and 0.0013 , RFS: $P=0.0374$ and 0.0001). Notably, patients with negative AFP and low circPTK2 expression had a superior OS than those with negative AFP but high circPTK2 expression ($P=0.0386$).

Conclusion: CircRNA and NCL are closely related to the metastasis of HCC and are effective prognostic indicators to patients with LT for HCC.

Abstract Submission No. 100513

O-0544

Mitochondria-targeted Icaritin Induces Immunogenic Cell Death in Hepatocellular Carcinoma

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Background: Icaritin (ICT), a novel small molecule from traditional Chinese medicine, induces mitophagy and immunogenic cell death (ICD), showing promise for treating advanced unresectable hepatocellular carcinoma. However, its limited bioavailability restricts clinical

use. We developed amphiphilic copolymer-encapsulated Icaritin nanoparticles (Icaritin NPs) with mitochondrial targeting to improve its bioavailability, tumor-targeting, and anti-cancer immunogenicities.

Method: We synthesized a novel mitochondrial targeting amphiphilic copolymer OPDEA-PCL and self-assembled it with ICT into micelles, using polyethylene glycol-polycaprolactone (PEG-PCL) as a positive carrier. Confocal imaging and flow cytometry were utilized to analyze cellular uptake of OPDEA-PCL/ICT nanoparticles. In a mouse subcutaneous HCC model, free ICT, PEG-PCL/ICT, and OPDEA-PCL/ICT NPs were intravenously administered to tumor-bearing mice to evaluate their anti-tumor effects.

Results: OPDEA-PCL/ICT had an optimal ~140 nm particle size, 0.19 PDI, and 86% encapsulation efficiency. It rapidly internalized into H22 cells, targeting mitochondria. Post-intravenous injection, in vivo imaging revealed effective tumor accumulation. The tumor inhibition rate was 47%. Flow cytometry showed post-treatment, DC activation, increased cytotoxic CD8⁺ T cells, and decreased immunosuppressive Tregs and MDSC in tumor tissues. Blood, liver, and kidney indices showed no adverse reactions.

Conclusion: OPDEA-PCL efficiently encapsulates icaritin into mitochondrial-targeted nanoparticles, significantly boosting icaritin's bioavailability. This process amplifies mitophagy, inducing immunogenic cell death (ICD) and activating the immune microenvironment in HCC tumors, thereby achieving potent tumor suppression.

Abstract Submission No. 100586
O-0545

MSH2 suppresses HCC progression via regulating the cell cycle in response to DNA damage

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Although microsatellite instability is rare in hepatocellular carcinoma (HCC), we found that DNA mismatch repair deficient (dMMR) related mutational signatures increase with HCC progression. On the other hand, gene expression data from the TCGA database revealed that mismatch repair genes, particularly MSH2, are upregulated in HCC tissues. In the present study, to elucidate the role of MSH2 in inflammation-related hepatocarcinogenesis, we generated a hepatocyte-specific Msh2 deletion (Msh2 KO) mouse model and treated it with 0.02% thioacetamide for inflammatory stimulation. Msh2 KO mice developed liver tumors at a higher rate than controls (60% vs. 24%). Although a high number of mutations with dMMR-associated signatures were detected in Msh2 KO tumors than in controls, no common driver mutations were identified. Transcriptome analysis using liver tissue and liver cancer cell lines revealed that loss/reduction of MSH2 causes up-regulation of E2F2 and downregulation of CPT1A. In addition, MSH2 silencing increased the percentage of cells in S phase. Furthermore, exploratory immunostaining for differences in DNA damage response-related molecules by MSH2 silencing revealed increased expression of γ H2AX. These data suggested that MSH2 suppresses hepatocellular carcinoma progression not only by DNA repair, but also by regulating the cell cycle in response to DNA damage and by regulating lipid metabolism.

Abstract Submission No. 100648
O-0546

Targeting XPO1 inhibits proliferation of hepatocellular carcinoma cells by disrupting redox balance

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Background: Hepatocellular carcinoma (HCC) poses a significant threat to public health due to its complex pathological mechanism and poor prognosis. There is an urgent need to identify efficient targets and effective treatment strategies for HCC.

Methods: By analyzing public liver cancer databases, we found XPO1, an essential gene of liver cancer, was aberrantly expressed in the HCC and associated with poor survival. The effect of XPO1 inhibitor was investigated in cell lines and mouse models of HCC. A resistance screen was performed to identify the key gene in the drug resistance. To identify inhibitors that could synergistically function with XPO1 inhibitor, a compound screen was conducted.

Results: XPO1 inhibitor KPT330 inhibited the proliferation of HCC in vitro and in vivo. It caused cell cycle arrest through inducing the accumulation of reactive oxygen species (ROS). Mechanistically, the accumulation of nuclear receptor corepressor (NCOR1) in the nucleus by XPO1 inhibition, potentially leading to abnormal gene transcription that regulates the oxidative state. Through resistance screen, KEAP1 was identified as a key gene whose knockout induced the resistance of HCC cells to KPT330. Deletion of KEAP1 alleviated oxidative stress by activating the NRF2-mediated antioxidant pathway. The combination of XPO1 inhibitor and aldehyde dehydrogenase (ALDH) inhibitor, Disulfiram, synergistically suppressed the HCC development.

Conclusions: Our study illustrates the potential of XPO1 inhibitor and a drug combination strategy for the treatment of HCC. Furthermore, our data shed light on the mechanism that the response of HCC cells to XPO1 inhibitor is intricately tied to the redox balance.

Abstract Submission No. 100694
O-0547

Luseogliflozin attenuates nonalcoholic steatohepatitis and hepatocellular carcinoma in diabetic mice

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Since diabetes mellitus is a pandemic disease worldwide and is becoming a main cause of non-alcoholic steatohepatitis (NASH) and hepatocellular carcinoma (HCC), the strategies to prevent diabetes-related NASH and HCC are strongly desired. It was documented that sodium-dependent glucose cotransporter 2 (SGLT2) inhibitor could prevent pancreatic cancer growth in mice and had reno/cardioprotective properties in humans. However, the long-term protective effect on the liver remains unclear.

To address this issue, this study aimed to evaluate whether luseogliflozin (LG), a major SGLT2 inhibitor, can prevent diabetes-related NASH and HCC. Streptozotocin-induced diabetic mice fed a high-fat diet (STAM mice) were treated with LG (0.1% in diet) for 20 weeks and the liver phenotype was assayed. Co-administration of LG alleviated steatohepatitis and significantly reduced the number of liver

tumors. Mechanistically, LG markedly down-regulated the expressions of genes associated with pro-inflammatory cytokines, endoplasmic reticulum stress, p62-Nrf2 pathway, and cell division in non-tumorous hepatic tissue.

In conclusion, LG attenuates NASH and HCC in diabetic mice. This study may propose a novel solution for serious liver complications of diabetes.

Abstract Submission No. 100696

O-0548

Integrated multiomic analysis in HCC beyond the Milan criteria undergoing liver transplantation

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Objective: In patients with hepatocellular carcinoma (HCC) meeting the Milan criteria, liver transplantation (LT) is an extremely effective therapy. We aimed to explore the survival-related molecular biological features in patients with hepatitis B virus (HBV)-related HCC beyond the Milan criteria received LT and to identify the key molecular biology governing the prognosis.

Design: Among 699 consecutive HCC patients undergoing transplant between 2015 and 2019, 122 had tumors exceeding the Milan criteria on pathology and were enrolled in the study. Integrated analyses of tumor tissues were conducted using RNA sequencing (RNA-seq), transposase-accessible chromatin sequencing (ATAC-seq) and proteomic landscape profiling.

Results: At a median follow-up of 34.6 months, 45 patients had died, and 52 had experienced recurrence; the 5-year overall survival (OS) and recurrence rates were 45.0% and 52.0%, respectively. Unsupervised clustering based on transcriptomics identified three subgroups, namely, the low-risk group, medium-risk group and high-risk group. The transcriptomic subgroups significantly differed in OS (high-risk vs. low-risk, hazard ratio (HR) = 4.527). Deep bioinformatics analysis revealed that cancer-associated fibroblast (CAF)-induced cancer stemness may govern the adverse biological features of HCC in the high-risk group. The ATAC-seq identified key transcription factors bridging CAF infiltration and stemness. Proteomics further validated the transcriptomic subgroup model. Finally, we constructed a three stemness-related protein-based prognostic model to support the transcriptomic subgroup model.

Conclusion: Our observations provided the first multiomic landscape of patients with HCC beyond the Milan criteria undergoing LT. A CAF-stemness-governed classification was constructed to predict the outcomes of patients with HCC beyond the Milan criteria.

Abstract Submission No. 100712

O-0549

SIRPa overexpression induces AICD of tumor-infiltrating T lymphocytes in hepatocellular carcinoma

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Background and aim: Tumor-mediated Activation induced T lymphocyte death (AICD) of tumor-infiltrating T lymphocytes is more likely to be involved in tumor immune escape. In this study, we aimed

to explore the molecular mechanism in tumor-mediated AICD in hepatocellular carcinoma (HCC).

Method: Firstly, a genome-wide CRISPR/Cas9 knockout (GeCKO) library screening was performed to screen the key genes in the human leukemic T cell line Jurkat E6-1 cells, which were stimulated with ConA, PMA+PHA and PMA+Ionomycin, respectively, to induce AICD. The candidate genes were verified in T cells from HCC patient blood with the corresponding sgRNAs.

Result: By using GeCKO library screening, there were 121 sgRNAs that could be enriched in ConA group, PMA + PHA group and PMA + Ionomycin group. In addition, transcriptome sequencing indicated that the gene expression profiles of T cells in HCC tissues were different from those in adjacent tissues. An integrated analysis of the two datasets showed that SIRPa might induce AICD in T cells. In vitro study, SIRPa overexpression in Jurkat E6-1 cells, TCR-T cells, or T cells from HCC patient blood could enhance apoptosis while SIRPa depletion could significantly inhibit apoptosis. Importantly, CD3⁺SIRPa⁺ T cells in HCC tissues were more than those in adjacent normal tissues. Finally, the analysis of RNA-seq data of TCGA LIHC dataset revealed that the level of SIRPa in HCC was positively correlated with the frequency of tumor-infiltrated T cells.

Conclusion: SIRPa could induce AICD in T cells of HCC.

Abstract Submission No. 100742

O-0550

The effect of SRC1 inhibitors in hepatitis B-related liver cancer

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Background and Aims: Hepatitis B virus (HBV) infection is the leading cause of chronic hepatitis B, cirrhosis, and hepatocellular carcinoma (HCC). HBV x protein (HBx) interacts with and modulates a variety of signal transduction pathways leading to HCC, including Src family kinases (SFKs). This study aims to investigate the effect Src inhibitor on HBV infection in an in vitro model of HBV-related HCC.

Method: Hep3B, a HCC cell line with integrated HBV genome was treated with two SRC1 inhibitors, saracatinib (SAR) and dasatinib (DAS) with concentration ranging from 0.02 to 10.00 μ M for 24,48, and 72 hours. Lethal concentrations 50 (LC₅₀) of all treatments were calculated from cytotoxicity assay using MTT test. mRNA and protein expressions SFKs, including SRC/ASV1, FGR, YES, and FYN were assessed by qRT-PCR and Western blot, respectively.

Results: Cytotoxicity test showed dose-dependent toxicity of SAR with LC₅₀ of 2.0 and 3.1 μ M for 48 and 72 hours treatment, respectively. SAR and DAS treatments using concentration of 1.25, 2.5, and 5 μ M significantly down-regulated the expressions of SRC1 and FGR ($p < 0.05$), while FYN was reduced only by DAS, and YES by SAR. The down-regulation of SRC mRNA was also confirmed by the decrease of protein expression. Interestingly, positive correlations between HBV X gene and SRC1, FGR, and YES were noticed, showing direct association between HBV infection and SFKs.

Conclusion: The inhibition of the SFKs is associated with HBV infection, showing a potential linear correlation between host and pathogen.

Abstract Submission No. 100755

O-0551

Identification of developmental heterogeneity and potential therapeutic targets in HCC

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Intratumor heterogeneity remains a major obstacle in clinical cancer treatment with limited therapeutic options. In contrast to genetic heterogeneity, the concept of cellular developmental hierarchies and cell-state plasticity driven by non-genetic mechanisms has recently come into sharp focus. With the advancement of single-cell sequencing technology, the clonal evolution and dynamics of cell populations during cancer progression could be monitored at high resolution. To gain insights into HCC tumor heterogeneity, a hepatocyte differentiation model was established to mimic liver development in vitro and utilized to guide the clustering of tumor cells at single cell level from a HCC cohort containing 160 patients. A total of 5 clusters liver parenchymal cells annotated by lineage-specific signature genes were identified. Pseudotime analysis revealed that tumor subpopulations forms a developmental trajectory resembling normal hepatocyte differentiation. RNA velocity analysis indicated that cells at the “root” of developmental trajectory are highly plastic, and constitute the hierarchical heterogeneity with their progenies, which significantly contributed to the poor prognosis in HCC. Multi-color immunofluorescent staining of representative biomarkers further confirmed the existence of developmental heterogeneity in HCC patients. The establishment of hepatocyte differentiation model and algorithms for predicting driver events of the regulatory networks delivers potential therapeutic targets and preclinical candidate compounds, which show high therapeutic potency in patient-derived organoids and xenografts.

Abstract Submission No. 100760
O-0552

Prognosis prediction based on B cell markers through single-cell and bulk RNA-seq analysis for HCC

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Tumor-infiltrating immune cells greatly participate in regulating tumorigenesis and metastasis of hepatocellular carcinoma (HCC). B cell, as an important role of specific immunity, plays an indispensable role in antitumor immunity and regulate tumor development. In this study, we firstly identified 345 B cell marker genes of HCC based on single-cell RNA sequencing data. Subsequently, a B cell marker genes-related prognostic signature (BCPS) was developed in the cancer genome atlas (TCGA) cohort for risk stratification and prognosis prediction. The predictive value of the BCPS in prognosis was well validated in different clinical subgroups and two external datasets (ICGC-LIHC cohort, GSE14520 cohort). Moreover, multivariate analysis revealed the independent prognostic value of BCPS for OS in HCC. Further functional analysis indicated the BCPS was associated with basic cellular processes, that may contribute to the development and progression of HCC. Thereafter, immune characteristics as well as the therapeutic benefits in BCPS risk score-defined subgroups were analyzed. Patients with low-risk score exhibited immune-active status, manifested as higher immune scores, more infiltration of CD8+ T cells, and higher T-cell receptor (TCR) richness and diversity. Remarkably, the BCPS was negatively correlated with immunotherapy response-related signatures. In addition, the low-risk group exhibited significantly improved therapeutic benefits, either from immunotherapy or traditional chemotherapy and target therapy. Overall, the BCPS showed an

excellent predictive value for prognosis and therapeutic responses for HCC, which might also provide novel insights into better HCC management strategies.

Abstract Submission No. 100823
O-0553

The Urea Cycle Enzyme CPS1 Inhibits the Metastasis of HCC through Recruiting CD8+T cells

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Background: Carbamoyl phosphate synthetase 1(CPS1) is a metabolic enzyme involved in the production of urea. Our previous studies demonstrated the role of CPS1 in tumor growth and radioresistance in hepatocellular carcinoma (HCC). However, whether CPS1 regulates metastasis and immune evasion remains unclear.

Methods: Transwell and scratch assay were used to detect the function in vitro. Cytometry by time-of-flight was used to screen the differential immune cell groups in the metastasis model. Flow cytometry was utilized to detect the key immune cell subtypes in Cps1-associated tumor immune microenvironment.

Results: The expression of CPS1 was gradually downregulated in normal liver tissue, HCC and metastatic HCC. Overexpression of CPS1 could inhibit the invasion and migration of HCC in vivo and in vitro, respectively. Furthermore, a high level of Cps1 enhanced the infiltration of CD8+T cells and the production of IFN- γ , granzyme B and perforin, thus impeding the development of HCC. However, the inhibition effect mediated by Cps1 was offset after clearing the CD8+T cells in C57BL/6 mice. Mechanistically, the inactivation of CPS1 promoted MMP7 upregulation mediated epithelial-mesenchymal transition by activating AKT1/ β -catenin signal pathway. CPS1 could induce CD8+T cells to the tumor site to exert anti-tumor immune effect via stimulating the production of C-X-C motif chemokine ligand 13(CXCL13). Finally, high CPS1 subtype HCC could further potentiate the responsiveness to immune checkpoint blockade.

Conclusion: These findings indicate that urea cycle key metabolic enzyme CPS1 can hinder the development of HCC and remodel the immunoactive tumor microenvironment, thereby enhancing the efficacy of PD-1 checkpoint.

Abstract Submission No. 100856
O-0554

Image analysis highlights distinct fibrosis patterns in combined hepatocellular-cholangiocarcinoma

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Background: Combined hepatocellular-cholangiocarcinoma (cHCC-CCA) is a distinct entity of primary liver cancer defined by the presence of both hepatocellular carcinoma (c-HCC) and cholangiocarcinoma differentiation (c-CCA) and usually have stem cell-containing transitional zone (TZ) between the two components. Tumor fibrosis stroma more abundant in pure colangiocarcinoma (p-CCA) than pure HCC (p-HCC) and has been reported to be associated with tumor stemness, invasion and treatment effect. This study is to clarify the fibrosis characters of tumor stroma and its clinicopathologic significance using second harmonic generation/two-photon excitation fluorescence (SHG/TPEF) microscopy.

Methods: We use SHG/TPEF to analyze the collagen structures in 16 cHCC-CCAs, 15 p-HCCs and 15 p-CCAs. Total 16 fibrosis parameters, such as distributed and aggregated collagen for tumor and 184 parameters in the non-tumor were quantified using digital image analysis. Wilcoxon rank sum test was used in the analysis.

Results: c-HCC and c-CCA in cHCC-CCA had more distributed collagen than the p-HCC and p-CCA ($P=0.042$ and $P=0.031$, respectively), while there was no difference for the overall fibrosis area or aggregate collagen. TZ contained more distributed collagen than c-HCC ($P=0.039$), p-HCC ($P<0.001$) and p-CCA ($P=0.028$). For non-tumor liver, the liver of the p-CCA patients had lower degree of fibrosis than the cHCC-CCA patients for the parameters in portal tract and peri-portal regions ($p<0.05$) while there was no significant difference of liver fibrosis between p-HCC and cHCC-CCA cases.

Conclusions: In conclusion, distributed collagen could be a distinct fibrotic pattern in cHCC-CCA. Distributed collagen may be associated with stem cell niche and tumorigenesis of cHCC-CCA.

Abstract Submission No. 100864
O-0555

HCC-Derived GM-CSF Induces Leukotriene Production in CD163+ TAMs Contributing to Cancer Progression

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Background: Tumor-associated macrophages (TAMs) promote cancer progression through cell proliferation and immunosuppression. We observed that macrophages secreted leukotrienes (LTs) in the lung metastasis of hepatocellular carcinoma (HCC) and promoted metastasis. In this study, we investigated the interactions between HCC cells and TAMs and evaluated the potential for targeted therapy.

Methods: We evaluated the number of 5-LOX-positive cells in resected HCC tissue and multivariate analysis associated with overall survival (OS) in 86 patients. Mouse HCC cell line BNL was inoculated intraportally into BALB/c mice, 5-LOX inhibitor was administered, and GM-CSF-transfected BNL cells were injected. Co-culture was performed with mouse bone marrow cell-derived macrophages (BMDM) and HCC cells.

Results: In resected HCC tissues and TCGA-LIHC, the group of patients with high 5-LOX expression had poorer OS ($p < 0.05$). On multivariate analysis, 5-LOX positive cell count was associated with post-operative survival. In the tumor, CD163(+) TAMs expressed 5-LOX. In HCC mouse model, tumor growth was suppressed by 5-LOX inhibitor. In tumor tissues, GM-CSF expressing cells were tumor cells and increased 5-LOX, CD163, and PD-L1 expression in BMDMs. Moreover, overexpression of GM-CSF in tumor cells promoted the tumor progression. In the co-culture experiment, tumor cells derived GM-CSF increased 5-LOX and CD163 expression in BMDMs.

Conclusions: This study demonstrated a series of mechanisms by which HCC cell-derived GM-CSF promotes 5-LOX and CD163 expression and LT production in TAMs, promoting tumor proliferative potential. Furthermore, the suppression of LT production via GM-CSF from HCC cells regulates tumor progression, suggesting the possibility of a novel therapeutic target.

Abstract Submission No. 100892
O-0556

Inhibition of SFK and its effect on cancer stem cell markers expression in HBV-related HCC

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Background: Chronic infection of hepatitis B virus (HBV) remains the main etiological factor for hepatocellular carcinoma (HCC). HBV-related HCC pathogenesis has been associated with the expression of HBV X protein (HBx), which can interact directly with key regulatory protein including Src family kinase (SFK). HBx interaction with Src are important for regulation of stem-like properties and liver cancer formation. Here, we determined the effect of treatment with Src inhibitors on cancer stem cell (CSC) markers expression in HBV-related HCC.

Methods: Hep3B, a HCC cell line with integrated HBV genome, was treated with two Src inhibitors, saracatinib (SAR) and dasatinib (DAS) with increasing doses of 1.25, 2.5, and 5.0 μ M for 48 hours based on each of their LC₅₀ concentrations. mRNA and protein expressions of different CSC markers and other liver-related markers were assessed by qRT-PCR and flow cytometry.

Results: Hep3B cells highly expressed CSC markers EpCAM, CD13, CD133, and CD24, but only lowly expressed PD-L1, CD95 and its ligand CD95L. Treatment with SFKs inhibitors, SAR and DAS, reduced both Src gene and protein expressions. SAR treatment increased *CD133* ($p<0.01$) but reduced *CD90* expressions, while DAS treatment caused no changes in other CSC markers. In addition, SFK inhibitors also reduced fibrosis markers, *TGFBI*, *ACTA2*, *HGF*, *CTGF*, and *FSP1* and have no significant effects on liver marker AFP and albumin expressions, mostly noted for SAR.

Conclusion: Src inhibitors treatment may have anticancer effect by reducing the expression of CSC markers, as well as a possible antifibrotic effect in HBV-related HCC.

Abstract Submission No. 100900
O-0557

PSMP suppresses HCC progression through inhibiting macrophage M2 polarization via PI3K/Akt pathway

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Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver and represents a major global health-care challenge.

PC3 secreted microprotein (PSMP) is a novel chemotactic cytokine that can recruit peripheral blood monocytes and lymphocytes through CCR2. Our previous study found that PSMP promotes the progression of liver fibrosis by regulating the infiltration, activation and polarization of macrophages. However, the relationship between PSMP and the development of HCC remains unclear.

Through clinical samples, we found that PSMP is downregulated in human HCC tissues, and its expression level is positively correlated with the prognosis of HCC patients. *In vivo*, we found that genetic deletion of PSMP promotes subcutaneous and liver orthotopic tumor growth and metastasis in mice; Overexpression of PSMP inhibits the formation of subcutaneous tumors in nude mice. Mechanistically, deletion of PSMP substantially suppresses the infiltration of CD8⁺ lymphocytes while promoting the infiltration and polarization of M2 tumor-associated macrophages (TAMs) within the liver. *In vitro*, we observed that PSMP possesses the capacity to induce M1-polarization and suppress M2-polarization of macrophages. In addition, analysis of RNA sequencing results showed that PSMP may mediate the polarization of macrophages by regulating the PI3K/Akt pathway. Then, we verified that PSMP mediates its inhibitory effect on M2-polarization of macrophages through inhibition of p85 and Akt phosphorylation.

Collectively, PSMP may inhibit macrophage M2 polarization by downregulating PI3K/Akt signaling. The results are expected to clarify the role and mechanism of PSMP in the liver tumor microenvironment for the first time, which has important theoretical significance and potential application value.

Abstract Submission No. 101145

O-0558

Investigation on the Tumor suppressor role of miR-3185 in Hepatocellular Carcinoma

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Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related deaths worldwide. Serum miR-3185 has emerged as a potential biomarker in HCC, with higher levels associated with better prognosis. However, the role of miR-3185 in the disease remains unclear. This study aimed to elucidate the function of miR-3185 in liver cancer.

Methods: The miR-3185 target genes were predicted by using TargetScanHuman 7.2 and miRDB. HCC-derived JHH6 cells were transfected with miR-3185 mimic and scramble control. mRNA and protein expression of target genes were assessed at 24h, 48h, and 72h post-transfection. Putative targets were validated by using a 3'UTR miR-target gene reporter system. Cell viability, cell cycle and migration were evaluated to describe the roles of miR-3185 in the *in vitro* model.

Results: *In silico* analysis identified eight miR-3185 target candidates. Among those, *SLC39A11* was identified as the main miR-3185 target. miR-3185 mimic significantly reduced *SLC39A11* mRNA at 24h, 48h, and 72h and its protein expression at 48h and 72h. The 3'UTR miR-target gene reporter assay confirmed the targeting of *SLC39A11*, resulting in a 58% reduction in luciferase activity. The inhibition of *SLC39A11* expression resulted in significant decreased cell viability, increased G0/G1 phase cell cycle arrest and repressed cell migration.

Conclusion: *SLC39A11* is a miR-3185 target in HCC. The inhibition of this essential zinc transporter reduced cell viability and migration, thus supporting the role of miR-3185 as a tumor suppressor.

Abstract Submission No. 101245

O-0559

MEGF6 suppresses muscle differentiation and increases tumor proliferation in lenvatinib-treated HCC

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Background: Hepatocellular carcinoma (HCC) patients who received the treatment of Lenvatinib (LEN) are often accompanied by skeletal muscle loss, which has been correlated with a poor prognosis. Interactions between tumor and skeletal muscle may play a role in patient prognosis and tumor progression.

Methods: C2C12 cells, the mouse myoblast cell lines, were treated with LEN, ERK1/2, and Akt inhibitors. Differentiation suppression was assessed by Immunofluorescence (IF). Transcriptomes were compared between LEN-treated and untreated C2C12 cells. Multiple EGF-like domains 6 (MEGF6) were knocked down to verify its effect on C2C12 cells and mouse HCC tumor cells.

Results: Lenvatinib hindered the proliferation and fusion of C2C12 cells through the ERK1/2 and Akt signaling pathways. Through the transcriptomic analysis and knockdown experiments, we identified the MEGF6 gene, which elevated the myostatin (MSTN) expression to repress myosin heavy chain (MHC) protein expression in C2C12 cells. Moreover, MEGF6 could promote the proliferation of tumor cells when cultured with LEN-treated C2C12 cells medium, and impair the differentiation of C2C12 cells when cultured with LEN-treated tumor cells medium.

Conclusions: The MEGF6 produced from muscle cells and tumor cells could impair muscle differentiation and enhance tumor proliferation. Therefore, MEGF6 is worth further investigating as a target to improve the prognosis of HCC patients.

Abstract Submission No. 101272

O-0560

Disparity landscapes of HBV integration in liver cancer: mechanistic and functional implications

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Background: Hepatocellular carcinoma (HCC) is a leading fatal malignancy worldwide and chronic hepatitis B virus (HBV) infection accounts for ~50% of the cases. HBV DNA integrates into the human genome, disrupting the endogenous tumor suppressors/regulatory genes, or enhancing the activity of proto-oncogenes.

Methods: We determined the disparity landscapes of integration events among sample cohorts, tissue types, chromosomal positions, individual host/viral genes, as well as genic locations. Moreover, we performed mechanistic investigation on how HBV-*TERT* integration led to *TERT* activation and derived a score to predict patients' prognostication according to their clonal disparity landscape of HBV integration.

Results: We revealed the global geographical disparity of HBV integration that the landscape of HBV integration between HCC and non-

tumorous liver varied in regional cohorts, suggesting different degrees of clonal enrichment. Most HBV integrations were positionally enriched at telomeres and centromeres, and they highlighted the novel co-involvement of HBV integration, which likely introduces genomic instability. We constructed a large meta-cohort of multiple ethnicities to refine the landscape of HBV integration. This enables the gene-set/gene-family-level exploration. As *TERT* is the most frequently integrated gene, we further investigated the mechanistic modulation of *TERT* transcription activation and revealed the concurrent influence by the orientation and relative distance of HBV integration. Additionally, clonal disparity of HBV integration was observed among patients and the higher level of clonal disparity score indicates poor patients' prognosis.

Conclusions: Our study uncovered the different levels of clonal enrichment of HBV integration, mechanistic insights, and prognostic biomarker, to strengthen our understanding in HBV-associated hepatocarcinogenesis.

Abstract Submission No. 101384

O-0561

Unique pattern of cell-cell interaction in Cytoglobin knock-out mice promoting liver tumor formation

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Background: Cytoglobin (Cygb), the newest member of the mammalian globin family, has shown protective function in anti-fibrotic properties. This study investigated the cell-cell interaction in the liver tumor and non-tumor area of wild-type (WT), CYGB deficient (Cygb-KO), and Cygb overexpression (Cygb-TG) using both whole tissue transcriptomic (RNAseq) and single-cell RNA sequencing (scRNAseq) analysis.

Method: Mice were administrated with Diethyl nitrosamine (DEN) by percutaneous injection at 6 µg/g BW at 15-day-olds and observed for 12 months. RNA from liver tissues was used for RNAseq. Primary non-parenchyma cells isolated from DEN-treated livers were performed scRNA-seq by 10X Genomics.

Result: The mean number of liver tumors in WT was 4.76 compared to 1.51 in Cygb-TG, $p < 0.001$; and the maximum size of liver tumors was 7.4 mm in WT compared to 2.05 in Cygb-TG mice, $p < 0.01$. Heatmap analysis of whole liver transcriptomic data revealed the suppression of DNA-damage inducible genes and stimulation of antioxidant-related genes in TG livers. The integrated scRNA-seq data and annotation identified 10 cell types including 2 subtypes of macrophage and 2 subtypes of HSC. Liver sinusoid endothelial cell (LSEC) is the most abundant population. NicheNet analysis demonstrated a unique pattern in the KO niche which highlighted robust interactions of receptors in LSEC with the ligands from other non-parenchymal and immune cells in comparison with those of WT. These ligands are neuron growth factors from HSCs, transferrin from cholangiocytes and NKs, and galectin 3 from tumor-associated macrophages. The validation cohort of 364 patients with HCC demonstrated these factors are correlated with overall survival.

Conclusion: Both RNAseq and scRNAseq revealed the transcriptomic profile changing in various cell types between KO and WT mice, while the interaction with other non-parenchymal cells and immune cells from KO liver may drive functional characteristics in LSEC and promote tumor development.

Abstract Submission No. 101472

O-0562

Novel disease-associated hepatocyte state can predict the future risk of liver cancer development.

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Rationale: Hepatocellular carcinoma (HCC) constitutes approximately 80-90% of primary liver cancers and is frequently identified at an advanced stage, where treatment choices are limited, while prognosis and survival are poor. Conversely, early detection of HCC substantially improves outcomes, rendering it potentially curable. Presently, it is challenging to pinpoint which patients will develop HCC, as current methods for staging chronic liver disease (CLD) are ineffective for predicting HCC.

Our study: In our research, we utilised single-nucleus RNA sequencing (snRNA-seq) to delineate the cellular microenvironments in both healthy and pre-malignant livers via established mouse models (CDE, TAA, MUP-uPA). Subsequent analysis revealed a disease-associated hepatocyte (daHep) transcriptional state not found in healthy livers but increasing in prevalence with advancing CLD. Copy number variation (CNV) analysis of micro-dissected tissues indicated that regions enriched with daHeps harboured extensive structural variants, implying that these cells may be an intermediary to malignancy. Examination of three contemporary human snRNA-seq datasets corroborated the existence of similar cellular phenotypes in human CLD and indicated a higher mutational load. Crucially, elevated daHep levels were shown to predict oncogenesis, suggesting a greater risk of developing HCC.¹

Ongoing research: We are now employing Oxford Nanopore long-read sequencing to investigate genome-wide methylation patterns of human pre-malignant daHeps to establish a non-invasive assay using methylated cfDNA from blood samples and quantify daHep levels to assess the subsequent risk of HCC. These insights have the potential to revolutionise the staging, monitoring, and risk assessment of patients with CLD.

¹Carlessi et al. Cell Genomics 2023

Abstract Submission No. 101474

O-0563

Traditional Chinese medicine compound and anti-tumor immunity

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Background: The cell cycle inhibitor p21 triggers targeted immunokilling by p21-activated secretory phenotype (PASP). Qizhu Kangai formula (QZKAF) has anticancer functions but the underlying mechanisms involving PASP remain unclear.

Purpose: This study aimed to investigate the mechanisms of QZKAF in inhibiting the progression of hepatocellular carcinoma (HCC) related to PASP.

Methods: Cell proliferation was measured by Cell Counting Kit-8 (CCK-8), 5-Ethynyl-2'-deoxyuridine (EdU). Cell cycle was evaluated by flow cytometry, and senescence was detected by senescence-associated beta-galactosidase (SA- β -gal) staining. A diethylnitrosamine (DEN)-induced liver cancer model of C57B/L6 mice was constructed to evaluate the anticancer effect of QZKAF. The pathological features of liver were observed using hematoxylin and eosin (H&E) staining. The screening of PASP was performed by GeneCards, DisGeNet, Online Mendelian Inheritance in Man, and The Cancer Genome Atlas databases. Western blotting, immunofluorescence, and transwell assays were also used.

Results: QZKAF-containing serum enhanced p21 expression, accelerated cell senescence, triggered cell cycle arrest, and inhibited cell proliferation in Huh7 and MHCC-97H cells. QZKAF decreased the number and size of liver tumor nodules and enhanced p21 expression, SA- β -Gal staining of tumor lesions, and cytotoxic CD8⁺ T cell infiltration. Decorin, dermatopontin, hepatocyte growth factor, C-X-C motif chemokine ligand 14, and Wnt family member 2 were involved in HCC development and associated with the infiltration of natural killer cells and CD8⁺ T cells in the tumors.

Conclusion: QZKAF suppression of HCC progression may involve P21 up-regulation-mediated cell senescence, the secretion PASP, and reversing the immunosuppressive microenvironment. This study could help new strategies for improving HCC treatment.

Abstract Submission No. 101526

O-0564

Combinational therapeutic targeting of BRD4 and CDK7 induces anticancer effects in HCC

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Objectives: In hepatocellular carcinoma (HCC), oncogenes are continuously and robustly transcribed due to aberrant expression of essential components of the trans-acting super-enhancers (SE) complex. Preclinical are now being conducted on small-molecule inhibitors that target core-transcriptional components, including as transcriptional bromodomain protein 4 (BRD4) and cyclin-dependent kinase 7 (CDK7), in many malignant tumors. We aim to explore whether co-overexpression of BRD4 and CDK7 is a potential marker of worse prognosis and a combined therapeutic target in HCC.

Methods: The expression pattern of BRD4 and CDK7 and their correlation with prognosis in HCC from TCGA and GEO datasets were analyzed. The protein levels of BRD4 and CDK7 were determined by immunohistochemistry, and survival data of patients were analyzed using the Kaplan-Meier method. The mRNA expression levels of genes in HCC cells were evaluated by q-PCR. CCK-8 and colony formation assays were conducted to assess cell proliferation of HCC upon treatment with BRD4 inhibitor JQ1 or/and CDK7 inhibitor THZ1.

Results: Co-overexpression of CDK7 and BRD4 was a worse prognostic factor in HCC. Treatment with JQ1 or THZ1 alone had an inhibitory effect on cell proliferation; however, when JQ1 and THZ1 were combined, there was a more notable suppression of cell growth. At the same time, the combined use of JQ1 and THZ1 synergistically suppresses the expression of HCC driver genes.

Conclusion: Our research revealed that BRD4 and CDK7 coupled can be a useful biomarker in HCC prognosis and the combination of JQ1 and THZ1 can be a promising therapeutic therapy against HCC.

Abstract Submission No. 101534

O-0565

Development of the Liver Tumor-bearing Rat Model with Dual Optical Imaging

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PURPOSE: This study aims to develop the liver tumor-bearing rat model that stably co-expresses both luciferase and a red fluorescent, and is quantitatively and qualitatively monitorable by the optical imaging system.

Methods: The plasmids encoding both luciferase and red fluorescence proteins were transfected to the N1S1 rat hepatoma cell lines. Those cell lines were inoculated to the liver of the Sprague-Dawley rats (n=6). All animals underwent both in vivo bioluminescence and fluorescence imaging one week after tumor inoculation. Then, animals were assigned to receive hepatic artery embolization (HAE) (HAE group, n=3) or sham treatment (sham group, n=3). All animals underwent optical imaging again 24 hours after the procedure and liver tissues were harvested. Changes in the intensity of optical imaging were evaluated. The harvested liver tissues were observed by fluorescein microscopy.

Results: Liver tumors were identified by bioluminescence imaging in all 6 animals at 1 week after tumor inoculation (100%, 6/6). The signal intensity of bioluminescence significantly decreased after HAE (P<0.05), whereas it remained unchanged in the sham group (P=0.12). The tumor necrosis areas were more than 90% in the HAE group and less than 30% in the sham group, respectively. The tumor area of the unstained liver tissue could be identified in all animals (100%, 6/6) on fluorescence microscopy imaging.

Conclusion: Tumor-bearing rat model that stably co-expresses both luciferase and a red fluorescent was successfully developed. This model will be useful in the translational research of interventional oncology.

Abstract Submission No. 101554

O-0566

Rab14 potentiates CD147 cytoplasm translocation to promote HCC metastasis by NME1-mediated pathway

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The correct subcellular localization of proteins is essential for their physiological functions, cell homeostasis and signal network transmission. CD147, localized in the basolateral membrane of hepatocytes, functions as signal transduction molecule to regulate complicated pathway between extracellular to intracellular signals, to improve hepatocellular carcinoma (HCC) progress. However, few studies focused on the CD147 distribution. Here we found in comparison with HCC cells expressing wild-type CD147 (CD147^{WT}), mutated CD147 (CD147^{L249A}) showed cytoplasmic enrichment, enhancing HCC cells more aggressive phenotype characteristics with epithelial to mesenchymal transition (EMT) and invasion. Cytoplasm-anchored CD147

competitively bind to NME1 that interrupted the interaction between NME1 and STRAP, to stimulate TGF- β signal and disrupt PAR polarity complex. The cytoplasmic localization of CD147 was regulated by Rab14 in a nucleotide-dependent manner to increase HCC metastasis. In human HCC tissues, patients with cytoplasmic distribution of CD147 was significantly associated with AFP levels ($P < 0.0001$), PVTT ($P = 0.009$) and TNM grade ($P = 0.022$). HCC patients with cytoplasmic CD147 predicted poor overall survival ($P = 0.021$). Collectively, we discovered an unconventional localization of CD147 and dissected the underlying molecular mechanisms “Rab14-CD147/NME1-p-Smad2/p-Smad3-PAR polarity complex” that replenishes a novel molecular pathway in HCC progress.

Abstract Submission No. 101564

O-0567

CRISPR screen for kinase potentiating T cell-mediated cytotoxicity in hepatocellular carcinoma

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Background: Despite achieving durable clinical responses in multiple malignancies, the overall response rate to immune checkpoint blockade (ICB) for hepatocellular carcinoma (HCC) patients remains relatively low. This necessitates immediate efforts to identify the factors responsible for the resistance to immunotherapy and devise novel strategies that can augment antitumor activity of ICB through synergistic approaches. Cytotoxic T lymphocytes (CTLs) are the central effectors of anti-tumor immune response. Understanding the relationship between tumor intrinsic kinases and CTL-mediated cytotoxicity could reveal novel mechanisms in promoting responses to immunotherapy.

Methods: Cas9-expressing mouse HCC cells were overexpressed with ovalbumin (OVA), then transduced with kinome knockout library. Cells were co-cultured with activated OVA-specific OT-1 CD8⁺ T cells followed by next-generation sequencing of gRNA representation. MaGeCK analysis was used to define the top genes that affected tumor cell killing by cytotoxic T cells.

Results: Top hits from the screen were validated *in vitro* and loss of target gene was shown to reduce tumor burden in an immune-dependent manner. Mechanisms by which the target genes regulate T cell killing and modifications in tumor microenvironment are currently under investigation.

Conclusion: By identifying key genes involved in T cell-mediated cytotoxicity and validating their impact on tumor burden, the research emphasizes the importance of understanding the interplay between tumor intrinsic kinases and immune responses. These findings provide insights that can guide the development of novel therapeutic strategies to enhance the effectiveness of immunotherapy in HCC.

Abstract Submission No. 101631

O-0568

A Precision Therapy Targeting Replication Stress in Hepatocellular Carcinoma by WEE1 Inhibition.

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Background: The diversity of hepatocellular carcinoma (HCC) necessitates more individualized and effective treatment strategies for advanced cases.

Methods: We sequenced 178 proteomic and 94 transcriptomic clinical samples for HCC subtype identification. Employing Kinome CRISPR screening and patient-derived xenograft drug assays, we explored synergistic therapeutic combinations for different HCC subtypes. We verified the synergistic effect of oxaliplatin and adavosertib through *in vitro* and *in vivo* models. To elucidate the synergistic mechanism of oxaliplatin and adavosertib in HCC cells, we utilized whole transcriptomic sequencing, confocal imaging, Western Blot, and pDR-GFP or pimEJ5-GFP reporter systems for the detailed investigation.

Results: Both proteomic and transcriptomic subtyping analyses revealed that subtypes with hyperproliferative features have the worst prognosis and highest replication stress (RS) levels. Oxaliplatin, among the clinical first-line agents, heightened RS in HCC, with WEE1 as a synergistic point of action. We demonstrated the synergy between the WEE1 inhibitor adavosertib and oxaliplatin. Mechanistically, adavosertib inhibits oxaliplatin-induced homologous recombination repair and G2/M checkpoint activation, leading to fatal DNA damage and forcing cells with DNA damage into mitosis. High RS levels in HCC patients were associated with poorer prognosis but predicted a better response to the adavosertib-oxaliplatin combination, as confirmed by preclinical models through unsupervised clustering analysis.

Conclusions: Our study proposes a novel classification and treatment strategy for HCC based on tumor RS levels, potentially enriching precision medicine with direct clinical implications.

Abstract Submission No. 101710

O-0569

miR-485-3p as a predictive biomarker in Atezo/Beva therapy and analysis of PIAS3/STAT3/VEGF signal

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Objective: Atezo/Bev therapy has been shown to be effective for uHCC, and miRNA targeting VEGF is associated with therapeutic effect. In this study, we focused on the usefulness of miR-485-3p as a early predictive marker and analyzed the mechanisms related to PIAS3/STAT3/VEGF.

Methods: Sixty-six patients with uHCC treated with Atezo/Bev from 2020 to 2022 were included. Contrast-enhanced CT at 6 weeks was evaluated by modified RESIST and divided into response group (CR+PR) and non-response group (SD+PD). *In vitro*, HuH-7 and HU-VEC were co-cultured, miR-485-3p was transfected, and cell migration and proliferation ability were analyzed. mRNA expression was analyzed by RT-PCR and protein expression by Western blot.

[Results] Comparing 44 patients in the response group with 22 patients in the non-response group, 10 miRNAs were significantly elevated before treatment in the response group, especially miR-485-3p, which was higher than in the non-response group and further elevated 3 weeks later. Serum VEGF levels before treatment were not significantly different, but both groups decreased to below detection sensitivity the next day, and the 3-week/pre-treatment ratio was significantly lower in the response group than in the non-response group. In multivariate analysis, miR-485-3p elevation at baseline was a significant factor related to therapeutic response. *In vitro*, miR-485-3p transfection suppressed migration and proliferation in HuH-7, enhanced

PIAS3 expression, and suppressed STAT3/VEGF expression, which were more pronounced in cells co-cultured with HuVEC.

Conclusion: Serum miR-485-3p is useful for predicting early treatment response, and PIAS3/STAT3/VEGF signals are associated and may have clinical applications in biomarker and drug development.

Abstract Submission No. 101721

O-0570

In vitro therapeutic effects of Bosentan and Obeticholic acid on Hepatocellular Carcinoma Cells

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Background: Hepatocellular carcinoma (HCC) is the second liver tumor with a high mortality rate. High plasma endothelin-1 B (ET-1) level in HCC patients is an important marker of portal hypertension pathogenesis. Expression of Farnesoid X receptor Obeticholic acid (OCA), responsible for hepatoprotective effects are significantly reduced in human HCC tumor tissue.

Method: The *in vitro* anti-proliferative, cytostatic and cytotoxic efficacy of the Bosentan, OCA and Bosentan+OCA were investigated. EA.hy926 and HepG2 cell lines were treated with Bosentan, OCA and Bosentan+OCA for 48 h at various concentrations (0-200 μM). SRB cell viability and colony formation assays were performed in EA.hy926.

Results: GI50, TGI, and LC50 parameters representing the antiproliferative, cytostatic, and cytotoxic effects were calculated at 48h, respectively. Bosentan and OCA revealed lower cytotoxic effects on HepG2 cells compared to EA.hy926, control cell line, (LC50>200). Bosentan had lower cytostatic and antiproliferative effect than OCA on HepG2 cells. Bosentan 25 μM and Obeticholic acid 50-25 μM showed a slight reduction in colony number and size compared to control. Bosentan (50-200 μM) alone, OCA (100-200 μM) alone and Bosentan+OCA combination showed a dose-dependent reduction in cell viability and colony formation ability.

Conclusion: In this study, combined use of Bosentan and OCA were found to increase the cytotoxic effect in both cell lines by showing a synergistic effect. Higher doses of Bosentan+OCA causes loss of healthy cells due to resistance in HepG2 cells emphasizes the need for targeted therapies.

Abstract Submission No. 101746

O-0571

Transcriptome sequencing was used to analyze the mechanism of CENPF involved in regulation of hcc

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Objective: This study is based on analysis of the transcriptome study technology, to explore the mechanism of action of CENPF to participate in the regulation of HCC.

Methods and Results: In this study, the mRNA expression of 20 pairs of HCC tissue and paracancerous tissue samples was examined using

transcriptomics technology. By analyzing the differentially expressed genes between HCC and adjacent tissues. Ten target genes were selected for verification by RT-qPCR, and CENPF gene was screened. The expression levels in normal liver cells L02 and liver cancer cell lines HepG2, PLC, Huh7 and Hep3B were detected, and immunohistochemical staining and Western blot were performed on paraffin sections of liver cancer tissues. The results showed that CENPF was significantly increased in HCC tissues compared with normal liver tissues. Western blot was used to verify the expression of signal pathway related proteins in HepG2 and Huh7 cells with CENPF overexpression and knockdown. GO analysis revealed that CENPF was related to 243 biological processes, and CENPF was mainly involved in cytoskeleton formation, cell mitosis, protein binding and other processes. KEGG analysis showed that CENPF mainly involved in the AKT/mTOR, TNF, JAK - STAT signaling pathways are closely associated with cancer. There were significant differences in PI3K and p-AKT between the knockdown group and the overexpression group.

Results: CENPF is mainly involved in regulating the signaling pathway of liver cancer, which provides a new way to elucidate the mechanism of CENPF on HCC.

Abstract Submission No. 101843

O-0572

MicroRNA-491 ameliorates lenvatinib resistance in hepatocellular carcinoma cells

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Lenvatinib, a multi-kinase inhibitor, has demonstrated superior response rates in hepatocellular carcinoma (HCC) treatment. However, overall survival remains non-inferior to sorafenib, suggesting the development of resistance during treatment. Lenvatinib induces severe hypoxia in tumors by inhibiting VEGF receptors, potentially playing a critical role in multi-kinase inhibitor resistance. This study aims to elucidate the mechanism of lenvatinib resistance under hypoxia in HCC. Human HCC cell lines PLC/PRF/5, Huh7, Hep3B, and HepG2 were cultured under normoxic or hypoxic conditions. Hypoxia increased HIF1α expression without significantly affecting cell growth until 96 hours. Lenvatinib inhibited cell growth in a concentration-dependent manner, but this cytotoxicity was reduced under hypoxia, indicating resistance acquisition.

MicroRNA profiling revealed that 48 microRNAs were differentially expressed in lenvatinib-treated PLC/PRF/5 cells under normoxia (42 increased, 6 decreased). Of the 42 increased microRNAs, 28 showed decreased expression in lenvatinib-treated PLC/PRF/5 cells under hypoxia. Among these, miR-491 exhibited the most significant change in expression. Forced expression of miR-491 partially restored lenvatinib cytotoxicity under hypoxia. Similar results were observed in all tested cell lines. Genome-wide mRNA profiling identified 168 genes commonly altered by miR-491 forced expression in PLC/PRF/5, Huh7, and HepG2, associated with RNA splicing, cell cycle, and cell adhesion pathways.

In conclusion, miR-491 contributes to hypoxia-induced lenvatinib resistance in HCC, and modulating its expression partially restores lenvatinib cytotoxicity. These findings highlight the potential of targeting microRNAs to overcome lenvatinib resistance.

Abstract Submission No. 101857
O-0573

UBE2S promotes tumor glycolysis by enhancing K11-linkage ubiquitination at lysine 171 and 196 of VHL

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Background: Ubiquitination is widely involved in the progression of hepatocellular carcinoma (HCC) by regulating various cellular processes. However, systematic strategies for screening core ubiquitin-related genes, clarifying their functions and mechanisms, and ultimately developing potential therapeutics for patients with HCC are still lacking.

Methods: Cox and LASSO regression analyses were performed to construct a ubiquitin-related gene prediction model. Loss- and gain-of-function studies, transcriptomic and metabolomics analysis were used to explore the function and mechanism of UBE2S on HCC cell glycolysis and growth.

Results: Based on 1423 ubiquitin-related genes, a four-gene signature was successfully constructed to evaluate the prognosis of patients with HCC. UBE2S was identified in this signature with the potential to predict the survival of patients with HCC. E2F2 transcriptionally upregulated UBE2S expression by directly binding to its promoter. UBE2S positively regulated glycolysis in a HIF-1 α -dependent manner, thus promoting the proliferation of HCC cells. Mechanistically, UBE2S enhanced K11-linkage polyubiquitination at lysine 171 and 196 of von Hippel-Lindau tumor suppressor (VHL), thereby indirectly stabilizing HIF-1 α protein levels. In particular, the combination of cephalomannine, a small molecule compound that inhibits the expression of UBE2S, and PX-478, an inhibitor of HIF-1 α , significantly improved the anti-tumor efficacy.

Conclusions: This study identified UBE2S as a key biomarker among the thousands of ubiquitin-related genes and elucidated its mechanism in promoting glycolysis in HCC cells by regulating VHL/HIF-1 α signaling pathway, thus providing therapeutic candidates for the treatment of HCC.

Abstract Submission No. 101876
O-0574

Nimbolide reduces tumor growth and metastasis by regulating miR145 expression in liver cancer

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Background: Liver cancer remains a substantial public health problem and represents the 3rd leading cause of cancer-related deaths globally. However, many advanced therapies are in place, the prognosis remains poor. Here, we aimed to ascertain the anti-cancer and metastatic effects of Nimbolide (a major limonoid constituent of *Azadirachta indica*) by regulating specific microRNA 145 and its target genes in experimental liver cancer.

Methods: Diethyl nitrosamine and N-nitrosomorpholine-induced hepatocellular carcinoma (HCC) mice were administered Nimbolide (6mg/kg b.wt.) orally for four weeks following induction of HCC at 28 weeks.

Results: We found significantly decreased expressions of miR145 in HCC mice compared to naive. Following treatment with Nimbolide to HCC mice showed increased miR145 expression considerably. Moreover, miR145 direct target genes such as MUC1, ROCK-1, MMP-9 and ADAM 17 were significantly elevated in HCC and were downregulated following Nimbolide treatment. The epithelial-mesenchymal transition (EMT) markers E-cadherin expression decreased whilst N-cadherin expression increased in HCC mice. Furthermore, miR145 inhibitor treatment to HepG2 cells showed increased MUC1, ROCK-1, MMP-9, ADAM 17 and EMT marker expression. Nimbolide treatment positively regulated the above indices.

Conclusion: Our novel data suggested that Nimbolide treatment improved miR145 expression and decreased its target genes involved in cancer growth and metastatic development in HCC. Consequently, Nimbolide could be considered a future therapeutic approach in managing HCC pathogenesis.

Abstract Submission No. 101888
O-0575

FAN hinders metastasis and mitigates inflammation-related EMT by targeting FOXM1-ADAM17 axis in HCC

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Objective: Hepatocellular carcinoma (HCC) is a leading global cause of cancer-related death. Fangchinoline (FAN), derived from *Stephania tetrandra* S. Moore, shows pharmacological promise, yet its mechanisms remain unclear. This study aimed to discover the potential molecular target of FAN and examined its anti-tumor effect in both *in vitro* and *in vivo*.

Methods: FAN cytotoxicity was evaluated on HCC cell lines (HCCLM3, HepG2, SMMC7721, and McA-RH777). HCCLM3 and SMMC7721, identified for their heightened sensitivity to FAN, were further explored. Cell morphology alterations were documented through microscopic examination. FAN's impact on cell morphology, proliferation, metastasis, and epithelial-mesenchymal transition (EMT) was assessed. Its anti-inflammatory effect was confirmed using a cytokines ELISA kit. Molecular docking and a TCGA study explored FAN's potential targets. Mechanistic insights were derived from gene over-expression and silencing. Furthermore, FAN's anti-tumor efficacy was validated in an *in vivo* mouse xenograft model.

Results: FAN effectively inhibited the proliferation, invasion and epithelial-mesenchymal transition (EMT) of HCC cells. It also inhibited IL6 and IL1 β release and the expression of inflammation-related proteins including COX-2 and iNOS as well as the activation of NF- κ B pathway, thereby alleviating inflammation-related EMT. Furthermore, FAN bound directly to forkhead box protein M1 (FOXM1), disrupting the FOXM1-ADAM17 axis. *In vivo*, FAN impeded HCCLM3-xenograft tumor growth and lung metastasis. Increased FOXM1 in HCC tissue suggested targeting FOXM1 inhibition as a potential HCC therapeutic strategy.

Conclusion: This study elucidated the anti-tumor effects and potential pharmacological mechanisms of FAN, highlighting FOXM1 inhibition as an effective therapeutic strategy for HCC.

Abstract Submission No. 101980
O-0576

Cancer cell produce liver metastasis via intracellular gap formation in sinusoidal endothelial cells

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Background: Intracellular gap (iGap) formation in liver sinusoid endothelial cells (LSECs) is caused by the destruction of fenestrae under pathological conditions, but the role of LSECs-iGap in liver metastasis is still unclear.

Methods: Mouse models using acetaminophen or thioacetamide followed by intrasplenic injection of hepatocellular carcinoma (HCC) cell line, Hepa1-6 cells, to assess the LSECs-iGap formation. Functional effects of LSECs-iGap on cancer cells were analyzed using MMPs inducer, monocrotaline, and inhibitor, doxycycline. The data was collected using electron microscopic, RNA-sequencing, cytokine array, and endothelial trans-endothelial migration assay *in vivo* mouse models and *in vitro* co-culture system. Biopsy specimens from 98 patients with HCC were statistically evaluated using immunohistochemical staining.

Results: Acetaminophen-induced liver injury and thioacetamide-induced fibrotic liver resulted in LSECs-iGap formation, which positively correlated with increased numbers of metastatic foci after Hepa1-6 cells injection. In addition, Hepa1-6 cells induced IL-23-dependent TNF- α secretion by LSECs and triggered LSECs-iGap formation, toward which their processes protruded to transmigrate into the liver parenchyma. TNF- α caused depolymerization of F-actin and increased MMP9, ICAM1, and CXCLs expression in LSECs. Interestingly, moreover, high expression of ICAM1 and MMP9 was significantly associated with intrahepatic metastasis and overall survival of patients with HCC. Blocking MMP9 activity by doxycycline and an MMP-2/9 inhibitor eliminated monocrotaline or Hepa1-6 cells induced LSECs-iGap formation, which was accompanied with attenuated liver metastasis by Hepa1-6 cells.

Conclusion: This study revealed that cancer cells induced LSEC-iGap formation via pro-inflammatory paracrine mechanisms and proposed MMP9 as a novel target for blocking cancer cell metastasis to the liver.

Abstract Submission No. 102049
O-0577

Determinants of hepatocellular carcinoma in alcohol liver disease patients

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Background: This study aims to determine the drinking pattern and patient characteristics that make Alcohol Liver Disease (ALD) patients susceptible to develop Hepatocellular Carcinoma (HCC).

Methods: A Case Control study was conducted in Out Patient Department of tertiary care liver hospital from November 2022 to August 2023. ALD patients with HCC and without HCC were recruited as cases and controls respectively. Using questionnaire, data was collected on patient characteristics; anthropometry measurements were

done and biochemical test reports noted. Association between suspected risk factors and occurrence of HCC was determined by logistic regression.

Results: 220 ALD patients were enrolled. Mean age was 60.03 ± 9.161 years among cases and 52.70 ± 9.336 among controls; all were males. By univariable logistic regression, following factors had significant association with HCC development - age more than 60 years, family history of cancer, hepatitis C infection, diabetes mellitus, hypertension, smoking, alcohol consumption of more than 80gram per day, daily, for at least 10 years. By multivariable logistic regression, the factors were - age more than 60 years (aOR 9.297, 95% CI: 2.941-29.385), hepatitis C infection (aOR 13.037, 1.494-113.803), smoking (aOR 2.572, 1.180-5.606), alcohol consumption of more than 80gram per day, daily, for at least 10 years (aOR 2.233, 1.154-4.321)

Conclusion: Alcohol consumption more than 80 gram per day, daily, for at least 10 years; higher age, Hepatitis C infection and smoking increase predisposition of ALD patients to develop HCC. Vigorous screening, regular follow up and health education of ALD patients can aid early diagnosis and management.

Abstract Submission No. 200006
O-0578

The Impact of TIGAR on Tumor Microenvironment and Resistance to Ferroptosis in HCC

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Background: TP53-induced glycolysis and apoptosis regulator (TIGAR) is a p53 target protein that has critical roles in glycolysis and redox balance. The reports about the effect of TIGAR on prognosis and its biological role in hepatocellular carcinoma (HCC) are limited.

Methods: 386 patients with HCC who had undergone hepatic resection were enrolled. Immunohistochemical staining for TIGAR, cluster of differentiation (CD)8, CD68, programmed death-ligand 1 (PD-L1) and CD34 was performed. Additionally, the regulation of malignant activity and ferroptosis by TIGAR was investigated *in vitro*.

Results: Patients were divided into TIGAR-positive (n=80, 20.7%) and -negative (n=306, 79.3%) groups by immunohistochemical staining of TIGAR. In uni/multivariate analysis, TIGAR positivity was an independent prognostic factor (p<0.0001). In addition, TIGAR positivity was significantly associated with smaller number of CD8 positive T cells (p=0.0450), larger number of CD68 positive macrophages (p=0.0058), PD-L1 positive cases (p=0.0002) and vessels that encapsulate tumor cluster positive cases (p=0.0004). *In vitro*, TIGAR knockdown decreased cell motility (migration/invasion/colony forming abilities) and induced ferroptosis (down regulation of cell viability/ elevation of reactive oxygen species and lipid peroxidation) (p<0.05). TIGAR knockdown inhibited the phosphorylation of adenosine monophosphate-activated protein kinase and acetyl-CoA carboxylase. Ferroptosis induced by TIGAR knockdown was inhibited by liproxstatin and baicalin treatment (p<0.05). The combination of TIGAR knockdown and lenvatinib significantly further induced ferroptosis (p<0.05). **Conclusions:** High expression of TIGAR impacted the clinical outcome of HCC patients and TIGAR was associated not only with tumor microenvironment but also with resistance to ferroptosis.

Abstract Submission No. 200143

O-0579

Double knockout of P53/Pten induced an HCC mouse model shared a similar transcriptome to human HCC

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Background: HCC mouse models, play a vital role in studying the intricate interplay of factors contributing to HCC development. However, with a multitude of available HCC mouse models, choosing the one most closely resembles human HCC can be challenging. A comprehensive analysis of their characteristics and fidelity in recapitulating human disease is essential for selecting the most appropriate model for specific research objectives.

Methods: This study addresses this gap by conducting a comprehensive transcriptomic similarity analysis of widely used HCC mouse models. The researchers compared the gene expression profiles, immune microenvironments, and metabolic pathways of these models with those of human HCC.

Results: DEN+CCI4-induced HCC model: Showed the worst similarity to human HCC in terms of transcriptome profiles and DEGs. Had minimal metabolic differences between tumor and non-tumor tissues. p53&Pten KO model: Displayed a moderate level of similarity to human HCC in terms of transcriptome profiles and DEGs. Showed some enrichment of pathways similar to human HCC but also had unique enriched pathways. HBV+p53&Pten KO model: Demonstrated the highest similarity to human HCC across various parameters. Shared a high degree of overlap in DEGs between tumor and non-tumor tissues with human HCC. Exhibited a transcriptome profile and immune cell infiltration pattern closely resembling human HCC. Showed metabolic alterations similar to those observed in human HCC.

Conclusion: This study highlights the importance of selecting appropriate HCC mouse models for research. The HBV+p53&Pten KO model emerged as the most promising model due to its remarkable similarity to human HCC across various aspects.

Abstract Submission No. 100045

O-0580

Immunophenotyping and tumor microenvironments of HBV-positive and negative hepatocellular carcinoma

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Background & aims: HBV infection leads to hepatocellular carcinoma (HCC) and affects immunotherapy. Exploring tumor ecosystem in HCC help to gain a deeper understanding and design more effective immunotherapy strategies for HCC patients with or without HBV infection.

Methods: Single-cell RNA sequencing (scRNA-seq) series were integrated as a discovery cohort to interrogate the tumor microenvironment (TME) of HBV+ HCC and HBV- HCC. We further dissect the intratumoral immune status of HBV+ and HBV- HCC. An independent cohort, including samples treated with immune checkpoint blockade therapy (ICB), was used to validate the major finding and investigate the effect of HBV infection on response to immunotherapy.

Results: The interrogation of TME indicated that TREG, exhausted CD8+ T cell and M1-like Macrophage MMP9 were enriched in HBV+ HCC, while MAIT was enriched in HBV- HCC. All subclusters of T cells showed high expression of immune checkpoint genes in HBV+ HCC. TREG cells enriched in HBV+ HCC also showed more robust immunosuppressive properties, which was confirmed by cross-talk between immune cell subsets. The ability of antigen presentation with major histocompatibility complex (MHC)-II was down-regulated in HBV+ HCC and this phenomenon can be reversed by immunotherapy. Two types of HCC also present different responses to immunotherapy.

Conclusion: There is a more immunosuppressive and exhausted TME in HBV+ HCC than in HBV- HCC. This in-depth immunophenotyping strategy is critical to understanding the impact of HBV along with the HCC immune microenvironment and helping to develop more effective treatments in HCC patients.

Abstract Submission No. 100080

O-0581

Prognostic impact of Cyber-Knife as part of multidisciplinary treatment in hepatocellular carcinoma

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Backgrounds: Cyber-Knife (CK) is a stereotactic radiotherapy with high local control capability and is covered by insurance for the treatment of hepatocellular carcinoma (HCC) in Japan. We investigated the efficacy of CK as a multidisciplinary therapy in the treatment of HCC.

Methods: From January 2001 to December 2020, 568 patients with radically treated HCC were included. Of these, CK was added to 52 cases during the course of the study, and the remaining cases without CK were matched for age, gender, presence of HCV infection, tumor size, tumor number, ALBI score, and introduction of chemotherapy, and finally 40 cases each were selected to compare their backgrounds. The primary endpoint was overall survival (OS), and factors related to OS were also examined.

Results: The mean maximum tumor diameter and the mean number of tumors were 24 mm and 1.4, respectively, at the time of initial onset of HCC. The mean tumor diameter at the time of CK was 18 mm, and all the targets were one. The local control rate of CK was 96.8% at 1 year, 87.3% at 2 years, and 87.3% at 3 years. The overall survival rate from the initial treatment was 80.3% at 3 years, 70.8% at 5 years, and 39.1% at 10 years in the CK group, and 79.4% at 3 years, 52.9% at 5 years, and 22.7% at 10 years in the control group, with a significant difference ($P = 0.047$). In univariate analysis, ALBI score (HR 1.26 per 1 95%CI 1.08-1.48 $P < 0.01$) and application of CK (HR 0.56 95%CI 0.32-0.99 $P = 0.049$) were significant independent factors which contributed to OS.

Conclusion: Although it is difficult to determine the extent to which CK contributes to prolonged prognosis in a series of treatment courses, it was considered to be one of the effective treatments as a complement to standard treatment.

Abstract Submission No. 100244

O-0582

Similar recurrence after curative treatment of HBV-related HCC, regardless of HBV replication

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Background and Aims: Antiviral therapy (AVT) is required in patients with newly diagnosed hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC), if HBV DNA is detectable. We compared the risk of recurrence according to HBV replication activity at the curative treatment of HBV-related HCC.

Methods: Patients with HBV-related HCC who underwent surgical resection or radiofrequency ablation between 2013 and 2018 were enrolled in this retrospective cohort study. Patients were categorized into two groups according to HBV replication activity at the curative treatment of HBV-related HCC (group 1: patients who met the AVT indication for HBV-related HCC due to detectable HBV DNA but did not meet the AVT indication if without HCC; group 2: patients who met the AVT indication, regardless of HCC).

Results: In the entire cohort (n=911), HCC recurred in 303 (33.3%) patients during a median follow-up of 4.7 years. After multivariate adjustment, group 2 showed a statistically similar risk of HCC recurrence (adjusted hazard ratio [aHR]=1.18, $P=0.332$) compared to that of group 1. In addition, group 2 showed statistically similar risks of early (< 2 years; aHR=1.31) and late (≥ 2 years; aHR=0.83) recurrence than that of group 1 (all $P>0.05$). Propensity score matching and inverse probability of treatment weighting analysis also yielded similar risks of HCC recurrence between the two groups (all $P>0.05$, log-rank tests).

Conclusions: The risk of HCC recurrence in patients who received curative treatment for newly diagnosed HBV-related HCC was comparable regardless of HBV replication activity if AVT was properly initiated.

Abstract Submission No. 100261
O-0583

The impact of high body mass index on hepatocellular carcinoma in chronic liver disease

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Purpose: To investigate the association between body mass index (BMI) and hepatocellular carcinoma (HCC) in patients with various etiologies of chronic liver disease (CLD), considering age and sex.

Patients and Methods: 350,608 Korean patients with CLD who underwent routine health examinations from 2003 to 2006 were followed up until December 2018 through linkage to national hospital discharge records. Multivariable-adjusted hazard ratios (HRs) per 5 kg/m² increase in BMI for HCC risk in persons with BMI ≥ 25 using Cox models.

Results: HRs were 1.17 (95% CI, 1.06 to 1.28) for HBV, 1.08 (0.87-1.34) for HCV, 1.11 (1.00-1.23) for LC, 1.34 (1.14-1.58) for alcoholic liver disease (ALD), and 1.51 (1.17-1.94) for nonalcoholic fatty liver disease (NAFLD). In these CLD patients, the impact of BMI did not differ by co-morbid LC presence. In sex-specific analyses, HRs were 1.45 (1.23-1.70) in women and 1.06 (0.95-1.19) in men for HBV, while HRs were 1.27 (1.07-1.50) in women and 1.02 (0.90-1.16) in men for LC. In age-specific analyses, in patients aged <65, HRs were 1.17

(1.07-1.29), 1.33 (1.03-1.73), 1.20 (0.87-1.64) for HBV, HCV, and NAFLD, respectively, while corresponding HRs were 1.05 (0.70-1.59), 0.74 (0.50-1.10), and 2.40 (1.62-3.54), respectively, in patients aged ≥ 65 . In categorical analysis, a BMI of 27.5-29.9 showed statistically significantly higher risks of HCC in HBV, ALD, NAFLD, and LC (including HBV-LC).

Conclusion: Higher BMIs were associated with HCC risks in patients with HBV, ALD, NAFLD, and LC. Even being overweight, specifically with a BMI of 27.5-29.9, increased the HCC risk. Women had stronger risks associated with high BMIs in HBV and LC. In NAFLD, the impact of high BMI was more profound at an older age than at a younger age in viral hepatitis.

Abstract Submission No. 100371
O-0584

Identifying optimal candidates for HAIC over Sorafenib: A systematic review and meta-analysis

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Background: Sorafenib is pivotal in extending the survival of patients with advanced or unresectable hepatocellular carcinoma (HCC) though its efficacy is largely curtailed by low response rates. With interest revived in hepatic artery infusion chemotherapy (HAIC), it was found that patients may receive greater benefit from HAIC compared to Sorafenib. This study aims to find optimal candidates for HAIC over Sorafenib.

Methods: A rigorous literature search was conducted to collect available studies comparing patients' outcome differences between HAIC and Sorafenib. The pre-registered protocol was available at PROSPERO (CRD42023458845).

Results: A total of 26 studies with 6456 patients (HAIC:2648; Sorafenib:3808) were included. Chemotherapy-naïve patients (HR=0.66, 95%CI [0.56, 0.79]), individuals with Child-Pugh grade A liver reserve (HR=0.81, 95%CI [0.74, 0.89]), and those with major vessel invasion (MVI) but no extrahepatic metastasis (HR=0.58, 95%CI [0.45, 0.75]) could potentially benefit more by HAIC. However, for those who were refractory to trans-arterial chemoembolization (TACE), sorafenib demonstrated greater efficacy (HR=1.32, 95%CI [1.01, 1.73]) while patients with extrahepatic metastasis whether with or without MVI (EHS+MVI+:HR=0.72, 95%CI [0.44, 1.17]; EHS+MVI-:HR=1.35, 95%CI [0.65, 2.84]) presented similar survival after HAIC or Sorafenib monotherapy. Additionally, pooling HRs from multivariate Cox regression showed that MVI, EHV, and AFP >400ng/ml could be independent risk factors for patients' overall survive (OS), while HAIC treatment and lower BCLC stage were potentially protective factors.

Conclusions: Higher survival benefits could be expected from HAIC compared to sorafenib monotherapy in selected patients. A re-evaluation of HAIC as a potential treatment option in intermediate and advanced HCC is warranted.

Abstract Submission No. 100416
O-0585

Integrative translational research to study T cell exhaustion in hepatocellular carcinoma (HCC)

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Background: Reversal of CD8 T cell exhaustion plays key roles in the antitumor effects of immune checkpoint inhibitor (ICI) therapy, the current standard therapy for unresectable HCC.

Methods: Hepa1-6 liver cancer cells overexpressing gp33 glycoprotein were co-cultured with lymphocytes from P14 transgenic mice, which specifically recognized gp33, to measure antigen-specific anti-tumor immunity. Resistance to anti-PD1 in vivo was induced by repeated injection of anti-PD1 to Hepa1-6-bearing B6 mice. Transcriptional factors involved in T cell exhaustion were identified by single-cell RNA-seq analyses using SCENIC. T cell function and exhaustion in peripheral blood from HCC patients who received ICI therapy were monitored using spectral flow cytometry and analyzed using deep learning algorithms to predict ICI treatment response.

Results: Transcription factors involved in in vivo and in vitro resistance to anti-PD1 and induction of exhaustion, including RUNX2, HMGB2 and galectin-3, may serve as targets to develop exhaustion-reversal strategies. In 43 HCC patients who received nivolumab + ipilimumab therapy, the changes of function/ exhaustion status of peripheral blood T cells were correlated with objective response by imaging after 2 to 4 cycles of treatment. Deep learning algorithms for T-cell exhaustion markers yield good predicting power for ICI response, with area under receiver operating characteristic curve ranged from 0.64 to 0.73 (pre-treatment) and from 0.74 to 0.81 (post-treatment).

Conclusion: Our translational research platforms have the potential of developing biomarkers to predict response to ICI therapy for HCC and designing exhaustion-reversal strategies. (supported by NTU-CC-109L104702-1, NTU-CC-110L893301, NTU-CC-111L893301, NTUMC-NTUH-112C101-62).

Abstract Submission No. 100450
O-0586

ASAP algorithm demonstrates high sensitivity for HCC surveillance - a prospective study.

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Background: Hepatocellular carcinoma(HCC) surveillance with liver ultrasound and alpha-fetoprotein(AFP) has limitations of accuracy and patients' poor adherence with ultrasound examination. ASAP is a HCC risk algorithm based on Age, Sex, AFP, and Protein Induced by Vitamin K Antagonist-II (PIVKA-II) that may allow for a personalized surveillance protocol. We studied the performance of the ASAP algorithm in a prospective cohort of patients undergoing HCC surveillance.

Methods: Patients without prior HCC undergoing HCC surveillance in Singapore General Hospital Department of Gastroenterology and Hepatology between December 2017-October 2018 were enrolled.

Baseline AFP and PIVKA-II (Abbott ARCHITECT®) were assayed and prediction from the ASAP algorithm was calculated using the published model. The patients continued HCC surveillance with semi-annual ultrasound and AFP.

Results: There were 612 patients (60.9% male). Median age was 65 years (IQR 58-72). Most common liver disease was Hepatitis B (90%). By February 2023, after a median follow-up of 52.2 months (IQR 48.3-54.5), 15 patients developed HCC with 13 in BCLC stage 0/A. ASAP algorithm score had the highest AUROC (0.767) for HCC detection, compared to AFP or PIVKA-II alone (0.743 and 0.672 respectively). ASAP score's sensitivity/specificity/negative predictive value (NPV)/AUROC for HCC developing within 1 and 2 years of biomarker assessment were 100%/87.3%/100%/0.946 and 83%/87.3%/99.8%/0.889, respectively.

Conclusion: ASAP algorithm demonstrated high sensitivity, specificity and NPV for HCC detection in a prospective cohort of patients undergoing HCC surveillance. Hence, in view of patients' poor adherence to ultrasound imaging, substitution with regular assessment with the ASAP algorithm may be a feasible option.

Abstract Submission No. 100460
O-0587

A Multi-center Study on Predictors of Primary Resistance to Atezolizumab plus Bevacizumab Therapy

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Background: Atezolizumab plus bevacizumab (Atezo+Bev) therapy is the leading first-line treatment for advanced hepatocellular carcinoma (HCC). Despite various reports on prognostic markers for HCC patients receiving Atezo+Bev therapy, the predictors of primary resistance remain unknown.

Methods: We retrospectively analyzed 225 patients with advanced HCC who received Atezo+Bev therapy between October 2020 and September 2022 across seven hospitals. Best objective response (BOR) was assessed using the RECIST criteria (version 1.1). Primary resistance was defined as BOR of progressive disease. Non-primary resistance was defined as (1) BOR of stable disease and PFS of ≥ 180 days or (2) BOR of partial/complete response. Baseline characteristics were compared between the primary resistance and non-primary resistance groups.

Results: The median age was 72 years; 186 (82.7%) patients were male; and 113 (50.2%) patients had viral hepatitis. Fifty-one (22.7%) patients showed primary resistance, while 114 (50.7%) patients were categorized into the non-primary resistance group. Univariate analysis revealed significant associations between primary resistance and treatment line, CRP, neutrophil-to-lymphocyte ratio, AFP, and DCP.

Among those receiving Atezo+Bev therapy as first-line treatment (n = 152), 24 (15.8%) patients showed primary resistance, which was significantly associated with CRP, AFP, and DCP. The CRAFTY score, incorporating CRP and AFP, effectively stratified the primary resistance rates (11.8%, 30%, and 66.7% for CRAFTY scores of 0, 1, and 2 points, respectively).

Conclusions: About 15% of patients exhibited primary resistance to first-line Atezo+Bev therapy. The CRAFTY score seemed useful to predict the likelihood of primary resistance.

Abstract Submission No. 100634

O-0588

Association between Post-Ablation Fever and Prognosis in Initial Hepatocellular Carcinoma

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Background: Fever, a common complication in patients with hepatocellular carcinoma (HCC) following thermal ablation, yet its impact on prognosis remains unclear.

Materials and Methods: This retrospective study included initial HCC patients who underwent percutaneous microwave ablation at 13 hospitals between January 2007 and February 2021. Statistical models were employed to identify the impact and cut-off values of post-ablation temperature and fever duration on early recurrence. Primary outcomes included very early recurrence (VER) and early recurrence (ER), and secondary outcomes were disease-free survival (DFS) and overall survival (OS) rates. Survival analyses used the Kaplan-Meier method. **Results:** A total of 1458 BCLC stage 0-B HCC patients (mean age: 59 ± 11) with a median follow-up of 47 months. Compared to afebrile, patients who exhibited peak temperatures between 37.0-38.8°C and fever lasting 1-2 days (transient low-grade fever, TLF) showed independent protective effects against VER (HR, 0.73; 95% CI: 0.57, 0.95; P=0.017) and ER (HR, 0.66; 95% CI: 0.54, 0.81; P<0.001). Prolonged or high-grade fever (PHF) showed no differences in VER (P=0.964) and ER (P=0.171). Additionally, TLF patients displayed the highest 5-year DFS and OS rates of 42.6% and 73.2%, surpassing afebrile patients (33.2% and 69.3%, P=0.020 and 0.005) and PHF patients (44.1% and 66.7%, P=0.018 and <0.001). Notably, TLF patients exhibited the highest post-ablation lymphocyte counts increase (P<0.001 vs. afebrile and P=0.013 vs. PHF).

Conclusions: Transient low-grade fever following percutaneous microwave ablation in patients with hepatocellular carcinoma has demonstrated protective effects against early recurrence, possibly attributed to the activation of lymphocytes.

Abstract Submission No. 100640

O-0589

Assessment of Cases with Prolonged Elevation of Tumor Markers without Detectable HCC Recurrence

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Background: Tumor marker elevation is highly predictive of hepatocellular carcinoma (HCC) recurrence during post-treatment surveillance. However, some patients show persistent tumor marker elevation without imaging evidence of recurrence.

Methods: We reviewed 1,610 patients with naive HCC treated with radiofrequency ablation in our department from 1999 to 2021. We identified cases in which tumor markers were continuously above the cutoff value for more than 180 days prior to HCC recurrence. The AFP cutoff value was set differently according to active viral hepatitis status.

Results: Inclusion criteria were met in 228 cases of recurrence in 172 patients, including AFP >20 ng/mL in 122 cases, AFP >200 ng/mL in 42, DCP >200 mAU/mL in 50, and AFP-L3 fraction >15% in 130. The average tumor size at recurrence was 1.7 cm, with 106 cases of solitary tumors, 74 with 2-3 tumors, and 33 with 4 or more tumors. Distant metastasis was observed in 8 cases (3 with neoplastic seeding, 3 with lymph node metastasis, and 2 with lung metastasis). Vascular invasion was observed in 7 cases (6 with portal vein and 1 with bile duct invasion). Treatment modalities included local therapy in 177 cases, transarterial chemoembolization in 36, resection in 6, systemic therapy in 4, best supportive care in 3, and others in 2. Local cure was achieved in 170 (74.6%).

Conclusions: In cases with tumor marker elevation prior to imaging, curative treatment was possible in the majority with caution for vascular invasion and distant metastasis.

Abstract Submission No. 100782

O-0590

Immune Checkpoint Inhibitors for Downstaging HCC Before Liver Transplantation: A Systematic Review

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Background: There is a growing interest in the use of Immune checkpoint inhibitors (ICIs) in the downstaging of hepatocellular carcinoma (HCC) before liver transplantation (LT). We aim to investigate post-LT outcomes for HCC patients who received pre-LT ICIs.

Methods: PubMed, Web of Science, Scopus, and related congresses were searched by September 2023. We included any study types in which ICIs had been used in HCC cases before LT. Two authors screened and critically appraised identified and included studies.

Results: A total of 115 cases (28 publications) were identified and cases were mainly from China (n=66) and the USA (n=38). Nivolumab (n=38), pembrolizumab (n=20), and atezolizumab plus bevacizumab (n=8) were the most used ICI regimens (**Table 1**). We found 17 (25.8%), five (8.9%), and three (5.1%) patients with graft rejections, post-LT HCC recurrences, and death status respectively over the median (interquartile range) follow-up of 11.5 (7.0-17.2) months. Mean (standard deviation [SD]) ICI withdrawal days pre-LT were 24.2 (20.0) and 76.5 (81.8) in patients with and without rejection (P<0.001) and 57.6 (64.0) and 77.1 (85.5) in patients with and without recurrence (P=0.62). Mean (SD) ICI cycles were similar between those with and without rejection (11.2 [13.2], 8.5 [8.4], P=0.37), but it was shorter for

those with post-LT HCC recurrence vs. without (4.2 [1.1] vs. 11.5 [9.6]), $P < 0.001$).

Conclusions: Mean ICI cycles and withdrawal days pre-LT were associated with post-OLT outcomes. Prospective cohort studies and clinical trials are needed to determine the optimal strategy for using ICI before LT.

Abstract Submission No. 100852

O-0591

Improved Survival in BCLC 0/A HCC with Resection vs Ablation: A Propensity-Matched Multicentre Study

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The optimal treatment approach in very-early and early-stage hepatocellular carcinoma (HCC) is not precisely defined, with ambiguity in the literature around the comparative efficacy of surgical resection versus ablation as curative therapies for limited disease. We performed this real-world propensity-matched, multicentre cohort study to assess for differences in survival outcomes between those undergoing resection and those receiving ablation. Patients with Barcelona Clinic Liver Cancer (BCLC) 0/A HCC first diagnosed between 01/01/2016 and 31/12/2020 who received ablation or resection as initial treatment were included in the study. A total of 450 patients were included in the study from 10 major liver centres including two transplant centres. Propensity-score matching was performed using age, sex, transplant centre, HBV, alcohol, diabetes, smoking, platelet count, Child Pugh Score, Charlson Comorbidity Index and tumour category (single tumour 2cm or less, 2-3cm, >3cm and multiple tumour), 156 patients were available for analysis with 78 in each group. Patients who underwent resection had significantly improved overall survival (log-rank test $p=0.023$, Figure 1) and local recurrence-free survival (log rank test $p=0.027$, Figure 2) compared to those who received ablation. Similar results were seen in unadjusted analysis of the original unmatched cohort (overall survival, log-rank test $p<0.001$; local-recurrence free survival $p<0.001$). Based on real-world data, our study supports the use of surgical resection in preference to ablation as first line curative therapy in appropriately selected BCLC 0/A HCC patients.

Abstract Submission No. 101099

O-0592

Chronological changes in clinical characteristics of HCC patients undergoing systemic therapy

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Background: With the advancement in systemic therapy for hepatocellular carcinoma (HCC), the background of patients has significantly changed over time. In this study, we investigated the chronological change of the patients' characteristics in Japan.

Methods: Hepatoma Registry of Integrating and Aggregating EHR (electric health record): HERITAGE study is a registry study of systemic therapy at member institutions of the Japan Liver Cancer Association (JLCA). Patients were divided into three groups based on the initiation dates of systemic therapy: April 2015-2017 (cohort A), 2018-2019 (cohort B), and 2020-March 2022 (cohort C). They were then compared in terms of age at the start of therapy, etiology, mALBI grade, presence of vascular invasion (VI), and existence of extrahepatic metastases (EHS).

Results: A total of 4,669 patients were enrolled, and the regimens were sorafenib/ lenvatinib/ atezolizumab plus bevacizumab in the following order: A 1415/0/0, B 346/1495/3, C 111/742/557. The percentage of patients aged 70 years or older was 57%, 66%, and 71% in cohorts A, B, and C, respectively. For non-viral cases, the corresponding percentages were 47%, 55%, and 58% in the same cohorts. The mALBI grade was 1 or 2a in 57%, 59%, and 61% of the patients in cohorts A, B, and C, respectively. Additionally, 39%, 53%, and 55% of patients in these groups had neither EHS nor VI.

Conclusion: There was an increase in the proportion of non-viral elderly patients among those eligible for systemic therapy. Advances of therapy have expanded the range of cases treated.

Abstract Submission No. 101101

O-0593

Urban Rural Disparities at Presentation and Overall Survival of Hepatocellular Carcinoma in Taiwan

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Introduction: There are urban rural disparities in the management of hepatocellular carcinoma (HCC). The reasons are multifactorial. To investigate the degree of disparities, we initiated this study.

Methods: We assessed all HCC patients in the period of 2014 to 2019 from the database obtained from Integrative Medical Database, National Taiwan University Hospital (NTUH-IMD). NTUH has a main campus located in Taipei City (urban) and Yunlin branch (NTUH-YL)(rural). Demographic characteristics, BCLC staging, underlying liver reserve (Child Pugh class, and ALBI score), viral etiology, treatment method, and overall survival were analyzed.

Results: A total of 3368 patients in NTUH and 785 patients in NTUH-YL were collected. NTUH had 50.9% of HCC patients presenting as BCLC stage 0 or A, while NTUH-YL had 41.1% in BCLC stage 0 or A. NTUH had 25.0% of HCC patients presenting as BCLC stage C or D, while NTUH-YL had 41.7% in BCLC stage C or D. ALBI grade 1 was found in 53.6% NTUH patients, while it was 33.6% in NTUH-YL.

Curative treatment (transplantation, resection, RFA) were done in 61.9% of NTUH patients, while it was 47.9% in NTUH-YL. The median overall survival (OS) was 63.2 months in NTUH and 38.5 months in NTUH-YL ($p < 0.001$).

Conclusions: There were significant disparities in the stage at presentation, underlying liver reserve, treatment method, and median OS in HCC patients, between rural and urban areas even in the same medical system. To improve the OS in the rural HCC patients, earlier diagnosis is the urgent needs.

Abstract Submission No. 101126

O-0594

MOLECULAR CHARACTERIZATION OF HEPATOCELLULAR CARCINOMA IN ARMENIA, 2019-2020: INITIAL OBSERVATIONS

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Background: Within the large region encompassing the Caucasus, Middle East, and Central Asia, Armenia is the country where the incidence of liver cancer is the highest for both sexes.

Methods: A case-control study was conducted, and plasma samples were collected of 110 patients with hepatocellular carcinoma (HCC) and 167 patients with no tumor.

Results: HCV prevalence was 67.2% in the CLD group and 41.8% in the HCC and CLD group. HBV infection was less prevalent.

Free circulating DNA was analyzed for a mutated TERT gene promoter. 20.0% of HCC cases and only 1.7% of CLD patients (OR=13.5, $P=2.5 \times 10^{-7}$) had this.

In contrast, TP53 R249S mutant was rare (1.8% vs 3.6%, ns). The presence of TP53 suggests contact with Aflatoxin B1.

Concerning HBV, 6 HCC patients were infected with subtype D1 (66.6%), one with D3 (11.1%), and two with A2/D1 (22.2%). In CLD, we observed two D1 and a single A2 subtype. Subtype 3A of HCV was representing 64.0% ($n=16/25$) of isolates in HCC patients followed by subtype 1b (32%, $n=8/25$), and a single subtype 2a strain (4.0%).

Conclusion: 1. Conditions of living increased behavioral risk factors which resulted in increased rates of hepatitis and subsequent HCC.

2. HCV isolates correspond to the distribution of genotypes in this part of Eurasia.

3. Occult HBV is more prevalent than expected.

4. Small proportion of patients with severe liver disease has been exposed to Aflatoxin B1.

5. Circulating mutations in plasma are promising tools for diagnosis and monitoring treatments.

Abstract Submission No. 101199

O-0595

Clinical outcome of atezolizumab plus bevacizumab in HCC with major portal vein invasion

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Background: The prognosis of the patients with major portal vein invasion (Vp3-4) is still limited, and the median overall survival (OS) of Vp3 HCC treated with resection was within 18 months. We retrospectively investigated the clinical outcome of Vp3-4 HCC treated with atezolizumab plus bevacizumab (Atez+Bev).

Method: Between Oct 2020 and Sep 2023, 147 patients received Atez+Bev at our institution. Among them, 26 patients showed Vp3-4 at the baseline. The radiological evaluation was performed using RECIST v1.1.

Results: The median age was 74 years. Vp3 and Vp4 existed in 18 and 8 patients. Gastroesophageal varices were reported in 15 patients. The median ALBI score was -2.28, and 2 patients had extrahepatic metastasis. The median observation period was 13.1 months. The median OS in Vp3 and Vp4 were 24.5 and 21.5 months. The median progression-free survival (PFS) in Vp3 and Vp4 were 13.9 and 2.6 months. The objective response rates (ORR) and disease control rates (DCR) were 19.2% and 73.0%. One patient experienced varix rupture at 8 months after achieving partial response. In Vp4 patients, 6 of 8 patients are alive and received lenvatinib (LEN) ($n=1$), durvalumab ($n=1$), and intrahepatic arterial infusion chemotherapy (HAIC) ($n=2$) after Atez+Bev. In Vp3 patients, 3 patients achieved clinical complete response (CR) by resection or radiation.

Conclusion: The clinical outcome of Atez+Bev in patients with Vp3-4 HCC was better than resection. The patients with VP3 have possibilities for clinical CR by additional therapies. The patients with VP4 should be treated with HAIC or LEN after Atez+Bev.

Abstract Submission No. 101242

O-0596

Impact of complete tumor control, "so called cancer free", in patients with advanced-stage HCC

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Background: As the advent of highly efficacious systemic therapies in hepatocellular carcinoma (HCC), there have been reports of successful conversions to states amenable to curative treatments. Our study ventures to shed light on the profound implications of reaching a cancer-free and examined the outcomes for those achieving a cancer-free following advanced-stage HCC.

Methods: We established a database tracking the full clinical course of all HCC patients (from 2003-June 2022). We identified the initial instances of MVI or EHM. In this study, "Cancer Free" was defined by the following criteria. 1) Surgical cases: The absence of tumors and no recurrence in two distinct imaging evaluations spaced a minimum of two months apart. 2) Non-surgical cases: Two consecutive imaging evaluations (a minimum of two months apart) showed no tumors, with both evaluations indicating a complete response (CR) as per mRECIST.

Results: We identified 815 advanced-stage HCC patients. The cancer free rate was 8.6% (70/815). The median OS of patients who achieved cancer free was not reached (95% CI: 67.4-NA), and that of patients who did not achieve cancer free was 11.4 months (95% CI: 9.5-13.7) ($p < 0.001$). In the decision tree analysis in patients without extrahepatic metastatic spread, the number of tumors ≥ 8 was the strongest factor making it difficult to achieve cancer free.

Conclusions: The frequency of cancer free is low in the advanced-stage HCC. However, the OS is significantly longer in the patients who achieve it. Achievement is related to the number of intrahepatic tumors.

Abstract Submission No. 101243

O-0597

Systemic therapies for patients with intermediate stage HCC and the evolution of the prognosis

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Background: Systemic therapies for TACE-refractory/unsuitable patients in intermediate-stage hepatocellular carcinoma (HCC) has been discussed. However, the extent to which these treatment strategies have improved the prognosis of patients with intermediate-stage HCC, a heterogeneous population, has not been adequately investigated.

Methods: We reviewed the treatment outcomes of intermediate-stage HCC diagnosed at our hospital from 2004 to 2022. Patients were divided into three groups according to the date of diagnosis (period I: 2004-April 2009, period II: May 2009-August 2018, and period III: September 2018--2022). The classification was based on the time of approval of sorafenib and lenvatinib in Japan. Prognostic evolution of TACE-refractory/unsuitable patients was evaluated. We defined cancer-free as 6 months without recurrence and evaluated the evolution of the cancer-free rate.

Results: Of all 916 intermediate-stage HCC patients the frequency with which systemic therapy was initiated at the time of diagnosis has increased over time. As for TACE unsuitable, in patients with tumors number ≥ 8 , there was a trend toward improved survival in period III. And the prognosis from the time of TACE refractory has been prolonged. The improvement in cancer-free rates was also not evident over time. The number of intrahepatic tumors was an important factor in the difficulty of achieving cancer-free in the intermediate stage.

Conclusions: We evaluated the evolution of treatment outcomes for intermediate-stage HCC. It might be important to continue the development of treatment, including systemic therapy, with a focus on patients with multiple intrahepatic lesions.

Abstract Submission No. 101341

O-0598

Analysis of atezolizumab antidrug antibody in HCC patients treated with atezolizumab and bevacizumab

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Backgrounds: Atezolizumab+Bevacizumab (Atezo+Bev) is positioned as first-line chemotherapy for unresectable hepatocellular carcinoma (HCC). Although immune checkpoint inhibitors (ICIs) may induce an antidrug antibody (ADA), there is a lack of evidence for the relationship between ADA against Atezo (ATZ-ADA) levels and treatment outcome. In this study, we assayed ATZ-ADA levels and analyzed its association with therapeutic outcome in advanced HCC patients who were treated with Atezo+Bev.

Methods: Twenty-six patients with unresectable HCC treated with Atezo+Bev between 2020 and 2023 were included in this study. ATZ-ADA was assayed with ELISA using the stored serum samples at the time of 3 courses of treatment or the earliest time point.

Results: The backgrounds of 26 patients were as follows: male/female=8/18, median age 74 years, HCV/HBV/non B,C=7/7/12, BCLC stage B/C=16/10, Child-Pugh score 5/6=18/8, ALBI grade 1/2=7/19. Atezo+Bev was administered for a median of 4 courses, and the best responses with mRECIST were CR/PR/SD/PD=2/11/7/6. ATZ-ADA levels were assayed at 3/4-6/7-12/13-20 course administration (12/7/3/4 cases, respectively). The median ADA level (OD value) was 0.035 and did not correlate with the number of treatment courses. The median ADA level in each response group was CR/PR/SD/PD=0.031/0.035/0.036/0.038. Interestingly, a PD patient had the highest ATZ-ADA level (0.079). His treatment was switched to the STRIDE regimen with Tremelimumab+Durvalumab resulting in CR.

Conclusions: The ATZ-ADA levels in this study were generally low, suggesting the proportion of patients in whom ADA inhibited the therapeutic effect was small. It was suggested that patients with high ATZ-ADA should consider treatment switch as soon as possible.

Abstract Submission No. 101476

O-0599

Screening of Prognostic Markers and Predictive Analysis of Potential Traditional Chinese Medicine

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Background: Hepatocellular carcinoma (HCC) is a kind of malignant tumor with high risk of recurrence and metastasis. Novel prognostic biomarkers still need to be explored.

Methods: A total of 103 HCC patients and 50 healthy control were collected to extract PBMC for high-throughput sequencing. Bioinformatics analysis technology was used to analyze the difference of gene expression matrix, core genes were screened by Cytoscape, and immune infiltration analysis was improved by CIBERSORT deconvolution algorithm. KM-plot plotted survival curve and Coremine Medical to obtain targeted Chinese medicine.

Results: Nine core genes were identified, including SLC4A1, ALAS2, HBG1, AHSP, HBG2, HBB, HBD, HBA2 and HBA1. High expression of HBA2, AHSP and HBG2 was associated with shorter survival. It is involved in biological processes such as oxygen metabolism, enriched in lysosome, arachidonic acid metabolism, complement and coagulation cascade, and natural killer cell-mediated cytotoxicity. Survival analysis showed that the low expression of resting NK cells was negatively correlated with OS, and core genes were correlated with immune cells to varying degrees. Thirty kinds of traditional Chinese medicine including soft-shell turtle, ejiao, lotus leaf, tea tree root and corn beard were selected by targeted screening.

Conclusion: We clarified the expression of core genes and the mechanism of immune infiltration, and provided a new direction for the identification of HCC prognostic markers and the potential targeting of Traditional Chinese medicine.

Abstract Submission No. 101519

O-0600

Increased spleen volume during atezolizumab and bevacizumab: Predictive factors and clinical outcome

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Background: We previously reported a greater increased spleen volume in hepatocellular carcinoma (HCC) patients receiving atezolizumab plus bevacizumab (Atez/Bev) compared to lenvatinib (Oncology 2023). In malignant cases treated with immune checkpoint inhibitor, baseline spleen volume (SpV) and alternations in SpV were negatively associated with PFS and OS. The study aimed to investigate the relationship between changes in SpV and therapeutic outcome of Atez/Bev. Additionally, we also investigate the predictive factors associated with increased SpV.

Methods: This retrospective study included 164 HCC patients who did not have portal vein tumor thrombosis or a history of splenectomy or partial splenic embolization. SpV were calculated based on CT imaging and patient characteristic imbalances were adjusted by IPTW method.

Results: The median ages were 74 (IQR 68-80), with 135 (82.3%) patients being male. Baseline SpV was 184.6 (IQR 130.3-256.9) cm³. Enlarged SpV at baseline (>184cm³) were not significantly associated with PFS and OS in both crude and IPTW-weighted cohort. SpV increased in 100 (84.0%) patients during Atez/Bev treatment. In 119 patients who obtained CT imaging from 3 to 4 month after treatment, the median difference in SpV were 25cm³ (IQR 6-59). Predictive factors for increased SpV (>25cm³) included age, BCLC A or B, and FIB-4 index. Patients with greater changes in SpV (>25cm³) were not associated with the PFS and OS in both crude and IPTW-weighted cohort.

Conclusions: Enlarged baseline SpV and greater changes in SpV were not associated with the therapeutic outcomes of Atez/Bev. Alternation in SpV may be associated with liver fibrosis.

Abstract Submission No. 101548

O-0601

Diagnostic Assessment of PIVKA-II in the Detection of Hepatocellular Carcinoma in Indian Patients

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Aim: To investigate the potential application of prothrombin induced by vitamin K absence-II (PIVKA-II) and its combination with alfa

fetoprotein (AFP) in the diagnosis of Hepatocellular Carcinoma(HCC) and to establish the cutoff limits of PIVKA-II.

Methods: In this single-center case-control study from India, serum levels of AFP and PIVKA-II were measured in three groups: HCC patients (N=109), patients with chronic liver disease (CLD) (N=113), and healthy controls with normal liver function (N=100). The area under the receiver operating characteristic curve (AUROC), sensitivity, specificity, odds ratio and the ASAP model (combining age, sex, AFP, and PIVKA-II scores for analysis) were used to report the diagnostic accuracy of the biomarkers. Serum AFP and PIVKA-II values among the three groups were compared using a non-parametric Mann-Whitney test and R statistical software version 4.1.1(15). Two-tailed p-values <0.05 were considered statistically significant.

Results: PIVKA-II demonstrated superior diagnostic performance (AUROC:0.93, 95% CI:0.89-0.97) compared to AFP (AUROC:0.90, 95% CI:0.86-0.95) in the diagnosis of HCC, and the combination of AFP and PIVKA-II further improved the diagnostic performance (AUROC:0.95, 95% CI:0.92-0.99) for HCC patients. The ASAP model with refit coefficients showed better accuracy (96.2%) in diagnosing HCC, and in differentiating HCC from CLD (accuracy: 78.5%). The cutoff values for AFP and PIVKA-II were found to be 7.56 (95% CI:6.64-8.74) ng/ml and 49.41 (95% CI:44.81-60.66) mAU/ml respectively.

Conclusion: PIVKA-II is a promising biomarker for diagnosis of HCC, and its combination with AFP greatly improved the diagnostic accuracy of HCC. The ASAP score outperformed all single biomarkers, including AFP and PIVKA-II, in terms of diagnostic accuracy.

Abstract Submission No. 101561

O-0602

Single-cell profiling of the circulating immune cell predicts the immunotherapy for HCC

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Background: The combination of Atezolizumab and Bevacizumab (Ate/Bev) has revolutionized the clinical outcome for unresectable hepatocellular carcinoma (HCC), which has been shown to be superior to sorafenib in IMbrave150 trial. However, how to predict the response to Ate/Bev therapy in HCC patients remains elusive. Herein we investigated the circulating immune profile of patients with unresectable HCC receiving Ate/Bev therapy.

Methods: HCC patients were enrolled in a prospectively registered multicenter study and peripheral blood mononuclear cells (PBMCs) were collected from these patients treated with Ate/Bev. Single cell-RNA sequence was utilized to analyze PBMCs from 5 responders and 5 non-responders at pretreatment and 6 weeks after Ate/Bev therapy.

Results: First, 231,832 cells of 20 PBMCs from 10 patients were clustered into 30 subsets and annotated based on the gene expression in each cluster. Responders showed the higher frequencies of central memory CD4 T cells and B cells compared to non-responders at pretreatment (p= 0.0315, 0.0159, respectively), while non-responders showed the higher frequencies of monocytes than responders (p= 0.0315). The frequency of CD8 T cells was not significantly different between groups, but responder showed stronger expression of cytotoxicity-related genes in CD8 T cells compared to non-responders. Relustering of monocytes resulted in 7 types of subclusters, exhibiting the differential dynamic changes during Ate/Bev treatment.

Conclusion: The immune profiling of PBMCs potentially predicts the response to checkpoint inhibitors in patients with unresectable HCC.

Abstract Submission No. 101568
O-0603

Impact of genetic discrimination between MC and IM on the prognosis of recurrent HCC

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During the follow-up after HCC resection, genetic mutation patterns possibly change from multicentric occurrence (MC) to intrahepatic metastasis (IM), or vice versa, along with the recurrence. In the present study, we focused on patients who underwent repeated resection for recurrence and analyzed the prognosis along with the genetic mutation change.

Methods: We performed genomic analysis using an in-house HCC panel employing NGS for 200 cases of liver resection, involving 350 lesions. Among the 200 cases, we sequentially performed genetic discrimination (MC/IM) between the primary and recurrent nodules in 30 cases that underwent liver resection for recurrence.

Results: Among the 30 cases (primarily 18 solitary, 12 multifocal), there were 17 MC- and 13 IM-recurrence. Significantly better OS was detected in MC-recurrent cases compared to IM ones ($p=0.025$). Among primarily MC multifocal HCC ($n=8$) whose OS was significantly better than that in IM ones, 2 cases experienced IM-recurrence, and one had a poor prognosis, while another survived without recurrence. Meanwhile, 1 MC- and 3 IM-recurrence were observed among the 4 primarily IM multifocal HCC, with poor prognosis in all cases, suggesting a dismal impact of primary IM. Among the 13 IM-recurrent cases, the genetic change from IM to MC was seen in one case after a long tumor-free status, while the other cases experienced relatively poor prognosis.

DISCUSSION: Genetic IM in primarily multifocal HCC and recurrent HCC implies a poor prognosis, suggesting the need for early drug introduction. MC-recurrence after a long tumor-free status is a good marker even in IM-recurrent cases.

Abstract Submission No. 101578
O-0604

Conversion therapy for unresectable HCC in 944 patients following atezolizumab and bevacizumab

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Background: This study aimed to investigate the clinical outcome of conversion therapy following atezolizumab and bevacizumab (Atez/Bev).

Methods: A total of 944 hepatocellular carcinoma (HCC) patients who treated with Atez/Bev from October 2020 to September 2023 were included in this study.

Results: The median ages were 74 years (IQR 68.8-80.0), with 745 patients (78.9%) being male. Chronic liver diseases were HCV in 318 (33.7%), HBV in 156 (16.5%), HBV plus HCV in 1 (0.1%), alcohol in 209 (22.1%), and other causes in 260 (27.5%) patients. mALBI grade was 1, 2a, and 2b in 335 (35.5%), 244 (25.8%), and 350 (37.1%), and 15 (1.6%) patients, respectively. BCLC stage distribution was very early, early, intermediate, advanced, and terminal in 19 (2.0%), 54 (5.7%), 370 (39.2%), 485 (51.4%), and 16 (1.6%) patients, respectively. Conversion therapy was conducted in 40 (4.2%) patients, involving resection ($n=7$), ablation therapy ($n=24$), TACE ($n=14$), and radiation therapy ($n=1$), with treatment modalities overlapping. The objective response rates assessed by mRECIST were 75.0% and 34.0% in the conversion group and non-conversion group, with a statistical significance ($p<0.001$). The median overall survival (OS) was not reached in the conversion group, with a 1-year survival rate of 97.4%, and was 20.4 months in the non-conversion group, showing statistical significance ($p<0.001$). BCLC stage B was identified as a predictive factor associated with conversion therapy.

Conclusions: Patients with BCLC intermediate-stage HCC were likely to received conversion therapy and patients receiving conversion therapy achieved favorable clinical outcomes.

Abstract Submission No. 101609
O-0605

Constructing immune classification to predict clinical response of HBV-HCC after TACE treatment

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Background: Transcatheter arterial chemoembolization (TACE) can activate the immune system and regulate the tumor microenvironment. This study evaluates the clinical response of HBV-HCC patients after TACE treatment based on systematic immune classification.

Methods: A total of HBV-HCC patients ($n=80$) were tested for peripheral blood immune cell exhaustion phenotype and immune protein expression profile using a complementary technique of "Olink High Sensitivity Plasma Proteomics" and "Multicolor Flow Cytometry". An unsupervised clustering algorithm was used to classify different immune subtypes and obtain core indicators to evaluate the response of systemic immune classification to TACE treatment ($n=69$). The use of two technologies as new methods for detecting HBV-HCC synergistically reveals the mechanism of the disease and the prognosis of patients.

Results: Based on the combination of immune exhaustion phenotype and immune protein, a system immune classification was constructed: Cluster1 (immune activated), Cluster2 (intermediate), and Cluster3 (immune exhaustion or inhibitory). Cluster3 was found to have poor clinical features, prognosis, and high levels of immune checkpoint expression. In order to better evaluate the efficacy of TACE treatment for HBV-HCC, a focused scoring system was constructed based on five core indicators. This risk scoring system can predict the overall survival of patients at different times, with ROC areas higher than 0.8.

Conclusions: This study identified the system immune classification of serum protein mass spectrometry and cell flow cytometry associated with survival in HBV-HCC patients after TACE treatment, providing new basis for guiding immunotherapy and discovering non-invasive biomarkers in the future.

Abstract Submission No. 101619
O-0606

Prescription patterns of sorafenib and the following salvage treatment for advanced HCC in Taiwan

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Background: Sorafenib (SOR) was covered by National Health Insurance (NHI) since 2012. Two expansions in reimbursement and the introduction of salvage therapy post-SOR failure in 2019 Jun 1 have altered the treatment landscape. This study explores the prescription patterns in Taiwanese HCC patients.

Methods: Using the NHI database, we analyzed patients receiving their first prescription between Aug 1, 2012, and Dec 31, 2021. Patients were divided into 3 cohorts based on prescription dates: 1st cohort (before Oct 31, 2016) with extrahepatic spread or main/first branch portal vein (PV) thrombosis; 2nd cohort (Nov 1, 2016 to May 31, 2019) including BCLC B post 3 locoregional therapies (LRTs) within 6 months; 3rd cohort (after Jun 1, 2019) encompassing patients with thrombosis of first/second branch of PV and BCLC B post 3 LRTs within 12 months.

Results: 19,806 patients were included. LRTs were performed during the SOR in 5133 (25.9%) patients, TACE (n = 4343, 21.9%) as the most common. Fewer patients initially received standard SOR dose (1st vs. 2nd vs. 3rd cohort: 54.9% vs. 46.5% vs. 36.3%). The median OS was 6.1, 7.9, and 10.4 months for the 1st, 2nd, and 3rd cohort, respectively ($p < 0.001$). Salvage with SOR failure and Child A was reimbursed, 2264 patients discontinued SOR. Among them, 1323 (58.4%) received salvage therapy, including regorafenib, ramucirumab, and nivolumab, the median treatment duration of which was 3.3, 2.6, and 3.9 months, respectively.

Conclusions: Physicians often initiate lower doses of multikinase inhibitors. Less than 60% of patients received salvage therapy. There remains a significant unmet need for novel therapies.

Abstract Submission No. 101696
O-0607

Progression Pattern and Survival in Patients received Atezolizumab + Bevacizumab for advanced HCC

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Background: Although the combination of atezolizumab and bevacizumab (ATZ + BEV) is a standard treatment for advanced hepatocellular carcinoma (HCC), strategies for addressing treatment failure and prognostic factors of post-progression survival (PPS) remain unestablished.

Methods: We conducted a multicentre retrospective study to evaluate post-progression survival following ATZ + BEV treatment in patients with advanced HCC. We classified the patients into three groups: BCLC stage B and BCLC stage C without or with new extrahepatic lesions (BCLCp-C1 and BCLCp-C2, respectively) at the time of progression.

Results: Of the 204 patients who started ATZ + BEV treatment between October 2020 and September 2022, 110 showed disease progression, with 33, 55, and 22 showing the BCLCp-B, BCLCp-C1, and BCLCp-C2 stages of the disease, respectively. Specifically, patients with the BCLCp-B stage of the disease showed better PPS than those with the BCLCp-C1 and BCLCp-C2 stages [hazard ratios: 2.19 (95% confidence interval [CI], 0.61-7.86), 2.16 (95% CI, 1.13-4.11), and 2.97 (95% CI, 1.42-6.23) for HCC stages BCLCp-B2, BCLCp-C1, and BCLCp-C2, respectively]. We identified the BCLCp-C1 and BCLCp-C2 stages as a independent prognostic factor from performance status, Child-Pugh class, and alpha-fetoprotein for PPS. On time-dependent analysis, BCLC stage C was a independent poor prognostic factor for progression-free survival PFS using BCLC stage upon progression. These results may help in making decisions and planning a clinical study regarding subsequent treatment after ATZ + BEV.

Abstract Submission No. 101762
O-0608

Increased PD-1+TIGIT+ TIM-3+ in peripheral circulating cells predict poor prognosis of HCC patients

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Background: Previous studies had shown that co-inhibitory molecules were associated with tumor prognosis, but whether their co-expression is related with tumor outcome remains unclear. This study was to explore the relationship between the co-expression of co-inhibitory molecules and the progression and death of patients with hepatocellular carcinoma(HCC).

Methods: We prospectively enrolled 299 patients with HCC of whom 17 HCC patients with hepatectomy. We detected the expression levels of coinhibitory molecules on the surface of peripheral blood mononuclear cells(PBMC) and tumor-infiltrating T cells(TILs). Then clinical indicators and co-inhibitory molecular expression were incorporated into Cox regression to analyze the impact on progression and death of HCC.

Results: The proportion of CD8+PD-1+TIGIT+TIM-3+T cells in TILs was higher than that in PBMC, and the level was positively correlated with peripheral blood level($r=0.71$, $P=0.003$). COX multivariate regression analysis showed that, PVT(HR=1.77), neutrophil-to-lymphocyte ratio(HR=1.14), γ -GGT(HR=1.02), tumor size ≥ 5 cm(HR=1.76), proportion of CD8+PD-1+TIGIT+TIM-3+T cells(HR=1.12) were independent risk factors for survival of HCC patients, albumin(HR=0.96) was an independent protective factor. Compared with low level of CD8+PD-1+TIGIT+TIM-3+T cells, the hazard ratios of 3-year overall survival of high-level group were 1.88 in the KM analysis.

Conclusion: High levels of CD8+PD-1+TIGIT+TIM-3+T cells was associated with poor outcome of HCC, which can be contribute to assess the prognosis of HCC and provide theoretical basis for multi-target immune checkpoint synergistic therapy in the future.

Abstract Submission No. 101841
O-0609

The efficacy and safety of durvalumab + tremelimumab for unresectable hepatocellular carcinoma

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Background: In recent years, durvalumab + tremelimumab combination therapy (Dur+Tre) was approved for unresectable hepatocellular carcinoma (uHCC).

Method: Forty-two cases of Child-Pugh A who received Dur+Tre for uHCC from April to October 2023 were enrolled. The background was as follows. Male/Female: 38/4, median age 73 years, HBV/HCV/NBNC: 11/8/23, first line 16 cases, extrahepatic metastasis positive 17 cases, macroscopic vascular invasion positive 8 cases, BCLC 0/A/B/C: 1/3/17/21, Child-Pugh score 5/6: 30/12, mALBI grade 1/2a/2b: 24/8/10, AFP 30.3 ng/ml and PIVKA-2 528.5 mAU/ml (median values). The administration method was the STRIDE regimen. The efficacy and safety were investigated.

Results: The evaluation after one course of administration were follows, PR/SD/PD/NE: 6/14/19/3 cases(mRECIST). Overall response rate (ORR) was 14.3%, and disease control rate (DCR) was 47.6%. All 6 PR cases were treated as first line systemic therapy. In first line cases, ORR was 37.5% and DCR was 56.3%. Frequently occurring adverse events were pruritus in 34 cases (81.0%), fatigue in 25 cases (59.5%), anorexia in 23 cases (54.8%), skin rash in 13 cases (31.0%), and diarrhea in 11 cases (26.2%). Grade 3 or higher adverse events included anorexia in 5 cases (11.9%), diarrhea in 2 cases (4.8%), 2 fatigue in cases (4.8%), hyperamylasemia in 2 cases (4.8%), enterocolitis in 2 cases (4.8%) and interstitial pneumonia in 1 case (2.4%).

Conclusion: Dur+Tre is effective as a first-line systemic therapy for uHCC. On the other hand, severe immune-mediated adverse event (imAE) occurred in some cases, we need to pay attention to the occurrence of imAE.

Abstract Submission No. 101907
O-0610

Liver regeneration following partial hepatectomy in hepatocellular carcinoma: not only size matters

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Background: To investigate factors associated with liver regeneration capacity in patients with hepatocellular carcinoma (HCC) after liver resection (LR).

Methods: A total of 123 patients with HCC who underwent liver stiffness (LS) by shear wave elastography (SWE) prior to LR were retrospectively included. The future liver remnant (FLR) prior to LR, and postoperative liver remnant (PLR) after LR were measured. The standardized future liver remnant (sFLR), parenchymal hepatic resection rate (PHRR), and regeneration index (RI) were calculated. Patients were classified into two subgroups based on the extent of LR: low PHRR (<50%) and high PHRR (>50%). Spearman correlation analysis was used to investigate factors associated with RI, and receiver operating characteristic (ROC) curve was employed to evaluate the

diagnostic performance of these relative factors to predict a significant liver regeneration (RI>1).

Results: Strong correlation between RI and volume-related parameters, including FLR ($r=-0.754$, $p<0.001$) and sFLR ($r=-0.811$, $p<0.001$), were identified. Optimal cutoff values of 535ml for FLR and 0.452 for sFLR were used to predict a significant liver regeneration with an area under the curve (AUC) value of 0.967 and 0.980, respectively (all $p<0.001$). In the high PHRR subgroup, LS was the only non-volume parameter correlating with RI ($r=-0.526$, $p=0.012$). A cutoff value of 6.7kPa was used to predict a significant liver regeneration with an AUC value of 0.767 ($p=0.035$).

Conclusions: The remnant volume was the key to liver regeneration after LR for HCC. LS may serve as a potential predictor for liver regeneration in those with extensive loss of parenchymal.

Abstract Submission No. 101924
O-0611

Decoding HCC Survival: A Comparative Analysis of Early vs. Late-Onset Cases

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Background: Hepatocellular Carcinoma (HCC) often has a grim prognosis, with most cases diagnosed at advanced stages. Intriguingly, younger individuals tend to show higher prevalence and poorer outcomes.

Objectives: This study aims to compare survival rates between early and late-onset HCC patients at RSCM and identify factors influencing their survival.

Methods: A retrospective cohort study was conducted on HCC patients from Cipto Mangunkusumo Hospital's registry (2015-2022). Kaplan-Meier curves depicted survival, while Cox Proportional Hazard Regression with a backward method identified independent prognostic factors.

Results: Among 896 subjects, early onset patients had a median survival of 2 months (95% CI: 1.071-2.929), significantly lower than the 4 months (95% CI: 3.441-4.559) in late-onset patients ($p=0.021$). Early onset showed a higher event rate at 24 months (92.9%) compared to late onset (87.7%) ($p=0.032$). Multivariate analysis revealed hypertension (HR: 3.728) and lack of hepatitis treatment (HR: 2.48; $p=0.053$) as key factors in early onset survival. In late-onset cases, AFP levels ≥ 200 ng/mL (HR: 1.28), AJCC stage (highest risk at stage 4, HR: 4.52), supportive, and palliative therapies (HR: 5.23 and 1.66, respectively) were significant.

Conclusion: Early onset HCC patients have a median survival of 2 months, half of that in late-onset patients. Distinct prognostic factors were identified in each group, highlighting the need for tailored approaches in managing early and late-onset HCC.

Keywords: Survival, Early Onset, Late Onset, Hepatocellular Carcinoma

Abstract Submission No. 101977
O-0612

Utility of Lens culinaris agglutinin-reactive AFP (AFP-L3) in atezolizumab plus bevacizumab therapy

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Background: While combined immunotherapy has become the first-line treatment for unresectable hepatocellular carcinoma, there is an unmet need to identify biomarkers to determine efficacy during treatment. Lens culinaris agglutinin-reactive alpha-fetoprotein (AFP-L3) has been reported to be useful in the diagnosis of hepatocellular carcinoma and in predicting prognosis after transplantation or resection. This study aimed to clarify whether baseline AFP-L3 and its dynamics during the treatment are useful in predicting response to systemic therapy.

Methods: We enrolled 151 patients with unresectable hepatocellular carcinoma who received atezolizumab plus bevacizumab treatment. The radiological response was assessed by RECIST ver 1.1 at 6-8 weeks and every 8-12 weeks after that. Progression-free survival (PFS) was analyzed by the Kaplan-Meier method.

Results: Patients had a median age of 74 years, 116 were male, 51 had HCV as background liver disease, and 98 received treatment as the first-line therapy. The median PFS was 6.6 months. At baseline, AFP-L3 was not elevated (<0.5%) in 26(17%) patients and median value of AFP-L3 was 14.5%. Patients with AFP-L3<14.5% (n=70) showed significantly longer PFS (8.7 vs 4.6 months, p=0.009). Among 106 patients with AFP-L3>0.5% at baseline, AFP-L3 decreased below 80% within 6 weeks compared to the baseline in 19(18%) patients (AFP-L3 response). Patients who achieved AFP-L3 response showed significantly better PFS than those without (14.4 vs 5.1 months, p=0.04). A similar tendency was seen in patients with baseline AFP<400ng/ml (p=0.07); however, in patients whose baseline AFP ≥ 400ng/ml, the difference was insignificant since only two patients achieved AFP-L3 response.

Conclusion: AFP-L3 was useful in predicting PFS of patients who received atezolizumab plus bevacizumab treatment. AFP-L3 response was a useful on-treatment biomarker for patients whose baseline AFP-L3 is elevated at baseline.

Abstract Submission No. 101981
O-0613

Trends and forecast mortality of liver cancer to 2040 in the United States: A population-based study

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Objective: The burden of liver cancer varies across the world. Herein, we present updated estimates of the burden of liver cancer mortality in the United States (US) and provide predictions of age-standardized mortality rates (ASMR) to 2040.

Methods: Using CDC WONDER of the NVSS, we estimated the ASMR of liver cancer during 2006-2040. We used joinpoint regression to assess the trend of mortality. Prophet/ARIMA prediction modeling analysis based on trends from 2006-2022, we predicted mortality for 2023-2040 and stratified by etiology and sex.

Results: Among the 333,784 liver cancer-related deaths during 2006-2022, we found increasing annual percentage change(APC) of 2.8% and 0.6% for 2006-2013 and 2013-2016, followed by stable mortality trends, and observed ASMR (per100,000 persons) 8.31 in 2022 overall. By sex, the APC for 2019-2022 for female is 2.7% (95%CI1.7-4.3) and the ASMR will increase to 4.86 in 2040 compared with 4.46 in 2022. However, the APC for 2015-2022 for male is -0.8% (95%CI-1.4--0.4) and the ASMR will decrease to 10.86 in 2040 compared with 12.75 in 2022(Fig.1A). By etiology, HCV-related mortality reached a peak in 2015 and decreased rapidly after that. The ASMR rise was most pronounced in alcohol-associated liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD), especially ALD-related deaths will be to the leading cause of liver cancer deaths in 2026(Fig.1B/C). The proportion of ALD and NAFLD-related liver cancer deaths sharply rise during 2006-2022(Fig.1D).

Conclusions: ASMR for ALD and NAFLD increased at alarming rates during 2006-2022 in US with the fastest rise in ALD-related liver cancer.

Abstract Submission No. 102061
O-0614

Impact of Methylated SEPT9 Liquid Biopsy Test as a Prognostic Biomarker in Hepatocellular Carcinoma

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Objective: Several biomarkers are used for cancer diagnosis, treatment monitoring, and prognostic prediction. In hepatocellular carcinoma (HCC), the classical tumor marker, AFP is used as a diagnostic and monitoring marker. We have reported liquid biopsy based on a methylated SEPT9 (m-SEPT9) as a new candidate of HCC diagnostic marker (Hepatol Commun. 2020). In this study, we investigated the significance of m-SEPT9 as a prognostic biomarker.

Methods: We enrolled 787 HCC patients obtained from multi-centers during 2018-22. We measured m-SEPT9 using "combined restriction digital PCR assay" which was developed by us and examined its potential as a prognostic biomarker.

Results: The median age was 73 years with 563 males (71.5%). BCLC stages 0, A, B, C, and D were 107, 250, 138, 268, and 21 patients, respectively and Child-Pugh A, B, and C were 669, 101, and 14 patients, respectively. The multivariate analysis showed that AFP, DCP, and m-SEPT9 were independent prognostic predictors in addition to Child-Pugh and BCLC stage in overall HCC patients. Furthermore, Child-Pugh, m-SEPT9, and AFP were significant independent prognostic predictors in the BCLC C-D group, whereas Child-Pugh and AFP were extracted in the BCLC 0-B group. AFP and m-SEPT9 were independent prognostic markers in advanced stage. The patients with advanced HCC were stratified according to the combination of m-SEPT9 and AFP.

Conclusion: The m-SEPT9 liquid biopsy test has a great potential for a prognostic biomarker of HCC.

Abstract Submission No. 200062
O-0615

ICIs and anti-VEGF antibody/TKIs with or without TACE as First-line Treatment for Advanced HCC

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Background: The role of transarterial chemoembolization (TACE) in the treatment for advanced hepatocellular carcinoma (HCC) is unconfirmed. This study aimed to assess the efficacy and safety of immune checkpoint inhibitors (ICIs) plus anti-vascular endothelial growth factor (anti-VEGF) antibody/tyrosine kinase inhibitors (TKIs) with or without TACE as first-line treatment for advanced HCC.

Methods This nationwide, multicenter, cohort study included advanced HCC patients receiving either TACE with ICIs plus anti-VEGF antibody/TKIs (TACE-ICI-VEGF) or only ICIs plus anti-VEGF antibody/TKIs (ICI-VEGF) from January 2018 to December 2022. The study design followed the target trial emulation framework with stabilized inverse probability of treatment weighting (sIPTW) to minimize biases. The primary outcome was overall survival (OS). Secondary outcomes included progression-free survival (PFS), objective response rate (ORR), and safety. The study is registered with ClinicalTrials.gov, NCT05332821.

Results Among 1244 patients included in the analysis, 802 (64.5%) patients received TACE-ICI-VEGF treatment and 442 (35.5%) patients received ICI-VEGF treatment. The median follow-up time was 21.1 months and 20.6 months, respectively. Post-application of sIPTW, baseline characteristics were well-balanced between the two groups. TACE-ICI-VEGF group exhibited a significantly improved median OS (22.6 months [95%CI: 21.2-23.9] vs 15.9 months [14.9-17.8]; adjusted hazard ratio [aHR] 0.63 [95%CI: 0.53-0.75]; $P < 0.001$). Median PFS was also longer in TACE-ICI-VEGF group (9.9 months [9.1-10.6] vs 7.4 months [6.7-8.5]; aHR 0.74 [0.65-0.85]; $P < 0.001$) per RECIST v1.1. A higher ORR was observed in TACE-ICI-VEGF group, by either RECIST v1.1 or mRECIST (41.2% vs 22.9%, $P < 0.001$; 47.3% vs 29.7%, $P < 0.001$). Grade ≥ 3 adverse events occurred in 178 patients (22.2%) in TACE-ICI-VEGF group and 80 patients (18.1%) in ICI-VEGF group.

Conclusion This multicenter study provides adequate evidence showing improved efficacy by adding TACE plus ICIs and anti-VEGF antibody/TKIs as first-line treatment for advanced HCC, with an acceptable safety profile.

Abstract Submission No. 200276
O-0616

Safety and efficacy of microwave ablation for Child B early stage hepatocellular carcinoma

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Background: Since most of the subjects of clinical trials which verify feasibility of Microwave ablation (MWA) are hepatocellular carcinoma (HCC) patients who have preserved liver function, the influence regarding the impact of impaired hepatic reserve on treatment outcomes has not been well established.

Methods: This retrospective cohort study enrolled 624 microwave ablation treatments using Emprint ablation system (Covidien) during 2017 to 2022. Of those, 582 treatments were operated under the tumor settings of HCC with 3 or less lesions of 30 mm in diameter or single lesions of 50 mm. We compared patient background factors and treatment outcomes of 474 patients with Child A and 108 patients with Child B.

Results: Of the entire cohort, there were significant increase in the number of tumors and the maximum tumor diameter in Child B cases. However, 582 subjects finally enrolled in the analysis under the limited tumor settings, these factors were comparable in both groups. Not only factors related to hepatic reserve, platelet count and liver stiffness showed significant difference in each group. All of the outcomes showed worse result in Child B cases including severe complication rate (Child A 5/484 1.1% vs Child B 4/108 3.7%, $p=0.0441$), recurrence-free survival, and incidence of bile duct dilatation. Furthermore, ascites was extracted as a risk factor contributing to bile duct dilatation.

Conclusion: Child B patients are at increased potential risk which may contribute to poor treatment outcomes. Aside from considering liver transplantation, taking proactive preoperative measures is needed for effective and safe MWA procedure.

Abstract Submission No. 200279
O-0617

Four-year Overall Survival from the HIMALAYA Study in Unresectable Hepatocellular Carcinoma

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Background: In the primary analysis (data cut-off: 27 August 2021) of the phase 3 HIMALAYA study (NCT03298451) in uHCC, STRIDE (Single Tremelimumab Regular Interval Durvalumab) significantly improved OS versus sorafenib; durvalumab monotherapy was

noninferior to sorafenib (Abou-Alfa et al. *NEJM Evid* 2022). Here, we report an updated 4-year OS analysis of HIMALAYA.

Methods: Participants with uHCC and no previous systemic treatment were randomized to STRIDE, durvalumab or sorafenib. Data-cut off was 23 January 2023. OS and serious treatment-related adverse events (TRAEs) were assessed. Baseline demographics and disease characteristics were assessed in long-term survivors (LTS; participants surviving ≥ 36 months beyond randomization).

Results: Follow-up duration was approximately 4 years across treatment arms (Table). The OS HR versus sorafenib (0.78; 95% CI, 0.67-0.92) and estimated 36-month OS rate (30.7%) for STRIDE were consistent with the primary analysis. The 48-month OS rate remained higher for STRIDE (25.2%) versus sorafenib (15.1%). No new serious TRAEs occurred after the primary analysis for STRIDE (17.5%). Durvalumab OS noninferiority to sorafenib and safety was consistent with the primary analysis. Baseline demographics, clinical characteristics and subsequent therapies, including tremelimumab rechallenge, for LTS in the STRIDE arm were generally consistent with the full analysis set, suggesting that LTS were not from any particular subgroup.

Conclusions: These data reinforce the sustained, long-term OS benefit of STRIDE versus sorafenib, demonstrating unprecedented 3- and 4-year OS rates and longest follow-up to date in phase 3 uHCC studies. STRIDE maintained a tolerable safety profile, with no new serious safety events.

Clinical Trial identification: NCT03298451

Abstract Submission No. 200280

O-0618

Outcomes by occurrence of immune-mediated adverse events in HIMALAYA study in unresectable HCC

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Background: In the Phase 3 HIMALAYA study (NCT03298451) in uHCC, STRIDE (Single Tremelimumab Regular Interval Durvalumab) significantly improved overall survival (OS) vs sorafenib, and durvalumab monotherapy was noninferior to sorafenib. This exploratory analysis assessed the association between imAEs and outcomes in HIMALAYA.

Methods: Safety was assessed in participants who received ≥ 1 dose of STRIDE or durvalumab. imAEs were AEs of special interest associated with drug exposure and consistent with an immune-mediated mechanism of action with no found alternate etiology.

Results: In this analysis, 388 participants (STRIDE) and 388 participants (durvalumab) were included. Any grade imAEs, Grade 3/4 imAEs, and imAEs leading to discontinuation occurred in 139 (35.8%), 49 (12.6%), and 22 (5.7%) participants, respectively for STRIDE and

64 (16.5%), 25 (6.4%), and 10 (2.6%), respectively for durvalumab. imAEs requiring high-dose steroids occurred in 78 (20.1%) participants for STRIDE and 37 (9.5%) for durvalumab. OS improved with STRIDE in participants with vs without imAEs (HR, 0.73; 95% CI, 0.56-0.95; Table). OS rates at 6, 12, and 24 months were higher for STRIDE in participants with vs without imAEs (Table). The association between imAEs and OS was less clear for durvalumab (Table). In a landmark analysis of participants with vs without imAEs within 6 months of STRIDE (n=307) or durvalumab (n=287), OS HRs (95% CIs) were 0.65 (0.47-0.90) and 1.39 (0.95-2.04), respectively.

Conclusions: In HIMALAYA, imAEs with STRIDE or durvalumab were manageable and generally low grade. The occurrence of imAEs was associated with improved OS for STRIDE.

Clinical Trial identification: NCT03298451

Abstract Submission No. 200281

O-0619

Temporal patterns of immune-mediated adverse events in HIMALAYA study in unresectable HCC

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Background: In the Phase 3 HIMALAYA study (NCT03298451) in uHCC, STRIDE (Single Tremelimumab Regular Interval Durvalumab) significantly improved overall survival versus sorafenib with manageable safety (Abou-Alfa et al. *NEJM Evid* 2022). In this exploratory analysis, we assessed temporal patterns of imAEs with STRIDE.

Methods: Safety was assessed in participants who received ≥ 1 dose of STRIDE or sorafenib. imAEs were AEs of special interest associated with drug exposure and consistent with an immune-mediated mechanism, with no clear alternate etiology.

Results: Safety was assessed in 388 (STRIDE) and 374 (sorafenib) participants. Median (range) duration of exposure was 5.5 (0.4-41.9) months for STRIDE (durvalumab exposure) and 4.1 (0.1-38.6) months for sorafenib. Any grade treatment-related AEs (TRAEs) and Grade 3/4 TRAEs were less frequent for STRIDE (75.8% and 25.8%, respectively) versus sorafenib (84.8% and 36.9%, respectively). Any grade imAEs and max Grade 3/4 imAEs occurred in 35.8% and 12.6% of participants, respectively, for STRIDE. imAEs with STRIDE occurred at all time points assessed and were most likely to occur within the first three months (Table). For STRIDE, any grade imAEs of gastrointestinal disorders and skin and subcutaneous tissue disorders were most common within the first month after treatment; any grade imAEs of endocrine disorders were most common between >1 and ≤ 2 months.

Conclusions: AEs with STRIDE were manageable and generally low grade. Although imAEs with STRIDE could occur at any time, most were observed within the first three months after treatment. Findings continue to support STRIDE for treatment of uHCC.

Clinical Trial identification: NCT03298451

Abstract Submission No. 100070
O-0620

Impact of NAFLD on the efficacy of immunotherapy for CHB-related Hepatocellular carcinoma

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Objective: To investigate the impact of non-alcoholic fatty liver disease (NAFLD) on immune checkpoint inhibitors (ICIs) in patients with chronic hepatitis B (CHB)-related hepatocellular carcinoma (HCC).

Method: A total of 94 patients with chronic hepatitis B virus (HBV) infection-related HCC who received immunotherapy in Department of Hepatobiliary Oncology, Tianjin Second People's Hospital and Tianjin Medical University Cancer Institute and Hospital from April 2021 to October 2022 were included in this study. According to the presence or absence of NAFLD, the patients were divided into concurrent NAFLD and CHB (NAFLD-CHB) group and the CHB group. SPSS 26.0 statistical software was used to analyze the demographic, laboratory, and tumor-related baseline data, and evaluate the efficacy and immune status of the two group patients.

Result: There was no significant difference in CR, SD, PR, ORR, and DCR between the two groups (all $P > 0.05$). Median progression-free survival (mPFS) in NAFLD-CHB group was significantly lower than that in CHB group (NAFLD-CHB group 7.0 months vs CHB group 11.6 months; $P < 0.05$). CD19+B cells (CHB group 9.79% vs NAFLD-CHB group 12.53%; $P < 0.05$) and CD3+CD4+CD8+T cells (CHB group 26.17% vs NAFLD-CHB group 16.07%; $P < 0.05$) in blood samples of NAFLD-CHB group were significantly lower than those of CHB group ($P < 0.05$). The percentages of CD4+PD1+T cells (CHB group 8.89% vs NAFLD-CHB group 17.56%; $P < 0.05$) and CD8+PD1+T cells (CHB group 7.42% vs NAFLD-CHB group 10.50%; $P < 0.05$) in the blood samples of NAFLD-CHB group were significantly higher than those of CHB-related HCC patients.

Conclusion: Concurrent NAFLD seems induce poorer efficacy and shorter progression-free survival (PFS) when treated with immune checkpoint inhibitors in patients with CHB-related HCC, and this also might be attributed to the decrease of CD19+B cells, CD3+CD4+CD8+T cells and the increase of percentages of CD4+PD1+T cells and CD8+PD1+T cells.

Abstract Submission No. 100103
O-0621

An Online Risk Stratification Model for Predicting Survival Duration of Older Patients with HCC

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Background: The objective of this study is to identify the prognostic factors of older patients with HCC and to construct a new prognostic model for predicting their overall survival.

Methods: 2,721 HCC patients aged ≥ 65 were extracted from SEER. 101 patients were from the Hospital.

Results: We found that the nomogram provided a good assessment of OS at 1, 3, and 5 years in older patients with HCC (1-year OS: (training set: AUC = 0.823 (95%CI: 0.803-0.845); internal validation set: AUC = 0.847 (95%CI: 0.818-0.876); external validation set: AUC = 0.732 (95%CI: 0.521-0.943)); 3-year OS: (training set: AUC = 0.813 (95%CI: 0.790-0.837); internal validation set: AUC = 0.844 (95%CI: 0.812-0.876); external validation set: AUC = 0.780 (95%CI: 0.674-0.887)); 5-year OS: (training set: AUC = 0.839 (95%CI: 0.806-0.872); internal validation set: AUC = 0.800 (95%CI: 0.751-0.849); external validation set: AUC = 0.821 (95%CI: 0.727-0.914)). The calibration curves showed that the nomogram was with strong calibration. The DCA indicated that the nomogram can be used as an effective tool in clinical practice. The risk stratification of all subgroups was statistically significant ($P < 0.05$). In the stratification analysis of surgery, Larger Resection (LR) achieved a better survival curve than Local Destruction (LD), but a worse one than Segmental Resection (SR) and Liver Transplantation (LT) ($P < 0.0001$). With the consideration of the friendship to clinicians, we further developed an online interface (OHCCPredictor) for such a predictive function (https://juntaotan.shinyapps.io/dynomapp_hcc/).

Conclusion: The online web interface of the predictive model provide easily-obtained access for clinicians.

Abstract Submission No. 100291
O-0622

Estimating the Appropriate Observation Period After Hepatitis C Virus Eradication

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Background: The Hepatitis C Virus (HCV) globally causes hepatocellular carcinoma (HCC). Direct-Acting Antivirals (DAA) have enabled virus eradication in most patients, significantly reducing HCC incidence and recurrence in HCV-infected individuals. However, some develop HCC over 10 years post-HCV eradication, necessitating prolonged patient observation. Given the decreasing risk for HCC over time has been seen in real clinical practice, we aimed to estimate an optimal observation endpoint.

Methods: We studied 680 patients (367 males, 313 females) treated with DAAs at our hospital from January 2015 to June 2023. We determined incidence and recurrence rates post-hepatitis treatment using the Kaplan-Meier method. We adopted the Weibull distribution for the approximation curve and minimized residuals between observed and theoretical values.

Results: The Weibull distribution parameters for incidence were 0.87 (shape) and 60.2 (scale), and for recurrence were 0.52 and 7.03. The 5-year and 8-year cumulative incidence real (estimation) values were 10.2 (10.6)% and 13.2 (13.8)%, and recurrence rates were 52.5 (55.4)% and 58.8 (59.0)%. The approximation curve indicated over 15 years post-DAA treatment for annual incidence (17.1 years) and recurrence (25.9 years) rates to drop to 1%.

DISCUSSION: The Weibull distribution closely approximated observed values. The time post-DAA treatment required for rates to drop to 1% aligns with clinical experiences.

Conclusion: Post-HCV treatment, the theoretical HCC onset and recurrence risk persist long-term.

Abstract Submission No. 100357

O-0623

New FP therapy for long-term prognosis in patients with advanced hepatocellular carcinoma

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Introduction: In Japan, hepatic arterial infusion chemotherapy (HAIC) is recommended as an optional treatment in the 2021 guidelines. In 2021, New FP therapy (NFP) was reported to have a longer prognostic effect than sorafenib in advanced hepatocellular carcinoma with intrahepatic lesions.

Objectives: I will show the performance of NFP in this study at our hospital.

Subjects: We perform 2 courses using the temporary indwelling catheter system via the left brachial artery, and then we remove the temporary reservoir during hospitalization. We repeat this treatment 3 to 5 times with an interval of about 2 months. We aim for cancer free by performing conversion therapy when PR or CR is obtained by NFP. We performed NFP on 290 patients with advanced with vascular invasion.

Results: There is almost no deterioration liver function. A total of 200 patients (69%) responded to NFP therapy, of which 80 patients achieved cancer-free outcome. 32 patients became cancer-free outcome with only NFP. We were able to add hepatic resection to 33 patients. Median OS (MST) after HAIC in all patients was 18 months. MST in patients who responded was 29 months, and in patients who achieved cancer-free outcome, it was extended to 67 months. The 5-year survival rate of all patients was 22%, and 67% for patients who got cancer-free outcome.

Conclusions: NFP has a high response rate and contributes to improve or maintain liver function by controlling PVTT. In response cases, long-term survival can be obtained by adding conversion therapy.

Abstract Submission No. 100165

O-0624

Monocyte to High Density Lipoprotein-Cholesterol Ratio Predicts Prognosis of MAFLD-related HCC

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Background: The incidence of non-B and non-C hepatocellular carcinoma (NBNC-HCC) is increasing globally. Metabolically associated fatty liver disease (MAFLD) has been a contributing factor to this

rising trend in NBNC-HCC incidence. The monocyte-to-high-density lipoprotein-cholesterol ratio (MHR) is a new prognostic marker that connects systemic inflammation with disorders of lipid metabolism. Therefore, MHR may be a potential prognostic predictor of patients with MAFLD-related HCC (MAFLD-HCC).

Patients and methods: This retrospective study of patients with MAFLD-HCC included training (n=112) and internal validation (n=37) cohorts. Univariate and multivariate Cox proportional hazard regression analysis was conducted to identify independent risk factors of survival. A visual nomogram was constructed to assess the performance of the two groups. Furthermore, receiver operating characteristic (ROC) curves and calibration curves were used to verify the prognostic discriminative ability of this nomogram, even in the MHR, ALBI grade, and MHR-ALBI model.

Results: Univariate and multivariate analyses revealed that extrahepatic metastases, Vascular invasion, Barcelona staging B, C, D, elevated ALBI Grade 3, C-reactive protein (CRP), and MHR were independent risk factors for the prognosis of MAFLD-HCC. Moreover, calibration plots showed good discrimination and consistency when the significant factors were entered into the nomogram. Meanwhile, the MHR strongly correlated with the prognosis of cancer under a background of MAFLD-HCC, with a sensitivity of 88.89% and a specificity of 79.61%.

Conclusion: The novel nomogram demonstrated good value in predicting the overall survival of patients with MAFLD-HCC. The MHR may be a potential predictor of prognosis.

Abstract Submission No. 100168

O-0625

Comparison of atezolizumab plus bevacizumab and lenvatinib for hepatocellular carcinoma with PVTT

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Background/Aim: Atezolizumab plus bevacizumab and lenvatinib are currently available as first-line therapy for the treatment of unresectable hepatocellular carcinoma (HCC); however, comparative efficacy studies are still scarce. This study aimed to investigate the effectiveness of these treatments in HCC patients with portal vein tumor thrombosis (PVTT).

Methods: We retrospectively included patients who received either atezolizumab plus bevacizumab or lenvatinib as first-line systemic therapy for HCC with PVTT. Primary endpoint was overall survival (OS), and secondary endpoints included progression-free survival (PFS) and disease control rate (DCR) determined by Response Evaluation Criteria in Solid Tumors, version 1.1.

Results: A total of 52 patients were included: 30 received atezolizumab plus bevacizumab and 22 received lenvatinib. The median follow-up duration was 6.4 months (interquartile range, 3.9-9.8). The median OS was 10.8 months (95% confidence interval [CI], 5.7-not estimated) with atezolizumab plus bevacizumab and 5.8 months (95% CI, 4.8-not estimated) with lenvatinib ($P=0.26$ by log-rank test). There was no statistically significant difference in OS (adjusted hazard ratio [aHR], 0.71; 95% CI, 0.34-1.49; $P=0.37$). The median PFS was similar ($P=0.63$ by log-rank test), with 4.1 months (95% CI, 3.3-7.7) for

atezolizumab plus bevacizumab and 4.3 months (95% CI, 2.6-5.8) for lenvatinib (aHR, 0.93; 95% CI, 0.51-1.69; $P=0.80$). HRs were similar after inverse probability treatment weighting. The DCRs were 23.3% and 18.2% in patients receiving atezolizumab plus bevacizumab and lenvatinib, respectively ($P=0.74$).

Conclusion: The effectiveness of atezolizumab plus bevacizumab and lenvatinib was comparable for the treatment of HCC with PVTT.

Abstract Submission No. 100171

O-0626

Efficacy and safety of multitherapy for Locally Advanced, Unresectable Hepatocellular Carcinoma

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Background: Recently, lenvatinib plus PD-1 inhibitors combined with or without hepatic arterial infusion chemotherapy (HAIC) has shown promising survival benefits for advanced hepatocellular carcinoma (HCC). This study aimed to explore the safety and efficacy of multitherapy versus transarterial chemoembolization (TACE) for locally advanced HCC patients.

Methods: Clinical data for initially unresectable HCC with PVTT from January 2018 to January 2023 in Tsinghua Changgung Hospital were collected. Conversion therapy, objective response rate (ORR, mRECIST), overall survival (OS), and adverse reactions were analyzed.

Results: 51 HCC patients with PVTT were enrolled, 32 (62.7%) receiving combination therapy (Vp2/Vp3/Vp4:4/20/8, Japanese Typing) and 19 (37.3%) receiving TACE (Vp2/Vp3/Vp4:1/11/7). In the combined group, the median overall survival (mOS) was not reached, the one-year OS rate was 90.1%, while in the TACE group, the mOS was 14 months (95% CI, 10.0-18.0) and the one-year OS rate was 59.7%. OS in the combined group was longer than that in the TACE group (HR 0.23 ; 95% CI, 0.09-0.59 ; $p=0.0021$). In combined group, ORR was 50%, 10 (31.2%) patients converted successfully and underwent hepatectomy, of these, 3 (30%) patients reached pathological complete response (pCR), and 3 (30%) reached major pathological remission (MPR); in TACE group, ORR was 26.3%, 3 (15.8%) patients converted successfully and underwent hepatectomy, of these, 1 (5.3%) patient reached MPR. There was no significant difference in adverse events in the two groups.

Conclusions: For patients with initially unresectable HCC with PVTT, local therapy in combination with systematic treatment have more prolonged survival and a relatively high surgical conversion rate in carefully selected patients with ECOG 0-1.

Abstract Submission No. 100234

O-0627

Experience of tremelimumab plus durvalumab in patients with unresectable hepatocellular carcinoma

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Background: Tremelimumab plus durvalumab (Tre+Dur) is the first combination therapy of anti-CTLA-4 and anti-PD-L1 antibodies approved for unresectable hepatocellular carcinoma (u-HCC) in Japan and has been used since March 2023. We investigated the clinical outcomes of the therapy in real-world practice.

Methods: Patients who received Tre+Dur at our hospital from April 2023 were analyzed retrospectively. Imaging evaluations were performed using RECIST v1.1 with MDCT every 6-8 weeks after the administration of Tre+Dur. Adverse events were evaluated based on CTCAE ver 5.0.

Result: Between April and September 2023, 22 patients were treated with Tre+Dur. Eight patients were without viral infection. The treatment line was 1st (n=2), 2nd (n=4), 3rd (n=4), 4th or later (n=12). BCLC stage was B (n=5) and C (n=17). The median ALBI score was -2.09 and 13 patients were ALBI grade 2b. The objective response rate was 22.2% and disease control rate was 66.7% within the 3rd -line, and 10.0% and 30.0% in the 4th -line or later patients. Tre+Dur has been continued in 5 patients (23%) and post-treatments were introduced in 10 patients. 7 patients were converted to BSC. Grade 3 immune-mediated adverse events (imAE) were observed within 4 weeks in 8 patients, including colitis (n=5), adrenal insufficiency (n=2), and renal failure (n=1). All 5 patients with colitis required steroid therapy, and 3 patients had a poor response to steroids. These 3 patients recovered after the administration of infliximab.

Conclusion: In Tre+Dur therapy, the radiological response of patients who received 1st- to 3rd-line treatment was comparable to that in the phase 3 study.

Abstract Submission No. 100111

O-0628

Lung metastasis from HCC is more powerful in predicting brain metastasis rather than bone metastasis

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Purpose: Brain metastases from hepatocellular carcinoma (HCC) are relatively rare. However, the incidence of brain metastases seems to have increased in recent years. The aim of this study was to characterize the incidence proportion and survival of newly diagnosed HCC with brain metastases.

Materials and Methods: Between January 2009 and December 2020, 942 advanced HCC patients with either metastatic or locally advanced disease untreatable by locoregional therapies were enrolled in clinical trials of first-line systemic chemotherapies in Kindai University Hospital. Total 276 HCC patients who developed extrahepatic metastases were retrospectively enrolled in this study, and the clinicopathologic features and survival times of those were analyzed.

Results: The median age at diagnosis of extrahepatic metastases was 71.0 years. 222 patients were male, and 54 patients were female. 48 patients were infected with hepatitis B virus (HBV), 120 patients were infected with hepatitis C virus (HCV), and 108 patients were not infected with HBV or HCV. Thirteen patients (4.7%) were found to have brain metastasis. The median interval from the diagnosis of HCC to brain metastases was 56.9 months. Extrahepatic metastases and chronic kidney disease were brain metastasis risk factors for HCC patients. Lung metastasis was the strongest risk factor for brain metastasis ($p<0.001$) rather than of bone metastasis ($p=0.051$).

Conclusions: The patients having brain metastases from HCC had poor prognosis.

This study can guide patients with high-risk brain metastases from HCC to undergo diagnostic brain imaging tests, early diagnosis, and treatment to prolong the survival of patients.

Abstract Submission No. 100112

O-0629

Fatal ARDS after a single dose of ATZ/BV for HCC, autopsy findings: a case report

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The combination of atezolizumab (PD-L1 inhibitor) and bevacizumab (VEGF inhibitor) has been used to unresectable hepatocellular carcinoma (HCC) as first-line therapy. Various adverse events are associated with these therapies, including hepatitis, endocrine disorders, nephritis, dermatitis, and interstitial lung disease. It is believed these adverse events occur in part due to their additive effects on tumor growth and their reprogramming of the immunosuppressive microenvironment into an immunostimulatory microenvironment. These events usually occur after several months and rounds of treatment. Here we present a case of a 63-year-old male with HCC who experienced acute respiratory distress syndrome (ARDS) after only a single dose of combination therapy with atezolizumab and bevacizumab. He presented with high grade of dyspnea and bilateral lung consolidation; twelve days after admission he died. Histologic examination revealed that immune-mediated inflammation destroyed the alveolar capillary barrier (alveolar epithelium and endothelium), increased its permeability and caused intra-alveolar hemorrhage and edema. PD-L1 staining was positive in the lung interstitium, suggesting that antibody-mediated injury played a significant role in the pathogenesis of ARDS. Additional studies ruled out an infectious etiology. Immune checkpoint inhibitors are increasingly more common, and it is important clinicians are aware patients can present with ARDS early in the course of treatment.

Abstract Submission No. 100359

O-0630

A Predictive Model to assess Recent Recurrence after Hepatectomy for Hepatocellular Carcinoma

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Background and Aims: We still lack effective prediction models for recent recurrence (time to recurrence [TTR] < 2 years) after hepatectomy for hepatocellular carcinoma (HCC). This study focuses on the factors including sarcopenia which maybe related to recent recurrence of postoperative HCC patients, and attempt to fit an interventable prediction model.

Methods: We retrospectively analyzed 283 hepatitis B-related HCC patients who underwent curative hepatectomy for the first time and measured the preoperative skeletal muscle index (SMI). Cox multivariate analysis was performed to identify the risk factors of postoperative recurrence. A nomogram model was developed to predict the survival of HCC patients, and its predictive performance was validated.

Results: Multivariate analysis showed that sarcopenia, alpha-fetoprotein (AFP) $\geq 40\text{ng/ml}$, the maximum diameter of tumor > 5cm, and hepatitis B virus [HBV] DNA level $\geq 2000\text{IU/mL}$ were independent risk factors associated with postoperative recurrence of HCC. The SAMD model predicting the recurrence-free survival (RFS) of HCC patients was established based on the above factors. The area under the curve (AUC) of the SAMD model was 0.782 (95% CI: 0.705 - 0.858) in the training cohort (sensitivity 81%, specificity 63%) and 0.773 (95%CI: 0.707 - 0.838) in the validation cohort. Besides, a SAMD score ≥ 110 was better to distinguish the high-risk group of postoperative recurrence of HCC.

Conclusion: Sarcopenia is associated with recent recurrence after hepatectomy for HCC. A nutritional status-based prediction model is first established for postoperative recurrence of HCC, which is superior to other models and contributes to prognosis prediction.

Abstract Submission No. 100390

O-0631

No Impact of Sarcopenia in Prognosis of Transarterial Chemoembolization for Hepatocellular Carcinoma

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Background: Chronic liver diseases are associated with poor nutritional status especially when progress to advanced liver disease or liver cirrhosis, and such status is related to development of hepatocellular carcinoma (HCC). Sarcopenia may reflect nutritional status. Transarterial chemoembolization (TACE) is a standard of care for intermediate-stage HCC, although treatment response varies. Whether sarcopenia affect prognosis of TACE remains unclear.

Methods: We recruited 161 adult HCC patients who were TACE-naïve from 2015 to 2018. Skeletal muscle index (SMI), a height squared-adjusted cross-section area of the muscles at the third lumbar vertebra on CT or MRI, is an indicator of sarcopenia.

Results: Among these 161 patients, 118 were male and 43 were female. The average age was 67 years old. 32 male patients (27.1%) had sarcopenia and 23 female patients had sarcopenia (53.5%). 156 patients (96.9%) had liver cirrhosis. 41 patients (25.5%) had infiltrative type HCC. The average tumor number was 5.4. After TACE, 15 patients had progressive disease (PD), 38 patients had complete remission (CR), 89 patients had partial response (PR), and 15 patients had stable disease (SD).

In univariate Cox regression analysis, infiltrative type, vascular invasion, necrosis, tumor number, largest tumor size, and post-TACE AFP had impact on OS (overall survival), while in multivariate Cox regression analysis, vascular invasion, ECOG-PS, pre-TACE ALT, and post-

TACE platelet count had impact on OS. Sarcopenia had no impact in both univariate and multivariate Cox regression analysis.

Conclusions: Our data suggest that sarcopenia has no impact on the prognosis of TACE for intermediate-stage HCC.

Abstract Submission No. 100422

O-0632

Time-to-interventional failure in hepatocellular carcinoma

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Background: Several curative-intent treatments are often applicable depending on the recurrence pattern in patients with hepatocellular carcinoma (HCC) undergoing hepatectomy; therefore, recurrence-free survival (RFS) is not considered an appropriate surrogate for overall survival (OS) in HCC. We assessed whether the time interval between the initial hepatectomy and the emergence of recurrence not indicated for curative-intent treatments, defined as time-to-interventional failure (TIF), is a better indicator of OS in patients with HCC undergoing hepatectomy.

Methods: We retrospectively reviewed patients who underwent initial curative hepatectomy for HCC in our hospital between 2009 and 2018. Recurrence not indicated for curative-intent treatments were defined as multinodular (≥ 4) intrahepatic recurrence, macroscopic vascular invasion, and/or extrahepatic lesions. We compared the correlation between RFS and TIF with OS and investigated the similarities of prognostic factors among RFS, TIF, and OS.

Results: In total, 266 patients were included. With a median follow-up of 56 months, 146 patients experienced any type of recurrence, and 103 patients experienced recurrences not indicated for curative-intent treatments. The median OS, RFS, and TIF were 59, 25, and 45 months, respectively. TIF had a stronger correlation with OS than with RFS ($r^2 = 0.808$ vs. 0.476). Multivariate analysis revealed that macroscopic vascular invasion, poor grade of tumor differentiation, and F3 or 4 were independent prognostic factors to TIF and OS, while macroscopic vascular invasion, maximum tumor size >5 cm, and R1 resection were factors to RFS.

Conclusions: TIF was a more appropriate surrogate for OS than for RFS in patients with HCC.

Abstract Submission No. 100435

O-0633

Usefulness of a novel microcatheter insertable port ReMAP/System-i for transarterial therapy of HCC

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Purpose: Transarterial therapy (TAT) for HCC plays an important role in the treatment of HCC. However, the invasiveness and difficulty of the TAT procedures should be improved. Recently, a novel microcatheter insertable port for intermittent TAT "ReMAP/System-i" was developed in Japan. In the study, we assessed the feasibility and safety of ReMAP/System-i.

Methods: In the placement of ReMAP, a side-holed indwelling catheter (Anthon PU catheter, TORAY Medical Co., Ltd) was inserted into

the femoral artery, and the catheter tip was placed in the descending artery. ReMAP was connected to the tail of the catheter and subcutaneously implanted into the femoral region. A high-flow microcatheter can be inserted into ReMAP and inserted into the targeted artery for treatment. Using this system, transcatheter arterial chemoembolization (TACE) and HAIC can be repeatedly performed. The feasibility and safety of ReMAP/System-i were assessed in the study.

Results: ReMAP/System-i was implanted in 58 patients. The most frequent reason chosen ReMAP/System-i was "need of TAT for several tumor-feeding arteries (48%)". The median procedure time for ReMAP implantation was 42 min (25-94). Among 58 patients, 6 cases had a complication regarding the procedure (3 wound dehiscence, 3 wound infection). By using ReMAP/System-i, repeated TATs have been performed from not only the hepatic arteries but also other tumor-feeding arteries, repeatedly.

Conclusions: ReMAP/System-i is a promising device, which allows us to perform repeated TATs for any arteries with less invasiveness.

Abstract Submission No. 100472

O-0634

Association between SGLT-2 inhibitors and death from hepatobilio-pancreatic cancer

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Background: Association of sodium-glucose cotransporter-2 inhibitors (SGLT-2i) with all-cause and hepato-bilio-pancreatic cancer-related mortality remains unknown in patients with diabetes mellitus (DM).

Methods: Data of adult patients with newly diagnosed DM (hemoglobin A1c $\geq 6.5\%$ or fasting plasma glucose of ≥ 7 mmol/L) were retrieved from a territory-wide healthcare database in Hong Kong between 2010 and 2022. Primary outcomes were mortality from cancer of liver, bile duct, gallbladder and pancreas. Secondary outcome was all-cause mortality. Primary exposure was SGLT-2i use (including canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin), which was treated as time-varying variable to address immortal time bias. Patients were followed from index date (DM diagnosis) till death or study end date (December 2022). Multivariable Cox model was used to calculate adjusted hazard ratios (HRs) of outcomes with SGLT-2i use by adjusting for 25 covariates including age, sex, DM complications, comorbidities, and concomitant use of medications (Table 1).

Results: Of 324,111 eligible subjects (mean age: 59.6 $\pm$ 11.3) years; male: 181,480 [53.0%]; median follow-up: 7.0 years [IQR: 4.7-9.9], 32,684 (9.6%) were SGLT-2i users (Table 1). There were 22,547 (6.6%) all-cause deaths (liver cancer: 901; gallbladder cancer: 76; bile duct cancer: 243; pancreatic cancer: 710). The aHR of death from liver, bile duct, gallbladder, and pancreatic cancer was 0.39 (95% CI: 0.21-0.70), 0.45 (95% CI: 0.25-0.81), 0.74 (95% CI: 0.10-5.43) and 1.03 (95% CI: 0.64-1.66), respectively. SGLT-2i use also associated with lower risk of all-cause mortality (aHR: 0.52; 95% CI: 0.47-0.59).

Conclusion: SGLT-2i use associated with lower risk of all-cause mortality including death from liver and bile duct cancer. This provides additional insight into the choice of anti-diabetic drugs in clinical practice.

Abstract Submission No. 100526
O-0635

Differences in hemodynamics of lenvatinib based on liver function for hepatocellular carcinoma

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Background: The aim of this study was to assess the safety and efficacy of lenvatinib in real-world practice, with a focus on plasma concentration analysis.

Methods: This multicenter, nonrandomized, open-label prospective study was conducted at 10 medical facilities in Japan (jRCTs031190017). Eligible patients had advanced hepatocellular carcinoma and were suitable for lenvatinib treatment. The study included patients with high tumor burden (with >50% intrahepatic tumor volume, main portal vein invasion, or bile duct invasion) and Child-Pugh B status. Plasma concentrations of lenvatinib were monitored on days 1 (multiple times), 8, and 15.

Results: From December 2019 to September 2021, a total of 59 patients were analyzed, with 47 classified as Child-Pugh A and 12 as Child-Pugh B. Patients with Child-Pugh B exhibited a higher frequency of grade 3 or higher adverse events (AEs) and a higher discontinuation rate compared to patients with Child-Pugh A. The median overall survival was 19.7 and 4.1 months in Child-Pugh A and B, respectively. Plasma concentrations were found to be higher in Child-Pugh B patients on days 8 and 15, and higher concentrations were correlated with dosage adjustments and reduced relative dose intensity (RDI).

Conclusions: Patients with inadequately maintained liver function may exhibit an inclination toward elevated plasma concentration of lenvatinib, potentially leading to a higher incidence of AEs and lower RDI.

Abstract Submission No. 100529
O-0636

Combining selective locoregional treatment with atezolizumab plus bevacizumab for unresectable HCC

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Background: Various locoregional treatments for localized HCC have been developed. This study investigated the safety and feasibility of

combining on-demand selective locoregional treatment for residual lesions after tumor shrinkage (complete response [CR]-oriented) or for solitary or few drug-resistant lesions (progressive disease [PD] salvage) with first-line atezolizumab plus bevacizumab (atezo/bev) for unresectable HCC.

Methods: This retrospective study included twenty-nine patients with unresectable HCC. The Response Evaluation Criteria in Solid Tumors, version 1.1, were modified in determining PD: neither tumor growth nor the appearance of a new tumor was regarded as PD if the tumor could be radically cured with locoregional treatment.

Results: Fourteen locoregional treatments were performed (CR-oriented, 7; PD salvage, 7) in 10 patients in the combination therapy group. There were no significant differences in the characteristics of the combination therapy and atezo/bev alone groups at the initiation of atezo/bev treatment. The objective response rate of the combination therapy group (80.0%) was higher than that of the atezo/bev alone group (21.1%; $p=0.005$). Progression-free survival (PFS) and overall survival (OS) were longer in the combination group (medians for PFS and OS: not reached) than in the atezo/bev alone group (median PFS, 224 days; median OS, not reached) (PFS, $p=0.001$; OS, $p=0.004$). The albumin-bilirubin score did not change, and no severe complications occurred with locoregional treatment.

Conclusions: On-demand locoregional treatment with first-line atezo/bev could be a treatment option for unresectable HCC, if locoregional treatment can be performed safely and with minimal invasion.

Abstract Submission No. 100536
O-0637

A tertiary hospital experience of atezolizumab & bevacizumab for advanced hepatocellular carcinoma

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Background: Hepatocellular carcinoma (HCC) contributes as the 7th most frequently diagnosed cancer, with approximately 80% of patients presenting with intermediate or advanced stage HCC. The combination of atezolizumab plus bevacizumab (A+B), have become first line treatment of advanced HCC not amenable to resection or locoregional therapy since 2020.

AIM: To characterise the cohort who received A+B at in Liverpool Hospital, Sydney, Australia and assess its efficacy and safety

METHODS: Patients who received Atezolizumab 1,200 mg plus bevacizumab 15 mg/kg intravenously every 3 weeks at Liverpool Hospital between October 2020 and March 2023 were identified from prospectively maintained HCC database.

Results: Table 1 summarises our patients' demographics. Barcelona Clinic Liver Cancer (BCLC) stage of patients were C in 31 patients (63.3%) and B in 17 patients (34.7%). One patient (2.0%) with BCLC 0 was given A+B because of recurrent HCC following tumour resection. Table 2 summarises patient outcomes as of March 2023. Adverse events of any grade occurred in 29 patients (59.2%). The most common adverse effects were fatigue ($n=10$, 20.4%) and diarrhoea ($n=7$, 14.3%). Grade 3-4 adverse events that occurred were diarrhoea ($n=4$, 8.2%), pyrexia ($n=3$, 6.1%), proteinuria ($n=3$, 6.1%), and gastrointestinal bleeding ($n=2$, 4.08%). The median overall survival was 14 months (95%CI, 12.4-20.3).

Conclusion: Treatment cessation was majority due to HCC progression. The rate of any adverse events was high, however significant side effects were uncommon. Longer follow-up duration and larger patient

cohort would provide better assessment of A+B treatment efficacy and safety in the real-world setting.

Abstract Submission No. 100572
O-0638

Prediction of prognosis in atezolizumab plus bevacizumab for unresectable HCC

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Background: Atezolizumab plus bevacizumab combination therapy (ATZ/BV) is recommended for unresectable hepatocellular carcinoma (u-HCC) patients. The present study aimed to clarify whether tumor marker response can predict efficacy and prognosis in ATZ/BV.

Methods: A total of 73 patients with u-HCC who received ATZ/BV were included. The definition of early tumor response (ETR) and early disease control (EDC) was complete response (CR) + partial response (PR) and CR + PR + stable disease (SD) after 6 weeks, respectively. Early tumor marker response (ETMR) was defined as a reduction in tumor markers after 3 weeks.

Results: Initial therapeutic response was CR 0, PR 22 (30%), SD 24 (33%), PD 20 (27%), respectively. Although no significant difference was seen in overall survival between ETR and non-ETR groups, there was a significant difference between EDC and non-EDC groups ($p < 0.001$). MST of EDC and non-EDC groups were 14.6 and 6.3 months, respectively. Independent pre- and post-treatment factors contributing to survival were performance status (PS), albumin-bilirubin score, lens culinaris-agglutinin-reactive fraction of alpha-fetoprotein (AFP-L3), and EDC. Independent pre- and post-treatment factors contributing to EDC were PS, prior tyrosine kinase inhibitor treatment, AFP-L3, and AFP- and des-gamma-carboxy prothrombin (DCP)-ETMR. The area under the receiver operating characteristic curve for predicting EDC with AFP-, AFP-L3-, and DCP-ETMR and ETMR combination were 0.734, 0.621, and 0.682, 0.766, respectively. Sensitivity, specificity, and accuracy of prediction for EDC using ETMR combination were 0.848, 0.700, and 0.803, respectively.

Conclusions: ETMR can predict disease control and prognosis of ATZ/BV for u-HCC.

Abstract Submission No. 100609
O-0639

Serum Insulin Growth Factor-1 as a Disease Course Predictor in Hepatocellular Carcinoma Patients

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Background: The insulin-like growth factor (IGF) axis has important autocrine, paracrine, and endocrine roles in growth promotion. Alterations of the IGF system have recently been implicated in the pathogenesis of several malignancies, but the relation to hepatocellular carcinoma (HCC) risk is unclear. This study aimed to determine whether

serum IGF-1 level predict the progression and survival in HCC patients.

Methods: We conducted a comprehensive literature search (September-October 2023) from PubMed, EMBASE, and Cochrane databases with the search terms “Insulin-like Growth Factor 1” AND “Hepatocellular Carcinoma” that were published within the year of 2000 to 2023. We screened 184 records after checking duplicates between databases. We examined 48 full-text articles and excluded 35 articles as they did not meet the inclusion criteria. A total of 13 cohort studies with calculation of relative risk (RR) of serum IGF-1 for HCC time-to-progression (TTP) and overall survival (OS) were subjected to statistical analysis using STATA 17. We assessed the ability of serum IGF-1 to predict HCC progression and survival using random effect model to estimate pooled RR. Heterogeneity among studies was assessed by the Cochran's Q and I² statistics. Publication bias was analysed using Begg funnel plot and Egger test.

Result: The meta-analysis of selected studies showed that low level serum IGF-1 significantly predicted shorter TTP (RR 2.36; 95% CI 1.51-3.68) and poorer OS (RR 2.17; 95% CI 1.72-2.74) in HCC patients, p value=0.00.

Conclusions: Serum IGF-1 level independently predicted the progression and survival in HCC patients. Further studies are needed for better causation explanation.

Abstract Submission No. 100659
O-0640

mRNA based HBV-specific TCR T-Cell Infusions can Induce Broad HBV T-cell Response in HBV-related HCC

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Background: LioCyx-M, autologous T-cells modified with mRNA encoding HBV-specific-TCR, has shown promise in advanced and recurrent HCC patients. We report safety and biomarker findings from a phase 1b study (NCT04745403) post LioCyx-M infusions in primary HBV-related HCC patients not amenable to/failed conventional treatment.

Methods: A 71-year-old male, who failed two prior systemic treatments, received 8 LioCyx-M infusions at escalating doses (1×10^5 , 1×10^6 , $3-5 \times 10^6$ cells/kg) intravenously bi-weekly, without lymphodepletion. For pharmacodynamic and immunological biomarker analysis, a whole blood assay (WBA) detected LioCyx-M function in peripheral blood (response to single target HBV-peptides) and explored evidence of epitope spreading (response to other HBV-peptides). Plasma protein levels, assessed through Proximity Extension Assay (PEA), elucidated systemic immune responses and their relationship with clinical symptoms.

Results: LioCyx-M infusions were well-tolerated, with manageable grade 1-2 fever and CRP elevation at highest doses (5×10^6 cells/kg). These infusions transiently elevated NLR (neutrophil/lymphocyte ratio), PLR (platelet/lymphocyte ratio) and reversible liver inflammation (ALT & AST), indicating on-target effects. A 2.62-fold reduction in

serum HBsAg was observed post treatment. along with AFP reduction starting at dose 1×10^6 cells/kg. WBA revealed dose-dependent T-effector cytokines increase, particularly Granzyme-B, IFN γ , IL-2 and IL-4. T-cell responses to non-target HBV peptides, suggestive of epitope spreading, were prominent from 5th-8th infusions. Transient elevation of CXCL9, CXCL10, and other cytokines/chemokines following the highest dose correlated with clinical inflammation, indicating induction of systemic immune response.

Conclusion: Our findings shed light on the safety and immunological responses to LioCyx-M, indicating its potential to trigger a broader immune response targeting various facets of HBV-related HCC.

Abstract Submission No. 100684
O-0641

M2BPGi correlated with immune biomarkers and stratified risk of hepatocellular carcinoma recurrence

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Background: Novel biomarkers reflecting liver fibrosis and immune microenvironment might correlate with the risk of hepatocellular carcinoma (HCC) recurrence. The aim of this study was to evaluate the prognostic value of serum biomarkers in predicting HCC recurrence. **Methods:** Serum biomarkers including M2BPGi, IL-6, IL-10, CCL5, VEGF-A, soluble PD-1, PD-L1, TIM-3, LAG-3 and CTLA-4 in 247 patients with HCC receiving surgical resection were measured. Factors associated with recurrence-free survival (RFS) and overall survival were evaluated. ERASL-post model and IMbrave 050 criteria were used to define HCC recurrence risk groups.

Results: Serum M2BPGi level significantly correlated with FIB-4 score, APRI, ALBI score, AFP, ALT, AST, IL-10, CCL5, VEGF-A, soluble PD-1, PD-L1, TIM-3 and LAG-3 levels. M2BPGi, VEGF-A, soluble PD-1 and TIM-3 levels significantly correlated with RFS. By multivariate analysis, M2BPGi >1.5 COI (hazard ratio (HR)=HR=2.100, p<0.001), tumor size >5 cm (hazard ratio (HR)=1.859, p=0.002), multiple tumors (HR=2.562, p<0.001), AFP >20 ng/mL (HR=2.141, p<0.001) and microvascular invasion (HR=1.954, p=0.004) were independent predictors of RFS. M2BPGi level significantly stratified the recurrence risk in ERASL-post and IMbrave 050 risk groups. An M2BPGi-based model further stratified the recurrence risk into low-, intermediate- and high-risk groups (RFS of 87.8, 27.3 and 5 months, respectively, p<0.001). M2BPGi >1.5 COI was also an independent predictor of OS after resection (HR=2.707, p<0.001).

Conclusions: Serum M2BPGi level significantly correlated with surrogate markers of liver fibrosis, liver function and immunology. M2BPGi is a significant predictor of HCC recurrence and survival after resection and could be incorporated into recurrence-prediction models.

Abstract Submission No. 100708
O-0642

CEUS for Differentiation of Benign Vs Malignant PVT in HCC - A Systematic Review with Meta-analysis.

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Background: Patients with cirrhosis and hepatocellular carcinoma (HCC) can develop both benign and malignant portal vein thrombosis (PVT). Characterizing the nature of PVT is important for planning an optimal therapeutic strategy. In the absence of typical findings or contraindications to CT or MRI, contrast-enhanced ultrasound (CEUS) could help in this differentiation. The present meta-analysis aimed to evaluate the performance of CEUS for characterizing PVT in patients with HCC.

Methods: Electronic databases of PubMed, Embase, and Scopus were searched from inception to 31st December 2022 for studies analyzing the role of CEUS in the differentiation of benign and malignant PVT in HCC. Using the bivariate random effect model, pooled sensitivity and specificity were calculated, and the summary receiver operating characteristic (sROC) curve was plotted.

Result: A total of 12 studies with data from 712 patients were included in the meta-analysis. The pooled sensitivity and specificity of CEUS for the diagnosis of TIV were 97.0% (95% CI: 93.0 - 98.7) and 96.8% (95% CI: 92.1 - 98.7), respectively, without significant heterogeneity. A sROC curve was plotted, and the area under the receiver-operating characteristic was 0.99 (95% CI: 0.98 - 1.00). Despite the presence of publication bias, sensitivity analysis did not show any change in sensitivity and specificity.

Conclusion: CEUS is an effective diagnostic modality differentiation of benign and malignant PVT in patients with HCC and can be an alternative modality to CT or MRI. Further studies are required to study the role of CEUS as a first-line diagnostic modality for the characterization of PVT in HCC

Abstract Submission No. 100746
O-0643

Nonselective β -blocker use does not impact on mortality in patients with hepatocellular carcinoma

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Background: Hepatocellular carcinoma (HCC) contributes to a substantial burden of mortality across the globe. Increasing evidence supports the role of non-selective beta-blockers (NSBB) in reducing liver decompensation and prolonging survival in cirrhotic patients. However, the effect of NSBB on liver-related mortality in HCC patients remains unestablished.

Materials and methods: All patients with HCC and esophageal and/or gastric varices from January 2000 to December 2020 were identified from a territory-wide database in Hong Kong. Participants were

classified into three groups using a time-dependent covariate (i) propranolol users (ii) carvedilol users (iii) NSBB non-users. The primary endpoint was liver-related mortality in 5 years. Cause-specific hazard model was used for competing risk analysis. Liver transplantation and non-liver-related mortality were considered as competing events.

Results: A total of 5,454 patients with 4119 propranolol users, 86 carvedilol users, 1249 non-users (mean age 60.4±11 years, male 82.0%) were included in the analysis. Most patients had viral cirrhosis (78.3%). The use of propranolol and carvedilol did not have a significant impact on liver-related mortality (adjusted cause-specific hazard ratio [aC-SHR] 1.03, 95% CI 0.97-1.12, $p=0.42$; aC-SHR 0.90, 95% CI 0.57-1.43, $p=0.67$) and non-liver-related mortality (aC-SHR 0.99, 95% CI 0.86-1.15, $p=0.94$; aC-SHR 1.40, CI 0.75-2.65, $p=0.293$).

Conclusion: In this territory-wide retrospective study, use of NSBB did not impact on liver-related and non-liver-related mortality in HCC patients over a follow-up period of 5 years.

Abstract Submission No. 100797
O-0644

First-line lenvatinib ± pembrolizumab for advanced hepatocellular carcinoma: LEAP-002 China subgroup

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Background: The global, randomized, phase 3 LEAP-002 study (NCT03713593) was conducted to evaluate lenvatinib plus pembrolizumab compared with lenvatinib plus placebo as first-line therapy in patients with advanced hepatocellular carcinoma (HCC). Efficacy and safety results for patients enrolled in LEAP-002 in China are reported.

Methods: Eligible patients had confirmed HCC, Child-Pugh class A liver score, ECOG PS score 0 or 1, and no main portal vein invasion. Patients were randomly assigned 1:1 to receive oral lenvatinib (8mg/day [bodyweight <60 kg] or 12mg/day [bodyweight ≥60kg]) plus either pembrolizumab (200mg IV every 3 weeks [Q3W]; ≤35 cycles) or placebo (saline IV Q3W). Dual primary end points were OS and PFS per RECIST v1.1 by blinded independent central review (BICR). Secondary end points included ORR per RECIST v1.1 by BICR and safety. Database cutoff was June 21, 2022.

Results: One hundred fifty patients were enrolled in China (lenvatinib plus pembrolizumab, $n = 76$; lenvatinib plus placebo, $n = 74$). Median follow-up (time from randomization to database cutoff) was 31.9 months (range, 28.1-37.5). Median OS was 32.3 months for lenvatinib plus pembrolizumab and 26.0 months for lenvatinib plus placebo (HR, 0.76 [95% CI, 0.50-1.17]). Median PFS was 8.3 months for both groups (HR, 0.86 [95% CI, 0.61-1.23]). Additional results are summarized in the Table.

Conclusion: China subgroup results were consistent with those of the global LEAP-002 population. OS, PFS, and ORR were numerically improved with the addition of pembrolizumab to lenvatinib, with a similar safety profile.

Abstract Submission No. 100878
O-0645

RFA of progressive HCC after introduction of chemo therapy, may extend life prognosis.

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Background: Molecular target agent (MTA) for hepatocellular carcinoma (HCC) is improving and plays a significant role in treatment of patients with medium to advanced stage of HCC. However, once chemotherapy is ineffective and cancer is evaluated as progressive disease (PD), supportive treatment is the only possible option for these patients. Radio frequency ablation (RFA), a minimally invasive treatment for HCC, can be useful for mass volume reduction and extend life prognosis of such patients.

Objective: To evaluate the clinical effects of RFA on patients with PD HCC.

Method: From September 2009 to December 2021, 32 out of 186 patients with a diagnosis of HCC and were evaluated as PD or discontinued MTA due to its adverse events, underwent RFA. We analysis survival lengths after performing RFA.

Results: The patients included 27 men and 5 women. The median age is 71 (range 50-88). The MTA before RFA for 22, 9 and 1 patient were Sorafenib, Lenvatinib and Regorafenib respectively. Child-Pugh score were A in 28 patients (88%) and B in 4 patients (12%). RFA were performed for the following reasons; volume reduction for uncountable liver lesion in 12 patients (37%), recurrence of lesions in liver in 11 patients (34%), disseminated lesions in 6 patients (18%), others in 3 patients (9%). No early complications have been observed after RFA. Median survival after performing RFA is 13.2 months.

Conclusion: Our experiences suggest that RFA after MTA introduction may reduce mass volume of tumors and extend life prognosis.

Abstract Submission No. 100895
O-0646

Serum HBcAb level can predict the occurrence of hepatitis B related hepatocellular carcinoma.

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Background: Serum hepatitis B core-related antibody (HBcAb) have always existed in the course of hepatitis B infection since the acute stage. Previous literatures have found that the quantitative detection of HBcAb is related to the occurrence of hepatitis B related hepatocellular carcinoma (HCC). In order to further explore the predictive significance of serum HBcAb levels in patients with chronic hepatitis B (CHB) for the occurrence of hepatitis B related HCC, we conducted this retrospective study.

Method: A total of 454 patients treated in our hospital from October 2018 to October 2019 were included. Serum HBcAb levels, surface antigen level, alpha fetoprotein (AFP) level, liver function and other clinical indicators were quantitatively measured at enrollment. The

time of diagnosis of chronic viral hepatitis B, the time of initiation of antiviral therapy, and the time of diagnosis of primary hepatocellular carcinoma were retrospectively recorded.

Results: The optimal cut-off value of HBcAb level as a predictor was determined by ROC curve analysis to be 3.513 (sensitivity 0.494, specificity 0.759, AUC area 0.610). Univariate and multifactorial COX regression analysis showed that HBcAb >3.513 was a protective factor for the development of HCC after treatment with nucleoside analogues (NAsHCC), HR0.561 ($p < 0.05$). In addition, univariate and multivariate COX regression showed that baseline HBeAg positive and abnormal AFPN were risk factors for NAs HCC (HR1.949 ($p = 0.006$), HR2.493 ($p < 0.005$)).

Conclusion: In patients with CHB, serum HBcAb level >3.513 is a protective factor for the development of NAsHCC, HR0.561 ($p < 0.05$). In addition, positive HBeAg and abnormal AFPN are risk factors for NAsHCC.

Abstract Submission No. 100937
O-0647

ALBI vs CTP- Predictor of post-TACE hepatic decompensation in intermediate stage HCC

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Background: The treatment of choice for intermediate stage hepatocellular carcinoma (HCC) traditionally has been trans-arterial chemoembolization (TACE). Post-TACE hepatic decompensation is an important complication and is predicted based on Child-Pugh score (CTP). The albumin-bilirubin (ALBI) score is emerging as an important tool for this. We compared the performance of ALBI score and CTP score in predicting post-TACE decompensation for intermediate stage HCC patients.

Methods: A total of 56 consecutive intermediate stage HCC patients who underwent TACE (DEB TACE) during January 2020-March 2023 were studied. Demographics and biochemical tests pre and post-TACE were recorded. Time-dependent receiver operation Curves (ROC) were used to compare ALBI grade and CTP score for predicting TACE hepatic decompensation.

Results: Of the 56 patients, 37 (66.1%) were males; median age was 58 years (range 37-74 years); 37 (66.1%) were CTP A, 19 (33.9%) were CTP B. The etiologies of liver cirrhosis were alcohol ($n = 8$, 14.3%), Hepatitis B ($n = 20$, 35.7%), Hepatitis C ($n = 17$, 30.4%), Non-Alcoholic Steatohepatitis ($n = 4$, 7.1%), Cryptogenic ($n = 7$, 12.5%). Post TACE decompensation was seen in 14/56 (25%) patients.

In the logistic regression analysis, ALBI Score was a significant predictor of post-TACE hepatic decompensation ($p < 0.0005$, OR = 0.026, 95% CI = 0.004 to 0.181; AUROC 0.944 Vs 0.4, $p < 0.0005$). Using Youden's index, ALBI score > -1.75 was found to predict post-TACE decompensation (sensitivity 85.7%, Specificity 95.2%, accuracy 92.86%).

Conclusions: In patients with intermediate stage HCC, compared to CTP score, pre-TACE ALBI grading has a better accuracy and discriminatory ability to predict post-TACE decompensation.

Keywords: Child-Pugh score; ALBI score/grade; post-TACE hepatic decompensation; intermediate HCC

Abstract Submission No. 100971
O-0648

Comparison of Alpha-Fetoprotein with Viral & Non-Viral Etiology in Hepatocellular Carcinoma Patients

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Background: Alpha-fetoprotein (AFP) in serum is one of the diagnostic markers currently available for Hepatocellular Carcinoma (HCC). In Indonesia, HCC is the fourth most common cancer with an incidence of around 5.4%, while chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) are the main etiology of HCC in all Asia-Pacific, western countries, and Africa, followed by non-viral etiologies. The efficacy of AFP monitoring is controversial and varies based on the etiology of chronic liver disease in patients with HCC. The aim is to analyze the correlation between alpha-fetoprotein serum and the etiology of hepatocellular carcinoma subjects.

Methods: This study was a retrospective database analysis of HCC patients diagnosed in Wahidin Sudirohusodo Hospital between 2018 and 2022. Information on patients' demography, laboratory (liver biochemistry/serology/virology), and radiology data were collected. Diagnosis of HCC according to the Asia-Pacific Association for the Study of the Liver (APASL). The threshold of AFP level of 400 ng/mL was evaluated against the etiologies of the subject.

Results: During the study period, a total of 337 HCC subjects were found. The majority were male with 257 (76.3%) patients and a mean age of 53.6 years old. Causes of the underlying liver were viral infection 244 (72.4%) and non-viral 93 (27.6%). Of the total patients, 172 (51.04%) had AFP over 400 ng/mL. Viral etiologic was associated with higher AFP levels in serum (130 subjects vs 35 subjects, $p < 0.01$).

Conclusions: Hepatocellular carcinoma with etiologic of viral infection was associated with a higher level of alpha-fetoprotein

Abstract Submission No. 101023
O-0649

2D- SHEAR WAVE ELASTOGRAPHY OF TUMOR - A NOVEL PREDICTOR OF RESPONSE TO TACE IN PATIENTS WITH HCC

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Background and Aims:

Early prediction of Tumor Response is paramount for identification of failure of TACE as well as guidance of future therapy. A recent study has shown that a higher baseline Tumor Elastography is associated with incomplete response to TACE. We aimed to study the association between Tumor Shear Wave Elastography (SWE) and response to TACE.

Methods: 57 patients were enrolled in our study over a period of 1 year. 3 were excluded. Baseline characteristics were analysed. All patients underwent 2D-SWE of Tumor and Liver parenchyma at least 2cm away from the focal lesion before TACE, 48 hours and 6 weeks Post-TACE. Tumor response was assessed at 6 weeks by mRECIST criteria.

RESULTS: The mean age was 59.94 ± 7.6 years. 44 (84.18%) were male. 20 (37.04%) had complete response, 10 (18.52%) had partial response, 9 (16.67%) had Stable disease and 15 (27.78%) had Progressive disease post-TACE. Mean SWE of focal lesion (FOL) at baseline was significantly lower in patients with CR (14.82 ± 4.76) compared to other groups PR (18.59 ± 5.31), SD (35.93 ± 8.7), PD (38.22 ± 14.07) ($p=26kpa$ (AUC=0.95, CI: 0.854 to 0.991; Sensitivity 100%, Specificity 79.1%, $p=20kpa$ (AUC=0.79, CI:0.657-0.889, Sensitivity=83.3%, Specificity=67.7%). On Multivariate analysis, Lower baseline SWE FOL (aOR: 0.811, $p=0.004$) and lower AFP (aOR: 0.988, $p=0.026$) were found to be independently associated with Tumor Response.

Conclusion: Baseline Tumor Shear Wave Elastography and AFP can be used as predictors for Tumor response of HCC to TACE.

Abstract Submission No. 101027

O-0650

The distribution of BCLC 2022 stages among patients with Hepatocellular carcinoma

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Objective: Primary liver carcinoma ranks as the seventh most prevalent cancer globally. Hepatocellular carcinoma (HCC) represents the predominant form of liver cancer, accounting for approximately 75% of all cases. The objective of this study is to ascertain the distribution of BCLC stages among patients presenting with HCC at a tertiary care hospital.

Method: A descriptive cross-sectional, observational study was carried out in the gastroenterology department of the Aga Khan University Hospital. The study included all patients, who presented in liver tumor board clinic with the diagnosis of HCC.

Result: A total of 66 patients were enrolled in the study, with mean age of 54.7 years. The primary cause of HCC was found to be Non-B non-C CLD in 39 cases (65%). BCLC -2022 staging was performed, with the majority of patients ($n=42$, 63.7%) falling into the BCLC-C category, followed by BCLC-D ($n=26$, 39.3%).

Conclusion: The study highlights that a significant proportion of HCC patients are initially categorized as BCLC-C where some management can be offered. Early detection of HCC is recommended to offer improved treatment options to patients.

Abstract Submission No. 101041

O-0651

A comparison of surgical resection and RFA for early-stage HCC patients with Child-Pugh class B

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Background: This study compared surgical resection (SR) and radiofrequency ablation (RFA) for early-stage HCC patients with Child-Pugh class B.

Methods: This retrospective study included 497 HCC patients with ≤ 3 nodules and tumors ≤ 3 cm in diameter who initially received either SR ($n=41$) or RFA ($n=456$). The significant differences in patient background were adjusted by IPTW.

Results: The median ages were 72 and 68 years old in the SR and RFA group ($p=0.3$), with 26 and 305 patients being males ($p=0.7$). Child-Pugh score were 7, 8, and 9 in 34, 6, and 1 patients in the SR group and 262, 124, and 70 patients in the RFA group, respectively ($p=0.003$). The number of nodules was 1, 2, and 3 in 35, 6, and 0 patients in the SR group and 309, 109, and 38 patients in the RFA group, respectively ($p=0.034$). The maximum tumor diameter 2.2 and 1.8 cm in the SR and RFA group ($p=0.002$). The 5-, and 10-year RFS rates were 48.6%, and 30.4% in the SR group and 43.6%, and 34.9% in the RFA group, which did not reach a statistical significance ($p=0.6$). The 5-, and 10-year OS rates were 47.6%, and 19.5% in the SR group and 43.2%, and 15.3% in the RFA group, without a statistical significance ($p=0.5$). In the IPTW-weighted cohort, the differences in the RFS and OS rates between two groups were not observed ($p=0.5$ and 0.9 , respectively).

Conclusions: RFA may be equally effective compared to SR for early-stage HCC patients with Child-Pugh class B.

Abstract Submission No. 101078

O-0652

Evaluation of circular RNA SMARCA5 as a novel biomarker for hepatocellular carcinoma

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Background: Hepatocellular carcinoma (HCC) is the sixth and fourth common cancer in worldwide and Egypt, respectively. Most patients with HCC are diagnosed at their advanced stages due to lack of early diagnosis biomarker, so they lose the best opportunity for therapy.

Objective: The aim of this study is to evaluate the level of circular RNA SMARCA5 and SMARCA5 mRNA gene expression as novel biomarkers for early detection of HCC.

Patients and methods: The study was conducted as a case control study included 159 subjects, they collected from inpatient and outpatient pathology clinics of national liver institute, Menoufia university and they were equally divided into 3 groups; Group I: 53 control subjects, Group II: 53 HCV cirrhotic patients and Group III: 53 HCC patients. Each patient underwent full history taking, thorough clinical examination, radiological examination and assessment of serum Alpha-fetoprotein (AFP) and detection of circular RNA SMARCA5 and SMARCA5 mRNA genes by quantitative real time polymerase chain reaction (PCR).

Results: There were statistically significant difference among studied groups regarding AFP, SMARCA5, and CircSMARCA5 (P -value= 0.001, 0.001 & 0.001, respectively). CircSMARCA5 and SMARCA5 mRNA were significantly reduced in HCC group when compared to

HCV cirrhotic patients and controls. ROC analysis for early diagnosis of HCC showed that the area under curve (AUC) of CircSMARCA5 at cut off point 4.55 yielding specificity of 83.8% and sensitivity of 91.7% while the AUC for AFP at cutoff point 515 ng/ml yielding specificity of 89.2% and sensitivity of 91.3%

Conclusion: CircSMARCA5 may serve as a potential predictor of HCC disease with better sensitivity than AFP.

Abstract Submission No. 101142
O-0653

Integrative Characteristics of HBV -HCC after NUCs Long-term Antiviral Therapy

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Aims: The integrated characteristics of Hepatitis B Virus (HBV)-related liver cancer after long-term antiviral treatment remain incompletely understood. This study aimed to explore the influence of integration events on clinical factors of HBV-related liver cancer using a long-term follow-up cohort undergoing antiviral therapy. Additionally, we aimed to analyze the characteristics of integration patterns.

Methods: This study enrolled 22 patients with HBV-related liver cancer, monitoring clinical indicators including HBV DNA and Hepatitis B Surface Antigen (HBsAg). Genome-Wide Association Study (GWAS) analyzed liver cancer tissues and detected HBV integration sites. Among them, 17 cases had HBV integration (Int group), while 5 cases had no HBV integration (N-int group). We analyzed clinical differences between the two groups and compared dynamic changes in HBsAg levels. Additionally, we explored genomic features at the HBV integration breakpoints.

Results: The participants were followed for nearly 11 years. Among them, 77.3% demonstrated HBV integration. The Int group consistently exhibited higher levels of HBsAg compared to the N-int group, accompanied by a slower decline. In the Int group, there were significant increases in telomerase reverse transcriptase (TERT) gene copy number, single nucleotide variations (SNVs) deletion number, and substitution number compared to the N-int group ($P < 0.05$). Integration events primarily transpired close to chromosome termini and centromeres, indicating a preference for specific human genomic elements. Essential functional elements of the HBV genome were prone to integration.

Conclusion: After long-term antiviral therapy, HBV integration could still sustain a certain level of HBsAg. HBV integration resulted in an increased number of interrupted gene SNVs and could potentially impact chromosome stability and mitosis. Host genomic elements cooperated with HBV functional elements in integration events.

Abstract Submission No. 101185
O-0654

The causes of HCC in Turkey

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Background: The incidence of HCC has been increasing despite the reducing incidence of chronic hepatitis infections. Also, the etiology

of HCC has been changing with a growing role of metabolic (dysfunction) associated fatty liver disease (MAFLD).

Method: We analyzed the publications related with the causes of HCC in Turkey. HBV is the major cause of HCC in Turkey. There are many reports that HCC has a geographic variability for the etiology in Turkey.

Results: In the previous study, HBV, HCV and alcohol were the main causes of HCC with (56%), (23.2%) and (15.9%) in 207 patients respectively. The etiologic risk factors for HCC were HBV in 555 patients (57.6%), HCV (16.5%), and chronic alcohol (14.2%). Yalcin reported that HBV infection alone (45%), HDV co-infection (29%), HCV infection (15%) and unknown etiology (10%) were causes of HCC in southeastern Turkey. The result of another multicenter, retrospective cohort study including 1802 patients showed that HBV was the most common etiology (54%), followed by HCV (19%), NAFLD (10%), cryptogenic (8.6%), alcohol-related liver disease (3.6%), autoimmune liver diseases (0.9%).

It was reported that HBV infection (68.2%) was the leading etiology, followed by HCV infection (17.2%), HDV infection (5.5%), alcohol (6.4%), and NAFLD (3.5%).

Conclusions: Despite the national immunization program, HBV remains the leading cause of HCC in Turkey, followed by HCV, alcohol-related liver disease, cryptogenic MAFLD and HDV. Recently, MAFLD is increasingly involved in the etiology of HCC.

Abstract Submission No. 101187
O-0655

The factors contributing to prolonged survival in the intermediate stage HCC using survival model.

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Backgrounds: The increase of treatments have made it possible to the more curative state in unresectable hepatocellular carcinoma. However, we do not know how much these therapies contribute to prognosis in real clinical practice. We applied our new developed survival model and compared them with actual survival, and analyzed the factors contributing to prolonged survival.

Methods: 101 cases from BCLC stage B from 2018 to 2023 were grouped by Kinki criteria as B1/B2/B3=37/56/8. 1) Overall survival was analyzed by Kaplan meier method. 2) Actual survival was determined in B1/B2/B3=26/41/6 cases. We compared them with predicted survival time calculating with survival model. The proportion of cases that exceeded the predicted survival time were extracted. The t-test was used to evaluate the survival factors contributing to the prolongation of the actual survival period.

Results: 1) Overall survival was 42.6/25.2/16.45 months. The mean predicted survival was 28.6/22.6/15.8 months. 2) Actual survival exceeded prediction in 17 patients (65.4%) in B1 and 23 (56.1%) in B2. Statistical analysis showed that actual survival time significantly exceeded predicted survival. Factors associated with prolonged survival were multiple TACE and RFA treatment in B1, and multiple TACE, ATZ+BV induction with treatment effect, and RFA treatment in B2.

Conclusion: Using our developed survival model, we analyzed the relationship of treatment contributing to prolonged survival in the intermediate stage. With the success or failure of TACE treatment is the key in the intermediate stage and ATZ+BV being effective in the B2 stage.

Abstract Submission No. 101314

O-0656

Safety of STRIDE regimen for advanced hepatocellular carcinoma and its optimal management

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Background: Durvalumab/tremelimumab combination therapy (STRIDE) has been approved for advanced hepatocellular carcinoma (HCC). However, STRIDE, which contains a CTLA-4 inhibitor, is associated with a high incidence of immune-related/mediated adverse events (irAEs/imAEs), which are often difficult to manage. We analyzed clinical data on irAEs/imAEs that occurred after STRIDE administration at our hospital and investigated the management of irAE/imAE.

Methods: We retrospectively collected clinical data on 43 patients treated with STRIDE for advanced HCC between April and August 2023.

Results: IrAEs/imAEs requiring treatment with glucocorticoids occurred in 13 cases (30.2%), and high-dose glucocorticoids (≥ 1 mg/kg) were required in 7 cases (16.3%). The median duration from the start of STRIDE to the first irAE/imAE was 16 days (range: 6-51). IrAEs/imAEs leading to treatment discontinuation occurred in 4 cases, and disease progression was observed in 4 cases. In one case of enteritis, remission was not achieved with glucocorticoids alone and infliximab was added. In addition, in one case of cytokine release syndrome, remission was not achieved with glucocorticoids alone, necessitating tocilizumab. After tapering of glucocorticoids, durvalumab was reintroduced in 5 cases, with only one case of enteritis recurring.

Conclusions: STRIDE-induced irAE/imAE can be effectively managed by prompt administration of glucocorticoids in severe cases. It is also important to have adequate knowledge of additional treatment options in cases of inadequate response to glucocorticoids. Although there is a risk of recurrence of irAE/imAE, retreatment with durvalumab may be considered after successful control of irAE/imAE with glucocorticoids, especially if supported by the risk-benefit assessment.

Abstract Submission No. 101322

O-0657

Exploratory Effectiveness of Atezolizumab + Bevacizumab against uHCC Beyond Radiological Progression

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Background: The IMbrave150 trial allows the continuation of atezolizumab (Atezo) plus bevacizumab (Bev) beyond radiological PD until clinical benefits cease. This study investigates the effectiveness of continuing ICIs after initial radiological PD.

Methods: 122 unresectable HCC patients treated with Atezo plus Bev across 8 liver centers were enrolled. Patients with clinical benefits, despite PD as per RECIST 1.1, could continue treatment until unacceptable toxicity developed. Those who received two or more cycles of Atezo plus Bev after first PD were defined as beyond PD group. Their outcomes were compared with those who either switched to alternative therapies or discontinued chemotherapy post-first PD.

Results: 24 patients continued with Atezo plus Bev, 26 switched to other chemotherapies, and 15 discontinued treatments after the first PD. The median overall survival (OS) was 21.3 months in the beyond PD group versus 13.6 months in those who switched or discontinued treatment. Additionally, those who switched to alternative chemotherapy had a median OS of 23.1 months, while those receiving palliative therapy had 7.0 months. Macrovascular invasion (MVI) was identified as a significant prognostic factor in the beyond PD group, based on the Cox proportional hazard model. Notably, in the patients without MVI, beyond PD group had a significantly longer median OS compared to others.

Conclusion: The study suggests that there are patients who may benefit from continuing Atezo and Bev beyond PD, especially in those without MVI. Nevertheless, due to selection bias, more research is needed to find predictors defines treatment efficacy.

Abstract Submission No. 101330

O-0658

Significance of Complete Response in Atezolizumab-Bevacizumab for Advanced Hepatocellular Carcinoma

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Objective: To evaluate the characteristics and prognosis of patients who achieved complete response (CR) by mRECIST in patients with advanced hepatocellular carcinoma (HCC) treated with atezolizumab-bevacizumab (Atz/Bev).

Methods: 129 patients who received Atz/Bev in our hospital were included. The median age 75 years; Male 106 cases; ECOG-PS 0 96 cases; Child-Pugh score 5 82 cases; BCLC stage B 60 cases; median AFP 50.1ng/ml; median PIVKA-2 599mAU/ml.

Results: The best antitumor response (CR/PR/SD/PD+NE) to Atz/Bev alone was 16/45/36/32 in mRECIST (CRR 12.4%; ORR 47.3%). Median PFS was 258 days; for mRECIST, CR 588 days; PR 442 days; SD 209 days; PD+NE 42 days. Median OS was 644 days, with mRECIST: CR not achieved; PR 886 days; SD 644 days; PD+NE 173 days. Predictors of CR were fewer than 4 HCCs and no portal vein tumor thrombosis at baseline. The median time to mCR was 105 days; AFP ratio was 0.330 at 2 weeks, 0.160 at 4 weeks, and 0.11 at 6 weeks; PIVKA-2 ratio was 0.575 at 2 weeks, 0.470 at 4 weeks, and 0.240 at 6 weeks. Six patients who underwent additional TACE achieved CR. Including these 6 patients, the median OS of the 22 CR patients was not reached. Of these, 18 patients achieved drug-free status.

Conclusions: Patients who achieved CR in mRECIST with Atz/Bev showed significant reductions in AFP and PIVKA-2 early in the course of treatment. CR achieved with Atz/Bev alone and with the addition of TACE can be expected to have an extremely favorable prognosis.

Abstract Submission No. 101333

O-0659

India Pabulum Index predicts short term mortality in patients with HCC : A Prospective study

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Background and Aims: The presence of systemic inflammation predicts poor outcome in patients with malignancy. We attempted to evaluate the association of the inflammatory component of diet with mortality in patients with Hepatocellular carcinoma (HCC) using a novel score, India Pabulum Index (IPL index) and compared it with existing prognostic indices.

Method: We performed a prospective study of 6 months in 84 patients with Decompensated Chronic Liver Disease (DCLD) and HCC. Basic clinical parameters were obtained. IPL index was formulated as Prognostic Nutritional Index $[(10 \times \text{serum albumin [g/dL]}) + (0.005 \times \text{lymphocytes } [\mu\text{L}])]$ evaluated in a South Indian cohort. Variables associated with Mortality were identified using Regression analysis and compared with other scores using ROC curves.

Results: The Short-term Mortality was 34.5% at 6 months. On univariate analysis, the predictors of mortality were IPL index ($p < 0.001$), BCLC score ($p < 0.001$), Portal Vein Thrombosis ($p = 0.038$), Hepatic Encephalopathy ($p < 0.001$), Child status ($p < 0.001$), Alpha fetoprotein > 256 ($p < 0.007$) and Neutrophil Leucocyte Ratio (NLR) ($p = 0.000$). However, on multivariate analysis, IPL index < 34.8 ($p = 0.001$) and NLR > 2 ($p = 0.039$) were significantly associated with mortality. ROC curve of IPL index estimated a cut-off value of 34.8 with sensitivity-89.66, specificity-90.91, positive predictive value-83.9 and negative predictive value-94.3. ROC for IPL index (0.926) was higher than BCLC (0.838), Hong Kong Liver Cancer (0.786) and NLR (0.778). Kaplan Meier analysis showed that the mean survival was 5.887 ± 0.069 months in the high IPL index group (> 34.8) and 2.968 ± 0.346 months in the low IPL index group (≤ 34.8) ($p < 0.001$). Multivariate analysis of the prognostic power of IPL index and BCLC using Cox regression model showed that a low IPL index had a Hazard ratio of 18.29 (95% CI (5.23-63.93)) vs 2.05 (95% CI (0.79-5.33)) for BCLC.

Conclusion: An IPL index of < 34.8 predicts Short-term Mortality in patients with DCLD and HCC. It is an easy-to-use, sustainable and viable prognostic score that can be applied at bedside, to identify patients for dietary recompensation as a powerful tool to improve their survival.

Abstract Submission No. 101338

O-0660

Clinical Characteristics And Barcelona Clinic Liver Cancer Staging In Patient With HCC.

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Objective: This cross-sectional prospective study, conducted at the Gastroenterology Department of Jinnah Postgraduate Medical Center in Karachi between January 2018 and December 2022, aims to assess the distribution of Barcelona Clinic Liver Cancer (BCLC) stages in patients with Hepatocellular Carcinoma (HCC) in a tertiary care hospital. The study seeks to provide valuable insights into the clinical characteristics and staging of HCC within a specific population.

Methods: A total of 566 patients of both genders, all with confirmed HCC diagnoses, were included in the study. Data analysis was conducted using SPSS version 25.

Results: The study population had an average age of 59.3 years, with 58% being male and 42% female. The mean Model for End-Stage Liver Disease (MELD) score was 15 ± 6 . Hepatitis C Virus (HCV) was the leading cause of HCC, accounting for 70% of cases. The most frequently reported presenting complaints were abdominal distention and

abdominal pain, followed by upper gastrointestinal bleeding. Upon Barcelona Clinic Liver Cancer (BCLC) staging, the majority of patients were classified as BCLC-D (40%), followed by BCLC-C (36%).

Conclusion: The study highlights a concerning trend in our population, with a significant proportion of HCC patients presenting in advanced stages, particularly within the BCLC-D category. Abdominal pain emerged as the most common symptom. Early detection of HCC is crucial to enable the timely implementation of more effective treatment strategies. These findings contribute to the global understanding of HCC presentation and staging, facilitating improved clinical management and patient outcomes on a broader scale.

Abstract Submission No. 101371

O-0661

Decoding the importance of AFP in HCC : Is it all it's touted to be?

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Introduction: Serum alpha-feto protein (AFP) is the most widely used serological marker to establish a diagnosis of HCC and is a part of most standard guidelines on screening and diagnosis. We aimed to study the clinical relationship of AFP levels and tumor characteristics in patients diagnosed with HCC on surveillance.

Methods: A total of 126 patients (99 men, age $55 (\pm 13.1)$ years) diagnosed with HCC on surveillance were recruited. AFP producing tumors (AFP+) were defined as $\text{AFP} \geq 10$ ng/ml. Clinical and tumor characteristics were compared between patients with AFP producing versus non-AFP producing tumors (AFP-).

Results: A total of 85 (67.4%) were AFP+. Median CTP, MELD and ALBI score were 7 (IQR 5-14), 13 (IQR 6-35) and -1.7014 (IQR -3.63 — 0.53) respectively. The most common etiology was Hepatitis B ($n = 47$; 37%) followed by NASH ($n = 37$; 29.1%). AFP- had fewer number of lesions (9.8% vs 16.4%) but, the median size of the lesions was similar (5cm vs 5cm). AFP+ had a higher incidence of microvascular (30.5% vs 19.5%, $p = 0.17$), macrovascular invasion (portal vein: 28.2% vs 12.2%; $p = 0.045$, hepatic vein: 10.6% vs 7.3%; $p = 0.558$) and extra hepatic metastases (16.5% vs 9.8%; $p = 0.313$). Curative intent therapy could be offered to 20 (23.5%) Vs 22 (53.6%) in AFP+ and AFP- respectively.

Conclusions: AFP producing tumors have higher number of lesions, and increased incidence of vascular invasion and hepatic disease. Curative intent therapy could be offered to greater proportion of patients who were AFP-. Need better biomarkers for less aggressive disease.

Abstract Submission No. 101392

O-0662

Influence of Enterobacteria on the Response to Atezolizumab and Bevacizumab in patients with HCC

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Background: Numerous studies suggest that alterations in the microbiome can impact the efficacy of immune checkpoint inhibitors. The use of proton pump inhibitors or antibiotics is considered a risk factor

for diminished survival, while the presence of butyrate-producing enterobacteria appears to have a potentially positive effect. However, the specific influence of enterobacteria on patients with hepatocellular carcinoma (HCC) remains unclear.

Methods: We conducted a retrospective analysis of 747 HCC patients undergoing treatment with atezolizumab and bevacizumab, examining the impact of orally administered butyrate-producing enterobacteria on treatment efficacy and overall survival. Additionally, we reviewed reports examined the effects of proton pump inhibitors and antibiotics on treatment outcomes.

Results: While the objective response in patients taking butyric acid-producing enterobacteria was higher compared to the control group (29.7% vs. 26.4%), no statistically significant differences were observed. Similar trends were observed in disease control rates (77.8% vs. 72.7%). Median survival time showed no significant difference between the two groups (20.0 months vs. 21.4 months), even after adjusting for patient background. Despite one study reporting a connection between pretreatment antibiotics and reduced therapeutic response, our analysis did not reveal a significant impact of antibiotics or proton pump inhibitors.

Conclusions: Our study did not identify a clear influence of enterobacteria on the treatment outcomes of patients with hepatocellular carcinoma receiving atezolizumab and bevacizumab; however, prospective study is needed to confirm the effect.

Abstract Submission No. 101443
O-0663

Durable response and its significance in atezolizumab plus bevacizumab therapy

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Background: Immune checkpoint inhibitor therapy has dramatically benefited cancer patients, particularly patients undergoing long-lasting effectiveness. However, durable responses are not well elucidated in real-world clinical practice. We aimed to clarify the durable response rate and the significance of atezolizumab plus bevacizumab (Atez+Bev).

Methods: This single-center retrospective study enrolled 134 patients with unresectable hepatocellular carcinoma (HCC) who underwent Atez+Bev treatment. We evaluated radiological response according to RECIST ver 1.1 at 6-8 weeks and every 8-12 weeks thereafter. The "durable response" was defined as a maintained response (CR/PR/SD) >6 months and received Atez+Bev >6 months.

Results: Among enrolled patients, 84 patients received AtezBev as the 1st-line treatment. In the 1st-line treated patients, SD/PR/CR was achieved in 42(50%)/20(24%)/2(2%), respectively. Among these, durable response was achieved in 40% of SD, 75% of PR, and 100% of CR. Patients who achieved durable responses survived significantly longer than those who did not ($p=0.02$). The durable response rate was significantly higher in the 1st-line group than in the 2nd or later-line treated patients (40% vs. 18%, $p=0.02$). The durable response rate in the 2nd or later-line group was 24% for patients who achieved SD and 67% for patients with PR. Patients whose AFP decreased under 80% compared to the baseline achieved significantly higher durable response rates compared to those who did not (51% vs. 25%, $p=0.006$).

Conclusion: Patients who achieved durable response showed better prognosis. Three-fourths of patients without AFP response could not maintain a response over six months.

Abstract Submission No. 101452
O-0664

Efficacy Outcomes of Atezolizumab-Bevacizumab Therapy for Unresectable Hepatocellular Carcinoma

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Introduction: Atezolizumab-bevacizumab is the recommended first-line systemic therapy for unresectable hepatocellular carcinoma (uHCC). We aimed to present the efficacy of atezolizumab-bevacizumab combination treatment in patients with uHCC.

Methods: Twenty consecutive uHCC patients who received atezolizumab-bevacizumab were included. Antitumor responses 12 weeks after initiation of atezolizumab-bevacizumab were assessed using Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 and the modified RECIST (mRECIST). Overall survival (OS) and progression-free survival (PFS) were estimated using Kaplan-Meier analysis.

Results: All patients had advanced HCC with a median tumor size of 10 cm. Ten (50%) had macrovascular invasion while 4 (20%) had extrahepatic metastasis. Median number of cycles was 6 with median follow-up period of 10 months. The median OS and PFS were 24 and 14 months, respectively. Child-Pugh A and alpha-fetoprotein less than 400 ng/mL were independently associated with OS. The ORR and DCR were 35% and 76%, and 44% and 75% using RECIST AND mRECIST, respectively. Two (10%) patients had significant downstaging and underwent successful curative-intent microwave ablation.

Conclusions: Response rates in this real-world cohort were comparable to the registration trial. Atezolizumab-bevacizumab followed by curative microwave ablation was achieved in two cases.

Abstract Submission No. 101499
O-0665

LUS and ICG Fluorescence Navigation in Laparoscopic Anatomical Liver Resection

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Anatomical resections, which include the complete removal of an anatomical area that is defined by the vascular supply of the Glissonian branches, have been shown to significantly improve the oncological outcomes and to reduce local recurrence compared with nonanatomical resections in patients with HCC. By approaching the hilum according to specific gates and landmarks including Laennec's capsule, one could identify and divide the pedicle of each segment or subsegment, aiming to a true anatomical resection. The hepatic intersegmental/sectional plane is defined by the border or watershed of each order portal venous territory. Hepatic veins coursing intersegmental/sectional planes are defined as intersegmental/sectional veins. They can play a role of landmark to divide the liver parenchyma appropriately by continuously exposed in the cutting plane. LUS and ICG staining are

recognized as real-time intraoperative tools for identifying intersegmental planes during LALR. The intersegmental planes are visualized not only on the liver surfaces but also on the deep raw surfaces during the liver transection using the ICG fluorescence images.

Abstract Submission No. 101517

O-0666

Elderly patient with advanced HCC who received atezolizumab/bevacizumab and achieved CR by mRECIST

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Case: 80S, male. Chief complaint: body weight loss, appetite loss. Medical history: 10 and 5 years ago, respectively, he received cataract surgery and spinal canal stenosis. Two years ago, he received transfusion for colonic diverticular bleeding. He does not have any tattoos or drug abuse. He drunk one cup of alcohol daily. He regularly went to local doctor for hypertension and diabetes mellitus. Present illness: He decreased body weight (-10 kg/6 months). Two months ago, he felt appetite loss. He was introduced to our department due to multiple liver tumor and suspected lung tumor of right apex area. Present status: The patient's body length and body weight were 172 cm and 65 kg, respectively. His blood pressure, pulse rate, O₂ Saturation and body temperature were 169/67 mmHg, 62/min, 97% and 36.4 °C, respectively. He was conscious, his conjunctiva were no icteric or no anemic, and liver tumor was palpable in right hypochondriac region. No edema exist on foot. His performance status was PS1. Laboratory data: WBC5400/ μ L, Hb 12.0 g/dL, Plt 23,500/ μ L, PT 93%, INR 1.04, TP 6.8 g/dL, Alb 3.7 g/dL, AST 85 IU/L, ALT 18 IU/L, ALP 103 IU/L, G-GTP 690 IU/L, T-BIL 0.42 mg/dL, TCHO 143 mg/dL, Cre 1.12 mg/dL, eGFR 48.7 mL/min, UN 4.2 mg/dL, BS 102 mg/dL, HbA1c 6.4%, HBsAg (-), HCVAb (-), ANA<40, AFP 22,771 ng/mL, AFP-L3 66.0%, PIVKA-II 27 mAU/mL. Computed tomography: 110 mm and other HCC nodules were observed in S4, S5 and S8 of the liver. P4 portal vein was disrupted and swelling of lymph nodes was observed in the paraaortic lesion and other sites. Clinical course: We diagnosed him as HCC stage IVA and started treatment of atezolizumab plus bevacizumab for unresectable HCC and after 6 cools of these combination, complete response was judged by the criteria of modified Response Evaluation Criteria in Solid Tumors (mRECIST). Tumor markers were returned to within normal limits: AFP 1.8 ng/mL, AFP-L3 <0.5%, PIVKA-II 17 mAU/mL.

Conclusion: Combination treatment of atezolizumab plus bevacizumab was effective for elderly patient with unresectable HCC without any serious adverse events.

Abstract Submission No. 101551

O-0667

Baveno VI criteria is inaccurate in predicting high-risk varices in advanced HCC

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The Baveno VI criteria (LSM <20kPa and platelet >150 x 10⁹/L) has been well established in the use of predicting varices needing treatment (VNT) in patients with liver cirrhosis. Yet its use in patients with advanced hepatocellular carcinoma (HCC) has not been validated. HCC alone is accompanied with a higher variceal bleeding risk due to its association with liver cirrhosis and portal vein thrombosis. The use of systemic therapy in advanced HCC has been thought to further augment this risk.

This is a post-hoc analysis of a prospective study on 200 patients with advanced HCC. Patients underwent transient elastography with paired oesophagogastroduodenoscopy within 6 months. Within the entire cohort, 46 patients fulfilled the Baveno VI criteria; 40/46 (87%) patients were correctly identified as not having VNT, while 6/46 (13%) of patients had VNT missed by Baveno VI criteria. Amongst 154 patients who did not fulfil the Baveno VI criteria, 39/154 (25%) patients had VNT. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of Baveno VI criteria for predicting VNT were 86%, 25%, 25% and 86%, respectively.

Of the 135 patients with Child A cirrhosis, 39 patients fulfilled the Baveno VI criteria, with 12% VNT missed rate. In patients with favourable Baveno VI criteria, 0/4 (0%) of BCLC-A patients, 3/14 (21%) of BCLC-B patients and 3/28 (11%) of BCLC-C patients presented with VNT.

In conclusion, favourable Baveno VI criteria are not appropriate to rule-out the presence of high-risk EV, in patients with advanced HCC

Abstract Submission No. 101570

O-0668

Surgical Management of Hepatocellular Carcinoma in Octogenarians: Insights of our Institution

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Background: With the rapid aging population, the opportunity for surgeries among individuals aged 80 years and older has increased. This study aims to evaluate the appropriateness of such procedures.

Methods: A retrospective review of cases involving liver cancer surgeries in patients aged 80 years and above, performed at our hospital from January 1, 2013, to December 31, 2022, was conducted.

Results: The study encompassed 44 cases: 28 males and 16 females, with a median age of 82 years (range: 80-89). Surgical cases gradually increased from 2013-2017 (20 cases, 16.2%) to 2018-2022 (24 cases, 19.8%). Background liver diseases included HBV (3), HCV (17), MASLD (6), alcohol-related (4), and others (14). Pre-existing malignancies were observed in 17 cases (38.6%). Most cases (86.3%) were independent in activities of daily living (ADL), while 13.6% required some form of support. Surgical techniques varied, with partial resection (41%) and anatomical major liver resection (59.1%) being predominant.

Conclusion: Surgical interventions in liver cancer patients aged 80 and above at our institution displayed satisfactory short-term outcomes and comparable long-term results to national surveys. However, cases revealed early discontinuation of follow-up due to declining ADL and a lack of preparedness for appropriate post-recurrence treatments.

Ethical dilemmas regarding invasive surgeries in this age group warrant the establishment of standardized guidelines.

Abstract Submission No. 101611
O-0669

A case of HCC with bone metastasis successfully treated with radiation and cancer immunotherapy.

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Abstract: A 84-year-old man, who refused antiviral therapy for chronic hepatitis C, had been followed up every 6 months for surveillance of hepatocellular carcinoma (HCC). In June X-1, a 20mm hypoechoic mass was found in S8 of the liver. Further examination with EOB-MRI and CT angiography findings were undiagnostic for HCC. In January X, he noticed a 6-cm mass in the left anterior chest wall, and visited us. Chest CT showed bone tumors on 1st and 7th rib. Biopsy of the mass showed plates of cords of cells lined by endothelium and immunostaining of the hepatocyte marker HEP-PAR1 was strongly positive. This led to the diagnosis of rib metastasis of HCC. EOB-MRI of the liver revealed the enlarged S8 mass with intrahepatic metastasis in S6 lesion. With a diagnosed as HCC stage IVB and his liver function as Child-Pugh class A, a combination of atezolizumab and bevacizumab (Atezo/Bev) were initiated in May X. For rib metastases, extracorporeal radiation therapy was also added. The bone tumors shrank in August X. The patient is currently receiving 16 courses of Atezo/Bev and maintaining CR for 1.5 years. **Discussions:** It has been suggested that the combination of immune checkpoint inhibitors and radiation therapy may have a synergistic effect, in which neoantigens resulting from DNA damage in irradiated tumors stimulate antigen-presenting cells, which activate T cells and exert an anti-tumor immune effect on residual tumor cells after irradiation. In this case, combination use of radiation therapy may have enhanced the effect of immune checkpoint inhibitors.

Abstract Submission No. 101617
O-0670

Evaluation of liver functions after liver radiotherapy using blood tests and imaging examinations

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Purpose: Several studies have shown that liver function after radiotherapy using galactosyl human serum albumin (GSA) liver scintigraphy and enhanced MRI. However, there are no reports investigating the relationship between imaging and blood tests.

Therefore, we investigated the changes that occur in the liver between before and after radioltherapy by combining imaging (GSA, CT, and MRI) with blood tests that assess total liver function (albumin-bilirubin (ALBI) grade, ICG-R15).

Methods: 12 patients underwent GSA, MRI, and ICG-R15 testing before treatment, 1 month after treatment, and 3 months after treatment. All patients underwent imaging studies and blood tests at the beginning of treatment, 1 month after treatment, and 3 months after treatment ended. The evaluation items were as follows: 1) changes over time in Child-Pugh classification, ICG-R15, and ALBI values before and after SBRT; 2) changes over time in GSA count and ICG; and 3) selection of the optimal sequence for recognizing radiation hepatitis on MRI.

Results: The ICG values were 14.4 before RT, 17.1 after 1 month, and 17.6 after 3 months. ICG worsened after 1 month of treatment, but was similar after 3 months. ALBI values were -2.61 before RT, -2.67 after 1 month, and -2.71 after 3 months. ALBI worsened slightly over time.

Conclusion: Regarding the ICG-R15, there was an average worsening of 2.8 after 1 month of treatment compared with before SBRT, but only of 0.5 between 1 month and 3 months after SBRT. Therefore, evaluation using ICG-R15 after SBRT after 1 month alone may be sufficient.

Abstract Submission No. 101624
O-0671

TACE with a fine cisplatin powder and porous gelatin particles for TACE-naïve multifocal HCC

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Purpose: A Japanese Interventional oncology group showed the efficacy and safety of nonselective transcatheter arterial chemo embolization (TACE) with a fine cisplatin powder (65mg/m2) and porous gelatin particles without lipiodol for extensive multifocal hepatocellular carcinoma (HCC)(1). The aim of this study is to evaluate the efficacy and safety of this type of TACE for the whole liver in a single center.

Material and methods: We retrospectively reviewed our medical records of TACE-naïve multifocal HCC patients (Child Pugh A, up to 7 out) who had undergone TACE for the whole liver with a fine cisplatin powder and porous gelatin particles between 2006 and 2019.

Results: There was 60 patients. The median age of the patients was 71 years (range 35-88). Child Pugh 5 was 41 patients (68.3%). The median maximum size of tumors was 26mm (range 8-184mm). Overall survival was 30.3 months. Progression free survival was 4.8 months. Initial evaluation with contrast enhanced CT was done (mean 45days later) with modified RECIST (Response Evaluation Criteria in Solid Tumors). Overall response rate was 65% (complete response 13, partial response 26). Disease control rate was 86.7% (stable disease 13, Progressive disease 8). At the time of initial evaluation, 8 patients' liver function had dropped to Child Pugh B (13.3%).

Conclusion: Although TACE with a fine cisplatin powder and porous gelatin particles for the whole liver was effective for the tumor reduction, we have to be careful not to lose liver function for further post-treatment.

Abstract Submission No. 101658
O-0672

Current status of initial treatment for elderly patients with hepatocellular carcinoma

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Background: To decide the treatment strategy for hepatocellular carcinoma (HCC), not only hepatic reserve and tumor conditions, but also comorbidities and age are considered. There are no clear criteria for comorbidities and age as indications for treatment for HCC.

Methods: We reviewed 317 patients who underwent standard treatment (resection or RFA) for HCC of less than 3 cm and 3 or less during the period from January 2009 to December 2018 at our institution and analysis background liver disease, tumor conditions, hepatic reserve, and prognosis. Furthermore, we compared across the age groups of 65 years (WHO criteria for elderly patients) and 80 years (age group excluded from the SURF study).

Results: In 293 of 317 patients (92%), prognosis, including recurrence and cause of death, was traceable. Overall, 62.8% had a single tumor, mean tumor diameter 18.9 mm, Child-Pugh Score A in 79.4%, median OS 70 months, median RFS 24 months, 3-year survival 78.9%, 5-year survival 55.8%, cause of death 37.5% liver cancer death and 39.8% other disease death. Of the 317 patients, 91 were younger than 65 years, 178 were 65-79 years, and 48 were older than 80 years. Tumor conditions and liver reserve were similar for all ages. For patients <65/65-79/80+ years old, median OS was 85/68/55 months, median RFS was 27/24/24 months, 3-year survival rate was 82/79/69%, 5-year survival rate was 69/59/48%. The cause of death in 43/37/33% of the patients was death from liver cancer and 31/39/53% from other diseases. 2 in the 65-79 age group and 2 in the 80+ age group had comorbidity as a prognostic factor before initial treatment, and only one of each of these patients actually died of other causes.

Conclusion: Tumor conditions and hepatic reserve were similar in each generation, but the prognosis was significantly worse in the elderly, with more deaths from other causes. It should be noted that these results were obtained even in a population in which the standard of care was judged to be appropriate after discussion at the Cancer Board. The results suggest that a new criteria for determining Fit or Unfit for standard treatment is needed.

Abstract Submission No. 101761
O-0673

Cardiovascular profile of patients with hepatocellular carcinoma: Kazakhstan study population

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Aim: To study the cardiovascular profile of patients suffering from hepatocellular carcinoma who were treated with TACE.

A retrospective analysis of the medical records of 130 patients with hepatocellular carcinoma for the period from 2020-2022 was carried out. The analysis was carried out within the framework of the grant project of the Ministry of Education and Science of the Republic of Kazakhstan IRN AR 19176025 (2023-2024).

Results: Of 130 patients with hepatocellular carcinoma, 71 (54.7%) were men. The average age of the patients in the sample was 63.8±5.78 years. The average duration of the disease was 17.8 months. All patients received targeted therapy with sorafenib in combination with TACE of the hepatic artery. Cardiovascular diseases were present in 47% of patients, among whom arterial hypertension was in the first place and the development of chronic heart failure with a preserved left ventricular ejection fraction. After the diagnosis of hepatocellular carcinoma, 4 patients were exposed to chronic coronary syndrome and two developed atrial fibrillation. Echocardiography analysis shows an increase in the transverse size of the left atrium in patients without

cardiovascular diseases (40,8±0,6mm, p<0,05), as well as the tendency to prolong the PQ interval on electrocardiography (19,8±0,9mm, p>0,05), but having no statistically significant difference.

Conclusion: these data are the initial stage of a prospective study to study the state of the cardiovascular system in patients with liver cancer who are on different schemes of antitumor therapy and reflect the prerequisites for the development of cardiotoxicity.

Abstract Submission No. 101776
O-0674

ECG markers of cardiotoxicity of TACE in patients with primary liver cancer

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Relevance of the study: The cardiotoxic effect of chemotherapy can be manifested by a large spectrum of changes on the ECG, among which tachycardia, changes in the ST segment and T wave, ectopic atrial rhythms, intraventricular blockages, prolongation of the QTc interval, prolongation of the PQ interval are leading.

Aim: To describe the effect of chemotherapy in patients with liver cancer on ECG changes in the electrical activity of the heart.

Findings: The results of the thesis are a sub-analysis in a prospective study under the grant of the Ministry of Education and Science of the Republic of Kazakhstan IRN AR 14870224 (2022-2024). ECGs of 59 patients over 18 years old were analyzed, 23 received traditional systemic chemotherapy and 36 underwent TACE. The average age of patients was 60.8±11.1 years. The average duration of disease is 9.1±7.2 months. Incomplete blockage of the right leg of the His bundle, complete blockage of the right leg of the His bundle and blockage of the anterior-upper branching were recorded in 4 patients, 2 of them received gemcitabine and 2 oxaliplatin therapy. Resting heart rate was significantly higher in the targeted therapy group (88.4±12.8 per minute versus 71.1±9.1 per minute in the traditional chemotherapy group, p = 0.042). Also, resting heart rate was significantly higher in the targeted therapy group versus the TACE group (88.4±12.8 per minute versus 74.3±10.8 per minute, p=0.047).

Conclusions: Early detection of initial abnormalities, including on an ECG, can help to correct chemotherapy and prevent fatal complications in this group of severe patients.

Abstract Submission No. 101792
O-0675

Impact of surgical resection of initially unresectable HCC after LEN or ATZ+BEV treatment

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Background: Recent introduction of immune-checkpoint inhibitors or targeted therapy has facilitated the surgical resection after drug therapy for initially unresectable hepatocellular carcinoma (HCC).

Methods and Patients: Between 2018 and 2023, 39 consecutive patients who received lenvatinib (LEN) or atezolizumab + bevacizumab (ATB) for initially unresectable HCC. Unresectable HCC involved

patients with 4 or more nodule ($n = 14$), refractoriness to TACE ($n = 11$), extrahepatic diseases ($n = 16$) or vp3 or vv3 ($n = 8$) and others ($n = 3$).

Results: Responses to LEN and ATB were PR in 5% and 20%, SD in 53% and 40%, PD in 10% and 0%, respectively in mRECIST. No significant difference was found in the disease control rates between LEN and ATB (63% vs 40%, $p = 0.15$). Surgical resection was performed in five patients (13%) who received LEN ($n = 2$) and ATB ($n = 3$). Progression survival was better in 5 patients who underwent surgery than in 18 patients who continued non-surgical treatments after first therapy (median, 18 vs 6 months, $p = 0.02$). However, no significant difference was found in disease specific overall survivals between patients undergoing surgery and non-surgical treatments (median, 23 vs 22 months, $p = 0.24$).

Conclusion: Aggressive surgery for initially unresectable HCC after LEN and ATB treatments offered favorable progression free survival. Local therapy after systemic therapy may play an important role in the treatment of advanced HCC.

Abstract Submission No. 101817
O-0676

Influence of DOAC on bleeding events of atezolizumab and bevacizumab therapy

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Background: Bevacizumab has the bleeding risk, because bevacizumab inhibits angiogenesis. DOACs (Direct Oral Anti Coagulants) are increasingly used in cancer patients because of their attractive characteristics such as no coagulation test monitoring required. There are concerns that the combination of bevacizumab and DOACs may increase bleeding events. We analyzed the influence of DOACs on bleeding risk during atezolizumab and bevacizumab regimens (Atezo/Bev).

Methods: The retrospective study included 59 patients with hepatocellular carcinoma (HCC) and 82 patients with lung cancer who received Atezo/Bev. Exclusion criteria were the administration of antithrombotic agents other than DOACs.

Results: No significant difference was observed in bleeding events between the DOAC group (1/11 patients, none with Gr.2 or higher) and the no-antithrombotic drug (14/130 patients, 4 patients with Gr.2 or higher) groups ($p = 1.000$). Regarding factors contributing to bleeding events, DOAC administration had a HR of 1.357; 95% CI: 0.175-10.54; $p = 0.770$. Multivariate analysis showed that hypoalbuminemia was an independent factor contributing to bleeding (HR 0.298; 95% CI: 0.105-0.847; $p = 0.006$). As for analysis of only patients with HCC, bleeding events were not observed in the DOAC group (5 patients), but occurred in 8 patients in the no-antithrombotic agent group (8/54 patients, 3 patients with Gr.2 or higher) with no significant difference ($p = 0.808$). High ALBI score was an independent factor contributing to bleeding (HR 9.083; 95% CI: 1.118-73.76; $p = 0.039$).

Conclusions: In the DOAC group, there were no cases in which Atezo/Bev was discontinued due to bleeding. Atezo/Bev may be safely administered under surveillance in patients taking DOAC.

Abstract Submission No. 101824
O-0677

Development of a new model to predict survival duration with HCC patients in BCLC C stage

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Background: Systemic therapy is mainly indicated for HCC patients in advanced stage. It is difficult to evaluate the individual therapy whether it is appropriate or not in real world. Recently, we have developed a Weibull model prediction of survival duration in patients with intermediate stage (Sci Rep 2023). Based on this model, we next aimed to develop a new model to predict survival duration in patients with advanced stage.

Methods: 750 patients from 2005 to 2017 were enrolled in this cohort. Any therapies were admitted but just one TKI, Sorafenib, could be used. The survival related factors were extracted by the cox proportional hazard regression model. The expectation of survival duration model was developed by exponentiated Weibull distribution.

Results: The median ALBI score was -2.18. Macrovascular invasion shown 76.7% and extrahepatic metastases was 35.3%. The multivariate Cox proportional hazards analysis showed significant difference in ALBI score including with T-bil, albumin and AFP, age, naïve or recurrence, the number of nodules, the size of the largest nodule, the presence of macrovascular invasion and extrahepatic metastases. The survival curb continuously corresponded with exponentiated Weibull distribution. The new survival model for patients with BCLC C stage was developed based on these nine factors.

Conclusion: This survival model is useful in epidemiologic research and in clinical practice for patient counseling, prognostication and comparison with survival duration after multi MTA era.

Abstract Submission No. 101853
O-0678

Biomarker discovery for HCC detection and prognosis via plasma cfDNA methylome profiling

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Purpose: This study aims to develop methods for detection, prognosis and stratification of HCC using plasma cfDNA methylome profiling using whole genome bisulfite sequencing (WGBS) and targeted bisulfite sequencing (TBS).

Experimental Design: Plasma cfDNAs were isolated from a total of 311 participants including 70 healthy individuals, 46 patients with HBV, 45 patients with cirrhosis, and 150 HCC patients. Two cfDNA

methylation sequencing assays were performed using WGBS and TBS, respectively, and a machine learning method for cancer detection based on genome wide differentially methylated regions (DMR) between HCC and other groups was used to establish early detection, prognosis and stratification model for HCC.

Results: WGBS analysis achieved overall sensitivity of 85.37% at 82.35% specificity to discriminate all stages of HCC patients from healthy people, and sensitivity of 92.31% at 88.24% specificity to discriminate early stage HCC patients from healthy people, while the TBS analysis showed better performance of 95.65% sensitivity at 83.33% specificity to discriminate all stages of HCC patients from healthy people, and sensitivity of 85.71% at 83.33% specificity to discriminate early stage HCC patients from healthy people. Additionally, a number of significant DMRs between HCC and none-cancer groups were identified, providing candidate biomarkers for HCC detection and prognosis.

Conclusions: This study provides preliminary proof for the feasibility of plasma cfDNA methylomes profiling for HCC detection, staging and prognosis. WGBS showed genome wide methylation profile while TBS provide in-depth analysis of highly relevant genomic regions with discrepancies of methylation levels between different groups yielding potential biomarkers for HCC detection.

Abstract Submission No. 101867

O-0679

Risk of HCC occurrence after antiviral therapy for CHC: A systematic review and meta-analysis

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Background: The risk of hepatocellular carcinoma (HCC) occurrence following anti-viral therapy in patients with chronic hepatitis C (CHC) remains unclear. The study aimed to estimate HCC occurrence rate following sustained virological response (SVR), among different subgroups.

Methods: A search was performed for articles published between January 2017 and July 2022. Studies were included if they assessed HCC occurrence rate in CHC patients following anti-HCV therapy. Random effects meta-analysis was used to synthesis the results from individual studies.

Results: A total of 27 studies including 33,500 patients (IFN-based=6, DAA=21; prospective=10, retrospective=17) were included in the review. HCC occurrence was significantly lower in CHC with SVR (1.52 patient-year (py), 95% CI 1.45, 1.61) in CHC patients who achieved SVR which was significantly lower than those in non-responders (6.23 py, 95% CI 5.29, 7.34). Stratified by HCV treatment regimens, HCC occurrence following SVR was 1.11 per 100 py (95% CI 0.95, 1.30) and 1.59 per 100 py (95% CI 1.50, 1.68) in IFN- and DAA-treated based studies. HCC occurrence was 1.18 per 100 py (95% CI 1.12, 1.24) across all fibrosis stages and rose to 1.62 per 100 py (95% CI 1.39, 1.89) in studies focused on advanced fibrosis or cirrhosis. Further

meta-regression analysis showed that neither treatment type nor liver fibrosis stage was associated with a higher HCC occurrence rate.

Conclusion: HCC occurrence was significantly lower in SVR population than in NR population. However, we found no significant difference in HCC risk following SVR between two therapies or different fibrosis stages.

Abstract Submission No. 101911

O-0680

Association of ABO blood groups and Rh<stro

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Background: Primary liver cancer (PLC) is one of the most common cancers worldwide. ABO blood groups and Rhesus (Rh) factor are inherited characteristics. Their association with the presence of PLC remains unclear in cirrhotic patients.

Methods: Patients with liver cirrhosis who were consecutively admitted to our hospital from January 1, 2010 to June 30, 2014 were retrospectively screened. Logistic regression analyses were performed to explore the association of ABO blood groups and Rh factor with PLC in cirrhotic patients. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were calculated after adjusting for gender, age, family history of liver cirrhosis, HBV-DNA positivity, and etiology of cirrhosis. Subgroups analyses were performed according to different etiologies of liver cirrhosis.

Results: Overall, 1158 cirrhotic patients without PLC and 240 cirrhotic patients with PLC were included. After adjusting for confounding factors, non-O blood group (aOR=0.763; 95%CI=0.449-1.298, p=0.319), A blood group (aOR=0.643; 95%CI=0.332-1.246, p=0.191), B blood group (aOR=0.835; 95%CI=0.453-1.540, p=0.564), AB blood group (aOR=0.888; 95%CI=0.363-2.170, p=0.795), and Rh (+) (aOR=0.239; 95%CI=0.036-1.571, p=0.136) were not independently associated with PLC in cirrhotic patients. In the subgroup analysis of HBV-related cirrhotic patients, the proportion of A blood group was significantly lower in cirrhotic patients with PLC than those without (24.17% vs. 33.99%, p<0.001); however, in those of HCV and alcohol-related cirrhotic patients, the proportions of ABO blood groups and Rh factor were not significantly different between the two groups.

Conclusions: ABO blood groups and Rh factor may not be associated with the presence of PLC in liver cirrhosis.

Abstract Submission No. 101921

O-0681

Non-contrast Abbreviated MRI for the Detection of Hepatocellular Carcinoma

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Background/Aim: Given limited ultrasound sensitivity in hepatocellular carcinoma (HCC) surveillance, and few prospective studies exploring non-contrast abbreviated MRI (NC-AMRI) for this purpose,

this study aimed to assess diagnostic performance of NC-AMRI in detecting HCC.

Materials and Methods: This ongoing prospective study involves cirrhotic patients with LI-RADS LR-2, LR-3, and LR-4 findings in MRI. Patients underwent one to three complete contrast-enhanced MRI rounds (CE-MRI). NC-AMRI included diffusion-weighted (DWI), T1-weighted gradient imaging (T1WI), and T2-weighted imaging (T2WI-FS). Diagnostic performances of surveillance protocols were analyzed.

Results: In 101 follow-up CE-MRI examinations, the median (IQR) age of patients is 64 years (55-70), comprising 61% males and 39% females. Hepatitis C (37%) and hepatitis B (33%) were the predominant underlying liver diseases, followed by alcoholic liver disease (15%) and steatotic liver disease (6%). T1WI, T2WI, and combined T1WI/T2WI exhibited identical sensitivities at 91.7%(95%CI:61.5-99.8), while NC-AMRI (T1WI,T2WI,andDWI) and DWI alone showed similar sensitivities at 90.0%(55.5-99.7). Combined T1WI/T2WI demonstrated highest specificity (95.5%,95%CI:88.9-98.8), the highest PPV (73.3%,95%CI:44.9-92.2), and highest diagnostic accuracy (95.0%,95%CI:88.9-98.4). AUROCs and NPVs were similar across all surveillance protocols. Ten patients(9.9%) diagnosed with HCC had mean solitary lesion sizes of 2.1±1.3cm. Staging revealed 7 BCLC-0, 1 BCLC-A, and 2 BCLC-B cases, mostly CTP-A (9 patients) and one CTP-B. Median(IQR) AFP among HCC patients was 4.46 ng/mL(1.79-22.8). Only one HCC case escaped NC-AMRI detection, a single 0.8 cm lesion in segment V with an AFP of 1.21 ng/mL.

Conclusion: NC-AMRI proves clinically feasible, and exhibits high diagnostic performance in detecting HCC demonstrating superior accuracy compared to ultrasound.

Abstract Submission No. 101966
O-0682

Effectiveness and tolerability of camrelizumab therapy for elderly patients with advanced HCC

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Objective: There is a lack of effective PD-1-targeted immunotherapy with good tolerability in elderly patients with advanced hepatocellular carcinoma (HCC). We aimed to assess elderly patient outcomes after combined camrelizumab and molecular targeted therapy in China.

Methods: The study included 99 advanced HCC patients (27 patients aged ≥65 years and 72 patients aged <65 years), 84 out of them received camrelizumab combined with molecular targeted therapy from 01/01/2019-03/03/2021. Overall survival (OS), progression-free survival (PFS), objective response rate (ORR), disease control rate (DCR), and adverse events (AEs) were assessed.

Results: The median follow up was 12.1 months. For patients aged ≥65 years, the OS probability at 12-months, ORR and DCR were 67.8%, 44.4% and 74.1%, respectively, and the median PFS was 6.4 months (95%CI 3.0-12.4), which were comparable with patients aged <65 years. The median OS for elderly patients group was unavailable, and 18.9 months (95%CI 8.9-20.5) for patients aged <65 years(Fig.1). In multivariate analysis, macrovascular infiltration (MVI), but not sex, age, HBV etiology, extrahepatic metastasis, Child-Pugh B or AFP >400ng/ml associated with 6-months PFS (HR2.60, 95%CI1.14-5.96, P=0.024) and DCR (HR3.96, 95%CI1.67-9.39, P=0.002). Any and grade 3/4 immune-related AEs occurred in 51.9% and 25.9% in elderly patients group, similar to young patients. In both groups, the most common AEs were immune thrombocytopenia(28.3%).

Conclusion: The effectiveness and tolerability of camrelizumab combined with molecular targeted drugs therapy in the elderly patients with unresectable/advanced HCC is similar to patients aged <65 years. MVI was associated with suboptimal immunotherapy response and poor prognosis.

Abstract Submission No. 101984
O-0683

Factors enhancing local control of TACE recommended in BCLC strategy 2022-update for BCLC-0&A HCC

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Backgrounds: BCLC strategy 2022-update recommended TACE as an alternative treatment when curative treatment is not possible. This study aims to clarify therapeutic effects of TACE on single, treatment-naïve HCC corresponding to BCLC stage 0&A HCC. Factors enhancing local control effect of TACE were retrospectively evaluated.

Methods: This study investigated cases of Lip-TACE performed between 2010 and 2019. Factors contributing to local control effect were age, sex, Child-Pugh Score, tumor diameter, tumor location, AFP, PIVKA-II, number of vessels to tumor, and Lipiodol accumulation around tumor. Local recurrence free survival (LRFS) was statistically evaluated using Kaplan-Meier curves.

Results: Seventy-three cases were included in this study. Median LRFS for 73 nodules was 73.6 months. The peripheral tumor-location group, the single feeder group, and the group with Lipiodol accumulation around tumor had a longer LRFS than the central tumor group, the multiple feeder group, and the group without Lipiodol accumulation around tumor, respectively (median LRFS: Unreached vs. 9.9 months; Unreached vs. 10.9 months; Unreached vs. 5.6 months). In multivariate analysis, the central tumor group, the multiple feeder group, and the group without Lipiodol accumulation around the tumor showed a high hazard ratio for shortening LRFS (hazard ratio; 3.81; 1.80; 1.98). LRFS was significantly longer in these 3-factor integration group than in the others (Unreached vs. 16.2 months). The 1-year local control rate was 85.1% vs. 54.9%, and Both 3- and 5-year local control rates were 77.6% vs. 36.5%.

Conclusions: Factors enhancing local control effect of TACE for BCLC stage 0&A HCC was identified.

Abstract Submission No. 102028
O-0684

Insulin Growth Factor-1 Level as a Disease Course Predictor in Hepatocellular Carcinoma Patients

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Background: The insulin-like growth factor (IGF) axis has important autocrine, paracrine and endocrine roles in growth promotion. Alterations of the IGF system have recently been implicated in the pathogenesis of several malignancies, but the relation to hepatocellular carcinoma (HCC) risk is unclear. This study aimed to determine whether serum IGF-1 level predict the progression and survival in HCC patients.

Methods: According to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines, we systematically searched Pubmed, EMBASE and Cochrane Central database through the end of October 2023 to identify all studies reporting association between serum IGF-1 level and HCC. A total of 13 cohort studies with calculation of relative risk (RR) of serum IGF-1 for HCC time-to-progression (TTP) and overall survival (OS) were subjected to statistical analysis using STATA 17. We assessed the ability of serum IGF-1 to predict HCC progression and survival using random effect model to estimate pooled RR. Heterogeneity among studies was assessed by the Cochran's Q and I² statistics. Publication bias was analysed using a Begg funnel plot and Egger test.

Results: The meta-analysis of selected studies showed that low level of serum IGF-1 significantly predicted shorter TTP (RR 2.36; 95% CI 1.51-3.68) and poorer OS (RR 2.17; 95% CI 1.72-2.74) in HCC patients, *p* value=0.00.

Conclusions: IGF-1 serum level independently predicted the progression and survival in HCC patients. Larger scale studies are needed to investigate the relationship explanation.

Abstract Submission No. 102044

O-0685

Efficacy and safety of arterial infusion chemotherapy in patients with Child-Pugh class B

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Introduction: Although many treatment options are available for patients with advanced hepatocellular carcinoma and Child-Pugh class A, those for patients with Child-Pugh class B remain limited. We aimed to assess the safety and efficacy of hepatic arterial infusion chemotherapy using 5-fluorouracil and cisplatin in patients with advanced hepatocellular carcinoma and Child-Pugh class B.

Methods: Sixty patients who received hepatic arterial infusion chemotherapy with 5-fluorouracil and cisplatin at Kurume Chuo Hospital between April 2012 and March 2021 were recruited. Cisplatin (30 mg administered over 2 hours) and 5-fluorouracil (1,250 mg, 72-hour constant infusion) were administered to the tumor-feeding artery every 2 weeks. The primary endpoint was overall survival, while the secondary endpoints were progression-free survival and adverse effects.

Results: Among the 60 patients, Child-Pugh class A and class B were noted in 30 patients each. Overall survival did not significantly differ

between the two classes. After 4 weeks of hepatic arterial infusion chemotherapy with 5-fluorouracil and cisplatin, 12 patients in the class B group exhibited improved Child-Pugh scores relative to those at the start of treatment. There was a significant difference in overall survival between patients whose Child-Pugh scores had improved and those whose scores remained unchanged or had worsened.

Conclusions: Hepatic arterial infusion chemotherapy using 5-fluorouracil and cisplatin is effective and safe for patients with Child-Pugh class B, and improvements in Child-Pugh scores after 4 weeks of this therapy may represent a predictive marker of treatment efficacy regardless of pretreatment Child-Pugh score in Child-Pugh B patients.

Abstract Submission No. 102050

O-0686

Systemic Therapy in HCC Patients with Marginal Liver Function: Atezolizumab/Bevacizumab vs Sorafenib

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Background and Aim: The superiority of the combination of atezolizumab with bevacizumab (atezo/bev) in unresectable hepatocellular carcinoma (uHCC) patients with marginal liver function remains uncertain. The goal of the study is to compare the efficacy and safety of atezo/bev to sorafenib in real-world patients with uHCC with marginal liver function.

Method: This single institution retrospective cohort study analyzed patients with uHCC whose liver function improved from Child-Pugh B to Child-Pugh A through supportive care, and subsequently received atezo/bev (*n*=32) or sorafenib (*n*=32) as first-line therapy between August 2020 and February 2023. Outcomes were progression free survival (PFS), overall survival (OS), and adverse events (AEs).

Results: In patients with baseline liver function of Child-Pugh B, atezo/bev had significantly better PFS than sorafenib (mPFS 4.3 vs. 2.7 months, log rank *p* = 0.024) and a tendency to improved OS (mOS 8.3 vs. 6.6 months, log rank *p* = 0.13). When compared to sorafenib, atezo/bev significantly improved PFS, particularly in patients with Child-Pugh B7 (mPFS 4.3 vs. 2.4 months, log rank *p* = 0.009) or a serum AFP level of 200 ug/ml or higher (mPFS 2.9 vs. 2.4 months, log rank *p* = 0.038). The two groups reported different types of AEs, but there was no difference in the incidence of overall AEs including bleeding.

Conclusion: Atezo/bev may be recommended as the first-line treatment of choice for patients with marginal liver function, especially for those with Child-Pugh B7, based on both efficacy and safety.

Abstract Submission No. 102077

O-0687

Liver resection for hepatocellular carcinoma focused on the fourth branch of the portal vein

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Background: The third branch of the portal vein could be removed in the segmentectomy for hepatocellular carcinoma (HCC). This study aims to investigate whether removing the fourth portal branch affects the outcome after liver resection (LR) for HCC less than segmentectomy.

Methods: Patients who received LR less than segmentectomy for solitary HCC between 2015 and 2022 were evaluated. Compared presurgical to postsurgical dynamic-computed tomography (CT), patients were divided into two groups; patients who received the removal of the fourth portal branch which was the tumor responsibility as Anatomical (A) group, and the other as Non-anatomical (NA) group.

Results: Of the 258 LRs for HCC, 96 were eligible. Maximum tumor diameter was 2.2 (0.7-10) cm, and the proportion of portal and hepatic venous invasion were 18%, and 15%. Median operation time and blood loss were 315 (118-874) minutes, and 66 (0-3007) ml. The 5-year overall survival (OS) rate was 74.8%, and median survival time (MST) for recurrence-free survival (RFS) was 54 months. Comparing groups A (n=51) and NA (n=45), oncological covariates were similar, but group A showed lower total bilirubin (T-bil) (0.80 vs. 0.90mg/dl, P=0.04), type IV collagen 7S (IV-C7S) (4.35 vs. 5.10ng/ml, P=0.04). The 5-year OS was similar, but the RFS was better in group A (MST; 55 vs. 17 months, P=0.004). After risk-adjusted with T-bil and IV-C7S, group A showed a significantly lower risk for recurrence (aHR 0.44, 95%CI 0.21-0.91, P=0.02).

Conclusions: LR for HCC with the accurate removal of the fourth portal branch might lead to a reduction of short-term recurrence in the remnant liver.

Abstract Submission No. 102081

O-0688

the prediction models for post-hepatectomy liver failure based on the type IV collagen 7s domain

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Backgrounds: We aimed to develop the prediction models for post-hepatectomy liver failure (PHLF) based on the type IV collagen 7s domain (7s collagen) in patients with hepatocellular carcinoma (HCC).

Methods: We retrospectively collected the data from 972 patients with HCC who underwent initial and curative liver resection between February 2000 and December 2020 in our hospital. Multivariable logistic regression analysis using a restricted cubic spline was performed to evaluate the effect of 7s collagen on the incidence of PHLF. The nomogram was developed based on 7s collagen.

Results: PHLF grade B or C was identified in 104 patients (11%), of which 98 patients (10%) for PHLF grade B, 6 patients (1%) for PHLF grade C. In multivariate logistic regression analysis, preoperative serum level of 7s collagen was significantly associated with a proportional increase in PHLF risk. Its correlation with PHLF risk was confirmed in both laparoscopic and open liver resections. Alanine aminotransferase, Child-Pugh class B, 7s collagen, open liver resection, and extent of liver resection were found to be independent risk factors for PHLF. We developed the nomogram based on 7s collagen with a concordance index of 0.763.

Conclusion: 7s collagen is a useful predictive factor for PHLF. The current nomogram using 7s collagen would be useful to predict PHLF risk.

Abstract Submission No. 102087

O-0689

Outcomes of surgical resection of hepatocellular carcinoma with non-alcoholic fatty liver disease

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Background: It has been reported that there are oncological differences between hepatocellular carcinoma (HCC) related to non-alcoholic fatty liver disease (NAFLD) and HCC related to viral infections. However, the surgical short-term and long-term outcomes of NAFLD-related HCC remain unclear.

Methods: We retrospectively analyzed patients who underwent hepatectomy for HCC among a total of 1,047 cases. Patients with NAFLD and those with viral hepatitis infection were included in the analysis. Clinical, surgical, and pathological results were compared between the two groups. Postoperative survival rates and patterns of recurrence were also analyzed for both groups.

Results: The NAFLD group consisted of 57 patients, while the viral hepatitis (VH) group consisted of 727 patients. Body mass index (BMI) and serum HbA1c levels were significantly higher in the NAFLD group than in the VH group (BMI: 23.8 vs. 22.6; p=0.003, HbA1c (%): 6.4 vs. 5.3; p<0.001). There were no significant differences in serum albumin, serum bilirubin levels, Child-Pugh classification, or degree of liver damage between the two groups. In terms of short-term outcomes, there were no significant differences in operative time, bleeding volume, complication rates, or length of postoperative hospital stay between the groups. Pathologically, tumor size was significantly larger in the NAFLD group than in the VH group (4.7 cm vs. 2.7 cm, p=0.003), and there was a tendency for more advanced UICC stage in the NAFLD group. Overall survival and recurrence-free survival did not significantly differ between the two groups (5-year overall survival rate (%): 58.1 vs. 52.8, p=0.827; 5-year recurrence-free survival rate (%): 29.6 vs. 21.3, p=0.827). However, the NAFLD group had a significantly higher incidence of extrahepatic recurrence compared to the VH group (15.1% vs. 3.8%, p<0.001). Furthermore, in a subgroup analysis with matched tumor sizes, NAFLD-HCC patients demonstrated better postoperative outcomes (5-year overall survival rate (%): 78.6 vs. 55.3, p=0.023; 5-year recurrence-free survival rate (%): 83.3 vs. 19.8, p<0.001).

Conclusions: Surgical outcomes following hepatectomy for NAFLD-HCC were found to be comparable to those for VH-HCC. For NAFLD-HCC patients, early detection, surgical resection, and active intervention for extrahepatic metastasis and recurrence may lead to improved prognosis.

Abstract Submission No. 200007

O-0690

2D-SWE in HCC: Accessing and Predicting Liver Function

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Aim: The present study aimed to observe the dynamic changes in liver function from the pre- to post-hepatectomy period, and explore the correlation between hepatic two-dimensional shear wave elastography (2D-SWE) measurement and pre- and post-hepatectomy liver function in patients with hepatocellular carcinoma (HCC) and chronic hepatitis B (CHB).

Material and Methods: From August 2019 to August 2023, 250 patients with treatment-naïve HCC as well as CHB and undergoing hepatectomy were consecutively enrolled. Before reaching the study endpoint (recurrence, death, or initiation of subsequent treatment for HCC), patients were followed up for one year. Liver function and other relevant indicators of liver condition were collected at postoperative day 5, 1 month, 3 months, 6 months, and 12 months, respectively. Statistical analysis was conducted to explore the correlation between 2D-SWE measured liver stiffness (LS) and liver function during the follow-up.

Results: Correlation analysis showed that the pre-operative measurement of LS was positively correlated with pre-operative liver function indicators (represented by the most commonly used Child-Pugh and albumin-bilirubin systems, both with $p < 0.05$), and there was a significant positive correlation between pre-operative LS and liver function at post-operative 5 days, 1 month, 3 months, and 1 year (all with $p < 0.050$). But the correlation between LS and liver function at different time points from pre-operative to post-operative was inconsistent, and receiver operating characteristic analysis revealed that the LS cutoff values for distinguishing different liver function grades were not consistent at different time points.

Conclusion: Pre-operative 2D-SWE LS measurements appeared to have a certain degree of assessment and predictive value for liver function in HCC patients with concomitant CHB, and can assist in the non-invasive and straightforward evaluation of liver function and the assessment of recovery in HCC surgery patients.

Abstract Submission No. 102010

O-0691

Effectiveness and tolerability of camrelizumab therapy for elderly patients with advanced HCC

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Objective: There is a lack of effective PD-1-targeted immunotherapy with good tolerability in elderly patients with advanced hepatocellular carcinoma (HCC). We aimed to assess elderly patient outcomes after combined camrelizumab and molecular targeted therapy in China.

Methods: The study included 99 advanced HCC patients (27 patients aged ≥ 65 years and 72 patients aged < 65 years), 84 out of them

received camrelizumab combined with molecular targeted therapy from 01/01/2019-03/03/2021. Overall survival (OS), progression-free survival (PFS), objective response rate (ORR), disease control rate (DCR), and adverse events (AEs) were assessed.

Results: The median follow up was 12.1 months. For patients aged ≥ 65 years, the OS probability at 12-months, ORR and DCR were 67.8%, 44.4% and 74.1%, respectively, and the median PFS was 6.4 months (95%CI 3.0-12.4), which were comparable with patients aged < 65 years. The median OS for elderly patients group was unavailable, and 18.9 months (95%CI 8.9-20.5) for patients aged < 65 years (Fig.1). In multivariate analysis, macrovascular infiltration (MVI), but not sex, age, HBV etiology, extrahepatic metastasis, Child-Pugh B or AFP > 400 ng/ml associated with 6-months PFS (HR2.60, 95%CI1.14-5.96, $P=0.024$) and DCR (HR3.96, 95%CI1.67-9.39, $P=0.002$). Any and grade 3/4 immune-related AEs occurred in 51.9% and 25.9% in elderly patients group, similar to young patients. In both groups, the most common AEs were immune thrombocytopenia (28.3%).

Conclusion: The effectiveness and tolerability of camrelizumab combined with molecular targeted drugs therapy in the elderly patients with unresectable/advanced HCC is similar to patients aged < 65 years. MVI was associated with suboptimal immunotherapy response and poor prognosis.

Abstract Submission No. 200009

O-0692

Assessment of Liver Function by 2D-SWE in HCC at Different HBV Infection Status

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Purpose: Liver function is one of the most relevant influencing factors in the prognosis of patients with hepatocellular carcinoma (HCC). Liver stiffness (LS) measured by two-dimensional shear wave elastography was reported to be able to assess preoperative liver function in HCC patients. However, the influencing factors of which was not well address. The present study aimed to evaluate the feasibility of LS in assessing liver function in patients with HCC and chronic hepatitis B (CHB), as well as to assess potential influencing factors thereof in different hepatitis virus infection status and different hepatitis B viral (HBV) DNA levels.

Methods: Between August 2018 and May 2021, 284 patients were retrospectively recruited and were classified into two groups according to serum HBV-DNA levels [HBV-DNA ≥ 100.00 IU/mL as Pos group ($n=200$) and < 100.00 IU/mL as Neg group ($n=84$)]. Correlation analyses and receiver operating characteristic analyses were performed to evaluate the relationship between LS and liver function.

Results: The two groups showed no significant difference regarding LS ($p=0.453$) and Child-Pugh (CP) score ($p=0.200$), while a significant difference was shown regarding albumin-bilirubin (ALBI) score ($p=0.036$). A significant correlation was found in both groups between LS and liver function indexes ($p < 0.05$). When alanine aminotransferase (ALT) ≤ 40 U/L, LS was correlated with liver function ($p < 0.05$), but the LS cutoff value to differentiate a CP 5 score was higher in the Neg group (9.30 kPa) than Pos group (7.40 kPa). While when ALT > 40 U/L, LS was not very accurate in differentiating different liver function scores ($p > 0.05$).

Conclusions: LS was correlated with most liver function indexes in patients with CHB and HCC, while the correlation was different according to the levels of HBV-DNA and transferase.

Abstract Submission No. 200017
O-0693

Conversion surgery for hepatocellular carcinoma; relationship between the necrosis rate and outcome

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Background: We have performed conversion surgery for patients with unresectable locally advanced hepatocellular carcinoma (LA-HCC) using hepatic arterial infusion chemotherapy (HAIC). Here, we examine the relationship between pathological tumor necrosis rate and prognosis.

Methods: Patients with LA-HCC who have performed conversion surgery after HAIC from 2013 to 2022 were enrolled. The tumor necrosis rate was classified into A (complete necrosis), B (necrosis $\geq 90\%$), and C (necrosis $< 90\%$). The overall survival rates (OS), disease free survival rates (DFS) were compared and the type of recurrence in each group was investigated.

Results: Conversion surgery was performed for 31 cases. The 5-year DFS and OS was 40% and 63%. The tumor necrosis rate was as followings, A (n=7), B (n=10), and C (n=14). The 5-year OS of A, B, and C were 100%, 90%, and 19%, with significant differences observed between A and C and between B and C. However, there was no difference between A and B. The 5-year DFS for A, B, and C was 67%, 44%, and 17%, with significant differences observed in each group. Recurrence was observed in 2 patients in A, 5 patients in B, and 10 patients in C. Regarding the type of recurrence, multiple intrahepatic recurrences and extrahepatic metastases were more frequent in C.

Discussion/ Conclusion: Although the overall prognosis for conversion surgery appears to be favorable, we found that it differs depending on the tumor necrosis rates. In particular, type of recurrence affected outcome of C and adjuvant chemotherapy should be indicated.

Abstract Submission No. 200067
O-0694

Cancer-Associated Fibroblasts (CAFs) Promote the Growth of HCC Cells Through Expressing Activin-A

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Aim: Cancer-associated fibroblasts (CAFs) are one of the most important components of the tumor microenvironment (TME) and exhibit a critical role in the proliferation and growth of cancer cells. We investigated the role of CAF-derived Activin-A in cancer cell growth in living samples obtained from tumor and nontumor tissues of patients with hepatocellular carcinoma.

Materials and Methods: Samples from tumor and peri-tumoral tissues of patients with HCC were transformed into single cells with an enzyme mixture called liberase and containing collagenase. CAFs and fibroblasts were identified according to the level of α -smooth muscle actin (α -SMA) and vimentin. The HCC cell line HepG2 was co-cultured with fibroblast and CAFs from tumor and peritumor tissues.

Results: Luciferase cell growth experiments showed that CAFs increased the growth of HepG2 cells by 4 times. A cytokine array was performed with the media from co-growth experiments. CAF-derived Activin-A increased the growth of HepG2 cells, and this effect was

reduced by neutralizing antibodies against activin-A. Activin-A increased the growth of HepG2 cells when co-cultured with CAFs, and this effect was reduced in the presence of neutralizing antibodies against Activin-A. In the presence of neutralizing antibodies, this effect disappears. Experiments were proven in two separate setups with both luciferase and FALS techniques. Activin-A and its receptors were less expressed in tumor tissue.

Conclusion: CAFs in the TME of HCC promote the growth of HCC cells by Activin-A that can be inhibited by neutralizing antibodies and this molecule may be a novel target in the treatment of HCC.

Abstract Submission No. 200074
O-0695

Lenvatinib Combination Therapy VS Monotherapy in Unresectable Hepatocellular Carcinoma

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Background: The efficacy of Lenvatinib as a novel TKI has been acknowledged for first-line treatment of unresectable hepatocellular carcinoma (HCC). Lenvatinib combination therapy with PD-1 inhibitors has shown promising results. Studies which compared combination and monotherapy are still limited.

Aims: To compare the efficacy and safety of Lenvatinib-PD-1 inhibitor combination therapy and lenvatinib monotherapy in patients with HCC.

Methods: The review was performed based on the PRISMA guideline. Articles from PubMed, ScienceDirect, Cochrane, and ProQuest were identified up to November 2023 for analysis based on overall survival (OS), progression-free survival (PFS), objective response rate (ORR), and disease control rate (DCR). The risk of bias was assessed according to Cochrane Risk of Bias (ROB). The pooled effect was shown in mean difference (MD) and odds ratio (OR) with 95% confidence interval (CI).

Results: 5 studies were included which analyzed Lenvatinib combination with pembrolizumab, camrelizumab, sintilimab, or nivolumab compared to Lenvatinib only for DCR, ORR, PFS, and OS. Lenvatinib-PD-1 inhibitor combination showed a significant DCR (OR 1.891, 95% CI: 1.182 - 3.026), ORR (OR 2.237, 95% CI: 1.435 - 3.486), and OS (mean difference 0.306, 95% CI: 0.084 - 0.528) compared to Lenvatinib monotherapy. 6 studies for PFS were also in favor of Lenvatinib-PD-1 inhibitor combination (mean difference 0.143, 95% CI: 0.030 - 0.256) with significant p-value result.

Conclusions: Lenvatinib-PD-1 inhibitor combination showed promising efficacy compared to lenvatinib monotherapy. Further investigations are required among combinations to analyze which may be the best choice.

Keywords: efficacy, hepatocellular carcinoma, lenvatinib, PD-1 inhibitor

Abstract Submission No. 200095
O-0696

Impact of albumin-lymphocyte-platelet-CRP index

on outcome in hepatocellular carcinoma

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Background: We have created new markers calculated from albumin, lymphocyte, platelet, and c-reactive protein (CRP). We investigated the prognostic value of preoperative albumin-lymphocyte-platelet-CRP (ALPC) index in patients with hepatocellular carcinoma (HCC) undergoing hepatectomy.

Methods: 1. We analyzed 512 patients with HCC after hepatectomy from 2001 to 2019. For cross-validation, the cases were divided into the training and testing cohort.

Using the receiver operating characteristic curve, the cutoff value and the area under the curve (AUC) of ALPC were determined in the training cohort.

2. Clinicopathological factors were evaluated to identify predictors of overall (OS) and recurrence-free survival (RFS) after hepatectomy for ALPC. Univariate and multivariate analyses were performed, using the Cox proportional hazards model.

3. We examined the relationship between P-Nrf2 and ALPC index.

Results: 1. The AUC value of ALPC was 0.664. The cutoff for the ALPC index was 0.13.

2. In the training cohort, 149 of 256 patients had ALPC of more than 0.13. High ALPC was correlated with small tumor size, low BCLC stage, low rate of poor differentiation and low rate of microscopic intrahepatic metastasis. OS and RFS were better in the high ALPC group. Multivariate analyses for prognosis factor showed that ALPC was an independent predictor RFS ($P < 0.01$) and OS ($P < 0.01$).

In the testing cohort, 159 of 256 patients had high ALPC index. Multivariate analyses for prognosis factor showed that ALPC was an independent predictor RFS ($P < 0.01$) and OS ($P = 0.03$).

3. P-Nrf2 and ALPC index were found to be associated.

Conclusions: High ALPC index was the independent prognostic factor for HCC.

Abstract Submission No. 200121

O-0697

Laparoscopic Drainage Basin Hepatectomy Based on Cone Unit

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Background: Laparoscopic anatomical hepatectomy is mainly for liver malignant tumors, but most HCC has the basis of cirrhosis, does not allow large-scale hepatectomy. For patients with small HCC and severe cirrhosis, according to portal vein supply, the liver resection reduces the volume of hepatectomy and achieves the purpose of anatomical hepatectomy.

Methods: 12 patients with cirrhosis underlying liver cancer underwent Cone Unit-based resection. After enhanced CT or MRI, 3D reconstruction constructs the Glissonian pedicle composition where tumor is located, each small pedicle blood supply area acts as a cone unit, two methods determine the cone unit resection range, (1) liver gate Laennec membrane dissection is applied, one or several cone unit blood supply pedicle is isolated and ligated, ICG reverse staining determines 1 or several cone unit ranges for resection; (2) Another method: ultrasound localization of cone unit Glissonian pedicle and puncture portal injection of ICG, anatomical excision by puncture one or several cone unit blood supply pedicles according to preoperative planning.

Results: In all 12 patients with small HCC, 8 cases were reverse stained and 4 cases were orthostained. The median duration of surgery was 89 ± 15 minutes and the average estimated blood loss was 103 ml. There was no liver failure. Follow-up results showed the mean DFS was 24.7m and OS 38.9month.

Conclusion: Hepatectomy based on cone unit is a safe and effective surgical method for small HCCs with severe cirrhosis, which reduces the incidence of postoperative liver failure and reduces bleeding, thereby increasing DFS and OS of patients.

Abstract Submission No. 200275

O-0698

ICI and Systemic Therapy Comparison on Progression-Free Survival of Advanced HCC: Metaanalysis of RCT

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Background: Recent randomized controlled trials (RCTs) in Immune-Checkpoint-Inhibitor (ICI) and systemic therapy showed promising results in advanced stage of hepatocellular carcinoma (HCC). We aimed to compare the efficacy between ICI and TKI/anti-VEGF on progression-free survival (PFS) outcome, giving particular attention to the benefits in subgroups of viral/non viral-related etiology of HCC patients.

Methods: Randomized controlled trials (RCTs) reporting PFS following either ICI or TKI/Anti-VEGF and placebo in advanced-stage HCC were included in this study. We also compare the benefit on viral or nonviral-related etiology. We pooled Hazard Ratio (HR) of PFS using random effect model; Subgroup and sensitivity analyses were additionally performed. Heterogeneity among studies was assessed by the Cochran's Q and I² statistics. Publication bias was analysed using a Begg funnel plot and Egger test.

Results: Meta-analysis of 15 trials showed that ICI is better in improving PFS (HR 0.7; 95% CI 0.61-0.79), p value=0.00, compared to TKI/anti-VEGF with PFS (HR 0.81; 95% CI 0.73-0.90), p value=0.00. From subgroup analysis of etiology, we identified that ICI therapy was significantly more effective in patients with viral hepatitis compared to nonviral-related HCC, whereas no differences related to etiology were observed in patients treated with TKI/anti-VEGF.

Conclusions: ICI therapy demonstrated superior efficacy than TKI/Anti-VEGF in improving survival of advanced-stage of HCC patients, especially in viral etiology HCC.

Abstract Submission No. 100114

O-0699

Deep learning model based on CEUS improves diagnostic ability on differentiating HCC and ICC

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Background: The treatment and prognosis of hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC) are quite different, but it is difficult to differentiate them through conventional image examination.

Purpose: To develop a deep learning (DL) model based on contrast-enhanced ultrasound (CEUS) to help radiologists differentiate HCC and ICC.

Methods: We collected the CEUSs from 51 centers to train and validate the DL model through four algorithms (BNInception, mobilenetv2, resnet50, and VGG). CEUSs from another two independent centers were collected as external test set A and B to assess model performance and robustness. Six radiologists (junior, midlevel and senior radiologists, each two) were invited to compare diagnostic ability and explore the cooperation with DL model in the external test set C from a third independent center.

Results: 1005 CEUSs were included and divided to training (n=753) and validation (n=252) sets. 26, 97 and 50 CEUSs were included as external test set A, B and C. Resnet50 model had highest AUC in test set A (AUC=0.932, 95%CI 0.911-0.941) and B (AUC=0.934, 95%CI 0.912-0.944). In test set C, DL model had higher AUC than junior (0.913vs0.748, $p<0.001$) and midlevel radiologists (0.913vs0.789, $p=0.011$), and comparable to senior radiologists (0.913vs0.871, $p=0.209$). With model assistance, the AUC of junior (0.748 to 0.855, $p=0.017$), midlevel (0.789 to 0.899, $p=0.011$) and senior (0.871 vs 0.948, $p=0.049$) radiologists were all improved.

Conclusions: DL model based on CEUS had excellent diagnostic performance and robustness, and can help various levels radiologists improve ability to differentiate HCC and ICC.

Abstract Submission No. 100321

O-0700

Ultrasound-Derived Fat Fraction (UDFF) for quantification of steatosis with reference to biopsy

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Background & Aims: Ultrasound-derived fat fraction (UDFF) has recently developed as a noninvasive quantitative method for steatosis, which combines both attenuation and backscatter coefficients. This study analysed the diagnostic accuracy of grading steatosis with reference to liver histology.

Methods: From April 2022 to January 2023, 73 patients with liver disease underwent both UDFF and liver biopsy. UDFF cutoffs for histologically-proven steatosis grade were determined using area under the receiver-operating characteristic curve (AUROC) analyses. Linearity was evaluated using correlation coefficients between UDFF and fat accumulation in liver section. We assessed the association between clinical parameters including histology and UDFF.

Results: Median age was 66 years (IQR, 54 - 74 years), and 33 (45%) were female. UDFF values showed a stepwise increase in steatosis grade, and there was a significant correlation between UDFF and grade of steatosis ($p<0.001$). Linearity analysis showed good agreement between UDFF and fat accumulation. The AUROCs for distinguishing steatosis grade ≥ 1 , ≥ 2 , and 3 were 0.957 (95% CI, 0.912 - 1.00), 0.931 (95% CI, 0.868 - 1.004), and 0.964 (95% CI, 0.902 - 1.00), respectively. UDFF cutoff of more than 6% had sensitivity of 94.8% and specificity of 82.3% for diagnosing steatosis grade 1. Multivariate regression analysis showed that BMI ≥ 25 kg/m² and fat accumulation in liver $\geq 5\%$ were independent factors associated with more than 6% UDFF.

Conclusions: UDFF shows excellent diagnostic accuracy for grading steatosis as defined by histology. UDFF has a high correlation with liver fat accumulation, and can be a useful tool in clinical practice.

Abstract Submission No. 100398

O-0701

A new stage in the transformation from cirrhosis to hepatocellular carcinoma defined by ALARM model

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Background: Transition from cirrhotic nodules to hepatocellular carcinoma (HCC) involves progressive accumulation of molecular and cellular alterations in hepatocytes. Our study endeavors to create and validate a model using multi-phase enhanced computed tomography (CT) and clinical variables, to identify the earliest stage between cirrhosis and HCC, referred to as Transition Stage.

Methods: We analyzed 1858 cirrhotic patients from 11 institutions, collecting triphasic CT images and lab results 3-12 months before HCC diagnosis or final non-HCC follow-up. Using radiomics, deep learning, and aMAP HCC risk scores, we developed an early detection model with the discovery cohort (DC, n=924). This was then validated using an external cohort (EVC, n=703) across 10 institutions and an internal cohort (IVC, n=231).

Results: The ALARM model, integrating radiomics, deep learning, and aMAP scores, proficient at identifying individuals undergoing nodular tumorigenesis preemptively, exhibited excellent discriminatory ability in distinguishing early HCC or not for cirrhotic nodule with AUC of 0.929 (95%CI: 0.918-0.941) in the DC, 0.902 (95%CI 0.818-0.987) in the IVC, and 0.929 (95%CI:0.898-0.961) in the EVC. By applying optimal thresholds of 0.21 and 0.65, the malignant (n=221, 11.9%) and potentially malignant (n=433, 23.3%) groups (referred to as Transition Stage), which covered 94.4% (84/89) of the worsening nodules, had significantly higher rates of deterioration in comparison to the benign group (n=1204, 64.8%) (24.3% vs. 6.4% vs. 0.42%, $p<0.001$) (Figure).

Conclusions: The ALARM model is a valuable tool for early nodular tumorigenesis detection, introducing a novel "Transition Stage" that enhances clinical decision precision and enables early HCC treatment initiation.

Abstract Submission No. 100828

O-0702

Reduced glymphatic system activity induces elevated GABA level in hepatic encephalopathy patients

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Background: Hepatic encephalopathy (HE) is one of the most severe complications of decompensated cirrhosis, but its pathogenesis is still not completely understood. This study explored HE pathogenesis through diffusion tensor image analysis along the perivascular space (DTI-ALPS) and measuring GABA levels in the thalamus of cirrhosis patients.

Methods: Forty-eight decompensated cirrhosis patients were enrolled and allocated into three groups (LC, n=22; MHE, n=19; HE, n=7). DTI and MRS GABA were performed in all patients.

Results: No significant differences in sex, education years, and Child-pugh scores among the three groups were observed. The MHE (1.21±0.23) and HE groups (1.20±0.26) showed significantly lower ALPS index levels than the LC Group (1.47±0.35) ($p < 0.05$), and this difference persisted after adjustment for sex, age, and years of education. Meanwhile, ALPS index was notably correlated with psychometric tests (NCT-B, DST, SDT, and PHES) ($p < 0.05$). The volume of thalamus was decreased and the level of thalamus GABA/Water and GABA/Cr was increased in the MHE group ($p < 0.05$). Finally, through correlation analysis, there was a strong negative correlation between ALPS index and GABA levels ($p < 0.05$).

Conclusion: The occurrence and development of HE may be related to the exclusion of related neural wastes such as GABA due to intracranial glymphatic dysfunction. An effective glymphatic pathway that can help clear brain waste agents may have potential clinical implications.

Abstract Submission No. 101295

O-0703

Development of a new hepatic tumor diagnostic method using Sonazoid contrast-enhanced ultrasonography

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Background: Hepatocellular carcinoma (HCC) and other liver tumors are closely related to blood flow, and Contrast Vector Imaging (CVI) is a new system that tracks, records, and analyzes the trajectory of microbubbles with high frame rate. In this study, we performed contrast-enhanced ultrasonography (CEUS) of liver tumors and intra-tumor blood flow analysis using CVI to investigate its usefulness in qualitative diagnosis of liver tumors and grading of hepatocellular carcinoma.

Methods: Subjects included 232 nodules in 232 patients who underwent CEUS and CVI. Tumors included hepatocellular carcinoma (HCC, n=158), liver metastasis (meta, n=9), intrahepatic cholangiocarcinoma (ICC, n=3), hepatic hemangioma (HEM, n=33), focal nodular hyperplasia (FNH, n=10), hepatocellular adenoma (HCA, n=11), hepatic angiomyolipoma (AML, n=4). Median tumor diameter was 25.0 mm. Aplio i800 (Canon) was used. CEUS imaging conditions were as follows: bolus Sonazoid 0.005 ml/body, receiver frequency: h3.3HF, Focus: tumor lower margin, MI: 0.20, FR: 29-41 fps. All patients The CVI ROI was placed over the entire tumor area, and velocity, direction (In-Flow ratio), and density were measured. The contrast pattern of CT was classified as Type 1-4, reflecting tumor differentiation

and the usefulness of this classification in the diagnosis of tumor grade was examined.

Results: There was no significant difference in Velocity and Bubble density between tumors. On the other hand, In-out ratio was significantly lower than the others in FNH, which means nutrient vessels extending radially from the center toward the outside.

Velocity by CT type for HCC were 18.1/18.5/22.1/23.9 mm/s for Type-1/2/3/4, showing an increase in Velocity with a decrease in predicted differentiation ($P < 0.05$). Bubble density was predominantly lower in type 4 ($p = 0.0035$).

Conclusion: The usefulness of CVI in qualitative diagnosis of liver tumors and grading of HCC has been demonstrated; quantitative assessment of fine blood flow in liver tumors using CVI has the potential to improve the objectivity of CEUS.

Abstract Submission No. 101886

O-0704

Multiparametric MRI-based Radiomics Nomogram Predicts the Recurrence of stroke

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Background: This study aimed to develop and validate a radiomics model based on multiparametric magnetic resonance imaging (MRI) for predicting recurrence in patients with hepatocellular carcinoma (HCC) following postoperative adjuvant transcatheter arterial chemoembolization (PA-TACE).

Methods: In this retrospective study, 117 HCC patients (81 for training, 36 for validation) treated with PA-TACE were included. Multiparametric radiomics features were extracted from three MRI sequences. Least absolute shrinkage and selection operator (LASSO)-COX regression was utilized to select radiomics features. Optimal clinical characteristics selected by multivariate Cox analysis were integrated with Rad-score to develop a recurrence-free survival (RFS) prediction model. The model performance was evaluated by time-dependent receiver operating characteristic (ROC) curves, Harrell's concordance index (C-index), and calibration curve.

Results: Fifteen optimal radiomic features were selected and the median Rad-score value was 0.434. The median RFS of patients with low-risk signature was 47 months, much higher than those with high-risk signature ($P < 0.0001$). Multivariate Cox analysis indicated that neutrophil-to-lymphocyte ratio (NLR) (hazard ratio (HR)=1.49, 95% confidence interval (CI): 1.1-2.1, $P=0.022$) and tumor size (HR=1.28, 95% CI: 1.1-1.5, $P=0.001$) were the independent predictors of RFS after PA-TACE. A combined model was established by integrating Rad-score, NLR, and tumor size in the training cohort (C-index 0.822; 95% CI 0.805-0.861) and validation cohort (0.823; 95% CI 0.771-0.876). The calibration curve exhibited a satisfactory correspondence in two cohorts.

Conclusion: A multiparametric MRI-based radiomics model can predict RFS of HCC patients receiving PA-TACE and a nomogram can be served as an individualized tool for prognosis.

Abstract Submission No. 100059
O-0705

MRI iron-corrected T1 mapping may have utility to monitor NASH following weight loss interventions.

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Background: Bariatric surgery is a viable treatment for obesity (a risk factor for nonalcoholic steatohepatitis [NASH]). Studies have related weight reduction with changes in NASH, however, few have used imaging to investigate effects on liver health. We evaluated differences in response to intervention using disease activity (corrected T1 [cT1]), and liver fat (proton density fat fraction [PDFF]).

Methods: 34 morbidly obese patients were included; 13 underwent laparoscopic sleeve gastrectomy (LSG) alongside intraoperative liver biopsy, and N=21 underwent a lifestyle-modification program (LMP). All patients had multi-parametric MRI at baseline and 4-months follow-up. Diagnostic accuracy to identify NASH was assessed using area under the curve (AUC).

Results: 31% of patients in the LSG group had NASH (NAS $\geq$ 4) on liver biopsy and had significantly higher cT1 ($p=0.031$), but not PDFF, compared to those without NASH. PDFF and cT1 correlated with the NAS score ($r=0.81$, 0.70 , $p<0.05$, respectively). There was good AUC for cT1 (0.89) and PDFF (0.83) to identify NASH. At follow-up, weight reduction -22.8%, ($p=0.013$) vs. -1.3%, ($p=0.262$) resulted in cT1 reduction of -8.04% ($p=0.025$) vs. -3.87%, ($p=0.083$) in the LSG vs. LMP group, respectively. Significant differences between interventions were observed for %PDFF decrease ($p=0.001$). Both biomarkers were significantly reduced in the LSG group ($p<0.05$), while only PDFF ($p=0.012$) was significantly reduced in the LMP group.

Conclusions: MRI biomarkers have utility to monitor NASH following intervention in patients with morbid obesity allowing objective comparison between intervention strategies. Compared to lifestyle modification, bariatric surgery was more effective in improving liver health (especially fat).

Abstract Submission No. 100984
O-0706

Myosteatosis and sarcopenic obesity independently predict mortality of patients with PBC

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Background: There is limited research on the factors influencing sarcopenia and myosteatosis in patients with primary biliary cholangitis (PBC). Our study aimed to evaluate the risk factors associated with sarcopenia myosteatosis in PBC patients, as well as to determine whether these conditions correlate with the biochemical response rates and risk for death in PBC.

Methods: In this retrospective study, patients with PBC were enrolled. Sarcopenia and myosteatosis were defined using the L3 skeletal muscle index (SMI) and intramuscular adipose tissue content (IMAC) obtained from CT imaging.

Results: 151 patients with PBC were included. 100 (66.23%) and 64 (42.38%) patients were with sarcopenia or myosteatosis, respectively. 23 (15.23%) patients were with sarcopenic obesity (Fig. 1). The UDCA response rate was 43.7%. Mean follow-up was 58 months, and 11 patients died. Patients with sarcopenia were older, with a lower BMI and a higher prevalence of myosteatosis, as well as lower visceral adipose tissue index (VATI) and subcutaneous adipose tissue index (SATI) levels ($p < 0.05$). Patients with myosteatosis were older and had higher levels of albumin, SMAI, and VATI ($p < 0.05$). They also had a higher prevalence of sarcopenia and sarcopenic obesity ($p < 0.05$). In the multivariate analysis, the presence of sarcopenia, myosteatosis and sarcopenic obesity didn't affect the biochemical response rates of PBC patients. However, myosteatosis and sarcopenic obesity were found to be significant risk factors of mortality in PBC patients according to the multivariate Cox analysis.

Conclusions: Myosteatosis and sarcopenic obesity were independent risk factors for mortality of PBC patients.

Abstract Submission No. 101189
O-0707

EUS multi-actuation liver biopsy better than percutaneous in adequacy and pain with equal safety

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Introduction: Endoscopic ultrasound-guided liver biopsy (EUS-LB) is a potential alternative to the percutaneous route (PC-LB). We aimed at comparing sample adequacy and safety of multiple actuation EUS-LB and compared with PC-LB.

Methods: A total of 40 consecutive EUS-LB done between June to October 2023 were compared to 40 historical controls of percutaneous LB. All EUS-LB were performed with 19G Franseen core needle by heparinised wet suction technique. Percutaneous liver biopsy was done with 18G biopsy gun and 2-4 passes were taken. Outcome measured were total and longest specimen length (TSL and LSL), number of complete portal tracts (CPT), definitive histological diagnosis, post procedural pain and adverse events (AE). An adequate specimen was defined as TSL $\geq$ 20 mm and CPT $\geq$ 11.

Results: In EUS-LB mean number of actuation taken per pass were 6.19 (± 1.73). The percentage of adequate samples in EUS-LB vs PC-LB were 97.5% vs 77.5% ($P<0.01$) and histological diagnosis was possible in 97.5% vs 87.5% ($P=0.202$). The mean TSL and CPT were 7.74cm (± 3.54) vs 4.5cm (± 2.02), $P<0.00001$ and 25.36 (± 10.2) vs 13.25 (± 6.81), $P<0.00001$. Post-procedural pain was seen in 18% of PC-LB group while none in the EUS-LB group had pain ($P<0.033$). Minor AE in form of sub capsular hematoma were seen in 3 patients in PC-LB group while 2 patients in EUS-LB group had sedation related vomiting in the post procedure period ($P=0.64$).

Conclusion: EUS-LB with multiple actuation has better sample adequacy, pain tolerability with comparable safety in comparison to PC-LB.

Abstract Submission No. 101340
O-0708

Exploring the utility of EUS in Budd-Chiari syndrome : a multicenter multiobserver prospective study

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Background and Aims: The diagnosis of Budd-Chiari syndrome (BCS) relies primarily on radiological methods, crucial for devising appropriate therapeutic strategies. This study aimed to evaluate the accuracy of Endoscopic ultrasound (EUS) in diagnosing Budd-Chiari syndrome (BCS).

Methods: A prospective multi-center observational study enrolled 50 consecutive patients with a confirmed diagnosis of BCS. Each patient underwent a thorough EUS examination conducted by three independent endosonographers, all of whom were blinded to the anatomical details of the venous obstruction and the findings of their peers. This was subsequently compared with conventional angiography (when available) or Magnetic Resonance Venography (MRV).

Outcome measures included were inter-observer agreement, sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy in diagnosing pathological lesions associated with BCS.

Results: Among the 50 BCS patients (mean age 34 years; range 13-65 years) subjected to EUS, the results showed good overall agreement among endosonographers for diagnosing right hepatic vein (RHV) ($\kappa=0.716$) and left hepatic vein (LHV) lesions ($\kappa=0.722$). There was moderate agreement for middle hepatic vein (MHV) lesions ($\kappa=0.660$) and very good agreement for inferior vena cava (IVC) lesions ($\kappa=0.823$). EUS demonstrated high sensitivity and positive predictive value along with low inter-observer variability, and an overall high diagnostic accuracy for detecting lesions associated with BCS.

Conclusions: In summary, EUS is a safe and promising diagnostic tool for the management of patients with BCS. It can provide accurate mapping of hepatic veins, intrahepatic collaterals, and the IVC.

Abstract Submission No. 101458

O-0709

RETROSPECTIVE ANALYSIS OF THERAPEUTIC ERCP IN A TERTIARY CARE HOSPITAL IN FAISALABAD

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Abstract

Objective: (ERCP) is common treatment used for therapeutic purposes while treating a variety of pancreato-biliary illnesses. Study was aimed at determining the indications of the ERCP and comparing the ultrasonography and ERCP findings.

Methodology: This study was an observational, retrospective study that was conducted in the Department of Gastroenterology, The ERCP data were collected between September 2019 and December 2021. The study included 277 patients who had been diagnosed with common bile duct stones and were over the age of 18. Different ERCP indications were identified and radiographic and ERCP cholangiographic results were compared. For quantitative variables, the mean and standard deviation were documented. Qualitative variables were computed as frequencies and percentages.

Results: A total of 277 cases of CBD stones were included. There were 96 male patients (34.6%) and 181 female patients (65.4%). The mean age was 51.68 ± 15.67 years. Findings of ERCP were similar to USG, CT, and MRCP findings in 218 (78.7%) patients whereas dissimilar in 53 (19.1%) patients. Sphincterotomy, balloon Sweeps, and CBD Stenting had been performed in 221 (79.8%), 163 (58.8%) and 109 (39.4%) patients respectively. ERCP was successfully performed in 235 (84.8%) patients and unsuccessful in 42 (15.2%).

Conclusion: Most common indications for ERCP was CBD stone. A more successful method for stone removal was endoscopic sphincterotomy combined with balloon sweep of the common bile duct.

Keywords: Endoscopic retrograde cholangiopancreatography, common bile duct, sphincterotomy.

Authors Professor DR Hafiz Mughees Ather, Dr Umair Waheed But,

Abstract Submission No. 101556

O-0710

Stiffness on SWE as Potential Microenvironment Biomarker for Predicting Recurrence in HBV-Related HCC

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Background: To explore the pathologic basis and prognostic value of tumor and liver stiffness measured pre-operatively by two-dimensional shear wave elastography (2D-SWE) in hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC) patients who undergo hepatic resection.

Methods: A total of 191 HBV infected patients with solitary resectable HCC were prospectively enrolled. The stiffness of intratumoral tissue, peritumoral tissue, adjacent liver tissue and distant liver tissue were evaluated by 2D-SWE. The correlations between stiffness and pathological characteristics were analyzed in 114 patients. The predictive value of stiffness for recurrence-free survival (RFS) were evaluated and Cutoff Finder was used for determining optimal cut-off stiffness values. Cox proportional hazards analysis was used to identify independent predictors of RFS.

Results Pathologically, intratumoral stiffness was associated with stroma proportion and microvascular invasion (MVI) while peritumoral stiffness was associated with tumor size, capsule and MVI. Adjacent liver stiffness was correlated with capsule and liver fibrosis stage while distant liver stiffness was correlated with liver fibrosis stage. Peritumoral stiffness, adjacent liver stiffness and distant liver stiffness were all correlated to RFS (all $p < 0.05$). Higher peritumoral stiffness (>49.4 kPa) (HR=1.822, $p=0.023$) and higher adjacent liver stiffness (>24.1 kPa) (HR=1.792, $p=0.048$) were significant independent predictors of worse RFS, along with tumor size and MVI. The nomogram based on these variables showed a C-index of 0.77 for RFS prediction.

Conclusions: Stiffness measured by 2D-SWE could be a tumor microenvironment and tumor invasiveness biomarker. Peritumoral stiffness and adjacent liver stiffness showed important values in predicting tumor recurrence after curative resection in HBV-related HCC.

Abstract Submission No. 101589

O-0711

Diagnostic and prognostic ability of CEUS and biomarkers in hepatocellular carcinoma subtypes

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Objectives: To investigate the diagnostic and prognostic value of contrast-enhanced ultrasound (CEUS) and clinical indicators of the vessels encapsulating tumor clusters (VETC) pattern and macrotrabecular-massive subtype in hepatocellular carcinoma (MTM-HCC)

Materials and methods: A total of 273 HCC patients (182 in the training cohort and 91 in the validation cohort) were included in this

prospective study. All patients received conventional ultrasound and CEUS examination, followed by surgery within one week and obtain pathological diagnosis. Multivariable logistic regression was performed to selected independent correlated factors of VETC-HCC and MTM-HCC to develop the nomogram. Nomogram models were assessed by receiver operating characteristic (ROC) curves, calibration plots, and decision curve analysis (DCA). Kaplan-meier curves analysis and Cox regression analysis were conducted to assess the association between risk stratification and early postoperative recurrence.

Results: VETC-HCC and MTM-HCC were found in 109 (39.9%) and 51 (18.7%) patients, respectively. Multivariate logistic regression analysis revealed that AFP level [OR 2.26 (1.49-3.42), $P < 0.001$], intratumoral non-enhancement [OR 2.40 (1.02-5.64), $P = 0.044$] and perfusion pattern in CEUS arterial phase [OR 2.27 (1.05-4.91), $P = 0.038$] were independent predictors of VETC-HCC. Besides, the first two indicators were also independently associated with MTM-HCC [OR 2.36 (1.36-4.09), $P = 0.002$ for AFP level and OR 3.72 (1.02-13.56), $P = 0.046$ for intratumoral non-enhancement]. The area under curve (AUC) value of VETC-HCC nomogram and MTM-HCC nomogram models were 0.78 (0.71-0.84), 0.80 (95% CI: 0.73-0.87) in training cohort and 0.72 (0.60-0.84), 0.78 (95% CI: 0.64-0.93) in validation cohort. Both of the two models had good discrimination, calibration and generalization ability. Kaplan-Meier curves analysis indicated that predicted VETC-HCC or MTM-HCC exhibited higher rates of early recurrence (Log rank $P < 0.001$ and $P = 0.002$, respectively). Cox regression analysis showed that high risk of VETC-HCC was independently correlated with early recurrence ($P = 0.011$).

Conclusions: Based on CEUS images and clinical data, this study established and verified non-invasive nomogram models for predict VETC-HCC and MTM-HCC, which were helpful in preoperative prognosis prediction and individualized therapy decisions making.

Abstract Submission No. 101915

O-0712

A tricky Case of Pleosis Hepatis : case report

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Peliosis hepatis is a rare vascular condition of the liver characterized by a proliferation of the sinusoidal hepatic capillaries that results in cystic blood-filled. We present a case of a 40-year-old female who first presented by acute abdomen and hemoperitoneum and managed surgically.

Case Presentation: A 40-year-old female presented to by acute abdomen and shivering. Regarding medical history She is hypertensive, has psoriatic arthritis and fibroid uterus on OCP. She has a family history of cancer pancreas. On evaluation, Hb was 8.8 g/dl, Platelets 345, WBCs 10.5 c/dl Alt was elevated 329 u/l, AST 63u/l, S. albumin 3.8 g/dl, total bilirubin 1 mg/dl, direct bilirubin 0.50 mg/dl. Abdominal ultrasound revealed the presence of sizable heterogenous lesion in the epigastric region measuring 10*12 cm with mildly turbid fluid collection in perihepatic and pelvic region. CT scan showed large heterogenous soft tissue lesion at the mid abdomen. MRI abdomen revealed large exophytic mass from segment III on left hepatic lobe with hemorrhagic component and mild hemoperitoneum and suggested large hepatic adenoma with hemorrhage. Resection of segment III of liver with safety margin was done and histopathology showed large wide spaces filled with blood with no lining surrounded by areas of hemorrhagic necrosis confirming diagnosis of peliosis hepatis.

Conclusion: Peliosis hepatis is a rare vascular condition of the liver characterized by a proliferation of the sinusoidal hepatic capillaries. Healthcare providers should be aware of this condition when

interpreting imaging studies and managing patients with incidental findings of pleosis hepatis or presenting by complications.

Abstract Submission No. 200153

O-0713

Differentiating Renal Urothelial Carcinoma and Endophytic Renal Cell Carcinoma using US and CEUS

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Purpose: This retrospective study aimed to evaluate the value of conventional ultrasound (CUS) and contrast-enhanced ultrasound (CEUS) features in differentiating between renal urothelial carcinomas (RUC) and endophytic renal cell carcinomas (ERCC).

Methods: From July 2014 to November 2022, a total of 72 patients with RUC and 118 patients with ERCC confirmed by pathology were enrolled in this study. Both CUS and CEUS were performed in all patients within 4 weeks before the procedure. Univariable and multivariable analyses were used to select statistically significant variables of clinical, CUS, and CEUS features for the differentiation of RUC and ERCC. Sensitivity (SEN), specificity (SPE), and the area under the receiver-operating characteristic curve (AUC) were assessed for diagnostic performance. Inter- and intra-observer agreements of CUS and CEUS features were evaluated using the intra-class correlation coefficient (ICC).

Results: Multiple logistic regression analysis demonstrated that clinical (age and hematuria), CUS (size, echogenicity, regularity, and hydronephrosis), and CEUS (non-enhancement area, enhancement intensity in cortical phase, and rim-like enhancement) features were independent factors for differential diagnosis with all $p < 0.05$. When combining clinical characters with CUS and CEUS features into a diagnostic criterion, the AUC reached 0.917 (95% CI 0.873-0.961), with a sensitivity of 95.8% and specificity of 87.5%. ICC ranged from 0.756 to 0.907 for inter-observer agreement and 0.791 to 0.934 for intra-observer agreement for CUS and CEUS features.

Conclusions: Combining the imaging features of CUS and CEUS with age and hematuria provides a potentially effective diagnostic method in the differentiation of RUC and ERCC.

Abstract Submission No. 100478

O-0714

MSC-derived Extracellular Vesicles Alleviate Ischemia Liver Injury via Inhibiting NETs Formation

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Background: Transjugular intrahepatic portosystemic shunt (TIPS) is a highly efficacious approach for managing portal hypertension complications. However, portal venous shunt-related ischemia often results in liver dysfunction or failure following TIPS. This study aims to investigate the therapeutic potential of mesenchymal stromal cells (MSCs) in mitigating ischemic liver injury and elucidating the underlying mechanism.

Methods: We employed portal venous branch ligation to partially obstruct the blood supply to liver to establish a model of ischemic liver injury and performed transcriptome sequencing on liver tissue.

Additionally, we utilized MSCs derived from human umbilical cord to treat the mouse model of ischemic liver injury, elucidating the mechanism through both *in vitro* and *in vivo* experiments.

Results: The transcriptome sequencing and differential gene enrichment analysis revealed significant enrichment of cytokine pathways and glucose metabolism pathways. Additionally, the plasma levels of IL-6, IL-17A, MMP-9, and MPO, which serve as indicators of neutrophil activation, were found to be elevated in patients after TIPS and in mouse model. The average serum levels of AST, ALT, and bilirubin in the mice model treated with MSC were significantly reduced. MSC treatment inhibited the formation of neutrophil extracellular traps (NETs). We further confirmed that both MSC medium and MSC-derived extracellular vesicles (MSC-EVs) were able to inhibit the release of NETs from neutrophils by interfering with GSDMD shearing.

Conclusion: Both MSC and MSC-EV possess the potential to mitigate ischemic liver injury through hindering the NETs formation. They may be considered for the prevention of liver dysfunction after TIPS procedure.

Abstract Submission No. 101693

O-0715

Microwave ablation (MWA) antenna emprint visualization innovation

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Background: New-generation microwave ablation (MWA) has garnered attention due to its ability to generate larger ablation volumes in shorter durations compared to radiofrequency ablation (RFA). However, MWA faces a challenge in terms of visibility under ultrasound, as the MWA antenna is less conspicuous than an electrode used in RFA.

Purpose: The primary objective is to enhance the visibility of Emprint electrodes, especially in cases where observation is challenging (e.g., deep, obese, postoperative patients), ensuring safe cauterization.

Method and Results: In instances where visibility is compromised after Emprint antenna insertion into the liver, a novel approach is employed. The saline solution used for reflux is agitated to create microbubbles. Activation of the pump sends air and saline alternately. Utilizing contrast mode on the echo side (Aplio i800) and focusing on the expected needle tip, observation is conducted. Microbubbles, reaching the antenna needle tip, highlight its position.

Once confirmed, cauterization proceeds from the anticipated location.

Discussion: The discussion emphasizes that during contrast mode, refluxed microbubbles flow to the 4mm tip of the Emprint needle, where the sensor chip is situated. This structural feature of the Emprint is crucial for highlighting the needle tip, aiding in its visualization.

Conclusion: The innovative technique proves valuable for predicting the needle tip position in cases where Emprint visibility poses a challenge.

Abstract Submission No. 200184

O-0716

Sonodynamic therapy improves cancer immunotherapy after insufficient radiofrequency ablation.

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Background: Residual lesions and undetectable metastasis after **insufficient radiofrequency ablation (iRFA)** are associated with earlier new metastases and poor survival in cancer patients. **Programmed cell death protein 1(PD-1)** blockade has been reported to enhance RFA-elicited antitumor immunity, but its ability to eliminate residual lesions has been questioned. Thus, new adjuvant strategies are urgently needed to restrain iRFA-induced tumor cell progression. Here, we report a combined treatment modality post iRFA based on integrating an oxygen self-enriching PFH-Ce6 liposome@O₂ nanodroplets (PCL@O₂)-augmented noninvasive **sonodynamic therapy (SDT)** with PD-1 blockade.

Methods and Results: PCL@O₂ containing Ce6 as the sonosensitizer and PFH as O₂ reservoir, was synthesized as an augmented SDT nano-platform and showed increased ROS generation to raise effective apoptosis of tumor cells, which also exposed more calreticulin meaning stronger immunogenic cell death (ICD). Combining with PD-1 blockade post iRFA, this optimized SDT **induced a better anti-tumor response** in MC38 tumor bearing mouse model, which not only arrested residual primary tumor progression, but also inhibited the growth of distant tumor, therefore prolonging the survival. Profiling of immune populations within the tumor draining lymph nodes and tumors further revealed that **combination therapy effectively induced ICD, and promoted the maturation of dendritic cells, tumor infiltration of T cells, as well as activation of cytotoxic T lymphocytes.** Moreover, the combined treatment could significantly initiate **long-term immune memory.**

Conclusion: this study establishes the preclinical proof of concept to apply oxygen self-enriching SDT to augment cancer immunotherapy after iRFA.

Abstract Submission No. 200122

O-0717

Invitrogen 遂「 Vivofectamine 遂」 LNP Library for *in vivo* RNA delivery to liver from mouse to NHP

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The rapidly expanding use of mRNA as a therapeutic tool necessitates innovative delivery methods. Leveraging three decades of lipid-based delivery expertise, we have developed lipid nanoparticle (LNP) solutions that can efficiently deliver mRNA *in vivo* and *ex vivo*. Our leading candidates have been selected from a library of over 5000 synthesized lipids after rigorous *in vitro* and *in vivo* screening. They demonstrate high efficacy and safety across diverse applications like liver protein expression, vaccines, and immune cell targeting.

Our liver-specific ionizable lipids, formulated as LNPs, were tested in mice, rats, and non-human primates (NHPs). In mice using fLuc mRNA-LNP, we observed high levels liver-specific protein expression, on par or surpassing ionizable lipids in clinical trials and FDA-approved drugs. Initial data on genome editing at the TTR locus showed over 80% reduction in circulating TTR levels and more than 50% editing in the homogenized liver.

In NHPs, three of six lipids from our exploratory panel were evaluated for delivering hEPO mRNA. Collaborator data indicated superior efficacy and safety with our leading candidate compared to a benchmark ionizable lipid used in clinical-stage mRNA liver therapies. Moreover,

this lipid exhibited excellent tolerance in rats, even at a single 9 mg/kg dose or three repeated 3 mg/kg injections each. Our findings underscore the high efficacy and safety of liver-specific Vivofectamine 達「 LNPs, suitable for diverse applications, including protein expression and genome editing. Our LNP Library aims to expedite nucleic acid delivery from bench to clinic, offering solutions to our customers' delivery challenges. Research use only.

Abstract Submission No. 200278
O-0718

Overlapping and Power Ramping Ablation Zone Techniques using the Emprint Ablation System

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INTRODUCTION: Creating overlapping ablation zones is a technique common to thermal ablation in the liver to achieve ablative margins around larger tumors. Similarly, a power ramp-up technique is common, wherein power is increased in a stepwise approach to reduce tissue popping, a phenomenon related to fluid-to-vapor phase transition, by allowing heat and pressure to disperse over a slower initial heating period. This scientific work characterizes overlapping and power ramping ablation techniques using the Emprint™ ablation system within ex vivo bovine livers.

METHODS: Ablation zones (n=284) were created within temperature-controlled ex vivo bovine livers. For the overlapping technique, both pull-back (n=92) and side-by-side (n=103) overlapping ablations were created using two sequential activations of a single Emprint device at four device spacings (0.5,1.0,1.5,2.0cm), three power settings (50,100,150W), and three activation times per placement (90,300,600sec). For the ramp-up technique, single-placement ablation zones (n=89) were created using nine ramping protocols, each starting at 50W for 60 seconds. Ablation zone dimensions were measured following Triphenyltetrazolium chloride tissue staining.

RESULTS: The range of the mean for ablation volume, width, and length for overlapping pull-back was 5.8-110.3 cm³, 2.0-5.1cm, 2.6-7.2cm. The range of the mean for ablation volume, width-large, width-small, and length for overlapping side-by-side was 4.5-101.9 cm³, 2.0-6.2cm, 1.8-5.1cm, 2.1-5.3cm. Power ramping protocols resulted in ablation volume, width and length ranging from 4.4-61.5 cm³, 1.8-4.8cm, 2.6-5.1cm.

CONCLUSION: A wide range of ablation sizes and shapes are possible with the Emprint ablation system using an overlapping ablation technique, and power ramping with the system delivers small to large spherical ablations.

Abstract Submission No. 101059
O-0719

Refining Liver Fibrosis Assessment: Palm-sized Transient Elastography Guided with B-mode Imaging

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Transient elastography (TE), recommended by WHO and major clinical guidelines, has been an established method for assessing liver fibrosis via liver stiffness measurement (LSM). However, conventional TE is limited by large size and relies on difficult-to-interpret A-mode

imaging for liver localization, which hinders its widespread use in hepatology field. A palm-sized wireless TE system with real-time B-mode ultrasound imaging guidance was proposed. The performance of B-mode guided TE was prospectively evaluated in three tissue-mimicking phantoms (reference values: 4.66, 12.8 and 76.9kPa) and 60 adults with various chronic liver diseases (age, 52.9±12.2 years; BMI, 24.0±3.9 kg/m²; 30 women; 47% Chronic hepatitis B). Intra- and inter-operator reliability were further assessed in a subgroup of 30 patients using intra-class correlation coefficient (ICC). B-mode guided TE accurately estimated the Young's modulus of the reference phantoms (averaged bias: 4.4%; range: 2%-7.9%). Pairwise comparisons revealed significant inter-correlation of LSM among B-mode guided TE, conventional TE and two-dimensional shear-wave elastography, with strongest correlation ($r=0.80$) and highest agreement (mean difference of -0.51kPa, 95% LOA: -2.95 to 1.92kPa) observed at the pair of B-mode guided vs. conventional TE. Excellent intra-operator and good inter-operator reliability were established (ICCs: 0.883-0.925). B-mode guided TE presents a practical approach for achieving reproducible and valid LSM, comparable to other existing liver elastography techniques. Enhanced liver anatomy visualization under B-mode improves examination efficiency and shortens the learning curve for inexperienced practitioners. Its small footprint offers high portability, paving the way toward point-of-care liver fibrosis assessment.

Abstract Submission No. 101060
O-0720

Telemedicine for Hepatology Consultations in Myanmar: A Single Centre Experience

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Aim: Telemedicine has witnessed a significant surge in its adoption, particularly during the COVID-19 pandemic. Over the years, it has found utility in various facets of hepatology. The main objective of this study was to assess patient satisfaction regarding Hepatology consultations conducted through a telemedicine program in a private hospital in Myanmar.

Methods: This study encompassed a series of telemedicine consultations conducted by a hepatologist at a private hospital in Yangon, Myanmar. Patients and the hepatologist utilized various communication platforms, based on their individual preferences. The consultations were done via telemedicine when they led to a diagnosis and established a suitable plan for follow-up care. To assess patient satisfaction with the telemedicine approach, the study employed the Patient Satisfaction Questionnaire Short Form and the Telemedicine Satisfaction Questionnaire.

Results: A comprehensive dataset comprising 155 telemedicine consultations conducted by the hepatologist. Notably, all these consultations were successfully resolved through the telemedicine approach. The final diagnoses for the patients whose consultations were effectively managed via telemedicine encompassed chronic hepatitis B (70%), hepatocellular carcinoma (18%), non-alcoholic fatty liver disease (7%), and benign hepatic lesions (5%). Our findings revealed a notably high level of patient satisfaction with the telemedicine model, as evidenced by positive responses in both questionnaires utilized.

Conclusion: The outcomes of our study underscore the efficacy of telemedicine within the realm of hepatology. Our findings revealed a pronounced level of patient satisfaction, as evidenced by the use of prevalidated questionnaires, which bolsters the case for the continued utilization of telemedicine in hepatological practice.

Abstract Submission No. 101067
O-0721

Intravascular ultrasound-guided direct portal vein puncture for TIPS: A proof-of-concept study

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Background: Portal vein (PV) puncture is the most challenging and time-consuming step in the transjugular intrahepatic portosystemic shunt (TIPS) procedure. Conventional intravascular ultrasound (IVUS)-guided PV puncture separates the ultrasound probe and puncture needle in different veins, providing indirect guidance but increasing procedural complexity. The purpose of this study was to evaluate the technical feasibility and safety of IVUS-guided direct PV puncture via the right hepatic vein (RHV) for TIPS in a live canine model.

Methods: Five healthy beagle dogs were selected and anesthetized. The 6.6-millimeter diameter phased-array side-firing endoscopic ultrasound was introduced as the IVUS. The ultrasound probe was inserted into the RHV via a right jugular vein approach. Under direct ultrasound guidance, PV puncture was performed using a 21-gauge needle through the entrance of the RHV. Guidewire insertion, tract dilation, and stent placement were subsequently completed. The efficacy of IVUS-guided direct PV puncture via RHV was assessed.

Results: Among the five beagle dogs, one case cannot insert an ultrasound probe due to the small diameter of the jugular vein. The remaining four completed the IVUS-guided direct PV puncture via RHV and TIPS creation without technical problems or complications. No adverse events occurred in animals during the 6-month observation. Necropsy of animals revealed no evidence of stent displacement, stent stenosis, or puncture complications.

Conclusion: Our experimental model demonstrated that IVUS-guided direct PV puncture via RHV for TIPS is both technically feasible and safe, which may be the foundation of a specialized IVUS-guided integrated puncture system in TIPS creation.

Abstract Submission No. 101288
O-0722

Augmented Reality Navigation for Laparoscopic Liver Surgery: A Comparison with ICG Fluorescence

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Objective: Augmented reality (AR) is gradually becoming prevalent in the medical field, especially for surgical assistance. It is useful in overlaying preoperative 3D images with intraoperative visuals to understand the spatial relationship between tumors and blood vessels.

However, the accuracy of matching real organs with AR, considering abdominal organ deformation due to pneumoperitoneum or respiratory variations, remains unclear. This study aims to implement overlay displays considering liver deformation through non-rigid registration and compare it with the fluorescence regions identified by the Indocyanine Green (ICG) fluorescence method.

Subjects and Methods: Four cases identified using the ICG fluorescence method were selected. Annotations were made on liver silhouettes and fluorescence-stained areas for silhouette-based alignment. 3D liver models were created from CT images using SYNAPSE VINCENT (Fujifilm). AR display was conducted using the open-source program RBOT (Region-based Object Tracking) for pose estimation. Finally, registration of the liver silhouette was performed using the medical image registration library SimpleElastix. The Hausdorff distance and IOU (Intersection over Union) were calculated between the ICG fluorescence area and AR liver region mapping for accuracy evaluation.

Results and Discussion: The non-rigid registration before and after showed Hausdorff distances and IOU of 13.8 vs 13.1 mm and 0.58 vs 0.63, respectively, indicating a slight improvement in accuracy with non-rigid registration. While this method faces challenges, such as manual setting of initial positions, leveraging open-source programs and future enhancements including AI-based initial position estimation could lead to more accurate AR displays.

Abstract Submission No. 101329
O-0723

An Equivalence Design to compare two non-invasive tools to predict Esophageal Varices in Cirrhosis

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Background: We evaluated the diagnostic performance and Equivalence of Shear wave elastography (SWE), vibration controlled transient elastography (VCTE) and other non-invasive parameters in their predictive ability to detect the presence of esophageal varices and high-risk esophageal varices in patients with compensated cirrhosis of liver.

Methods: 108 patients with compensated cirrhosis of liver who underwent SWE, VCTE, endoscopy and base-line investigations were enrolled. Comparisons of the accuracy of prediction between groups were made by AUROCs. Regression analysis was performed for multiple variables.

Results: There were 64 males and 44 females, with a mean age of 51.73 ± 11.35 years. The predominant aetiologies were NASH (40%) and Alcohol (27%). Esophageal varices were detected in 63 patients, of which 36 patients had high-risk varices. The AUROC value of SWE (0.967) was comparable to that of VCTE (0.961) but significantly higher than other non-invasive parameters (platelet count, spleen diameter, platelet count/spleen diameter ratio, FIB-4, APRI). SWE had 92.1% sensitivity, 88.7% specificity, 90.6% PPV, and 88.6% NPV for predicting the presence of varices at an optimal cut-off value > 21.1 kPa, and 91.7% sensitivity, 88.6% specificity, 80.2% PPV, and 95.1% NPV for predicting high-risk varices at an optimal cut-off value > 24.6 kPa. No patient with SWE value < 20.3 kPa had varices.

Conclusion: The Equivalence of the predictive ability of SWE and VCTE to detect the presence of varices and high-risk varices is demonstrated in our study. The other non-invasive parameters were found to be inferior to them

Abstract Submission No. 101891
O-0724

Mimic nanovesicle with Enhanced PD-1 Expression Induce Immunomodulation for immunotherapy after iRFA

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Background: Radiofrequency ablation (RFA) was one of the most effective treatments for controlling early HCC. However, the recurrence rate remains as high as other treatment modalities owing to immunosuppressive tumor microenvironment. As reported, Lenvatinib blockade FGF Receptor 4, leading to the decrease the expression of tumor PD-L1 and restriction of Treg differentiation. Herein, we synthesis a macrophage-membrane modified nanovesicle with enhanced PD-1 expression for reversing the immunosuppressive tumor microenvironment and enhance the adaptive immune response after insufficient RFA (iRFA).

Methods: The synthesized nanovesicle LMP@Len was consisted of a lipid/macrophage-membrane (enhanced PD-1 expression) shell for carrying Lenvatinib. The characterization of LMP was evaluated by TEM and Nano ZS90. The fusion of lipid and membrane was detected by CLSMs and Flow cytometry assay. Cytotoxicity of LMP were detected by CCK-8 assay. Flow cytometry and immunofluorescence staining were applied to investigate the effect of LMP on reversing immunosuppressive microenvironment of residual tumor.

Results: The synthesized LMP@Len can significantly avoid the phagocytosis by kuffer cell in vitro and more effectively accumulated in tumor cite than the liposome in vivo. The combination therapy of Lenvatinib and the PD-1 antibody expressed on the macrophage-membrane effectively inhibited the recurrence of Hepa1-6 tumor. The infiltration percent of Tregs decreased to 1.02±0.50% in treatment group from 3.64±0.90%. Compared with iRFA group, the infiltration of CD8+T cells increased 2 folds with the combination therapy.

Conclusion: Blocking PD-L1 and Tregs was an attractive strategy to enhance the therapeutic efficacy of ICB with LMP@Len.

Abstract Submission No. 100725
O-0725

New oncolological resectability of CRLM and multidisciplinary treatment strategy

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Background: For colorectal liver metastasis (CRLM), selection of multidisciplinary strategy is not clearly determined. We advocate new resectability using maximum diameter×number, and show treatment strategy along with this resectability.

Methods: 1. CRLM patients who underwent up-front surgery (n=144) were enrolled, and definition of oncological R/BR/UR was investigated. Prognosis was compared with NAC cases (n=20).

2. Initially unresectable CRLM patients (n=78) were enrolled. Treatment strategy for conversion surgery was investigated.

Results: 2. Definition of oncological R/BR/UR:

Maximum Diameter x Number: MDN could stratify prognosis of patients who underwent up-front surgery. MDN<15 showed better prognosis than local therapy other than surgery, and defined as R. prognosis of MDN≥30 was comparable with initially unresectable cases, and defined as UR. 15≤MDN<30 was defined as BR. BR cases with adjuvant

chemotherapy showed tendency of better prognosis than without adjuvant chemotherapy (p=0.07), and there were long survivors with oxaliplatin base chemotherapy. On the other hand, adjuvant chemotherapy showed no effect in R cases. In R cases, prognosis was comparable with NAC cases (p=0.85).

2. Strategy for conversion surgery in initially unresectable cases

In initially unresectable cases, factors for conversion showed MDN≤70, no extrahepatic metastasis, FOLFOXIRI regimen were defined. Independent prognostic factors after conversion were FOLFOXIRI regimen and low MRI-ADC min value<0.7.

Conclusion: We advocated new resectability for CRLM using MDN. Our strategy along with oncological resectability as follows: Up-front surgery without adjuvant chemotherapy for MDN<15, oxaliplatin base adjuvant chemotherapy for 15≤MDN<30, conversion surgery with FOLFOXIRI regimen for 30≤MDN<70; MRI-ADC value can predict timing of hepatectomy.

Abstract Submission No. 100949
O-0726

FLNA cargo in exosome promote pre-metastatic niche formation in intrahepatic cholangiocarcinoma

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Background: Lymph node metastasis is a frequent occurrence in patients with intrahepatic cholangiocarcinoma (ICC), which makes patients suffer from worse outcome. Accumulating evidences have shown that pre-metastatic niche(PMN) formation play an irreplaceable role in lymph metastasis preferentially development. However, the biogenesis and media of PMN formation in ICC remains unclear.

Methods: Effects of exosome separated from ICC cell lines were confirmed by western-blot and other phenotype analyses. The exosomal protein for promoting Lymphatic metastasis were verified by intravenous injection of ICC-derived exosomes and sleeping beauty system. Mouse intrahepatic cholangiocarcinoma models via hydrodynamic were applied for scRNA-seq, aiming to detect the landscape of PMN in lymph node.

Results: Our results indicate that Filamin A (FLNA) as an oncogene in ICC, FLNA specifically regulate extracellular vesicle cargo selection. Incubating human lymphatic endothelium cell with ICC cell-secreted exosome increases tube forming capacity, which contributes to the formation of PMN in lymph node. We also found ICC cell-secreted exosome promoting the PD-1 expression of CD8+ T-cell, which consequently accelerates immune escape, both effects related with the FLNA expression in tumor. Moreover, FLNA level in serum exosome of ICC patients with lymph metastasis is significantly higher than those with negative lymph node.

Conclusion: Our results indicate that FLNA plays an important role in educating lymphocytes and endothelial cells, which associated with the formation of PMN in lymph node. The data from mouse and patient samples further reflect FLNA as a potential target for clinical diagnosis and treatment of intrahepatic cholangiocarcinoma lymph node metastasis.

Abstract Submission No. 101264
O-0727

Exploring genes involved in proliferation of intrahepatic cholangiocarcinoma using clinical samples

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Purpose: Our study aimed to elucidate the molecular pathology underlying intrahepatic cholangiocarcinoma (ICC) growth through comprehensive RNA analysis of clinical samples.

Method: RNAs were extracted from serum exosomes and tumor tissues of 24 patients (average age: 63.8 years) undergoing surgical resection for hepatobiliary tumors at our hospital. The cohort included 10 cholangiocarcinomas, 10 hepatocellular carcinomas, and 4 benign tumors. High-sensitivity microarray and in silico screening identified differentially regulated RNAs among tumor groups.

Results: High-ranked RNAs were selected by target database, resulting in a focus on microRNA-3648 (targeting LPL, SKI, and APC2). Assessment of these target mRNAs in the human ICC cell line (OZ), overexpressing microRNA-3648, revealed a 6.7-fold decrease in SKI protein expression compared to negative controls (ANOVA $p < 0.01$). SKI-overexpressing OZ showed increased p21 expression at mRNA, protein, and promoter luciferase levels (2.6-fold increase, 2.1-fold increase, 1.5-fold increase; ANOVA $p < 0.01$, < 0.05 , < 0.05), inhibiting cell proliferation and DNA replication factor CDT1 protein expression (1.8-fold decrease, 1.5-fold decrease; t -test $p < 0.01$, < 0.05) [vs. negative controls, respectively]. The p21 protein increase disappeared in OZ overexpressing SKIΔ, a plasmid with a deleted p21 transcription-related amino acid sequence (1.6-fold decrease vs. SKI plasmid, t -test $p < 0.05$). As a preliminary analysis, immunostaining in a mouse model of chemically induced precancerous bile ducts showed SKI-positive regions were Ki-67 negative.

Conclusion: Our findings suggest that SKI protein suppresses ICC growth (in vitro/in vivo) through p21 gene transcription (in vitro).

Abstract Submission No. 101582
O-0728

Prevalence of Chronic Liver Disease in Cholangiocarcinoma - A single arm metaanalysis of 113 studies

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Background: Chronic liver disease (CLD) is a well-associated risk factor for cholangiocarcinoma (CCA). Despite long-standing association, the population of patients with concurrent CCA and CLD remains poorly characterised. Recent data suggests potential prognostic implications of CLD in CCAs.

Methods: In this single-arm meta-analysis, we searched MEDLINE and EMBASE from inception to 6th June 2023 for English articles containing information for CCA patients with and without CLD.

Population data was pooled to obtain the prevalence of different CLDs within CCA population and stratified by geography and tumor location. **Results:** In total, 136346 CCA patients and 17909 CCA patients with concomitant CLD were identified. Amongst CCA patients, cirrhosis was the most prevalent CLD ($n = 6426$), followed by HBV ($n = 3936$), and HCV ($n = 1536$). Mean age of CCA patients with concomitant CLD was 62.3 years old while mean age of non-CLD CCA patients was 65.3 years old. Cumulative mean tumour size was 5.74 cm amongst CLD CCA patients and 5.92 amongst non-CLD CCA patients. Analysis of 113 studies showed overall prevalence of 24.8% (95% CI: 20.3 to 29.9%). By geography, CLD was most prevalent in the Eastern Mediterranean (42.4%, 95% CI: 38.2 to 46.7%), followed by Western Pacific (35.7%, 95% CI: 27.7 to 44.6%). By tumor location, CLD was most common in intrahepatic (36.3%, 95% CI: 28.8 to 44.5%) and perihilar CCA (24.8%, 95% CI: 10.7 to 47.5%) respectively.

Conclusions: Our results highlight the significant prevalence of CLD amongst the CCA population, allowing insight into a prominent CCA subgroup.

Abstract Submission No. 101873
O-0729

A nanodrug designed to maintain antitumor immunity in liver metastases after radiofrequency ablation

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Our study showed that the PD-1/PD-L1 blockade monotherapy failed to prolong the progression-free survival in patients following radiofrequency ablation (RFA) treatment for liver metastases from colorectal cancer. Furthermore, we found that the PD-1/PD-L1 immune checkpoint blockade (ICB) therapy after RFA in mice model only temporarily inhibited tumor progression due to the limited number of mature dendritic cells (DCs) and the insufficient tumor infiltration/activation of cytotoxic T lymphocytes (CTLs). In addition, stimulator of interferon gene (STING) activation, which affects tumor-infiltrating DCs and CD8⁺ T cells, was only transient after tumor RFA. (Figure 1) Therefore, a nanovesicle capable of spatiotemporally controlled release of the anti-PD-L1 antibody (α PD-L1) and STING agonist within the tumor was developed to evoke a robust anti-cancer immune response and immune memory for a long-term inhibition of tumor progression after RFA. The nanovesicle entrapping the hydrophilic STING agonist 5,6-dimethylxanthine-4-acetate sodium salt (DMXAAst) in its lumen and anchored α PD-L1 via an MMP-2-sensitive peptide linker was coated with PEG layer sheddable in the acidic tumor microenvironment. The nanodrug design allowed the PEG coating to block off-target interaction between α PD-L1 and PD-L1-positive normal cells in blood and normal tissues, thereby reducing the immune-related adverse effects (irAEs). α PD-L1 was first released in response to MMP-2 overexpressed in the residual tumor after RFA for ICB therapy, which promotes the intracellular delivery of DMXAAst to activate STING in DCs. The synergistic effect of α PD-L1, DMXAAst and RFA evoked a robust anti-tumor immunity and long-term immune memory for a potent cancer therapy. (Figure 2)

Abstract Submission No. 101970

O-0730

The Efficacy of Total Tumor Volume in Patients with Colorectal Liver Metastases

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Background: Few reports have discussed the association between total tumor volume (TTV) and prognosis in patients with colorectal liver metastases (CRLM). The present study aimed to evaluate the usefulness of TTV for predicting recurrence-free survival and overall survival (OS) in patients receiving initial hepatic resection or chemotherapy, and to investigate the value of TTV as an indicator for optimal treatment selection for patients with CRLM.

Methods: This retrospective cohort study included patients with CRLM who underwent hepatic resection (n = 93) or chemotherapy (n = 78) at the Kobe University Hospital. TTV was measured using 3D construction software and computed tomography images.

Results: A TTV of 100 cm³ has been previously reported as a significant cut-off value for predicting OS of CRLM patients receiving initial hepatic resection. For patients receiving hepatic resection, the OS for those with a TTV $\geq$ 100 cm³ was significantly reduced compared with those with a TTV < 100 cm³. For patients receiving initial chemotherapy, there were no significant differences between the groups divided according to TTV cut-offs. Regarding OS of patients with TTV $\geq$ 100 cm³, there was no significant difference between hepatic resection and chemotherapy (p = 0.160).

Conclusions: TTV can be a predictive factor of OS for hepatic resection, unlike for initial chemotherapy treatment. The lack of significant difference in OS for CRLM patients with TTV $\geq$ 100 cm³, regardless of initial treatment, suggests that chemotherapeutic intervention preceding hepatic resection may be indicated for such patients.

Abstract Submission No. 102030

O-0731

High-risk CRLM can provide excellent survival through multidisciplinary treatment including ablation

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Introduction: Beppu score can predict postoperative disease-free survival for patients with resectable colorectal liver metastases (CRLM). Based on the Beppu score, three groups were clearly estimated by recurrence-risk stratifications as low-risk ($\leq$ 6 points), moderate-risk (7-10 points), and high-risk ($\geq$ 11 points). For high-risk patients, hepatectomy following preoperative chemotherapy is recommended. We evaluated the treatment efficacy, focusing on the combination use of local ablation.

Patients and Methods: Between April 2016 and April 2022, twenty patients with CRLM diagnosed as technically unresectable or oncologically high-risk were evaluated.

After induction chemotherapy, conversion surgery using hepatectomy with or without local ablation was immediately attempted. Local ablation was permissive for patients with effective chemotherapy, CRLM $\leq$ 2cm, and $\geq$ 5mm distant from major vessels.

Results: The largest diameter and number of CRLM were 15cm and 46, respectively. Preoperative chemotherapy was performed for 18 patients, and all of them were judged as disease control. Local ablation was simultaneously conducted in 14 patients; all tumors were within the selection criteria: the median number was 3 (1-21), and the median diameter was 12.5mm (5-17mm). Local recurrence rates at the ablation sites were 7/82 (8.5%) per nodule. Three-year disease-free and five-year overall survival were 57.4% and 56.2%, respectively. There were no significant differences in patients with or without local ablation.

Conclusion: Our treatment strategy for patients with high-risk CRLM is feasible and can provide an excellent long-term prognosis instead of the additional use of local ablation on hepatectomy.

Abstract Submission No. 102045

O-0732

Hepatic arterial infusion is effective in patients with unresectable colorectal liver metastases

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We identified an effective chemotherapy regimen in patients who are refractory to standard chemotherapy. We included patients with unresectable colorectal liver metastases who underwent hepatic artery infusion chemotherapy and systemic chemotherapy between January 2015 and December 2022. Patients received either biweekly oxaliplatin and 5-fluorouracil through hepatic artery infusion chemotherapy as well as bevacizumab and leucovorin injected intravenously (HAIC-FOLFOX-B) or biweekly irinotecan and 5-fluorouracil by hepatic artery infusion chemotherapy and bevacizumab and leucovorin injected intravenously (HAIC-FOLFIRI-B). Of the 42 patients, 20 underwent HAIC-FOLFOX-B while 22 underwent HAIC-FOLFIRI-B treatment with response rates of 25% and 4.5%, respectively. The median overall survival and progression-free survival were 12.9 and 4.7 months and 17.4 and 7.7 months in patients undergoing HAIC-FOLFOX-B and HAIC-FOLFIRI-B, respectively. Of the 11 patients who had undergone oxaliplatin-based chemotherapy, eight received HAIC-FOLFOX-B and three received HAIC-FOLFIRI-B. The median overall survival and progression-free survival periods including the previous systemic chemotherapy period were 30.8 and 8.0 months, respectively. HAIC-FOLFOX-B and HAIC-FOLFIRI-B may improve survival in patients with unresectable colorectal liver metastases and in those who underwent both systemic oxaliplatin-based and irinotecan-based chemotherapies and were refractory to them. HAIC FOLFOX-B/FOLFIRI-B regimens may be effective therapeutic options for patients with unresectable colorectal liver metastases refractory to standard systemic chemotherapy.

Abstract Submission No. 102083

O-0733

IL-33 facilitates iCCA progression by increasing the secretion of IL-6 from CAFs

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Background: In the previous study, we reported that IL-33 level was elevated by hepatectomy, and intrahepatic cholangiocarcinoma (iCCA) cells growth were facilitated by adding cancer associated fibroblasts (CAFs) culture medium treated with IL-33, however the specific mechanism is still unknown.

Methods: We compared the proliferation and migration ability among following three groups: control group: iCCA cell were incubated in normal culture medium, IL-33(+) group: iCCA cells were incubated by adding condition medium of fibroblasts in cancer (CM-FiC) treated with IL-33, and IL-33(+)-anti-IL-6 group: iCCA cells were incubated by adding CM-FiC treated with IL-33 and anti-IL-6 antibody. Furthermore, murine experiments were performed and compared the tumor progression among following six arms: laparotomy arm, hepatectomy arm, laparotomy and co-transplantation with fibroblasts of murine iCCA cancer (mFiC) arm, hepatectomy and co-transplantation with mFiC arm, laparotomy and co-transplantation with mFiC treated with anti-IL-6 antibody arm, and hepatectomy and co-transplantation with mFiC treated with anti-IL-6 antibody arm.

Results: The malignant potencies of iCCA cells in both proliferation and malignant ability was facilitated by adding CM-FiC ($p < 0.001$, $p < 0.05$). Furthermore, both proliferation and migration ability were decreased by anti-IL-6 treatment ($p < 0.001$, $p < 0.05$). And in vivo experiments, the tumor size was larger in mFiC co-transplantation arms than not co-transplantation arms ($p < 0.05$), and the tumor size was reduced approximately 50% with anti-IL-6 treatment.

Conclusion: Our results suggested that IL-33 facilitated iCCA progression through increasing the secretion of IL-6 from CAFs.

Abstract Submission No. 200261

O-0734

Radio-Frequency Ablation of Hepatic Metastases from Sarcoma

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Background: The liver is the most common site of metastases from sarcoma. At present, surgery is considered to be the only therapy that offers the possibility of cure for patients with hepatic metastatic diseases. However, there are not many patients with the metastases treatable by the surgical resection, while remainings are treated with chemotherapy or best supportive care. This study was conducted to clarify the safety and efficacy of percutaneous radiofrequency ablation (RFA) for unresectable liver metastases from sarcoma.

Methods: 2004 to 2013, 143 patients with unresectable liver metastases from sarcoma were treated by RFA. The mean number and size of hepatic tumor foci were, 5.6 and 60mm, respectively. 114 patients had extrahepatic metastases. 97 patients were nonresponders to previous chemotherapy.

Results: 143 patients had received a total of 333 RFA procedures. There was no procedure-related mortality. 9 complications were observed. At the initial ablation, all the patients enjoyed the benefit of volume reduction ($>80\%$) of metastatic tumors. 1-, 2-year survival were 86% and 68%. Multivariate analysis showed no significant prognostic factors.

Conclusions: This study showed RFA could safely reduce the volume of hepatic metastases, and might improve the prognosis of patients with unresectable liver metastases from sarcoma.

Abstract Submission No. 100522

O-0735

Hepatic lymphoma diagnosed by liver biopsy: Clinicopathological features of 15 Japanese patients

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Background: Malignant lymphomas are sometimes associated with liver involvement.

Methods: Fifteen cases of hepatic lymphoma diagnosed by liver biopsy at our institution from January 2008 to October 2023 were included.

Results: The patients were 6 males and 9 females with a mean age of 70.1 ± 13.3 years at the time of liver biopsy. Pathological diagnoses based on liver biopsy included 6 cases of diffuse large B-cell lymphoma, 4 cases of intravascular large B-cell lymphoma, 3 cases of peripheral T-cell lymphoma, 1 case of unclassified T-cell lymphoma, and 1 case of follicular lymphoma. Mass formation in the liver was observed in 9 of the 15 cases. The remaining 6 cases were diagnosed by background liver biopsy. Of the 9 cases in which liver masses were detected, 2 cases had single, 1 case had two, and the rest had three or more. Most of the hepatic lesions were hypoechoic on ultrasound. Duct-penetrating sign within the mass was seen in 6 of the 9 cases. Special imaging findings included bile duct dilatation at the periphery of the mass in one case and low-density areas along the Glisson's capsule on computed tomography in one case. Lymph node lesion was observed at the time of liver biopsy in 6 of the 15 cases. In only 1 case, no lymphoma lesions other than the liver were detected. One patient required blood transfusion due to intra-abdominal bleeding after liver biopsy.

Conclusion: Liver biopsy is important in the diagnosis of lymphoma with liver involvement.

Abstract Submission No. 100532

O-0736

A case of spontaneous rupture of a giant hepatic hemangioma

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Background: Spontaneous rupture of a hepatic hemangioma is rare, but a large amount of bleeding can be fatal. In this report, we describe a case of spontaneous rupture of a hepatic hemangioma that was treated with transcatheter arterial embolization (TAE) followed by surgery.

Case: A 46-year-old woman was referred to our department for a close examination of a 10 cm-sized mass in the right lobe of the liver after a simple computed tomography (CT) scan of the abdomen for anemia and anorexia. She was diagnosed as hepatic hemangioma based on fill-in enhancement on contrast-enhanced CT. She developed right hypochondriac pain without any trigger and returned to our department. Contrast-enhanced CT showed a hematoma in the right paracolic gutter, and she was admitted to our department with a diagnosis of spontaneous rupture of a hepatic hemangioma. Angiography was performed on the same day, and TAE was performed on the distal, full-

distal, and posterior segment branches of the right hepatic artery to prevent rebleeding. At a later date, she underwent a laparoscopic S5 + S6 partial hepatic resection.

Conclusion: Among patients with hepatic hemangioma, absolute indication for surgery is considered to be bleeding or Kasabach-Merritt syndrome, but relative indications for surgery are not clearly defined. According to a previous report, hepatic hemangiomas larger than 10 cm have a significantly higher risk of bleeding, and surgery may be considered for lesions larger than 10 cm with abdominal symptoms or coagulopathy.

Abstract Submission No. 100564
O-0737

The Chemotherapy Response Prediction Based on Radiomics Method in Liver Metastasis: a Meta-Analysis

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Background: Addressing heterogeneous chemotherapy response in liver metastasis is challenging. The using of imaging modality in addition to RECIST evaluation is known to have positive impact regarding the accuracy level. Radiomics method as machine learning application is thought to provide more objective interpretation. The scope of this study was to perform meta-analysis about the application of radiomics method in the evaluation of chemotherapy response in liver metastasis patient.

Method: Literature was systematically searched from PubMed over the last five years. The articles were original research that using artificial intelligence to assess chemotherapy response based on radiology imaging in liver metastases. The data extraction was analysed in R-Studio by Dersimonian-Laird method.

Results: Three studies were included with total 426 number of datasets. All studies have colorectal cancer as primary tumour and computed tomography as imaging modality. Those included study has different chemotherapy regimens, including: FOLFOX-based therapy, HER2-targeted therapy, and Oxaliplatin-Irinotecan. The machine learning used is also different, including deep convolutional neural network, logistic regression modelling, and Gaussian Naïve Bayesian classifier. The meta-analysis showed that sensitivity was 0.956 (95% CI 0.885-0.984; $p=0.05$, $I^2=66\%$), specificity was 0.549 (95% CI 0.478-0.617; $p=0.25$, $I^2=29\%$), negative likelihood ratio was 0.091 (95% CI 0.030-0.274; $p=0.38$, $I^2=0\%$), positive likelihood ratio was 2.080 (95% CI 1.593-2.714; $p=0.326$, $I^2=11\%$), and diagnostic odds ratio was 27.148 (95% CI 7.813-94.337; $p=0.12$, $I^2=53\%$).

Conclusion: Radiomics method has good accuracy to predict chemotherapy response in liver metastasis patient and its significantly difference of sensitivity than conventional model that use the interpretation of oncological radiologist.

Abstract Submission No. 100987
O-0738

Liver-Directed Microwave Ablation of Oligometastatic Renal Cell Carcinoma in a Cirrhotic Patient

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Background: Metastatic renal cell carcinoma (RCC) to the liver is not uncommon and portends poor prognosis. However, studies illustrated that patients with cirrhosis have a decreased risk of acquiring liver metastases. No reports yet of liver-directed therapies in a cirrhotic patient with RCC. We present a unique case of oligometastatic RCC in a patient with liver cirrhosis who successfully underwent liver-directed microwave ablation (LD-MWA) prior to nephrectomy.

Case Description: A 64-year-old obese, diabetic female sought consult due to flank pain. Work-up revealed pyuria and microscopic hematuria, and a left renal mass on ultrasound. Computed tomography (CT) showed a 5x6x6 cm mass at the left kidney; with noted cirrhotic liver with hypodense lesions at right lobe; chest CT was unremarkable. Liver function was preserved, and AFP was normal. Same session ultrasound-guided percutaneous liver biopsy and microwave ablation of the lesions were done. Post-ablation imaging showed complete ablation. Liver biopsy exhibited carcinoma with clear cell features. Patient underwent laparoscopic radical nephrectomy with uneventful postoperative course.

Conclusion: Patients with oligometastatic RCC in a cirrhotic liver represent a challenging case requiring multidisciplinary management. LD-MWA as an alternative to surgical metastatectomy, may be offered in these cases. Further studies are needed to identify patients who will benefit most from this strategy.

Abstract Submission No. 101095
O-0739

Neoadjuvant FOLFOXIRI therapy for patients with colorectal liver metastasis

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Background: Based on our previous analysis, patients with H2/3 or ≥ 3 in number colorectal liver metastases (CLM) are considered high risk (HR)-CLM with poor prognosis even after radical resection. For these patients, we've performed FOLFOXIRI therapy (4 courses) as neoadjuvant chemotherapy (NAC). In this study, we investigated the safety and efficacy of NAC-FOLFOXIRI therapy in patients with technically resectable HR-CLM.

Methods: Fifteen patients diagnosed with HR-CLM and treated with NAC-FOLFOXIRI between 2020 and 2023 were included. Their treatment modalities and short-term outcomes were evaluated retrospectively. Values are expressed as median.

Result: Patient background was 64 years of age, 13 cases of synchronous metastasis, maximum diameter of liver metastasis 38 mm, and 4 tumors. About half of the patients had G3 or greater AEs, but all patients completed the scheduled NAC. The tumor reduction rate was 38.4%, and RECIST evaluation showed 8 cases of PR, 6 cases of SD, and 1 case of PD. 11 patients underwent hepatic resection, excluding 1 case of PD, 1 patient who died of other disease, 1 patient who refused surgery, and 1 patient with liver dysfunction. Five of the 11 patients underwent liver resection with more preserved liver function compared to the planned procedure before NAC. After operation, one patient died due to liver failure, but the others had no severe complications, and the median postoperative hospital stay was 11 days. The died patient had significant hepatic atrophy and liver dysfunction (ICG 18%) after NAC. Therefore we now consider a liver volume reduction of $<10\%$ and ICG $<15\%$ after NAC as an indication for hepatectomy.

Conclusion: NAC-FOLFOXIRI for technically resectable HR-CLM may contribute to liver parenchymal preservation, but liver dysfunction should be noted.

Abstract Submission No. 101434
O-0740

Title: Dark spots without a trace - a case of melanoma of unknown primary in the liver

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Background: Malignant melanoma (MM) is an aggressive neoplasm with increasing incidence. In 3.2% of cases, Melanoma of Unknown Primary (MUP) behaves as an occult melanoma where no primary is found. We report a case of MUP presenting as liver lesions.

Case report: A 54-year-old lady with no significant past medical history presented to hospital with unintentional weight loss. Computed Tomography (CT) scan showed prominent supraclavicular and hilar lymph nodes and multiple indeterminate hepatic lesions. There was no liver cirrhosis. In this admission, she was newly diagnosed with Pulmonary Tuberculosis (TB), and started on treatment. Laboratory tests done revealed an incidental past Hepatitis C infection, but liver function tests and alpha-fetoprotein were normal. With further Magnetic Resonance Imaging (MRI) of the liver, differential diagnoses were either multifocal hepatocellular carcinoma, liver metastases or hepatic tuberculosis, in view of newly diagnosed TB. She underwent a percutaneous liver biopsy of the lesions and histology confirmed a melanoma.

Full clinical examination identified no suspicious cutaneous lesions. Upper and lower endoscopy were negative for gastrointestinal malignancies. Ophthalmological evaluation revealed no uveal lesions and nasoendoscopy was normal. Positron emission tomography (PET) also demonstrated no obvious primary malignancy. Despite this, she remained well with no hepatic complications from the liver lesions and was started on immunotherapy of Nivolumab by the oncologist as treatment for MUP.

MM presenting as liver lesions is rare and requires thorough physical examination and corresponding investigations to search for the primary lesion. If the primary is not identified, MUP should be considered.

Abstract Submission No. 101481
O-0741

Patterns of liver metastasis in ovarian cancer

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Introduction: In ovarian cancer, the liver is involved via two mechanisms; liver parenchymal invasion (LPI) from perihepatic peritoneal metastasis (FIGO stage III) and hematogenous spread (FIGO stage IV) with the second one having shorter survival.

Case history: A 37-year-old female presented with loss of appetite & abdominal distension. CA 125 was 1888.5 IU/L. MRI showed bulky ovaries, ascites, lymphadenopathy, and nodules on the omentum & liver surface with right pleural effusion.

Ascitic fluid Cytology & US-guided FNAC of omental nodule confirmed Adenocarcinoma. Considering Ovarian Carcinoma, the 3# TP regimen was followed by cytoreductive surgery, followed by the 3 #

TP regimen. After 4 months, investigations showed progressive disease.

Oral metronomic therapy with oral CE (cyclophosphamide and etoposide for 1-5 days, every 21 days) was given. After 2 cycles the response was poor with PS-2 & CA 125 3830 IU/L. CECT showed progressive disease. **Gemcitabine + Cisplatin** (GC) regimen was started with D1, and D15 plans. This was being tolerated well. Post CT#2; Grade 2 thrombocytopenia resulted in to Gemcitabine dose reduction further. POST 3# GC regimen no response was seen. Weekly Paclitaxel was advised. As a last option, in case of no response after 2, the BSC regimen (Paclitaxel + Carboplatin + Bevacizumab) remains an option.

Discussion & Conclusion: This case had pleural as well as hepatic involvement. Resection of pleural & hepatic nodule was done. During surgery, with LPI, 1-2 cm resection margin & with liver portal lymph node metastasis, skeletonization is emphasized, not just lymph node dissection.

Key words: liver metastasis, ovarian cancer, Pattern

Abstract Submission No. 200198
O-0742

Reconsidering cholangiolocellular carcinoma from two cases presenting with different characteristics

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Cholangiolocellular carcinoma (CoCC) is small duct type intrahepatic cholangiocarcinoma (ICC) according to WHO classification. We experienced two patients with different clinicopathological findings, prompting us to reconsider CoCC characteristics.

Patients: A 76-year-old male with a mass on US, underwent CEUS revealing whole-tumor enhancement and washout within one minute. It (46 mm) showed arterial peripheral enhancement and equilibrium phase delayed enhancement on CECT. Retrospectively, the mass (6 mm) had appeared as arterio-portal shunt 9 years earlier. The tumor doubling time (DT) was 380 days. EOB-MRI showed decreased uptake in the hepatobiliary phase. CA19-9 was 43.7U/mL. As ICC/CoCC was suspected, partial hepatectomy was performed and yielded a CoCC diagnosis. He has remained recurrence-free for 1.5 years. Our other patient, a 58-year-old female, detected a mass during follow-up for NBNC hepatitis. It (72 mm) was hyper-enhanced in early-phase CECT, followed by washout. A CT from 22 months prior showed a 15 mm-mass. DT was 126 days. Uptake was decreased on EOB-MRI hepatobiliary phase. PET-CT revealed FDG uptake. AFP/PIVKA-II were slightly elevated. She underwent hepatectomy under a diagnosis of hepatocellular carcinoma. Histologically, the tumor had necrosis and tubular structures of various sizes with apical membranes positive for EMA, indicating CoCC. Postoperative lymph node and bone metastases were found 2 and 13 months, respectively.

Conclusion: DT was prolonged in both patients as compared to previous report in ICC cases. This implies good outcomes. One had a well-differentiated, however, the other a mixed well to poorly-differentiated tumors reflecting marked clinicopathological differences. Diversity exists among CoCC cases.

Abstract Submission No. 200226
O-0743

EUS Role in Defining Endoscopic and Histopathological Spectrum of Liver Lesions -South Asian Study

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Introduction: Conventionally liver lesions sample are acquired by transabdominal ultrasound guided procedure. Currently EUS guided liver biopsies demonstrated better diagnostic yield with lesser adverse event.

Aim: Aim of study to evaluate safety and diagnostic role of EUS in defining different endoscopic and histopathological spectrum of liver lesions in our region (South Asia).

Method: It is a descriptive study conducted at Endoscopy Suite, Aga Khan University Hospital from January 2021 to December 2023. All inpatient and outpatient with Liver lesion with or without organ involvement were included in study. Data were collected and analyzed using SPSS Version 22.

Results: Total 20 patients were included in the study. Majority of patients were male 15(75%) while 5(25%) were female. All patients were adult above 33 years ranging from 34 to 78 years. Main Indications for EUS guided biopsies were pancreatic mass with Liver Lesions 7(35%), Isolated liver lesion 4(20%) and Porta hepatis mass with Liver Lesions 3(15%). All procedures were done in conscious sedation and most of patient had ASA- score II 13(65%). In all procedures, 22G FNB needle with slow pull technique were used major of single pass 13(65%), diagnostic yield was 100% with no sedation and procedure related complication.

Histopathology analysis revealed common findings were metastasis of pancreatic origin 10(50%) comprising of adenocarcinoma (35%) and NET (15%), metastatic cholangiocarcinoma 3(15%) and Isolated liver lesions 4(20%) which includes HCC 2(10%) and benign 2(10%).

Conclusion: Our study concludes EUS guided liver lesion biopsies are safe with high diagnostic yield. Metastatic diseases comprising pancreatic adenocarcinoma is the commonest histological finding followed by cholangiocarcinoma and hepatoma.

Abstract Submission No. 100075
O-0744

Lower incidence of adverse liver outcomes and HCC in patients with chronic liver disease and HIV

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Background: People living with HIV (PLWH) show a high incidence of chronic liver disease (CLD). However, whether HIV is associated with major adverse liver outcomes (MALO) in patients with underlying CLD remains to be determined.

Methods: In this population-based cohort study, data were retrieved from the Swedish National Patient Register to identify PLWH and CLD (n=2,375) or CLD without HIV (n=144,346) between 1997 and 2020. The cumulative incidence of MALO was calculated while accounting for competing risks (non-MALO death). Incidence rates per 1000 person-years were compared between the exposure groups (HIV

vs. no HIV) with Cox regression to estimate adjusted hazard ratios (HR) and their 95% confidence intervals (CIs).

Results: The incidence rate per 1000 person-years of MALO was lower in PLWH (5.1, 95% CI 4.2-6.1) compared to patients without HIV (13.1, 95% CI 12.9-13.3). This translated into an adjusted HR of 0.77 (95% CI 0.64-0.93), driven by a lower rate of hepatocellular carcinoma (adjusted HR=0.61, 95% CI 0.43-0.86). Consistent results were noted across a range of subgroup analyses. The 10-year cumulative incidence of MALO was lower in PLWH (5.0%, 95% CI 4.1-6.1) than in patients without HIV (10.9%, 95% CI 10.7-11.0).

Conclusion: Among patients with CLD, the risk of MALO was lower in PLWH compared to those without HIV, primarily due to a lower incidence of HCC. These results suggest that HIV is not associated with a higher risk of MALO.

Abstract Submission No. 100085
O-0745

Genotype 4 HEV infection trigger the initiation and development of acute pancreatitis

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Background: The role of HEV infection in pancreatitis patients remains unclear.

Methods: 1000 eligible patients with AP, 1000 healthy controls (HCs) and 300 patients with AHE were enrolled. Rhesus macaques with HEV infection model was constructed to assess pancreatitis in rhesus macaques infected with HEV.

Results: The positive rates of anti-HEV IgG, anti-HEV IgM and HEV RNA in the AP patients were all significantly higher than HCs. With the increase of the severity of AP, the percentage of HEV infection also increased significantly. The percentage of patients with severe AP in the AP+AHE group was significantly higher than the AP- group. Moreover, HEV infection was one of the main independent risk factors and owned the high predictive power for the outcome of AP. High level of HEV titre would prolong the recovery time. Both ISH and IHC showed that HEV replicates in the pancreas of rhesus macaques. HE staining showed that the structure of the pancreatic islets was damaged and the tissue was loose after 272 dpi of HEV infection. After 770 dpi, a large amount of hyperemia appeared in the pancreatic islets. Both IFA and quantitative analysis of CD45 and F4/80 showed rhesus macaques infected with HEV caused a large number of inflammatory cells in the pancreas. Quantitative detection of HEV RNA in the serum, liver, and pancreas of rhesus macaques revealed that the pancreas and liver had a comparable viral load.

Conclusions: HEV infection plays an important role in the occurrence, development and prognosis of AP.

Abstract Submission No. 100438
O-0746

A nomogram for diagnosing infection in older patients with AoCLD: a nationwide prospective study

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Objective: The prevalence of acute-on-chronic liver diseases (AoCLD) in the older population has been steadily rising, with infection being the most prevalent complication and leading cause of mortality in this group. Therefore, the early and accurate diagnosis of infection in older patients with AoCLD holds significant clinical importance. This study aims to uncover the clinical characteristics and risk factors associated with infection in older patients with AoCLD and develop a specific diagnostic nomogram model for this population.

Methods: The study population was selected from the large-scale, prospective, multicenter CATCH-LIFE cohort established by Chinese Chronic Liver Failure (CLIF) Consortium, including 3970 patients with AoCLD. The t-test or Mann-Whitney U test was employed to compare clinical indicators between the infection and non-infection groups. Univariate logistic and lasso regression analysis was used to identify independent risk factors, and an easy-to-use nomogram was established. Performance was assessed using area under the curve, calibration plots and decision curve analysis (DCA).

Results: A total of 809 older patients with AoCLD were included. The comparison of baseline clinical characteristics between infected and non-infected older AoCLD patients were compared. Multivariate logistic regression analysis showed that cirrhosis, absolute count of eutrophic (N) and c-reactive protein (CRP) were independent risk factors for infection in older patients with AoCLD. The ROC curve based on these three variables accurately identified infection in older patients with AoCLD (AUC=0.805, P=0.000).

Conclusions: Our model will assist early and accurate diagnosis in older patients with AoCLD, subsequently facilitate early intervention to prevent adverse outcomes.

Abstract Submission No. 100538
O-0747

Imprinted SARS-CoV-2 humoral immunity induces a high Omicron reinfection risk in cirrhotic patients

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Background: The potential risk and related mechanism of Omicron reinfection after BA.5 breakthrough infection (BTI) in cirrhotic patients remain unclear.

Methods: We collected peripheral blood samples from 32 cirrhotic patients with different SARS-CoV-2 vaccination history 9 to 31 days after BA.5 infection to evaluate the hybrid humoral immunity. Serum neutralizing activity against Omicron subvariants was examined by pseudovirus neutralization assay. BA.5 specific B cell memory was evaluated by flow cytometry.

Results: Omicron BA.5 BTI elicited higher serum geometric mean titers (GMTs) against Wuhan-1 rather than BA.4/5 in cirrhotic patients with wildtype (WT)-based vaccination history regardless of 2-dose group and 3-dose group, but converse result was shown in unvaccinated patients. The serum GMTs against highly immune-evasive XBB.1.5 were lowest in all cirrhotic patients. In the 3-dose cohort, more than 80% of the BA.5 anti-receptor-binding domain (RBD)-binding memory B cells (MBCs) also bind to WT, indicating that BA.5 BTI mainly recalls cross-reactive MBCs elicited by WT-based vaccine, but rarely produces BA.5 specific MBCs. Besides, when compared with 2-dose group, cirrhotic patients with 3-dose vaccination did not show significant increased serum GMTs against BA.4/5 and XBB.1.5,

consistent with the frequencies of BA.5 specific MBCs and plasmablasts (PBs).

Conclusions: We reported the imprinted SARS-CoV-2 humoral immunity shaped by WT-vaccination in cirrhotic patients for the first time, which predicts their high risk of reinfection in next potential wave including XBB.1.5. Our results supported the consideration of incorporating the Omicron variants into subsequent vaccine design and performing more studies of alleviating immune imprinting in this vulnerable population.

Abstract Submission No. 100842
O-0748

CLINICAL PROFILE AND OUTCOME OF PATIENTS WITH HEPATIC TUBERCULOSIS

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Background: Tuberculosis (TB) infection continues to increase globally. Available data on hepatic tuberculosis is limited and outdated. Recent guidelines included case definition and ancillary tests not considered in previous studies. We aimed to provide an updated clinical profile and outcome of these patients.

Materials and Methods: Consecutive patients diagnosed with hepatic tuberculosis in a single outpatient hepatology clinic from February 2007-December 2022 were included. All patients were given anti-TB treatment intended for at least 12 months. Demographics, biochemistries, imaging findings and treatment outcomes were recorded.

Results: 40 patients were included, of which 23 (58%) were culture/GeneXpert-positive (bacteriologically confirmed) while 17 (42%) were clinically diagnosed (culture/GeneXpert-negative but consistent with TB on histology/imaging/clinical course). Biliary tree involvement (32.5%) and pulmonary TB (40%) were not uncommon. Majority (95%) presented with liver mass/es with a median size of 6 cm, while calcifications were seen in 50%. Despite previous TB treatment in 22.5%, only two patients (5%) had multi-drug resistant strains. Excluding 12 patients lost to follow up, 75% had treatment response, 14% had inadequate response and 11% developed biliary strictures despite initial response. No patient developed drug-induced liver injury from treatment.

Conclusion: Despite the advent of more sensitive tests to detect TB, like GeneXpert, the ability to confirm the presence of the bacteria in hepatic TB remains elusive, and empiric treatment in the background of a consistent clinical scenario may be needed. Response to treatment does not guarantee that biliary fibrosis as a response to the chronic inflammation of TB will not develop.

Abstract Submission No. 100995
O-0749

Molecular mechanisms of epigallocatechin gallate to treat granulomatous hepatitis caused by Q fever

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Coxiella burnetii, the etiological agent of Q fever, is a highly infectious and intracellular bacterium capable of causing granulomatous hepatitis, a severe and often chronic condition with limited therapeutic options. Epigallocatechin-3-gallate (EGCG), a polyphenolic compound found in green tea, has demonstrated anti-pathogenic potential against various infectious agents. This study aimed to elucidate the antipathogenic mechanisms underlying EGCG's efficacy against the pathogenesis of *C. burnetii* in granulomatous hepatitis using a bioinformatics model. A bioinformatics approach employing STITCH v.5.0 program was used to identify the protein targets and predict their functional role and virulence properties. EGCG was found to target ten important proteins of *C. burnetii*, including dihydrolipoyl dehydrogenase (lpdA), dihydrofolate reductase (folA), peptidyl-prolyl cis-trans isomerase surA (CBU_1980), DNA mismatch repair protein (mutL), (3R)-hydroxymyristoyl-ACP dehydratase (fabZ), aspartate aminotransferase (aspB), polyketide synthase (CBU_0788), methylated-DNA-[protein]-cysteine S-methyltransferase (ogt), hypothetical protein (1415), and ABC transporter permease (CBU_0933). Specifically, those identified virulence factors are essential in the survival of *C. burnetii*. It can be concluded that the anti-pathogenic mechanism of EGCG against *C. burnetii* in granulomatous hepatitis is through blocking several virulence factors associated with bacterial cell survival and metabolisms. However, the findings of this bioinformatics study need to be further proven and validated using *in vitro* and *in vivo* experiments.

Abstract Submission No. 101075
O-0750

***In vitro* and *in vivo* hepatitis A virus infection models for anti-HAV drugs screening**

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Aims: Developing a new *in vivo* HAV infection mouse model.

Methods: 1) Human hepatoma cell line Huh7 or HepG2 were infected with HAV GT-IB HM175 or GT-IIIa HA11-1299 strain and then transplanted into the back of nude mice as xenografts. 2) HAV RNA were measured by real-time RT-PCR in feces, sera, liver and intestinal tissues and tumors of the mice. 3) Tissues were stained by H&E. 4) Serum aminotransferases were measured by ELISA.

Results: 1) No difference in the bodyweight of HAV infected and uninfected mice. Mice transplanted with HepG2 cells and mice transplanted with Huh7 cells were sacrificed after 13 days and after 32 days of transplantation, respectively. 2) Mice transplanted with HepG2 cells of HAV infection - HAV RNA detected in tumors only. 3) Mice transplanted with Huh7 cells of HAV GT-IB HM175 infection - No tumor and no HAV RNA detected. 4) Mice transplanted with Huh7 cells of HAV GT-IIIa HA11-1299 infection - HAV RNA detected in feces, sera, liver and intestinal tissues and tumor. Hepatic necroinflammation was observed in the liver. Submucosal inflammation was partly observed in the intestinal tissues. Tendency of elevation in serum aminotransferases.

Discussion and Conclusion: Mice transplanted with Huh7 of HAV GT-IIIa HA11-1299 infection seems useful as *in vitro* HAV infection model for anti-HAV drugs screening. In this model, inflammation was histopathologically observed in the liver and intestinal tissues where HAV RNA was detected. We developed a xenograft mouse model with HAV GT-IIIa HA11-1299 infection.

Abstract Submission No. 101172
O-0751

An Immunocompetent Mongolian Gerbil Model for Hepatitis E Virus Genotype 1 Infection

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BACKGROUND & AIMS: Hepatitis E virus (HEV), primarily genotype 1 (HEV-1) accounts for approximately 20.1 million HEV infections, 44000 deaths, and 3000 stillbirths annually. Like HAV, HBV, HCV and HDV, current evidence demonstrated that HEV-1 only infects humans and no immunocompetent small animal model exists for the study of HEV-1 infection. We evaluated if Mongolian gerbils could serve as an alternative.

Methods: Mongolian gerbils were used for infection experiments with HEV-1 and HEV-3. HEV infection parameters, including HEV RNA, anti-HEV, antigen, liver function test and histopathology were determined.

Results: We adapted a clinical isolate of HEV-1 by serial passaging in the feces of aged male Mongolian gerbils. The resulting gerbil-adapted strain at passage 3 induce robust acute HEV infection characterized by stable fecal virus shedding, elevated liver enzymes, liver histopathological changes and seroconversion to anti-HEV. HEV-1-infected pregnant gerbils showed vertical transmission. HEV RNA or antigens were detected in the liver, kidney, intestine, placenta, testis and the neonates/feus liver samples. Intrahepatic transcriptomic analysis indicated activation of innate immunity. Tacrolimus prolonged the HEV-1 and HEV-3 infection in gerbils. Ribavirin significantly inhibit HEV-1 infection in gerbils. The protective efficacy of a licensed HEV vaccine candidate was validated by using this model. **Conclusions:** We updated the previous concept that HEV-1 only infects humans and demonstrated that HEV-1 can efficiently infect Mongolian gerbils. This HEV-1 infection gerbil model should be of value in investigating hepatitis E immunopathogenesis and evaluating vaccines and antivirals against HEV.

Abstract Submission No. 101424
O-0752

Plasma Exchange as a rescue therapy for severe prolonged cholestasis in Acute Viral Hepatitis

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Background: Most cases of acute viral hepatitis (AVH) resolve within weeks; however, a subset of patients develop severe prolonged cholestasis with disabling symptoms. This retrospective study aimed to investigate the etiology, management, and outcomes in patients of AVH complicated by prolonged cholestasis.

Methods: A retrospective analysis of 50 patients admitted with AVH complicated with prolonged cholestasis was done. Data was collected from medical records; clinical features, laboratory investigations, treatment and outcomes were analyzed.

Results: 50 patients, majority young males 88%(n=44) with mean age of 23.4±4.5 years were analyzed. Hepatitis A virus was the cause of AVH in forty-seven (94%) patients. Common symptoms included severe pruritis in 96% (n=48), disturbed sleep in 90% (n=45) and dry

cough in 70% (n=35). At the time of presentation, mean bilirubin was 30.3±5.9mg/dl, serum alkaline phosphatase (SAP) level was 166.3±47.2 IU/L, AST was 136±58.6 IU/L and ALT of 152.4±76.3IU/L. The mean bile acid concentration was 197.8±31.2 mg/dl. All patients received oral anti-pruritic medications for an average duration of 34.3 days. Thirty-Seven (74%) patients underwent standard volume Plasma Exchange (PLEX) with a range of 1-5 sessions. Twenty-Five (50%) patients received a short course of oral steroids (20 mg) after undergoing plasma exchange. Six (12%) patients received only steroids. Group that received combined PLEX followed by steroids exhibited significant improvements in symptoms, bilirubin and bile acids at 4 weeks (p=0.001) compared to the other groups."

Conclusion: PLEX followed by oral steroids is a novel strategy for managing severe prolonged cholestasis with incapacitating symptoms in AVH.

Abstract Submission No. 101456

O-0753

Small intestinal bacterial overgrowth in liver disease: Do jejunal cultures predict outcome?

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Introduction: There is limited data on bacterial translocation and small intestinal bacterial overgrowth (SIBO) in pediatric cirrhosis. We aimed to evaluate and interrelate the endotoxin assay, breath test and jejunal cultures in cirrhosis.

Methodology: A prospective study enrolled cirrhotic children for jejunoscopy, glucose hydrogen-breath test (GHBT, normal <12ppm above baseline), serum and ascitic lipopolysaccharide-binding protein (LBP, normal <5mcg/mL). Jejunal culture (aerobic and anaerobic media) antibiotic sensitivity (Kirby-Bauer disc diffusion method) and resistance genes (conventional polymerase chain reaction) were assessed. The median, minimum, and maximum areas under curve of GHBT were estimated using Ghoshal BreathCalc (Patent appl.No. 202111029055). Extrahepatic portal-venous obstruction patients were controls.

Results: Of the 56 cirrhotic children (pediatric end-stage liver disease score, PELD 15.4±4.3, 18 (32%) had evidence of ascitic fluid infection (AFI) with AF-LBP 7.6±3.3 mcg/mL (fig1). Twelve of 21 (57%) cirrhotics with positive jejunal culture had one or more morbidity outcomes (hospital readmission, systemic infection, renal dysfunction, recurrent AFI, persistent hyponatremia and relative adrenal insufficiency) over the next 6 months. Of these twelve, six had high AF-LBP (18±2.7), serum LBP (33±8.7) and jejunal culture multidrug antibiotic resistance (mecA, NDM-1, mcr-1, SHV-1, NDM-1 genes). All six patients died in next 8 (3-12) months. Serum LBP correlated with absolute neutrophil count (r=0.77, p<0.01) and pediatric end-stage liver disease (PELD) score (r=0.87, p=0.03). Serum LBP cut-off >7.8 mcg/mL (AUROC 89%, sensitivity 88%, specificity 64%, p=0.02) predicted short-term morbidity events. All ten patients with AF-LBP >10 mcg/mL had renal dysfunction.

Conclusions: Jejunal culture-positive SIBO in cirrhotics predicts short-term morbidity outcomes

Abstract Submission No. 101718

O-0754

Global, regional, and national burdens of HEV from 1990 to 2019 and forecasted incidence in 2030

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Aim: Hepatitis E virus (HEV) is the emerging cause of viral hepatitis. Here, we reported the trends of HEV burden at the global, regional, and national levels from 1990 to 2019, and predicted the forecasted incidence in 2030.

Methods: Using the data from the Global Burden of Diseases (GBD) 2019, we performed the trend analysis to report the incidence of HEV infection, disability-adjusted life years (DALYs), incidence per 100,000 population, average annual percentage changes (AAPCs), and social development index (SDI). Connection point regression analysis was performed to identify the years with the most significant changes in global trends. Furthermore, we predicted the incidence of HEV infection in 2030 using Bayesian age-period-cohort analysis.

Results: The incidence of global HEV infection decreased from 304.3 per 100 000 population in 1990 to 251.63 in 2019 with the AAPC as 0.13. The specific years for significant decrease of HEV incidence were 2006, 2009, 2014 and 2017. Regionally, Western Sub-Saharan Africa had the highest incidence and Southern Sub-Saharan Africa had the largest increase of incidence between 1990 and 2019. From 1990 to 2019, the highest incidence and DALYs rate of HEV infection was Low-middle SDI countries, while Middle SDI countries had the largest decrease in incidence and the High-middle SDI countries had the largest decline in DALYs. In 2030, the predicted global incidence of HEV infection is 275.34 per 100 000 population.

Conclusion: Global HEV incidence decreased between 1990 and 2019 but the incidences of individual regions and countries are still increasing year by year.

Abstract Submission No. 101780

O-0755

PERCUTANEOUS TREATMENT OF HYDATID CYSTS WITH THE ORMECI TECHNIQUE

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Background: The percutaneous route is accepted as the most convenient course in the management of Hydatid cysts (HC). The aim of this study is to analyze the efficacy of the ÖRMECİ technique used in the treatment of Hydatid cysts.

Methods: This is a retrospective cohort study. Patients with Hydatid cysts who presented to the Ankara University School of Medicine, Department of Gastroenterology since 1991 were included. Patients with WHO-CE types 1, 2, 3A-3B live cysts who were treated

percutaneously at least once and followed-up after a minimum of six months were analyzed.

Results: A total of 1556 cystic lesions in 1035 patients have been presented to our department since 1991. 544 live HCs in 479 patients were treated with the ÖRMECİ technique. The mean follow-up time was 59.29 months for females and 57.18 for males. The overall clinical success rate of all treated cysts with the ÖRMECİ technique was 94.5%. After the treatment, a statistically significant decrease was found in all WHO-CE cyst types in terms of cyst sizes ($p < 0.001$ for all). Mortality, abscess and fistula formation, sclerosing cholangitis, and drug toxicities were not detected. Only two patients experienced reversible anaphylaxis during the treatment among 544 cysts (0.36%). **Conclusion:** Hydatid cysts can be treated percutaneously by the ÖRMECİ technique with a high success rate for WHO-CE Type 1, 2, and 3B. The ÖRMECİ technique is an economic, simple, cheap, repeatable outpatient procedure. It can be chosen as the first-line therapeutic modality in suitable patients with Hydatid cysts.

Abstract Submission No. 200112
O-0756

Hepatitis E virus infects human testicular tissue and Sertoli cells

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Globally, hepatitis E virus (HEV) infections are prevalent. The finding of high viral loads and persistent viral shedding in ejaculate suggests that HEV replicates within the human male genital tract, but its target organ is unknown and appropriate models are lacking. We aimed to determine the HEV tropism in human testis and its potential influence on male reproductive health. We conducted ex vivo culture of human testis explants and in vitro culture of primary human Sertoli cells. Clinically derived HEV genotype 1 (HEV1) and HEV3 virions, as well as rat derived HEV-C1, were used for inoculation. Transcriptomic analysis was performed on testis tissues collected from tacrolimus-treated rabbits with chronic HEV3 infection. Our findings reveal that HEV3, but not HEV1 or HEV-C1, can replicate in human testis explants and primary human Sertoli cells. Tacrolimus treatment significantly enhanced the replication efficiency of HEV3 in testis explants and enabled successful HEV1 infection in Sertoli cells. HEV3 infection disrupted the secretion of several soluble factors and altered the cytokine microenvironment within primary human Sertoli cells. Finally, intratesticular transcriptomic analysis of immunocompromised rabbits with chronic HEV infection indicated a downregulation of genes associated with spermatogenesis. HEV can infect the human testicular tissues and Sertoli cells, with increased replication efficiency when exposed to tacrolimus treatment. These findings shed light on how HEV may persist in ejaculate of patients with chronic hepatitis E and provide valuable ex vivo tool for studying countermeasures.

Abstract Submission No. 100458
O-0757

Hepatic Tuberculoma Masquerading as Hepatocellular Carcinoma : A Case Report

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Hepatic Tuberculoma, a rarely-seen tuberculosis manifestation, presents a complex challenge to gastroenterologists due to its diverse clinical presentations. This case report sheds light on a unique instance of

liver tuberculosis in a region grappling with a high prevalence of HBV. In this particular case, it not only mimicked Hepatocellular Carcinoma but also exhibited symptoms characteristic of Charcot's Triad.

Our patient, a 35-year-old male, initially presented with a one-week history of right upper quadrant abdominal pain, jaundice, and fever. Initially suspected as Acute Cholangitis, further investigation through MRCP revealed a 2x2cm hypointense ovoid lesion in segment 5. This diagnostic puzzle led to a liver biopsy to rule out Hepatocellular Carcinoma. To our astonishment, the biopsy showed clusters of epithelial cells intermingled with poorly formed caseating granulomas alongside benign hepatocytes. Additionally, MTB-PCR analysis of tissue core fragments yielded positive to Mycobacterium tuberculosis. Subsequently, the patient commenced anti-koch's therapy, and at the time of this report, is on his third month of treatment with a remarkable resolution of the initial symptoms.

In conclusion, this case underscores the critical consideration of Hepatic Tuberculoma in the differential diagnosis of liver lesions, particularly in regions with a high HBV prevalence. It is vital to have a heightened index of suspicion, comprehensive histopathology confirmation to differentiate Hepatic Tuberculoma from Hepatocellular Carcinoma. This report contributes to the evolving body of literature concerning the distinctive presentations of tuberculosis. Timely diagnosis and prompt initiation of anti-koch's therapy play a pivotal role in achieving a favorable clinical outcome in such cases.

Abstract Submission No. 101453
O-0758

We did not look for it because it was everywhere : The Ubiquitous presence unveiled

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49 year old homemaker presented with c/o Jaundice for 2 weeks, Menorrhagia for 1 week and Generalised pruritus for 2 days

Past History - 8 months back she received Ormoxifene for 3 months for dysmenorrhea related to uterine fibroid

Examination revealed icterus, pedal edema, skin excoriation

Baseline investigation - Hb-5.6; LFT(TB/DB - 10.9/5.9 mg/dl SGOT/SGPT-761/283 U/L ; TP/Alb-5.2/2.4 g/L ; ALP- 127U/L GGT-29.5(50)U/L; INR- 1.63.

USG abdomen showed minimal ascites and mild coarsening of liver echotexture.

Ascitic fluid examination revealed high SAAG low-protein ascites without evidence of infection. Etiological evaluation of liver dysfunction done twice-no clue.

Clinical progression and treatment- Due to onset of encephalopathy, she was planned for superurgent liver transplantation. Due to non-availability of a matching donor, she underwent 3 cycles of Plasma-Exchange as bridge to transplantation. Trans-jugular liver biopsy (TJLB)-histopathology report was suggestive of Acute hepatitis with hepato-canalicular bilirubinostasis, and mild steatosis.

Extended investigations revealed HAV-RNA PCR positive. Even though HAV is endemic in India with >95% IgG-HAV antibody positivity among adults, we started Ribavirin as we were left with no other choice. Due to high suspicion of false positivity, HCV RNA-PCR was repeated 2 days later which confirmed the earlier positive report. Meanwhile there was dramatic response to Ribavirin in 2 weeks with near normalisation of LFT and complete resolution of ascites and encephalopathy

Take home Message- Time to think about occult Hepatitis A with Flare precipitated by the immunomodulatory effects of Ormoxifene,

a selective Estrogen receptor modulator, in a hyperendemic zone of HAV

Abstract Submission No. 200209
O-0759

Gas Sonogram within Ablation Zone: A Strong Indicator of Post-ablation Infection in Liver Malignancy

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Background: Patients with gas sonogram within ablation zone are more likely to develop post-ablation infections, but few researches focused on the relationship between the unique image and infection. This study aimed to explore the relationship between 'gas sonogram' within the ablation zone and post-ablation infection in liver malignancies.

Methods: This retrospective study reviewed patients between November 2011 and November 2021 who underwent percutaneous thermal ablation in liver malignancies. All patients with 'gas sonogram' within ablation zone were included as the case group (n=57), and two treatment date-matched control without gas sonogram were randomly selected for each case, following a nested case-control design. Gas sonogram was then divided into three classes according to ultrasound imaging.

Results: The post-ablation infection rate and severe infection rate in case group were significantly higher (54.4% (31/57) vs 6.1% (7/114), 26.3% (15/57) vs 0.9% (1/114)), while the hospital stay was significantly prolonged (5 days vs 2 days). No statistically significant difference was showed in recurrence and LTP rate. In case group, gas class III was a more dangerous type and strongly indicated infection. Multi-variable logistic regression showed the independent factors for gas sonogram were prior biliary intervention (OR=6.249), cancer type (OR=2.086), and proximity to bile ducts (OR=2.136), and the independent predictor for gas class III was gas range (OR=1.778).

Conclusions: Patients with 'gas sonogram' within ablation zone after thermal ablation in liver malignancies were prone to infection, especially gas Class III. Vigilance is required for these patients including early prophylactic antibiotic therapy and local catheter drainage should be instituted.

Abstract Submission No. 200256
O-0760

Hepatobiliary Tuberculosis Mimicking Hepatic Malignancy

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Background: Hepatobiliary tuberculosis (HBTB) is a rare form of tuberculosis (TB) infection, and frequently misguided into the diagnosis of hepatic malignancy.

Methods: Clinical data from two patients were collected from medical records. The essential features leading to the diagnosis of HBTB using pathological findings, AFS stain, TB culture, and radiological response to treatment were analysed.

Results: Both cases presented with abdominal fullness, body weight loss, low-grade fever, and initial medical imaging studies leading to suspicion of hepatic malignancy, but pathological finding of granulomatous inflammation with caseous necrosis leading to the diagnosis of HBTB. One case had axillary lymph node TB culture showing

mycobacterium tuberculosis complex. In one case, hepatic mass regressed completely. The other case had resolved hepatic infiltrative change, but persistent hepatic segmental atrophy.

Conclusion: The clinical and radiological features of HBTB remain the great masquerader of hepatic malignancy, sometimes leading to unnecessary surgery. Diagnosis usually requires pathological proof, but once the diagnosis is confirmed, response to therapy is usually optimum.

Abstract Submission No. 101342
O-0761

Contrast-enhanced Volume of the Hepatocellular Carcinoma Treated with Carbon-ion Radiation Therapy

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BACKGROUNDS: The most appropriate imaging modality for treatment evaluation of hepatocellular carcinoma (HCC) patients treated with carbon-ion radiation therapy (C-ion RT) has not yet been defined, and interpretation of treatment response is challenging.

METHODS: This retrospective study included the patients with HCC ≥ 5 cm who underwent computed tomography or magnetic resonance imaging examination before and 3 months after CIRT between April 2000 and March 2020 in QST Hospital. C-ion RT was performed at 45-48 Gy/2 fractions or 52.8-60 Gy/4 fractions. Modified Response Evaluation Criteria in Solid Tumors (mRECIST) values and contrast-enhanced tumor volumes (CETV) were measured on pre- and 3-month post-treatment imaging, and the 3-month change in each was determined.

RESULTS: Ninety-eight patients were included. The median follow-up duration was 32 (3-142) months. 2-year overall survival, progression-free survival and local recurrence rates were 73%, 43% and 84%, respectively. Local failure was observed in a total of 17 patients. There were significantly fewer local failures in patients with a greater change in CETV after treatment (23.1% vs. 67.7%, $p = 0.031$). After dividing patients into two groups based on median value, baseline mRECIST and mRECIST/CETV changes at 3 months were associated with local progression-free survival, with the difference in mRECIST change being statistically significant ($p = 0.047$). The 3-month CETV was also significantly associated with overall survival ($p = 0.003$).

CONCLUSION: Change in CETV at 3 months is associated with local control of HCC treated by C-ion RT. Prospective validation studies and standardization of imaging protocols are warranted

Abstract Submission No. 101729
O-0762

Comparison of carbon ion radiotherapy and transarterial chemoembolization for HCC larger than 3 cm

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Background: This study compared the clinical outcomes between carbon ion radiotherapy (C-ion RT) and transarterial chemoembolization (TACE) for patients with solitary HCC larger than 3 cm.

Methods: We examined 58 patients treated with C-ion RT (C-ion RT group) and 34 patients treated with TACE (TACE group) between January 2016 and December 2021. Propensity score matching (PSM) was performed to adjust for differences in baseline and tumor characteristics between the two groups. Overall survival (OS), progression-free survival (PFS), and local control (LC) were assessed.

Results: The median duration of follow-up was 34.2 months for all patients. Among the entire cohort, there was a significant difference between the two groups concerning etiology ($P = 0.038$), and AFP ($P = 0.012$). PSM identified 29 patients from each treatment group and successfully matched the two treatment groups. In the matched cohort, there were no significant differences between the two groups. The 3-year OS, PFS, and LC rates of each group (C-ion RT group vs. TACE group) were 74.4% vs. 54.4%, 45.2% vs. 16.1%, and 84.7% vs. 23.3%, respectively. The C-ion RT group showed better OS than the TACE group, however, there was no significant difference between the two groups ($p = 0.283$). The C-ion RT group showed better PFS ($p = 0.005$) and LC ($p < 0.001$) than the TACE group.

Conclusions: C-ion RT has better OS, PFS and LC rates than TACE for patients with solitary HCC larger than 3 cm.

Abstract Submission No. 101947
O-0763

Prognostic role of serum VEGF and HGF post SBRT in advanced hepatocellular carcinoma

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Background: Stereotactic body radiation therapy (SBRT) is a treatment option for hepatocellular carcinoma (HCC) patients who are ineligible for other local therapies. An early diagnosis is important for improving the survival rate of patients. Other than AFP and PIVKA II, markers for tumor progression, prognosis and recurrence are needed.

Methods: HCC patients ($n=18$) were subjected to SBRT dose of 30-50Gy in 5 fractions and serum level of HGF, VEGF and EGF were analysed using enzyme-linked immunoassay before SBRT, at the completion of SBRT and 30 days post SBRT. Cumulative survival rates were calculated using the Kaplan-Meier method and were compared using the log-rank test.

Results: Total of 18 patients were analysed over a median follow up period of 10 months (05-27 months). In patients, the median overall survival was 13 months (95% confidence interval [CI], 5-20.9) with SBRT. The 12 months local control and progression free (PFS) was 80% and 50% respectively. Patients with raised PIVKA-II at baseline and post SBRT showed increased concentrations of VEGF and EGF (Fig B-C). Patients with increased VEGF and HGF at 30 days post SBRT had poor PFS (Fig D). The median progression free survival (mPFS) was 6 months vs. 14 months in patients with increase in VEGF

(Fig D). Similarly, mPFS in patients with increase in HGF was 9 months as compared to 14 months post SBRT.

Conclusion: Along with PIVKA II, HGF, EGF and VEGF can be used as prognostic markers to predict the OS, PFS and metastasis in HCC patients.

Abstract Submission No. 101037
O-0764

Standardization of Robot-Assisted Right Side Hepatectomy in Our Hospital

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Introduction: Robotic-assisted liver resection surgery is now being introduced in many hospital. However, a standardized global approach has not been universally established due to limited device availability. Leveraging our institutional experience, we summarize our techniques.

Material: Beginning in December 2009, our hospital pioneered robot-assisted hepatectomies, conducting 191 cases by September 2023. This involved 32 cases with Da Vinci S, 20 cases with Si, 138 cases with Xi, and 2 cases with hinotori. Due to the different port configurations of each device, only 96 right-sided liver resections, mainly using the Xi system, were included in this study.

Port Placement: Fundamental port placement for right side hepatectomies includes a semi-lateral decubitus position, inserting ports in a semicircular arc pattern centered around the hepatoduodenal ligament following EZ access insertion on the lateral side of the rectus abdominis. The camera port is positioned slightly towards the left upper quadrant from the umbilicus. The surgery is conducted with the patient in a head-up position.

Liver Transection: Following the Pringle maneuver, liver parenchyma is transected using a combination of monopolar scissors and the crush-clamp technique with a Maryland dissector. In anatomical resections, Gleason sheath is secured by 'the peel off and sweep method' using Fenestrator and Maryland. Firefly mode was used in the ischemic area for the parenchymal dissection line of the liver.

(Results) Among the 96 Xi system cases, 41 involved partial resections, while 55 underwent anatomical resections.

Conclusion: Presently, utilizing the outlined approach, we ensure the safe conduct of nearly all cases.

Abstract Submission No. 101168
O-0765

Surgical techniques of liver parenchymal transection in robot-assisted liver resection

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Background: Liver parenchymal transection is the most important process in liver resection. Current study shows our clamp-crushing technique for robot-assisted liver resection (RLR) and evaluates its perioperative outcomes.

Methods: The da Vinci Surgical System Xi robot is used for RLR. During clamp-crushing technique, the right hand uses a Maryland bipolar connected to the Force Triad Macro mode on arm No.3 or No.4. The EndoWrist One Suction Irrigator is used on arm No.1 to perform all suction and irrigation with the surgeon's left hand. During this solo-surgery, after crushing with the Maryland bipolar in the right hand, suction is performed with the left hand. Small vessels are cauterized and separated with the Maryland bipolar, and vessels larger than 3 mm in diameter are clipped. When bleeding occurs, hemostasis could be efficiently achieved by using a bipolar system while suction and irrigation. A good surgical field of view could be maintained by alternately using suction and Maryland bipolar to hold up or down the liver dissection plane.

Results: From August 2022 to December 2023, a total of 17 patients underwent RLR. Median total operation time was 384 min, median console time was 305 min and median blood loss was 50 ml. There were no CD>3 postoperative complications, and median hospital stay was 10 days.

Conclusion: RLR could be safely performed by a clamp-crushing technique using EndoWrist One Suction Irrigator.

Abstract Submission No. 101960
O-0766

Robot-assisted liver resection guided by ICG fluorescence imaging and artificial intelligence

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Background: Although the number of robot-assisted liver surgery (RALS) has increased in recent years, the lack of haptic feedback remains an issue. Indocyanine green (ICG) fluorescence imaging has proven to be a high potential navigation tool and may be a way to overcome the limitation. Furthermore, we have developed a surgical support artificial intelligence(AI) system to improve the recognition accuracy of vascular structures. This study aimed to investigate the feasibility and clinical application of ICG fluorescence imaging and AI to guide RALS.

Methods: 11 patients who underwent RALS with fluorescence imaging for liver tumor were included. The da Vinci Xi system's Firefly mode was used to observe fluorescence, liver transection was performed under IOUS and ICG fluorescence guidance. The AI algorithm was evaluated at Anaut Inc.

Results: The subjects included 4 hepatocellular carcinoma, 6 colorectal liver metastasis, and one focal nodular hyperplasia. The mean operative time and blood loss was 354 minutes and 105g, there were no postoperative complications and mortality. In all cases, ICG fluorescence imaging successfully identified tumor localization and aiding in liver transection guidance. The pathological findings of all tumors indicated negative margins, defined as R0. The AI model accurately recognized vascular structures of any size in real-time and indocyanine green fluorescent imaging without visual discrepancies.

Conclusion: The ICG fluorescence imaging is a promising navigational tool, that can potentially overcome the limitations of RALS. Although this AI system is currently limited to preclinical application,

these results may support the realization of more accurate real-time navigation.

Abstract Submission No. 102037
O-0767

Robot-assisted Limited Anatomic Liver Resection: A Report on the Current Status

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Background: Since the inclusion of robot-assisted liver resection (R-LR) in insurance coverage, the number of cases has gradually increased in Japan. This report outlines the current status of minimally invasive liver resection (MI-LR) at a leading robotic hospital in Japan. **Methods:** In our institution, the Glissonean approach (GA) and indocyanine green negative staining (ICG-NS) are employed as fundamental techniques in minimally invasive anatomic resections (MI-AR). We aimed to analyze long-term outcomes of MI-AR and describe our approach for R-LR.

Results: Among 112 patients undergoing laparoscopic AR, the 5-year OS rates were 73% for hepatocellular carcinoma (HCC) and 60% for colorectal liver metastasis (CRLM). Of 42 R-LR cases (December 2021 to December 2023), 24 involved anatomic liver resection, 18 involved partial resection. Operative time averaged 384 minutes, blood loss 358ml, complications ($\geq$ Calvien-Dindo IIIa) occurred in 7 cases but were successfully treated. The average postoperative hospital stay was 14 days.

Conclusion: MI-AR exhibits favorable oncologic outcomes for HCC and CRLM. R-LR's advantages lie in its flexible approach to Glissonean pedicle and vessels due to multi-joint functionality. Ongoing improvements in near-infrared light cameras and liver transection devices anticipate the safer implementation of R-LR.

Abstract Submission No. 200033
O-0768

Robotic surgery will be the standard approach to highly complex minimally invasive liver resection

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Background: We have standardized surgical techniques of minimally invasive complex anatomic liver resection (MICAR) by extrahepatic Glissonean approach and hepatic vein root-at first cranial-to-caudal parenchymal dissection, based on Laennec's capsule.

Methods: We performed 260 MICAR including 3 trisectionectomies, 58 hemihepatectomies, 4 bisectionectomies, 70 monosectionectomies and 125 segmentectomies (laparoscopic: LCAR 180; robotic: RCAR 80) at our institution. Indications were HCC (n=151), metastatic tumors (n=73), intrahepatic cholangiocarcinoma (n=13) and others (n=23). Posterosuperior lesions were resected in 170 cases (65.4%). Repeat hepatectomies and reconstructive procedures were performed in 40 (15.4%) and 8 (3.1%) cases, respectively.

Results: In the entire MICAR cohort, the median operative time was 593 min and blood loss was 246g. Open conversion, major morbidity, bile leak/collection and 90-day mortality were 3.5%, 9%, 6.5% and 0.4%, respectively. Between propensity score-matched cohorts (64:64), compared to LCAR, RCAR had a lower rate of bile leak (1.6% vs. 11.1%, $P=0.028$), with comparable operative time, blood loss, conversion rate, morbidity, mortality and hospital stay. In MICAR for posterosuperior lesions and repeat hepatectomy, RCAR, which had worse tumor and procedural backgrounds than LCAR, still had comparable outcomes with LCAR. Reconstructive procedures were highly difficult laparoscopically, and no reconstruction-related complications were observed in RCAR. Postoperative long-term outcomes in newly developed HCC were comparable between LCAR ($n=90$) and RCAR ($n=26$). **Conclusions:** Robotics may potentially improve safety of MICAR by technical dexterity, particularly for posterosuperior lesions, redo hepatectomy and reconstructive procedures, with comparable long-term outcomes in HCC with laparoscopic surgery. Robotic surgery will be the standard approach to MICAR.

Abstract Submission No. 200233
O-0769

Long-Term Outcomes of Robotic Surgery for Initial Liver Resection of Colorectal Liver Metastases

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Background: Robotic surgery is becoming increasingly popular for liver resection, and although there are some reports on the short-term outcomes, there are few reports on the long-term outcomes for malignant tumors.

Methods: We compared the long-term outcomes of initial liver resection for colorectal liver metastases performed at our hospital during the 8-year period from 2010 to 2017 by dividing the patients into three groups: open, laparoscopic, and robotic surgery groups.

Results: There were 200 patients who underwent initial liver resection, 132 underwent open, 32 laparoscopic, and 15 robotic surgery. The number of cases of anatomic systematic resection was 90 (68.2%), 17 (53.1%) and 6 (40.0%), respectively, with more systematic resection cases in the open surgery group ($p=0.015$). The median and interquartile range of Beppu's Nomogram Score (BNS) were 10 (6-15), 7 (4-10), and 4 (3-7), with higher BNS in the open surgery group ($p<0.0001$).

The long-term outcomes of 5-year and 10-year survival rates were 53.5% and 33.5% in the open group, 67.4% and 51.4% in the laparoscopic group, and 54.2% and 54.2% in the robotic group, respectively, with no statistically significant difference ($p=0.12$).

Conclusion: This study did not show any superiority of robotic surgery in long-term outcomes.

Abstract Submission No. 200284
O-0770

Inventions of robot-assisted laparoscopic liver resection in our department

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Introduction: Robot-assisted surgery (RAS) for the liver resection in Japan has just been covered by insurance in 2022, and there is no robot-specific energy device that can be used laparoscopic liver resection, so there are Kanck & Pitfalls. We report on the innovations for it in the RAS in our department.

Results: RAS partial hepatectomy (PH) started in January 2023. 16 cases (11males, 5female), median age 60years (47-83), primary disease: colorectal cancer liver metastases 6, HCC 4, FNH 2, liver cyst 2, hemangioma 1, portal vein hepatic vein fistula 1, median operation time: 388.5min (233-580), median blood loss: ml (0-1020(including ascites)), Median postoperative discharge: days 6(5-12), C-D classification II or higher: 1 (cholecystitis C-D II).

Methods: RAS-PH in our department is performed by the clamp crush method using Maryland forceps. The most important factors are stable surgical field development and adequate tension on the hepatic transection plane using endoloop, organ retractor and thread suture traction which we named "parachute traction". In addition, continuous dripping of saline through the CV catheter increases hemostasis ability with saline enhanced coagulation and it allows identification of the bleeding point. Continuous aspiration with SECURE and atom tube, and the use of folded gauze called "Benz gauze" are also very useful.

Conclusion: The following innovations have been developed, the tension at the hepatic transection plane, short pitch clamp crush method, saline enhanced coagulation and moisture control of the transection plane.

Abstract Submission No. 100208
O-0771

Risk of vascular complications with living & deceased donor liver transplantation - A meta-analysis

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Background: Vascular complications commonly cause graft loss and morbidity after liver transplantation. Data suggest an increased risk of biliary complications with living donor liver transplantation (LDLT) compared to deceased donor liver transplantation (DDLT). However, comparative data on the risk of vascular complications are limited. Hence, the present meta-analysis was conducted to analyze the difference in vascular complications between LDLT and DDLT.

Methods: A literature search of three databases was conducted from inception to June 2023 for studies comparing the incidence of vascular complications with LDLT and DDLT. Odds ratios (OR) with 95% confidence intervals were calculated for all the dichotomous outcomes.

Results: A total of 19 studies were included in the final analysis. There was no difference in the odds of vascular complications between LDLT and DDLT with OR 0.94 (95% CI: 0.73 - 1.21; $I^2 = 0\%$). When comparing the individual vascular events, LDLT was associated with a higher incidence of hepatic artery thrombosis (HAT) with OR 1.95 (95% CI: 1.28 - 2.97; $I^2 = 0\%$). There was no difference in the odds of portal vein thrombosis between LDLT and DDLT with OR 1.85 (95% CI: 0.82 - 4.18; $I^2 = 18\%$). On the contrary, LDLT was associated with a significantly lower incidence of intraoperative bleeding with OR 0.63 (95% CI: 0.49 - 0.81; $I^2 = 0\%$).

Conclusion: Despite the overall risk of vascular complications being similar between LDLT and DDLT, LDLT was associated with a higher risk of HAT and a lower risk of intraoperative bleeding.

Abstract Submission No. 100404
O-0772

Impact of preoperative infection on the outcomes of liver transplant recipients

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Background: Impact of preoperative infection on liver transplantation (LT) needs further investigation.

Methods: From January 1, 2015 to December 31, 2022, 24,122 eligible patients receiving LT were enrolled from the China Liver Transplant Registry database. The outcomes of LT were compared after using the propensity score-matched analysis.

Results: Compared to patients without preoperative infection, those with preoperative infection were more likely to have effusion, infection, abdominal bleeding and biliary complications (all $P < 0.01$), and they also had shorter 30-day, 90-day survival and overall survival (OS) (all $P < 0.05$). Cox proportional hazards regression analysis revealed that recipient MELD score and cold ischemia time were risk factors for the OS in patients with preoperative infection (both $P < 0.05$). Besides, compared to patients with non-pulmonary infection, those with pulmonary infection were more likely to have effusion and infection (both $P < 0.0001$), and less likely to have abscess and early allograft dysfunction (both $P < 0.05$). Patients with non-abdominal infection also had a higher proportion of infection than those with abdominal infection ($P < 0.05$). Furthermore, compared to patients with single site infection, those with multiple site infection were more prone to effusion and infection (both $P < 0.05$), and they also had shorter 30-day and 90-day survival (both $P < 0.05$).

Conclusion: Preoperative infection can result in a higher incidence of early postoperative complications and shorter survival in liver transplant recipients. Different infection sites and the number of infection sites will also influence the prognosis of liver transplant recipients.

Abstract Submission No. 100457
O-0773

BMSCs ROS-Responsively Secreting Hepatocyte Growth Factor for Attenuating Hepatic IRI

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Background: Hepatic ischemia-reperfusion injury (IRI) impairs the clinical efficacy of liver transplantation. After liver reperfusion, reactive oxygen species (ROS) generated from stressed hepatocytes would aggravate liver damage. How to attenuate IRI and improve liver regeneration remains a key problem.

Methods: A ROS-responsive charge-reversal polymer B-PDEAEA has been synthesized and utilized for condensing plasmid DNA to

obtain polyplexes. Inspired by the increased ROS during hepatic IRI and the tendency of bone marrow-derived mesenchymal stem cells (BMSCs) to migrate to injured sites, we put forward constructing BMSCs ROS-responsively secreting hepatocyte growth factor (HGF-BMSCs), which could realize efficient and IRI-specific HGF releasing for attenuating IRI.

Results: B-PDEAEA showed limited cytotoxicity to both hepatocytes and stem cells. N/P ratio as 30 was identified as the optimal for gene transfection in MSCs, and the polyplexes exhibited excellent ROS responsiveness and high gene transfection efficiency. HGF-BMSCs have been constructed and could release HGF with the response to ROS. HGF-BMSCs could release over 60000 pg HGF per 10000 cells with low stimulation of H₂O₂, suggesting the ROS-responsiveness. CM-Dil was used to track stem cells and the biodistribution assay revealed an accumulation of stem cells in injured livers. Furthermore, both in vitro and in vivo experiments showed HGF-BMSCs could protect hepatocytes from IRI, with decreasing of inflammation.

Conclusions: A novel IRI protection system is constructed and promising to be established and to realize targeted and efficient gene/protein therapy, thus providing a theoretical and experimental basis for translational research on the repair and regeneration of transplanted liver.

Abstract Submission No. 100661
O-0774

Novel System for Organ Preservation: Feed Macrophages with Ceria Nanoparticles

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Background: Liver transplantation, a definitive solution for irreversible liver failure and malignant tumors, has encountered significant challenges predominantly attributable to sterile inflammation following ischemia-reperfusion injury caused by frail donor livers and inadequate preservation techniques. Ceria nanoparticles (CeO₂NPs) have antioxidant and anti-inflammatory effects, but their potential use in preserving donor livers remains unknown.

Methods: We created newly designed dextran-coated CeO₂NPs that we introduced to solutions used to infuse and preserve murine livers. The biodistribution of CeO₂NPs and their association with macrophages were investigated. Additionally, we used a liver transplantation mice model to investigate the roles of CeO₂NPs-containing preservation solution on liver injury, reactive oxygen species (ROS), inflammation infiltration and hepatocyte apoptosis. In addition, both in vivo and in vitro studies were carried out to investigate the involvement of CeO₂NPs in the potential mechanisms of liver transplantation.

Results: The distribution of CeO₂NPs in different organs indicates their specificity in murine liver and Kupffer cells. Additionally, CeO₂NPs have been shown to improve liver injury, reduce ROS production and inflammation infiltration, suppress hepatocyte apoptosis in mice that have undergone liver transplantation. Furthermore, the application of CeO₂NPs aligns with M2 macrophage polarization, implying that they alleviate sterile inflammation following donor liver implantation through interaction with M2 polarization.

Conclusion: A novel system for infusing and preserving donor livers can be accomplished by deploying CeO₂NPs in solution by alleviating sterile inflammation via M2 polarization, which may improve prognosis of patients after liver transplantation in the near future.

Abstract Submission No. 100811
O-0775

Long-term outcomes of fenofibrate for treatment of liver allograft ischemic cholangiopathy

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Background: Ischemic cholangiopathy (IC) after liver transplantation has no definitive treatment besides retransplantation. 90-days of fenofibrate--a medication which potently downregulates toxic bile acid production--was recently demonstrated to improve cholestasis by 75% in IC patients during the treatment period. We assessed if these responses were durable beyond 90-days and if fenofibrate was stopped in the previously reported patients.

Methods: Over 360 days, we monitored alkaline phosphatase (ALP) and endoscopic retrograde cholangiography needs of liver transplant recipients who received at least 90 days of fenofibrate.

Results: Of the original 10 patients who received fenofibrate, one patient died of unrelated causes, and one patient had stopped treatment before the 90-day timepoint. Of the remaining 8 patients, 3 patients stopped fenofibrate after 90 days, 3 patients stopped fenofibrate after 180 days, 1 patient stopped fenofibrate at 360 days, and 1 patient did not stop fenofibrate. The initial ALP response seen during the first 90 days of treatment was durable with or without extended fenofibrate treatment. ALP in all patients was 59% of the peak ALP at treatment initiation. No patient required retransplantation.

Conclusion: While IC is a progressive condition of biliary inflammation, fenofibrate therapy initiated early may help arrest its progression with or without long-term treatment.

Abstract Submission No. 100962
O-0776

Utilization of elderly donors in liver transplantation for patients with hepatocellular carcinoma

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Background: Profound organ shortages worldwide have led to the increased utilization of marginal organs from older individuals. However, the effectiveness of liver transplantation (LT) with organs from elderly donors for patients with hepatocellular carcinoma (HCC) remains controversial. The objective of the current study was to assess the overall survival (OS) and disease-free survival (DFS) of patients with HCC following LT using grafts from deceased donors over 60 years old.

Methods: Patients with HCC who underwent LT between 2015 and 2018 were identified in the China Liver Transplant Registry database. The overall survival and disease-free survival of older liver donors (OLDs) were compared with those of younger liver donors (YLDs) after propensity score matching.

Results: From January 2015 to December 2018, a total of 4971 HCC patients were enrolled in the study according to the screening criteria. The absolute and relative utilization of liver grafts from elderly patients over 60 years for HCC patients increased every year, from 65 (9.3%) in 2015 to 268 (14.5%) in 2018. Disease-free survival (DFS) was significantly lower in HCC patients with elderly donors (both $P < 0.05$) after propensity score matching. The OLD group had worse DFS than YLD group if patients had tumors beyond the Milan criteria ($P < 0.05$).

Conclusions: The use of older donors for LT has been growing quickly in the last few years in China. Grafts from older donors can be safely used in HCC recipients with similar OS and comparable perioperative complications.

Abstract Submission No. 101225
O-0777

The impact of age on liver regeneration after living donor right hemihepatectomy in elderly donor

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Background: The expanding donor pool includes marginal donors with steatosis, small-for-size grafts, and elderly donors. This study aimed to investigate liver volumetric regeneration after living donor right hepatectomy (LDRH) in elderly and younger donors, focusing on age impact.

Materials and Methods: From March 2012 to December 2022, 38 elderly donors (≥ 55 years) and 291 younger donors (< 30 years) underwent LDRH. Donors without preoperative liver fibroscan or post-operative follow-up CT scans after three months were excluded. Propensity score matching resulted in a final cohort of 55 younger and 30 elderly donors. Remnant liver volume was assessed via CT scans within one year after surgery. Comparative analysis conducted on pre- and post-operative clinical characteristics, as well as liver volumetric regeneration over time between the two groups. Additionally, binary logistic regression was used to analyze risk factors for poor liver regeneration.

Results: The mean age was 58.0 and 24.0 years for elderly and younger donor, respectively. Preoperative factors were similar between two groups. Rapid liver regeneration occurred within the first months (median 465.9mL, 77.8% of initial total liver volume (iTLV)), but elderly donors showed significantly lower liver regeneration rates than younger age donors throughout all time points (around 1 month: 83.5 vs. 75.5%, $P=0.001$; 3 months: 89.9 vs. 79.2%, $P<0.001$; 6 months: 94.7 vs. 86.2%, $P=0.001$, all compared to iTLV). Multivariate logistic regression analysis identified old age and low preoperative phosphate level (<3.5 mg/dL) as risk factors for liver regeneration below 80% of iTLV.

Conclusion: After LDRH, liver regeneration within one year reaches over 95% of the original volume in young donors but is less, at approximately 86% of the original volume, in elderly donors. Therefore, more conservative criteria for the remnant liver volume need in elderly donors compared to younger donors.

Abstract Submission No. 101665
O-0778

The Therapeutic Potential of Self-Assembled Rapamycin Nanoparticles in Allograft Rejection

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Background: Transplant rejection remains a formidable obstacle in the landscape of organ transplantation, emphasizing the imperative for post-transplant interventions. While Rapamycin (RAPA) stands as a potent immunosuppressant, its effectiveness is hampered by issues related to suboptimal solubility and delivery efficiency. This investigation explores the potential of a “self-assembly inhibitor” strategy to enhance RAPA’s efficacy against graft rejection.

Methods: Soluble supramolecular rapamycin nanoparticles (sRNP) spontaneously form in aqueous solutions via a simple reprecipitation scheme, rendering RAPA injectable and providing colloidal stability.

Results: Our results demonstrate the sustained maintenance of therapeutic drug concentrations with the sRNP platform, accompanied by commendable pharmacokinetic parameters and minimal toxicity, effectively overcoming the challenge of immunotoxicity. In murine allograft models, the administration of low doses of sRNP over a short duration leads to an increase in myeloid-derived suppressor cells (MDSC) and regulatory T cells (Treg), concurrently reducing Th1 and Th17 cells, surpassing the impact of oral RAPA on graft survival. Evidently, sRNP manages the reduction of effector T cells while amplifying the naive T cell cohort. Transitioning to the rat orthotopic liver transplantation model, a short-term low dose of sRNP (administered once every other day, totaling four times at 0.1mg/kg, intravenously) effectively inhibits T cell proliferation, mitigates inflammatory cell infiltration, significantly prolongs graft survival, and positively influences hepatic function.

Conclusions: This study illuminates the distinct advantages of sRNP over its oral RAPA counterpart in the context of allograft rejection, demonstrating the practical feasibility of employing self-assembled RAPA nanoparticles as a potent anti-rejection therapy.

Abstract Submission No. 101840
O-0779

Laparoscopic Anatomical Liver Resection with ICG Real-time Navigation

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Background: In order to perform safe and reliable laparoscopic anatomical liver resection (LALR), it is desirable to establish intraoperative navigation that accurately conducts the proposed surgical plan, in addition to preoperative simulation of local anatomy. In this report, we describe our techniques and innovations using ICG fluorescence imaging and artificial intelligence (AI) for LALR.

Methods: Preoperatively, 3D reconstructed images were created from volume data, and simulation of the staining area at ICG injection was performed in all patients. During surgery, three methods of positive staining (PS) were selected according to the case: (1) preoperative puncture with B-mode US before surgery, (2) intraoperative puncture, and (3) combination of the two methods. And, the introduction of a puncture route support system using 3D holography and the development of a new US probe attachment complement the puncture with a red laser. In addition, AI was utilized to assist in the recognition of vascular structures during liver dissection.

Results: LALR was performed in 27 positive staining cases and 13 negative staining cases, and ICG staining method enabled accurate navigation in the direction of hepatic resection by distinguishing not only the demarcation lines on the liver surface but also the boundaries in the deep dissection plane. 3D holography and US attachment

assisted the optimal puncture route to the portal pedicle branch. The AI recognized the hepatic vein and Gleason branch during dissection of the liver.

Conclusion: Real-time navigation using ICG fluorescence and AI can contribute to the realization of safe and precise LALR.

Abstract Submission No. 101932
O-0780

ALPPS vs Conventional Techniques in Hepatitis Related HCC: A Systematic Review and Meta Analysis

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Insufficient functional liver remnant (FLR) volume frequently serves as a major hindrance in performing hepatectomy in cases of primary liver cancers. Current studies show that ALPPS rapidly increase FLR leading to completion of liver resection compared with standard techniques in cases of colorectal liver metastasis. However, there is limited data on its benefit to hepatocellular carcinoma (HCC) associated with chronic hepatitis or cirrhosis.

A comprehensive systematic search was performed to include clinical studies that compared ALPPS vs either conventional techniques including TACE+PVE, LAPS, or PVE alone. The Cochrane risk of bias tool and Newcastle Ottawa Scale were used to assess the presence of bias. Data was analyzed using Revman5.4. The primary outcome measured was increase in future liver remnant volume. The secondary outcomes were 1-year and 3-year disease free survival (DFS) and overall survival (OS) rate, perioperative complication rate and liver failure rates.

The study included 4 comparative studies with 284 hepatitis related HCC. There is no statistically significant difference in terms of increase in FLR volume between the two groups [MD -4.84 (95%CI -17.98 - 8.30); p0.47]. The secondary outcomes of 1-year OS (1.19; 0.52-2.71), 3-year OS (2.72; 0.40-18.36), 1-year DFS (0.99; 0.58-1.71), 3-yr DFS (2.14; 0.37- 12.39), overall complication rate (1.15; 0.42-3.14), overall liver failure rate (1.51; 0.33- 6.83), has no statistically significant difference at 95% confidence interval.

Among patients with hepatitis related HCC, ALPPS can be an alternative technique in increasing FLR volume prior hepatectomy. However, there remains a need for larger studies to strengthen this evidence.

Abstract Submission No. 102022
O-0781

Central Hepatectomy with Vascular Reconstruction (Video Abstract)

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Aims and Objectives: Centrally located liver tumors are a surgical challenge that was traditionally treated with extended right or left liver resections leading to a frequent risk of post-hepatectomy liver failure due to inadequate functional liver remnant. Non-anatomic resections are marred by risks of hemorrhage and positive surgical margins.

Central hepatectomy is a feasible choice in such patients with acceptable risks.

Materials and methods: In this video, the central hepatectomy steps are shown or a large tumor occupying and right anterior sector and segment 4 followed by vascular reconstruction. The video first discusses adequate mobilization of the liver for exposure. The transaction lines are marked followed by central hepatectomy and reconstruction of the middle hepatic vein using a PTFE graft. Due to the recurrent thrombosis of the right portal vein, it was heparinized through a catheter left in the umbilical vein. Following the completion of the surgery, the patient had an uneventful recovery. The umbilical vein catheter was removed 5 days later.

Results and Conclusions: Central hepatectomy is a feasible surgery with acceptable outcomes. In case of the inability to save the middle hepatic vein due to tumor infiltration, an in-situ vascular reconstruction can be done to maintain outflow.

Abstract Submission No. 200026
O-0782

Risk Factors for Surgical Site Infection after Hepatectomy in Our Facility

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Background: We reported our treatment outcomes for surgical site infection (SSI) following hepatectomy, analyzed and discussed the risk factors.

Methods: The study included 1012 cases of hepatectomy without biliary reconstruction or combined resection of other organs from April 2012 to December 2022. Minimally invasive surgery (MIS), including laparoscopic and robot-assisted hepatectomy, was performed in 507 cases (50.1%). As a prophylactic antibiotic, either flomoxef or cefmetazole was administered 30 minutes before and within 24 hours after surgery. A closed abdominal drainage tube was removed 2-4 days post-operatively unless bile leakage was suspected. Perioperative glycemic control was achieved through insulin therapy.

Results: Postoperative SSI was observed in 99 cases (9.8%), with 24 cases (2.4%) of incisional SSI and 84 cases (8.3%) of organ/space SSI. Multivariate analysis revealed that poorly controlled diabetes (HbA1c $\geq 6.5\%$) (odds ratio [OR] 3.31, $p=0.0083$), major hepatectomy (OR 3.2, $p=0.022$) and MRSA colonization (OR 4.63, $p=0.0083$) were significantly associated with incisional SSI. Risk factors for organ/space SSI were age ≥ 65 years (OR 1.96, $p=0.029$), blood loss ≥ 1500 mL (OR 2.7, $p=0.0017$), operative time > 300 minutes (OR 3.31, $p < 0.001$), open surgery (OR 4.28, $p=0.0016$).

Conclusion: Adequate preoperative glycemic control might be effective in reducing the risk of incisional SSI after liver resection. Additionally, for indicated cases, selecting MIS and making efforts to shorten surgery duration and reduce intraoperative blood loss might lead to prevent the development of organ/space SSI.

Abstract Submission No. 100160
O-0783

Comparative study of laparoscopic left lateral liver resection vs ablation for single small HCC

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Background: There is a scarcity of studies comparing laparoscopic left lateral liver resection with radiofrequency ablation (RFA) in these cases.

Methods: We retrospectively compared the short- and long-term outcomes of Child-Pugh class A patients who underwent laparoscopic liver resection (LLR; $n = 36$) or RFA ($n = 40$) for a newly diagnosed single small (≤ 3 cm) HCC located in the left lateral segment of the liver.

Results: Overall survival (OS) was not significantly different between the LLR and RFA groups (94.4% vs 80.0%, $P = 0.075$). However, disease-free survival (DFS) was better in the LLR group than in the RFA group ($P < 0.001$), with 1-, 3-, and 5-year DFS rates of 100%, 84.5%, and 74.4%, respectively, in the LLR group vs 86.9%, 40.2%, and 33.4%, respectively, in the RFA group. The hospital stay was significantly shorter in the RFA group than in the LLR (2.4 vs 4.9 days, $P < 0.001$). The overall complication rate was higher in the RFA group than in the LLR group (15% vs 5.6%). In patients with an α -fetoprotein level of ≥ 20 ng/mL, the 5-year OS (93.8% vs 50.0%, $P = 0.031$) and DFS (68.8% vs 20.0%, $P = 0.002$) rates were greater in the LLR group.

Conclusions: LLR showed superior OS and DFS compared to RFA in patients with a single small HCC situated in the left lateral segment of the liver. LLR can be considered for patients with an α -fetoprotein level of ≥ 20 ng/mL

Abstract Submission No. 100254
O-0784

Is it possible to minimize liver I/R damage and increase regeneration capacity?

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Background: During ischemia and subsequent reperfusion in the liver resulting in apoptosis and necrosis. This study aimed to evaluate the possibility of preventing the reduction of regeneration capacity as a result of ischemia and also to evaluate the possibility of a faster recovery process.

Methods: Rats of equal age and approximately equal weight were grouped into 6 groups in total: Group1 = Sham; Group2 = Silymarin-curcumin; Group3 = Silymarin-glucosamine; Group4 = Ganoderma lucidum; Group5 = mixture of group B vitamins, amino acids, l-carnitine and sugar; Group6 = Phenoxy-2-methyl-2-propionic acid. Liver ischemia was achieved by ligating the hepatic artery under anesthesia for 45 minutes. mTOR, insulin, nesfatin, and leptin levels were checked in the 2nd postoperative week.

Results: Insulin levels were found to be low in the silymarin-curcumin group. Regarding blood nesfatin level, it was significantly higher in the 3rd group compared to the control group ($p=0.002$), and significantly lower in the 2nd group ($p=0.015$). The blood mTOR level was

significantly lower in the 3rd group compared to the control group ($p=0.051$). Other parameters were similar. C3, PCNA, Ki67, mTOR, HGF, and Calpain10 were found to be higher in all groups compared to the control group. VEGF and FGF were found to be higher in all groups except group 4 compared to the control group. In immunostaining, more necrosis, vacuolization, and sinusoidal obstruction areas were seen in the 3rd and 4th groups compared to the other groups.

Conclusions: Although all substances applied after I/R injury have been shown to positively affect the regeneration capacity of the liver, silymarin-glucosamine, and ganoderma lucidum have been shown to cause deterioration in the quality of regenerating liver tissue. Apart from this, it was noteworthy that insulin levels were low in the silymarin-curcumin group, which is also used for the treatment of steatotic liver disease.

Abstract Submission No. 101310

O-0785

Outcomes of patients with primary sclerosing cholangitis after liver transplantation

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Background and aim: In this study we present the complications and outcomes of PSC patients after liver transplantation in a predominantly LDLT center.

Materials and methods: Adult and pediatric patients who underwent liver transplantation for PSC between February 2008 and October 2020 were included in the study. The demographic characteristics, presence of co-existing diseases, indications for transplantation, type of transplantation, and immunosuppressive treatments used were recorded. Patient survival, survival times, cause of death, recurrences, rejection, and biliary complications were recorded.

Results: Thirty patients who underwent liver transplantation for PSC were included in the study. Twenty-seven patients (90 %) were living donor transplants. The 1-, 3-, and 5-year survival rates after transplantation were 75.9 %, 74.9 %, and 74.9 %, respectively. Biliary complications occurred in 15 patients (50 %). All patients with biliary complications were successfully treated with endoscopic and percutaneous interventional treatments. Chronic rejection occurred in three patients (10 %) and acute rejection occurred in five patients (13.3 %). PSC recurrence developed in five patients (18.5 %).

Conclusion: Biliary complications are the most common complication after liver transplantation in patients with PSC in our center, where LDLT is used extensively and PSC patients are followed closely with respect to biliary complications after transplantation

Abstract Submission No. 101506

O-0786

Alternative hepatic artery conduit in liver transplantation: A Bayesian Network-Meta Analysis.

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Introduction: Finding the best alternative recipient anastomosis in liver transplantation is hard

Methods: Following PRISMA and NMA guidelines, a comprehensive search of Cochrane Library, MEDLINE, and Scopus was done, analyzing all observational studies that included non-standard anastomosis in liver transplantation, either with the splenic artery, aorta, celiac, or branches from the gastric artery. The outcome parameters are intraoperative, complications, and survival.

Result: Thirteen studies with 9521 subjects were included in this study for quantitative analysis. Aortic anastomosis showed the least complication of thrombosis, stenosis, and biliary tract abnormality. However, inferior results were shown in graft and overall survival. The splenic artery anastomosis alternative showed higher risk of thrombosis, but low complications of stenosis (OR 1.12, 95%CI 0.13-3.14) and biliary tract abnormality (OR 0.79, 95%CI 0.36-1.55). Further, in splenic artery anastomosis, graft survival (OR 1.08; 95%CI 0.96-1.23) and overall survival (1 year survival OR 1.09, 95%CI 0.94-1.26; 5 year survival OR 1.95%CI 0.83-1.22) showed favorable results. Constraints to the use of the splenic artery were longer operation time and cold ischemic time. However, the duration of hospital stay (MD 1.36, 95%CI -7.47 to 10.8) was shown to be shorter and the need for blood transfusions was minimal (MD -1.74, 95%CI -10.2 to 6.7).

Conclusion: In the case of an unusable recipient's hepatic artery, the recipient's splenic artery can be considered as the first choice for anastomosis in liver transplantation.

Abstract Submission No. 101757

O-0787

Hepatic Artery Pseudoaneurysm with Arterio-Biliary Fistula Following Liver Transplantation

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Hepatic artery pseudoaneurysm is an uncommon complication in liver transplant recipients, and the development of an arterio-biliary fistula is extremely rare. Endovascular treatments are being employed as alternatives to surgery; however, no standardized treatments are available.

We present herein the case of a 40-year-old male, deceased liver transplant recipient, with a history of Salmonella bacteremia after transplantation, who presented with melena, fever, and jaundice three months after surgery. Initial diagnostic tests showed evidence of acute graft failure. Endoscopic studies and technetium-99m-labeled RBC scintigraphy failed to identify the bleeding source. Ascending cholangitis was entertained due to findings of severe biliary ectasia in MRCP, along with positive blood and stool cultures for Salmonella. ERCP confirmed the diagnosis of ascending cholangitis which demonstrated bile stones, pus, and blood along the common bile duct. A hepatic artery pseudoaneurysm with fistulization into the bile duct was later identified in the hepatic angiogram. A polytetrafluoroethylene (PTFE)-covered stent was deployed which successfully excluded both the pseudoaneurysm and fistula without the need for surgery. The patient maintained a patent hepatic artery and a preserved liver function on follow-up three months after treatment.

The formation of an arterio-biliary fistula in those who developed hepatic artery pseudoaneurysm after liver transplantation should be considered in those presenting with obscure gastrointestinal bleeding. The use of a PTFE-covered stent was successful in our case. Further research regarding the risk factors in the development of such complications following liver transplantation and the long-term success of endovascular treatments are highly suggested.

Abstract Submission No. 101897

O-0788

Clinical characteristics and correlation with liver stiffness post 1 year liver transplantation.

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Background: Liver biopsy is a gold standard investigation to assess post transplant fibrosis and steatosis. Its limited by cost and procedural risks. Vibration controlled elastography (VCTE) has shown promise to assess fibrosis and degree of Steatosis in post LT recipients. We present our analysis of VCTE and correlation with clinical characteristics of liver transplant recipients at post 1 year of transplantation.

Method: A total of 38 patients were included in the study who underwent liver transplantation 1 year or prior. VCTE was done for all patients through standard protocol. Pearson bivariate correlation was applied at 95 % CI, to assess any correlation.

Results: Of total 38 participants, 29 (76%) were male and 9 (14%) were female. Mean duration post transplant was 4.42 years and mean donor age was 28.16 years. Most were deceased liver transplant recipients (n=29). Mean graft weight was 865.62 grams. Mean liver stiffness values obtained were 6.71 kPa (Min- 4.3; max- 12.8 kPa). We observed that a longer cold ischaemia time was associated with lower liver stiffness ($r = -0.216$; $p = .193$). Higher donor age and graft weight were associated with increased liver stiffness ($r = .256$; $r = .143$ respectively). More stiffness was observed if patient's trough tacrolimus levels were high ($r = 0.181$).

Conclusion: Current study was aimed to assess as to what clinical parameters could influence the development of early fibrosis in the recipients. Duration of cold ischemia time pre-transplant had a strong correlation with degree of stiffness. Higher trough levels of tacrolimus were also associated with higher stiffness. The data presented here is an interim analysis of an ongoing study and further observations will be obtained in future.

Abstract Submission No. 101110

O-0789

The evaluation for causes and status of fatty liver after liver transplantation.

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Background: In recent years, steatosis in the transplanted livers has been observed in some cases. However, its impact is still unknown. In this study, we evaluated the causes and status of fatty liver after liver transplantation.

Methods: Fatty liver was diagnosed by abdominal ultrasound, CT (L/S ratio < 0.9), or histopathology (fat deposits $> 10\%$). We retrospectively examined the association between the postoperative fatty liver development in recipients and the background of the recipient or donor, including gender, age, existing steatosis, and the recipients' prognosis.

Statistical analysis was performed using the log-rank test, Kaplan-Meier method, and Cox proportional hazard model.

Results: The background of the total 75 patients was NASH or alcoholic liver disease (NASH/ALC) in 12 patients, HBV/HCV in 35 patients, and others in 28 patients. During the follow-up period (median 133 months), fatty liver was developed in 20 patients (27%). The background of 8 patients was NASH/ALC (67% of all NASH/ALC) and significantly frequent compared to other liver diseases ($p < 0.0001$). The fatty liver development in NASH/ALC (4.8 months) was significantly earlier than other liver diseases (88.7 months). The multivariate analysis evaluated that only the NASH/ALC of the recipient was associated with post-transplant fatty liver development ($p < 0.0001$, HR 18.61). However, fatty liver development after transplantation was not correlated with overall survival after liver transplantation.

Conclusion: These results suggest that some other factors adding to lifestyle may contribute to the development of fatty liver after liver transplantation in NASH/ALC. We need further investigation into the mechanism and the impact on their prognosis.

Abstract Submission No. 101903

O-0790

A comparative study of laparoscopic liver resection for the segment 4 superior and inferior area

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Introduction: The difficulty of laparoscopic liver resection (LLR) is greatly associated with the location of liver tumors. According to the IWATE difficulty scoring system, the location in Couinaud's segment 4 superior area (S4a) scores 4 and inferior area (S4b) scores 3. The difference between LLR for S4a and S4b remains unclear.

Objectives: The aim of this study was to investigate the differences of the surgical outcomes between LLR for S4a and S4b.

Materials and Method: Patients who underwent laparoscopic partial liver resection (LpLR) for the tumors in the S4a and the S4b at Kobe University Hospital between January 2014 and December 2022 were enrolled. We retrospectively investigated perioperative short-term outcomes including the patients' background, operative results, and complications.

Results: Fourteen patients underwent LpLR for S4. Among these patients, 7 patients underwent LpLR for S4a and 7 patients (50%) for S4b. There was no significant difference between the groups in operation time (274 vs 251 minutes, $P = 0.7016$), blood loss (31.4 vs. 7.9 mL, $P = 0.0841$), the incidence of postoperative complications (0 vs 1 cases, $P = 1.000$), and length of hospital stay (11 vs 12 days, $P = 0.7382$).

Conclusion: There was no difference between LpLR for S4a and S4b in perioperative short-term outcomes. Although the IWATE difficulty score between LLR for S4a and S4b were different, additional studies with larger number of patients in an independent cohort are necessary.

Abstract Submission No. 102043

O-0791

A multi-center nomogram to predict the difficulty of minimally invasive liver resection for HCC

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Background: Minimally invasive liver resection (MILR) has become a common surgical treatment for hepatocellular carcinoma (HCC). However, current difficulty scoring system was limited to small samples and single-center, and there was rare scoring system to assess surgery only for HCC. Thus, we developed a novel prediction system based on a multi-enters date to assess the surgical difficulty of MILR for treating HCC.

Methods: This retrospective multicenter cohort study collected a total of 776 cases of MILR for resectable HCC from June 2011 to November 2022 at eight minimally invasive surgical centers in China. The cohort was randomly divided into a training dataset (n = 582) and a dataset (n = 194) in a 3:1 ratio. The training dataset underwent logistic regression analysis to identify independent risk factors for surgical difficulty and construct a predication model. The performance of the model was validated by the validation dataset, and the discriminative ability, calibration, and clinical effectiveness were assessed through ROC curves and Decision Curve Analysis.

Result: We considered prolonged surgical time, massive intraoperative bleeding, and conversion to open surgery as crucial indicators of a difficult surgery. According to the above criteria, 346 patients underwent a difficult MILR surgery. Gender, Cirrhosis, tumor diameter, and tumor location are independent risk factors affecting the difficulty of MILR for treating HCC. The AUC was 0.785 for the training cohort and 0.723 for the validation cohort.

Conclusions: We developed and validated a novel nomogram to predict the difficulty of MILR for treating HCC based on eastern date.

Abstract Submission No. 102074

O-0792

Effect of Ursodeoxycholic Acid on SARS-CoV-2 Infection in Patients With Liver Transplantation

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Background: Immunosuppressed recipients of liver transplantation (LT) are more likely to develop coronavirus disease 2019 (COVID-19) and may have an increased risk of developing worse outcomes.

Aim: To assess the effect of ursodeoxycholic acid (UDCA) on preventing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in LT recipients.

Design: Adult patients (aged ≥18 years) who underwent LT between January 1st, 2015, and December 31st, 2022, were included and categorized into two groups according to their use of UDCA.

Methods: The prevalence and severity of COVID-19 among transplantation patients between the UDCA and non-UDCA groups were estimated and compared.

Results: Among the 897 LT patients who met the inclusion criteria, infection rate of SARS-CoV-2 was 78.4%, and the rate of severe illness was 5.1% from January 2022 to January 2023 in China. In the multivariate analysis, only UDCA treatment (P=0.006) was found to be a protective factor against SARS-CoV-2 infection. After propensity score matching, the SARS-CoV-2 infection rate in the UDCA group was lower than that in the non-UDCA group (74.1% vs. 84.6%, P=0.002). This rate was further reduced to 62.1% (P=0.002) when the oral administration dose was greater than 15 mg/kg/d. There was no difference in the rates of severe COVID-19 illness, ICU admission, or ventilation rate or length of hospital stay with or without UDCA treatment (all P>0.05).

Conclusions: The use of UDCA in LT patients significantly reduced the SARS-CoV-2 infection rate and showed a dose-dependent protective effect.

Keywords: SARS-CoV-2, Ursodeoxycholic acid, Liver Transplantation, Infection rate, Immunosuppress

Abstract Submission No. 200011

O-0793

Laparoscopy specific dorsal approach to the middle hepatic vein in performing left hemihepatectomy

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Background: Laparoscopic surgery can provide a surgical view that cannot be obtained by open surgery. Herein, we report the surgical procedure of laparoscopic left hemi-hepatectomy by the laparoscopy specific dorsal approach method.

Procedures: (1) Flip-up the left lateral segment and start liver transection from the dorsal surface of the liver around the root of left hepatic vein (LHV). As the root of middle hepatic vein (MHV) also locates near there, the MHV can be exposed easily and quickly. (2) The left Glissonean branch was encircled and cut. Grasping the stump of the cut Glissonean pedicle and flipping it up, continue liver resection with exposing the MHV toward its periphery direction. (3) After the MHV is exposed entirely and all venous branches to segment IV are cut, then flip-down the left-lateral segment to the original position and transect the liver parenchyma remaining on the ventral side of the MHV from caudal to cranial direction. (4) Finally, cut the LHV by a linear stapler device.

Results: Ten consecutive cases received this procedure. Regarding an anatomical factor, the perpendicular distance from the center of the Arantius plate to the MHV was 1.0 cm on average. The blood loss and operating time were 95 ml and 314 minutes in average. There were no severe postoperative complications.

Conclusions: This procedure enables us to contact the MHV easily and quickly. Moreover, we can avoid split-injury of venous branches during exposure of the MHV. This procedure may be a theoretical method in performing laparoscopic left hemihepatectomy.

Abstract Submission No. 200018

O-0794

Laparoscopic and open minor hepatectomy for patients with clinically significant portal hypertension

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Background: Liver resection offers substantial advantages over open liver resection (OLR) for patients with hepatocellular carcinoma (HCC) in terms of reduced blood loss and morbidity. However, there is limited evidence comparing the indications and perioperative outcomes with the open versus laparoscopic approach for resection. This study aimed to compare postoperative outcomes between patients undergoing laparoscopic liver resection (LLR) and OLR for HCC with clinically significant portal hypertension (CSPH).

Methods: A total of 316 HCC patients with CSPH (presence of gastroesophageal varices or platelet count $<100,000/\text{ml}$ and spleen diameter $>12\text{cm}$) undergoing minor liver resection at eight centers were included in this study. To adjust for confounding factors between the LLR and OLR groups, an inverse probability weighting method analysis was performed.

Results: Overall, 193 patients underwent LLR and 123 underwent OLR. After weighting, LLR was associated with a lower volume of intraoperative blood loss and the incidence of postoperative complications (including pulmonary complications, incisional surgical site infection, and paralytic ileus) compared to the OLR group. The 3-, 5-, and 7-year postoperative recurrence-free survival rates were 39%, 26%, and 22% in the LLR group and 49%, 18%, and 18% in the OLR group, respectively ($p = 0.18$). And, the 3-, 5-, and 7-year postoperative overall survival rates were 71%, 56%, and 44% in the LLR group and 76%, 51%, 44% in the OLR group, respectively ($p = 0.87$).

Conclusions: LLR for HCC patients with CSPH is clinically advantageous by lowering the volume of intraoperative blood loss and incidence of postoperative complications, thereby offering feasible long-term survival.

Abstract Submission No. 101194
O-0795

Optimal radiological assessment for HCC with macrovascular invasion during systemic therapy.

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Background & Aims: Macrovascular invasion (MVI) is a significant prognostic factor in advanced hepatocellular carcinoma (HCC). Existing radiological criteria for evaluating MVI lack clarity in assessing the impact of MVI on systemic therapy. We conducted this study to establish standardized criteria for the assessment of MVI.

Methods: We collected clinical data from advanced HCC patients with MVI undergoing first-line systemic therapy at four medical centers in Japan. We used MVI-PD to monitor MVI progression and cRECIST-PD to assess tumor enlargement and new lesions. We evaluated the prognostic impact of MVI-PD, cRECIST-PD, and MVI control with sorafenib, lenvatinib, atezolizumab, and bevacizumab.

Results: Of the 209 HCC patients with MVI, 20.9% had both MVI-PD and cRECIST-PD. In the landmark analysis, patients without concurrent MVI-PD and cRECIST-PD during the initial 3 months had the longest median OS at 19.7 months, while those with both had the shortest at 5.3 months. The median OS for patients who experienced only cRECIST-PD within the first 3 months was 8.8 months, and median OS for patients who experienced MVI-PD within the first 3 months was 7.2 months ($p < 0.001$). The correlation coefficient between PFS

and OS was similar for MVI-PD (0.451) and cRECIST-PD (0.472). Atezolizumab plus bevacizumab showed longer overall survival than lenvatinib and sorafenib and had a lower incidence of her MVI-PD within 3 months.

Conclusions: Our findings underscore the association between MVI progression and poor OS in systemic therapy for advanced HCC, emphasizing the need for an accurate evaluation method for MVI progression.

Abstract Submission No. 101914
O-0796

ATZ + BEV for advanced HCC: If liver function and PS can be maintained, post-treatment is possible.

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Purpose: To investigate the selection and outcome of “post-treatment” of ATZ+BEV in real-world clinical practice.

Methods: A retrospective multicenter study was conducted on 53 patients with advanced hepatocellular carcinoma treated with ATZ + BEV from September 2020 to December 2022. The final follow-up date was March 15, 2023. The primary endpoint was the rate of sequence active treatment after PD. Secondary endpoints were PS at the end of ATZ+BEV, liver function, proteinuria, posttreatment therapy, OS after starting posttreatment, OS after starting ATZ+BEV, and OS from the initial diagnosis day of HCC.

Results: The median age was 74 years. 13 patients were Stage III, 12 patients IV-A, 26 patients IV-B, 46 patients Child-Pugh A, and 7 patients B. After ATZ+BEV treatment, 40/53 patients (75%) completed. PS2 or higher at the end of ATZ+BEV was 7/40, Child-Pugh A 27/B 11, proteinuria 3+ 7/40. Post-treatment therapy included lenvatinib in 10 patients, ramucirumab in 2, cabozantinib in 4, TACE in 7, sorafenib in 2, and BSC in 16.

The rate of sequence active treatment was 59%. MST after initiation of active post-treatment was 9.2 months, MST after initiation of ATZ+BEV was 16.8 months, and MST from the first treatment was 7.0 years.

Conclusion: After completion of ATZ+BEV, sequence active treatment was possible for patients with preserved residual liver function and PS. The rate of sequence active treatment was 59%, and the MST was 9.2 months. It was suggested that sequence active treatment may contribute to further prolongation of survival.

Abstract Submission No. 100441
O-0797

irAEs: Immune Mediated Thrombocytopenia After Durvalumab Infusion for Hepatocellular Carcinoma

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Introduction: Durvalumab is an anti-PDL1 immune checkpoint inhibitor that has become one of the first line systemic treatment in patients with Hepatocellular Carcinoma. Its incidence is estimated to be as low as 0.5% with an absolute frequency that is still unknown. Physicians should be alert of the rare adverse effects such as severe thrombocytopenia. The most important questions that should be answered when dealing with irAE are how frequently to monitor, when to withhold or discontinue ICIs, when to initiate and how to escalate immunosuppression.

Clinical Presentation: This is a case of a 60-year-old male, known case of compensated liver cirrhosis secondary to non-alcoholic steatohepatitis and chronic hepatitis B infection complicated by Hepatocellular carcinoma BCLC C. Twenty four hours after initiation of Durvalumab, the patient presented with acute severe thrombocytopenia (32,000/mm³) from a normal baseline platelet count (162,000/mm³), accompanied by episodes of hemorrhoidal bleed.

An exhaustive work-up for possible causes of thrombocytopenia began which all revealed negative results for infectious, rheumatologic and hematologic causes.

Management: Given the temporal profile of thrombocytopenia occurring after Durvalumab infusion and the exclusion of other possible factors, patient was managed as a case of Grade 3 irAE, namely Immune Mediated Thrombocytopenia. Initially, the patient was started on steroids, however there was persistence of thrombocytopenia. He was eventually given IVIG and Eltrombopag which led to the gradual increase of his platelet count.

Conclusion: Immune checkpoint inhibitors have reshaped cancer therapy. Early and aggressive medical interventions are necessary to successfully achieve irAE improvement after initiation of ICIs.

Abstract Submission No. 100729

O-0798

Comparative Efficacy of Regorafenib, Cabozantinib, and Ramucirumab for unresectable HCC.

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Background: A comparison of the therapeutic efficacy of regorafenib, cabozantinib, and ramucirumab in late-stage treatment for unresectable hepatocellular carcinoma (u-HCC) has not been reported. This study aimed to retrospectively compare the outcomes of u-HCC and identify which of these should be used as prior therapy.

Methods: Twenty-seven patients with u-HCC treated with regorafenib, cabozantinib, and ramucirumab from July 2017 to January 2023 were analyzed; patients who received more than one of the three drugs were included in the prior drug group. All patients had received lenvatinib, atezolizumab/bevacizumab, or both as previous therapies. Disease control rate (DCR), progression-free survival (PFS), and overall survival (OS) were evaluated according to modified Response Evaluation Criteria in Solid Tumors (mRECIST).

Results: There were no significant differences among these three groups in DCR (regorafenib vs. cabozantinib vs. ramucirumab: 70% vs. 25% vs. 46%; $p=0.26$) and median PFS (3.4 months vs. 2.6 months vs. 2.0 months; $p=0.54$). Median OS was statistically shorter in the ramucirumab group than in the other two groups (regorafenib vs. cabozantinib vs. ramucirumab: 28 months vs. 13.6 months vs. 5.4 months; $p=0.030$). Although there were cases of long-term response in the regorafenib group, there was no statistically significant

difference in OS between the regorafenib and cabozantinib groups. There were no grade 3 or higher adverse events in the ramucirumab group. Discontinuation rates due to adverse events were not significantly different between these three groups ($p=0.14$).

Conclusions: Cabozantinib or regorafenib may contribute to OS when compared to ramucirumab.

Abstract Submission No. 101258

O-0799

Safety and efficacy of durvalumab monotherapy for unresectable HCC in the real-world practice

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Background: Following the HIMALAYA trial, durvalumab monotherapy is now available. However, its optimal use remains undetermined. We analyzed the safety and efficacy of durvalumab monotherapy in unresectable hepatocellular carcinoma (HCC) and identified potential treatment targets.

Methods: Clinical data were retrospectively collected from 15 patients treated with durvalumab monotherapy for unresectable HCC between January and August 2023. Anti-tumor efficacy was evaluated using RECIST and adverse events were assessed using CTCAE version 5.0.

Results: In this cohort, liver function at the start of durvalumab was 1/1/12/1 with mALBI grade 1/2a/2b/3. There were four cases of vascular invasion and one case of extrahepatic metastasis. Ten patients were administered durvalumab as first line and three cases as second line and two cases as third or later line. Three patients received durvalumab following prior treatment with immune checkpoint inhibitors. In terms of efficacy, the overall response rate was 0%, the disease control rate was 73.3% and the median duration of treatment was 4.2 months (95% CI, 2.1-NA). Six patients experienced adverse events (pruritus in two, hypothyroidism in one, diarrhea in one, fatigue in one and liver injury in one), but all events were grade 1 and no patients discontinued treatment due to adverse events. Analysis of the ALBI score during treatment using a mixed effects model showed that the mean ALBI score at the beginning of the treatment, 4, 8, and 12 weeks was -1.95/-1.97/-1.89/-1.69, which was not significantly different ($p=0.239$).

Conclusions: Durvalumab monotherapy may be a treatment option for patients with poor liver function.

Abstract Submission No. 101270

O-0800

Multicenter observational study to evaluate clinical outcomes of ABC conversion therapy

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Background: Atezolizumab plus bevacizumab (Atezo/Bev) followed by curative conversion therapy (ABC-C) outcomes for unresectable hepatocellular carcinoma (u-HCC) that achieved tumor shrinkage with Atezo/Bev therapy has attracted attention. We conducted a multicenter study of Atezo/Bev therapy and examined the outcomes of ABC-C.

Methods: We enrolled a multicenter cohort of 205 patients with u-HCC treated with Atezo/Bev therapy between 2020 and 2022. The decision to perform curative conversion therapy was based on each facility's discretion. Propensity score matching (1:3 ratio) was used to create two matched patient groups: the ABC-C group or the group that did not receive curative conversion therapy (Atezo/Bev group). We retrospectively compared the clinical outcomes, including overall survival (OS), progression-free survival (PFS), clinical cancer-free, and drug-free rates, between the two groups.

Results: The median follow-up time for all patients was 14 months. The modalities of curative conversion in 13 patients were as follows: resection, 4; ablation, 3; and super-selective TACE, 6. The clinical cancer-free and drug-free rates for the ABC-C and Atezo/Bev groups were 100.0%/7.7% and 69.2%/7.7%, respectively ($p < 0.01$). The OS and PFS in the ABC-C group were significantly higher than those in the Atezo/Bev group ($P = 0.001$ and $P = 0.009$, respectively).

Conclusion: ABC-C therapy may provide more clinical benefits than Atezo/Bev without conversion in u-HCC patients.

Abstract Submission No. 101858

O-0801

Metalloimmunology-based nanoclusters activate the immune to enhance pembrolizumab plus lenvatinib

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Background: Targeted therapy combined with immunotherapy has become the first-line option for advanced unresectable Hepatocellular carcinoma (HCC). The combination of pembrolizumab plus lenvatinib did not meet the dual endpoints of PFS and OS in LEAP-002. In recent years, the role of metals in the immune microenvironment has attracted attention, and the aim of this study was to explore the efficacy and mechanism of the metalloimmunology-enhancing pembrolizumab plus lenvatinib in advanced HCC.

Methods and Results: We found lenvatinib possesses an eFT-508-like effect to downregulate PD-L1 expression in HCC cells by computer simulation (CADD). Dual luciferase reporter gene assays demonstrated that lenvatinib could downregulate PD-L1 expression by modulating the uORF of PD-L1, and that cobalt ions could enhance this effect. Lenvatinib combined with cobalt ions had a synergistic inhibitory effect on the growth of HCC cells, and the synergy index (CI) indicated the strong synergistic effect. We constructed Co+Len@OVA drug-carrying nanoclusters, which could effectively inhibit the growth and invasion of HCC cells and could trigger the immunogenic death (ICD) by blocking autophagic flux and activating the cGAS-STING pathway. As a result, Co+Len@OVA promotes the antigen presentation function of DC cells as well as the activation of adaptive immunity dominated by CD8⁺ T cells. In *in vivo* experiments, Co+Len@OVA transformed HCC from "cold tumors" into "hot tumors". In addition, Co+Len@OVA combined with anti-PD1, as a novel combination of

pembrolizumab plus lenvatinib, can induce tumor vascular normalization and increase anti-PD1 intra-tumor penetration.

Abstract Submission No. 102040

O-0802

Association between tumor morphology and efficacy of atezolizumab plus bevacizumab for advanced HCC

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Background: In the IMbrave150 trial, atezolizumab plus bevacizumab (AtezoBv) showed a higher objective response rate (ORR) in advanced hepatocellular carcinoma (HCC). Although conversion local therapy after AtezoBv has been recently reported, markers predictive of its efficacy, especially radiological imaging markers, have not yet been identified. The present study focused on the tumor morphological appearance on radiological imaging and analyzed whether it could be associated with AtezoBv efficacy.

Methods: Ninety-five intrahepatic lesions in 74 patients who were administered AtezoBv for advanced HCC were selected for evaluation. The lesions were divided into two groups, simple nodular (SN group) and non-simple nodular (non-SN group), based on the gross morphology on pretreatment imaging, and were retrospectively assessed for treatment response and other relevant clinical outcomes.

Results: Of all the lesions selected for evaluation, 39 lesions were classified into SN group, and 56 were classified into non-SN group. While assessing the size of individual tumors after treatment, waterfall plots showed that tumor shrinkage in the non-SN group was higher than that in the SN group. The ORR was significantly higher in the non-SN group (39.3% vs 15.4%, $P = 0.012$), and the median time to nodular progression was longer in the non-SN group (21.0 months vs 8.1 months, $P = 0.119$). Six patients with non-SN lesions underwent sequential local therapy.

Conclusions: AtezoBv may show increased therapeutic efficacy against tumors with a higher potential for oncological behavior, such as non-SN lesions. Treatment strategies aimed at sequential local therapy may be crucial in patients with non-SN lesions.

Abstract Submission No. 100061

O-0803

Systemic plus hepatic arterial infusion chemotherapy in unresectable intrahepatic cholangiocarcinoma

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Introduction: Intrahepatic cholangiocarcinoma (ICC) is associated with poor survival. The resectability rate is low because at the time of diagnosis this disease is frequently beyond the limits of surgical therapy. Systemic chemotherapy has been disappointing in regard to its efficacy, with most regimens resulting in a median survival of 6 to 12 months. This meta-analysis study aims to evaluate the efficacy of hepatic artery infusion (HAI) chemotherapy in achieving favorable benefit in the terms of survival rate in patients with unresectable ICC who received systemic chemotherapy.

Methods: This study was performed using PRISMA guideline by searching associated literatures in PubMed/Medline library. All prospective studies that comparing the combination of HAI and systemic chemotherapy, and systemic chemotherapy in ICC were included in this study. The parameter of this study was overall survival. The data were pooled and analysed by RevMan 5.3. The survival was analysed by generic inverse variance using log hazard ratio. The bias of each study was described using Jadad score.

Result: Of the 25 articles screened, 3 prospective studies were included. This meta-analysis showed that there was significant advantage in overall survival (HR 10.88, 95%CI 5.45-16.31; $p < 0.01$). Only 1 study reported major toxic effect which was grade III anemia found in 1 person.

Conclusion: Chemotherapy delivered by hepatic arterial infusion (HAI) is a particularly promising strategy to improve overall survival in patients with unresectable ICC who have received systemic chemotherapy.

Abstract Submission No. 100748

O-0804

Comparison of therapeutic effects of lenvatinib and HAIC for unresectable HCC with vascular invasion

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We compared the therapeutic effects of lenvatinib (LEN) and hepatic arterial infusion chemotherapy (HAIC) as primary treatment for unresectable HCC with vascular invasion. 33 unresectable HCC with vascular invasion patients participated in this study who treated by LEN or HAIC as primary treatment at our hospital between April 2016 and March 2022. 16 patients were LEN group, 17 were HAIC group. Median age 69 years, 2/10/10/11 cases with Vp0/2/3/4, 28/2/3 cases with Vv0/2/3. We compared background factors, overall survival (OS), progression free survival (PFS), objective response rate (ORR), and disease control rate (DCR) between the two groups. We analyzed factors affecting OS and PFS. Age and DCP value were significantly higher in LEN group. Median OS was 9.8 months in LEN group and 7.6 months in HAIC group ($p = 0.430$). Median PFS was 4.7 months in LEN group and 3.2 months in HAIC group ($p = 0.542$). ORR and DCR by mRECIST were 43.8% and 68.8% in LEN group and 29.4% and 64.7% in HAIC group, with no significant difference. In the univariate analysis of poor OS factors, ALBI grade 2b or 3 was a significant factor in HAIC group. In univariate analysis of poor PFS factors, distant metastasis and AFP 400ng/mL or more were significant factors in HAIC group. Multivariate analysis revealed no significant factor. Compared with HAIC, LEN administration is less affected by background factors such as ALBI grade, distant metastasis, and AFP value. We think that LEN is more suitable as primary treatment for unresectable HCC with vascular invasion.

Abstract Submission No. 100793

O-0805

Validity of the 7-11 criteria in transarterial chemoembolization for intermediate stage

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Objective: To assess the validity of the 7-11 criteria in TACE for intermediate stage HCC.

Materials and Methods: We included patients who underwent TACE as their initial treatment for intermediate stage HCC between February 2007 and January 2018 and no concurrent therapy within 4 weeks after the initial TACE and a Child-Pugh score below 7. We evaluated the CR rate, PFS, and OS in accordance with the 7-11 criteria. For patients exceeding the up-to-11 criteria, we stratified them into two groups based on tumor number (≤ 3 versus ≥ 4) and compared their prognoses.

Results: A total of 126 patients were enrolled and categorized into three groups: within up-to-7 ($n = 40$), 7 to 11 ($n = 45$), and beyond up-to-11 ($n = 41$). The CR rates were 94.9%, 70.5%, and 50.0% (with $P = 0.004$ and 0.074). The median PFS was 47.9, 21.6, and 12.1 months ($P < 0.01$ and 0.77). The median OS was 77.6, 38.3, and 29.9 months ($P = 0.002$ and 0.55). After stratifying the beyond up-to-11 group by tumor number (≤ 3 versus ≥ 4), PFS and OS were significantly different between the 7 to 11 and the beyond up-to-11 group with a tumor number ≥ 4 ($P = 0.044$ and 0.002).

Conclusion: The 7-11 criteria effectively distinguish the CR rate and prognosis of intermediate stage HCC treated with TACE. Stratification of the beyond up-to-11 group based on tumor number is also a valuable tool. Our data suggest that TACE could be indicated in intermediate stage HCC, with the exception of patients in the beyond up-to-11 group with a tumor number ≥ 4 .

Abstract Submission No. 102063

O-0806

Efficacy of TACE guidance software for hepatocellular carcinoma in the caudate lobe

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Background: To evaluate the outcomes of conventional transarterial chemoembolization (TACE) using guidance software for hepatocellular carcinoma (HCC) in the caudate lobe.

Methods: Seventy-six treatment-naïve caudate lobe HCCs were eligible. TACE was performed using guidance software including automated tumor-feeder detection (AFD) functionality. Technical success was classified into three grades according to 1-week computed tomography findings: entire tumor embolized with a safety margin (5 mm for tumors < 25 mm and 10 mm for tumors ≥ 25 mm) (grade A); entire tumor embolized without a margin (grade B); and entire tumor not embolized (grade C). Tumor response was evaluated using the modified Response Evaluation Criteria in Solid Tumors. Tumor-feeder detectability by AFD, technical success, complete response (CR) at 2-4 months, and local tumor progression (LTP) rates calculated by the Kaplan-Meier method were compared in each tumor among three

subsegments: the Spiegel lobe (SP); paracaval portion (PC); and caudate process (CP).

Results: The mean tumor diameter was 18.6 ± 9.7 mm (range, 6-53 mm), and 107 (88.4%) of 121 tumor-feeders were detected by AFD. The rates of feeder detectability by AFD, grade A technical success, and CR in 32 SP, 33 PC, and 11 CP tumors were 73.7%, 96.9%, and 93.8%; 97.0%, 63.6%, and 60.6%; and 87.5%, 63.6%, and 81.8%, respectively. LTP rates of SP tumors were significantly lower than those of PC tumors ($P = 0.0019$).

Conclusion: AFD could detect 88.4% of tumor-feeders in the caudate lobe; however, the feeder detectability, technical success, and outcomes differed among the three subsegments.

Abstract Submission No. 200141

O-0807

TACE combined with donafenib plus PD-1 for unresectable HCC : a retrospective study

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Background: To retrospectively evaluate the effectiveness and safety of transarterial chemoembolization (TACE) combined with donafenib plus programmed cell death protein 1 (PD-1) for unresectable hepatocellular carcinoma (uHCC).

Methods: Patients with uHCC who received TACE combined with donafenib plus PD-1 from 1 Feb 2022 to Aug 2022 were included in this study. The primary endpoint were overall survival (OS), progression-free survival (PFS). The secondary endpoint were objective response rate (ORR) and disease control rate (DCR). The tumor response was evaluated according to the mRECIST standard. Safety was assessed by the occurrences of adverse events and the severity of the adverse events.

Results: A total of 144 patients were involved in this study. All patients were treated with TACE combined with donafenib and PD-1. Up to the time of follow-up, 24 patients died, 13 patients were lost, and 107 patients survived. The median OS of TACE combined with donafenib and PD-1 was 13 months, and the median PFS was 6 months. The ORR was 73.61% and DCR was 91.67%. No treatment-related death occurred in the follow-up time. Five patients experienced Grade 3 or Grade 4 AEs with diarrhea, rash or vomiting. Fifty-nine patients accompanied with Grade 1 or Grade 2 AEs. Drug reduction occurred in two patients due to adverse events.

Conclusion: The clinical effect of transarterial chemoembolization combined with donafenib plus PD-1 on unresectable hepatocellular carcinoma is probably significant and could improve the short-term response, PFS and OS in patients with unresectable hepatocellular carcinoma, with tolerable adverse reactions.

Abstract Submission No. 100417

O-0808

AFP Response Patterns after Radioembolization of Hepatocellular Carcinoma Predicts Disease Outcomes

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Purpose: To describe alpha-fetoprotein (AFP) response patterns and outcomes in patients with AFP-producing Barcelona Clinic Liver

Cancer (BCLC) stage B or C hepatocellular carcinoma (HCC) after Y-90 radioembolization.

Methods: This IRB-approved, single-center, retrospective study included 167 adults from 2009-2022 with AFP-producing HCCs (≥ 20 ng/mL) without extrahepatic metastases who underwent Y-90 radioembolization. The AFP treatment response was categorized into 3 patterns: 1) sustained response (sustained post-procedure AFP decrease by $\geq 20\%$; $n=42$), 2) transient response (decrease by $\geq 20\%$, followed by an increase thereafter; $n=67$), and 3) no response ($< 20\%$ decrease or increased AFP; $n=58$). Two fellowship-trained abdominal radiologists evaluated pre-treatment and post-treatment imaging for baseline stage and treatment response using mRECIST, respectively. Overall survival (OS), distant progression-free survival (DPFS), and progression-free survival (PFS) were estimated with Kaplan-Meier curves.

Results: 167 patients were included (37 women, 130 men; 80 Stage B and 87 Stage C; median age 65 years). Median OS of sustained, transient, and no response were 18, 13, and 6.4 months, respectively ($p < 0.0001$). Median DPFS of sustained, transient, and no response were 14, 7, and 3.4 months, respectively ($p < 0.0001$). Median PFS of sustained, transient, and no response were 11, 3.7 and 2.6 months, respectively ($p < 0.001$). The sites of extrahepatic metastases at first imaging examination showing progression were lungs (40%), lymph nodes (30%), bones (21%), peritoneum (17%), and adrenal glands (14%).

Conclusions: AFP response patterns correlate with clinical outcomes. Only about 1/4 of patients have sustained AFP response. Increased AFP after treatment should prompt imaging with attention to lungs, lymph nodes, and bones.

Abstract Submission No. 100785

O-0809

Early Response to HAIC Using Lipiodol, Cisplatin, and 5-FU for Locally Advanced HCC in Vietnam

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Background: This study aimed to evaluate the early response (ER) to hepatic arterial infusion chemotherapy (HAIC) utilizing Lipiodol, Cisplatin, and 5-FU in patients who had locally advanced hepatocellular carcinoma (HCC) with portal vein invasion (PVI).

Methods: We conducted a prospective study involving twelve patients, each receiving an implanted subcutaneous port for HAIC. The treatment regimen consisted of Lipiodol, Cisplatin, and 5-FU. Each treatment course spanned four weeks and included five days of chemotherapy per week during the first, second, and fourth weeks. One week after the first course, the patients were examined and categorized into complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD) using mRECIST criteria.

Results: Of the patients, 9 (75%) demonstrated early response (ER) to treatment, with one (8.3%) achieving CR and eight (66.7%) exhibiting PR. One patient (8.6%) experienced PD, while two (16.7%) had SD. Additionally, portal vein tumor thrombosis showed shrinkage in 3 patients (25%), and liver function improved in 2 patients. Complications occurred in four patients (33.3%), including infection, hematoma, thrombosed catheter, and catheter breakage.

Conclusions: The HAIC regimen consisting of Lipiodol, Cisplatin, and 5-FU demonstrated a notable rate of ER, substantial reduction in portal vein tumor thrombosis, and improved liver function. While complications were relatively common, they did not pose life-threatening risks.

Abstract Submission No. 101325
O-0810

Radioembolization with 90Y Resin Microspheres and Voxel-Based Dosimetry with Integrated 90Y PET/MRI

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Background: Radioembolization is a regional treatment modality that can be applied variety of primary and metastatic liver tumours. In this study we aimed to determine dosimetric parameters that could be useful in prediction of response to therapy.

Methods: In this study 34 patients treated with Y-90 resin microspheres prospectively included in the study. The patients were imaged with integrated PET/MRI system in 24 hours following radioembolization procedure. Total number of 70 lesions that could be delineated on pre-treatment FDG or DOTATATE PET were included in dosimetric analysis. Each lesion was classified as complete(CR), partial(PR), stable(SD), and progressive(PD) depending on follow-up PET findings.

Results: Of the treatments, 9 were hepatocellular carcinoma, 15 were colorectal carcinoma and the remainder were breast, thyroid, neuroendocrine and cholangiocellular carcinoma. Median Davg values for responder lesions (CR+PR) were 114.90Gy and for non-responder lesions(SD+PD) were 36.30Gy. Addition to average dose(Davg), D values from dose-volume histograms were significantly different within response groups. In ROC analysis to predict response(CR+PR) AUC for Davg, D70, D80, D90 were 0.850, 0.884, 0.889, 0.854 respectively. Furthermore, to predict CR AUC were 0.759, 0.792, 0.814 and 0.812, for Davg, D70, D80 and D90 respectively. High specificity cut-off for prediction of response were 101Gy, 50.5Gy, 32Gy, 18.5Gy for Davg, D70, D80 and D90 respectively.

Conclusion: Dosimetric analysis of Y-90 PET/MRI can predict response and complete response after radioembolization treatment and may help clinicians to take measures early on after the treatment.

Abstract Submission No. 101528
O-0811

Hepatic Artery Embolization Promotes T-cell Exhaustion in Rat Hepatocellular Carcinoma Model.

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Purpose: T-cell exhaustion is a state of T-cell dysfunction that occurs in chronic infections and cancer. This study was undertaken to evaluate the effects of hepatic artery embolization (HAE) on tumor-infiltrating lymphocytes (TIL) of an orthotopic rat hepatocellular carcinoma (HCC) model by focusing on T-cell exhaustion.

Materials and methods: A rat HCC model was established in Sprague-Dawley rats with the N1S1 cell line. Five animals each were assigned to receive HAE or sham treatment. HCC nodules were collected and digested to generate single-cell suspensions for immunological characterization at 5 days after treatment. The population of PD-1⁺LAG-3⁺ exhausted cells among the CD8⁺ TILs was evaluated by flow cytometry. In vitro cell culture study of splenic mononuclear cells was performed for 5 days under normoxic or hypoxic conditions in the

presence or absence of glucose with or without tumor lysate, and the population of exhausted cells was evaluated by flow cytometry.

Results: The population of PD-1⁺LAG-3⁺ cells among the CD8⁺ TILs was significantly larger in the HAE group as compared with the sham group ($p<0.05$). In vitro cell culture study revealed that the populations of exhausted CD8⁺ cells significantly increased when cells were cultured without glucose with tumor lysate in both normoxic ($p<0.05$) and hypoxic ($p<0.05$) conditions.

Conclusions: HAE promotes T-cell exhaustion in the tumor immune microenvironment of a rat HCC model. Metabolic stress with continuous antigen stimulation is a possible mechanism underlying T-cell exhaustion after HAE.

Abstract Submission No. 101584
O-0812

Efficacy of HAIC New-FP for Unresectable Advanced Intrahepatic Cholangiocarcinoma

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Background: Treatment with chemotherapeutic agents for unresectable Intrahepatic Cholangiocarcinoma (ICC) is still unestablished. We evaluated the efficacy of Hepatic Arterial Infusion Chemotherapy New-FP (NFP) compared with gemcitabine+cisplatin(GC) therapy for unresectable ICC.

METHODS: Patients with unresectable ICC who underwent chemotherapy between March 2015 and March 2023 in Juntendo university hospital were retrospectively evaluated. We evaluated the efficacy and safety of NFP, and anti-tumor effect was evaluated by RECIST and tumor volume reduction rate with contrast-enhanced CT.

Results: Totally 30 cases, each 15 in NFP and GC group were enrolled. Antitumor effects by RECIST in the NFP/GC group was 5 /1 PR (33.3%), 8/8 SD, and 2/6 PD, and the DCR was 86.7%/60 %. PR rate was higher (33.3% vs 6.6%) ($p=0.0374$) in the NFP group. Median tumor volume reduction more than SD cases (NFP/GC) was 23.8%/11.3%, time to best response was 155/87days, and median observation period was 248/464days. About Chemotherapy side effect in the NFP group, Grade ≥ 3 hepatic dysfunction was observed in all patients, but all of them improved within 1 week, Grade3 thrombocytopenia occurred in 1, Grade3 anemia in 1, Grade 2/3 renal impairment in 1/3, biloma in 1. In the GC group, Grade 4 neutropenia occurred in 1, Grade 2 renal impairment in 8, Grade 3 anorexia in 1, and vasculitis in 1.

Conclusion: To confirm the efficacy, we should accumulate more cases and perform prospective study.

Abstract Submission No. 101875
O-0813

Hepatic arterial infusion chemotherapy Survives as a Last Resort

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Objective: Review the outcomes of hepatic arterial infusion chemotherapy (HAIC) and systemic chemotherapy in our experience.

Methods: 875 cases of HAIC, 171 cases of Sorafenib, 226 cases of Lenvatinib and 85 cases of Atezolizumab + Bevacizumab were included in the analysis. Overall Survival of all cases and OS by Vp status were calculated.

Results: Median Survival Time (MST) for all patients of HAIC was 6.8 months. MST by Vp limited to Child-Pugh A for comparison with other drugs was 7.6 months with Vp and 10.8 months without Vp. The MST for the Sorafenib patients was 10.2 months, and the MST by Vp was 7.1 months with Vp and 14.3 months without Vp. MST for lenvatinib patients was 16.2 months, and MST by Vp was 7.0 months with Vp and 17.6 months without Vp. The MST for the ATZ + BEV patients was 18.7 months, and the MST by Vp was 16.1 months with Vp and 19.7 months without Vp.

Conclusion: The standard of care is ATZ + BEV, even in the presence of portal vein tumor invasion. However, for Child-Pugh B patients and those who do not respond to systemic chemotherapy, HAIC will survive as a “last-resort” therapy.

Abstract Submission No. 101928

O-0814

Secretome methods show an active arachidonic acid metabolism indicates TACE response in HCC patients

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Background: Arachidonic acid is a polyunsaturated omega-6 fatty acid that plays a crucial role in the inflammatory response within the body. It is found in the phospholipids of cell membranes and is released by the action of phospholipase A2 enzymes when cells are damaged or under stress. Most of the studies of TACE are post-operational and retrospective. Here, we adopted a prospective study RNA-Seq data to explore the relationship between Secretome and TACE responses of HCC patients. Understanding and manipulating this relationship can have therapeutic implications for improving the efficacy of TACE and potentially other cancer treatments.

Methods: Secretome data was obtained from The Human Protein Atlas database. The RNA-Seq data was utilized from the Gene Expression Omnibus (Accession: GSE104580) which shows the secretomes profile of TACE in HCC patients. R language and packages are used to explore data signatures and statistics.

Results: After the analysis of RNA-Seq data with prospective results of TACE of HCC patients, we found the differential expression of secreted proteins between response and non-response formed an obvious enrichment in the Arachidonic Acid Metabolic Process (GO:0019369).

Conclusion: The enrichment of secreted proteins in the Arachidonic Acid Metabolic Process shows a potential pathway to predict the efficiency of TACE in HCC patients before the operation. And the secreted proteins are easier to be detected in blood. The Arachidonic Acid

Metabolic Process proteins and metabolites are also promising means of prediction and therapeutic targets for HCC patients.

Abstract Submission No. 200042

O-0815

Transcatheter Arterial Embolization of hepatic hemangiomas: Efficacy and Predictors of Response

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Background: Hepatic hemangioma (HH) is increasingly treated with Transcatheter arterial embolization (TAE). Given the lack of detailed information on the factors influencing TAE's efficacy and the tumor's response to treatment, this study aims to evaluate the safety, efficacy and predictors of response of TAE to treat HH.

Methods: A retrospective analysis was conducted of consecutive HH patients who received TAE with bleomycin-Lipiodol emulsion and gelatin sponge particles at three institutions from January 2014 to January 2021. TAE effectiveness was defined as more than 50% reduction of tumor volume. The effectiveness, safety, and CT changes of hemangiomas after TAE were assessed. Factors affecting TAE efficacy on tumor size were analyzed with logistic regression analysis.

Results: A total of 102 patients with 109 HHs were included. After treatment, both the tumor diameter and volume were significantly reduced from 8.5 ± 3.9 cm to 5.9 ± 3.8 cm ($P < 0.001$) and 412.6 ± 742.3 cm³ to 102.0 ± 232.7 cm³ ($P < 0.001$), respectively. TAE effectiveness was achieved in 80.7% (88/109) of hemangiomas, which was characterized by progressive reduction in tumor volume over time. Atypical enhancement pattern ($p = 0.001$) and central arteriportal shunt (APS) ($p = 0.002$) associated with the tumor were independent predictors of TAE ineffectiveness. Postembolization syndrome and transient increase in liver enzymes were common without severe complications and death.

Conclusion: TAE was safe and effective in reducing HH size, with characteristic changes during follow-up CT. Lesion enhancement pattern and APS type were associated with TAE efficacy on HH size.

Abstract Submission No. 200054

O-0816

In-stent Restenosis After Stenting for Superior Mesenteric Artery Dissection

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Objective: To identify risk factors for in-stent restenosis (ISR) in patients undergoing stent placement for superior mesenteric artery dissection (SMAD) and to determine the hemodynamic mechanism underlying ISR.

Methods: Patients with SMAD who had ISR after stent placement were included in the ISR group, and age- and sex-matched patients with SMAD who did not experience ISR after stent placement were included in the control group. Structural and fluid dynamics

simulations were applied to determine the hemodynamic mechanism underlying the occurrence of ISR.

Results: The study population included 26 patients with ISR and 26 control patients. Multivariate analysis demonstrated that stent-to-vascular (S/V) ratio (OR, 1.14; 95% CI, 1.00-1.29; $p = .045$), stent proximal position > 10 mm away from the SMA root (OR, 108.67; 95% CI, 3.09-3816.42; $p = .010$), and high oscillatory shear index (OSI) area (OR, 1.25; 95% CI, 1.02-1.52; $p = .029$) were predictors of ISR. In structural and fluid dynamics simulations, a stent proximal position near the abdominal aorta (AA) or entering into the AA reduced the contact area between the proximal struts of the stent and the vascular wall, alleviated the distal lumen overdilation.

Conclusion: S/V ratio, stent proximal position away from the SMA root, and high OSI area are independent risk factors for ISR in patients with SMAD undergoing stent placement. Deploying the proximal end of the stent near the AA or entering into the AA appears to improve the hemodynamic environment in the SMA lumen and ultimately reduce the risk of ISR.

Abstract Submission No. 200055
O-0817

A Change in Strategy for Filter Choice Leads to Improved Filter Retrieval Rates

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Objective: To assess whether a new strategy for the choice of inferior vena cava filter placed would improve filter retrieval rates at our institution.

Methods: Consecutive patients who underwent retrievable filter placement for temporary embolic protection between January 2021 and January 2023 were considered for study inclusion. Risk factors for nonretrieval of short-term filters were identified in patients receiving filters between January 2021 and January 2022 (prestrategy group). For patients treated between February 2022 and January 2023 (poststrategy group), a long-term filter was recommended for those with these risk factors, and a short-term filter was recommended for those without these risk factors.

Results: The study population included 303 patients (prestrategy group, $n = 154$; poststrategy group, $n = 149$). Long-term immobilization (odds ratio [OR] = 38.000; 95% confidence interval [CI]: 6.858-210.564), active cancer (OR = 17.643; 95% CI: 5.462-56.993), and venous thromboembolism detected in the intensive care unit (OR = 28.500; 95% CI: 7.419-109.477) were identified as independent risk factors for nonretrieval of short-term filters. The total retrieval rate was significantly higher in the poststrategy group (87.2%) than in the prestrategy group (72.7%; $P = 0.002$); the short-term filter retrieval rate was also significantly higher in the poststrategy group (84.5%) than in the prestrategy group (68.5%; $P < 0.001$).

Conclusion: The proposed strategy for filter choice based on risk factors for short-term filter nonretrieval can accurately identify patients who need long-term filter placement while also increasing the retrieval rates for both short-term filters retrieval rates and overall retrieval rates.

Abstract Submission No. 100096
O-0821

The relationship between pancreatic hormone and liver in acute hepatic failure.

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A canine model of an acute hepatic failure was created by the administration of Dimethylnitrosamine (DMN) (30mg/kg) via portal vein. Using this model, the hepato-pancreatic relationship was studied by measuring the pancreatic endocrine function of portal blood and hepatic blood flow. As a result, while the plasma level of IRI of portal blood was higher than basal level of IRI when the hepatic damage was mild, the former was similar to control when the hepatic damage was severe. On the other hand, the more severe the hepatic damage was, the higher the plasma level of IRG of portal blood was. Hypoglycemia and a considerable high level of portal IRG were shown in an acute hepatic failure. These results strongly suggest that pancreatic endocrine function of portal blood may reflect the grade of hepatic damage and a hormonal or neural hepato-pancreatic relationship may exist between the liver and the pancreas.

Abstract Submission No. 100242
O-0822

Thymosin $\alpha 1$ improves immune imbalance in hepatitis B virus-related acute-on-chronic liver failure

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Background and aim: Thymosin $\alpha 1$ (Ta1) is safe for patients with hepatitis B virus (HBV)-related acute-on-chronic liver failure (ACLF) and significantly improves the 90-day survival rate without liver transplantation; however, the immune mechanism remains unclear.

Methods: This study was an open-label, randomized, controlled clinical trial including 73 patients with HBV-related ACLF (HBV-ACLF) (Clinical Trial ID: NCT 03082885). The control group (SMT group, $N=38$) received standard medical therapy, while the experimental group (Ta1 group, $N=35$) received SMT combined with Ta1 by subcutaneous injection. Blood samples and clinical data were collected for analysis.

Results: We found that patients with ACLF had a higher proportion of regulatory T cells (Tregs) than the healthy people, suggesting that differentiation of T cells into effector T cells was limited in patients with ACLF. At baseline, patients who had survived at 90 days had a higher proportion of effector T cells and a lower proportion of Tregs than did patients who were deceased. Analysis of the serum cytokine profiles of surviving patients also showed higher levels of the serum interleukin (IL)-6, tumor necrosis factor (TNF)- α , and interferon (IFN)- γ and lower levels of the serum transforming growth factor (TGF)- β , compared with those in the deceased patients. More importantly, we found that Ta1 treatment can inhibit worsening of the inflammatory storm and restore the immuno-inflammation balance, thus improving prognosis.

Conclusion: Ta1 can improve the prognosis of patients with ACLF-HBV infection by inhibiting excess inflammatory reactions and reversing immune paralysis.

Abstract Submission No. 100354
O-0823

Baicalin Alleviates ACLF by Promoting TREM2-dependent M2 Macrophage Polarization and Efferocytosis

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Background: Acute-on-chronic liver failure (ACLF) is a life-threatening syndrome characterized by sudden hepatic deterioration and systemic inflammation in the context of chronic liver disease. However, current therapeutic options are limited. This study investigates the potential of Baicalein, a natural flavonoid, to mitigate ACLF and explores the underlying molecular mechanisms.

Methods: Liver tissues from an ACLF mouse model, subjected to either Baicalein treatment or saline treatment, were collected. CD45+ immune cells were isolated via fluorescence-activated cell sorting and combined for single-cell RNA sequencing (total ten samples). Additionally, the study employed the BMDM cell line and mouse peritoneal macrophages for in vitro experiments. Furthermore, macrophage conditional TREM2 knockout mice were generated to confirm the initial findings. Lastly, peripheral blood samples were obtained from ACLF patients to quantify soluble TREM2 in serum and assess its correlation with the patients' 28-day prognosis.

Results: The study demonstrates that Baicalein significantly alleviates liver injury in an ACLF mouse model. Single-cell sequencing results reveal a substantial increase in TREM2+ macrophages in the livers of the Baicalein-treated group, suggesting the pivotal role of TREM2+ macrophages in the process of Baicalein-mediated liver injury alleviation. Through further experiments, it is established that Baicalein-induced macrophage phagocytic receptor TREM2 is necessary for the efferocytosis of apoptotic hepatocytes and the polarization of M2 macrophages. Serum TREM2 levels are also significantly linked to the 28-day prognosis of ACLF patients.

Conclusion: In summary, this study highlights the potential of Baicalein as a therapeutic approach for ameliorating ACLF by promoting TREM2-dependent M2 macrophage polarization and efferocytosis.

Abstract Submission No. 100364
O-0824

Prospective study of the effect of TPO on platelets and prognosis in patients with ACLF

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Objective: To evaluate the dynamic changes in platelet and liver function in ACLF patients with severe thrombocytopenia with rhTPO in a prospective cohort.

Methods: Seventy patients with ACLF with severe thrombocytopenia were prospectively enrolled and divided into a TPO group and a control group, with 35 patients in each group. The TPO group was given rhTPO for 7 consecutive days. The PLT counts and liver function were compared between the TPO group and the control group, and 90-day mortality and incidence of bleeding events were observed.

Results: There was no significant difference in 90-day mortality between the TPO group and the control group (8.6% vs. 17.1%, $P=0.284$). The incidence of bleeding events within 90 days was 11.4% in the TPO group and 22.9% in the control group ($P=0.205$), and no thrombotic events were found in either group. The PLT count in the TPO group was significantly higher than that at baseline at 7 and 14 days after

treatment ($28 \times 10^9/L$ vs. $64 \times 10^9/L$ vs. $73 \times 10^9/L$, $P=0.001$), and the PLT count peaked at 14 days. The serum HGF and TPO levels were significantly higher than those at baseline (serum HGF: 130.4 pg/ml vs. 195.4 pg/ml, $P=0.000$) and (serum TPO: 41.8 pg/ml vs. 143.7 pg/ml, $P=0.000$) in the TPO group at 7 days after treatment. The serum albumin level, INR and MELD score in the TPO group at 14 days after treatment were significantly improved compared with those before treatment (ALB 34.5 g/L vs. 28.2 g/L, $P<0.05$; INR 1.6 vs. 1.7, $P<0.05$; MELD 14.7 vs. 16.0, $P<0.05$).

Conclusion: rhTPO can significantly increase the PLT count in ACLF patients with thrombocytopenia, reduce the occurrence of bleeding events, and promote the improvement of liver function, and it has no significant effect on 90-day mortality.

Abstract Submission No. 100374
O-0825

Long-term efficacy and safety of three potent NAs in the treatment of HBV-ACLF: 144-week data

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Background: There are no data on long-term prognosis and safety of tenofovir alafenamide (TAF), tenofovir disoproxil fumarate (TDF) and entecavir (ETV) in the treatment of HBV-related acute-on-chronic liver failure (HBV-ACLF). Here we report the 144-week results of the three NAs in the treatment of HBV-ACLF.

Methods: A total of 199 patients were included in this study. After PSM, 44 patients for each group were remained for further analyses. The survival status, incidence of hepatocellular carcinoma, virologic response, liver and renal function were observed during follow-up.

Results: In the original cohort, one patient in each group developed hepatocellular carcinoma. No serious drug-related adverse events were observed. The log-rank test indicated that no significance was found among the groups' long-term survival rates ($p = 0.118$) (Fig A). Even in the subsets of with or without cirrhosis, there was still no significance ($p = 0.338$ and 0.052) (Fig B-C). There was no significant difference in the HBV DNA undetectable rate (Fig D) and liver function among the three groups, except for AST, which was significantly higher in the TDF group than in the ETV group at week 144 ($p = 0.001$). In terms of renal function, there was no significant difference among the three groups at other time points except that CR decreased and eGFR increased more significantly in the ETV group at week 48 (Fig E-F).

Conclusions: There were no significant differences in the survival rate, incidence of hepatocellular carcinoma, efficacy and safety of the three NAs in the treatment of HBV-ACLF for 144 weeks.

Abstract Submission No. 100378
O-0826

mNGS improves the efficiency of infection diagnosis and treatment in acute-on-chronic liver failure

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Introduction: The early diagnosis of infections in ACLF is still difficult. As a no-bias, sensitive pathogen diagnosis method, further research on mNGS in ACLF is needed.

Methods: A total of 275 ACLF patients with suspected or confirmed infections were recruited, who were divided into the mNGS group and the no-mNGS group. Differences between the two groups were assessed, including pathogen detection, diagnosis and treatment of infections, and clinical outcomes.

Results: The 1:1 PSM for balancing baseline produced 86 patients in each group. The overall microbiological positive rate (103/134, 76.9%) detected by mNGS, higher than culture (24/134, 17.9%). The positive rate of bacteria, fungi and viruses by mNGS were 32.8%, 14.9%, and 64.9%, higher than those of culture (15.7%, 2.2%, 0.0%).

The etiological diagnosis rates of pulmonary infection, thoraco-abdominal infections, bloodstream or catheter infections, and biliary tract infections in the mNGS group were 47.9%, 52.0%, 79.0%, and 44.4%, respectively, higher than no-mNGS (11.4%, 18.4%, 83.3%, and 12.5%). The etiological diagnosis can be confirmed 22.83±26.27 hours earlier. The 23.1% (31/134) mNGS results in 27 patients led to the modification of anti-infection treatment.

The patients with positive-effect-treatment mNGS results had a higher 90-day transplant-free survival rate in four different infections [53.8% (7/13) vs 37.1% (13/35), 63.2% (12/19) vs 52.6% (20/38), 66.7% (4/6) vs 50% (3/6), 33.3% (1/3) vs 50% (4/8)].

Conclusions: mNGS is a valuable diagnostic tool for ACLF with infections, especially for virus and fungi. By precise positioning of pathogens, earlier diagnosis (22h at least), and influencing the anti-infective therapy, mNGS can improve clinical outcome of ACLF co-infection.

Abstract Submission No. 100399

O-0827

CRRT in Children with Hepatitis A Virus associated Acute Liver Failure with Advanced Encephalopathy

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Objective Effect of CRRT on survival in children with HAV associated ALF with HE grade III/IV

Methods Analysis of all children between January 2018 to April 2023. All children were offered CRRT, 21 agreed to CRRT and 14 who refused were treated with standard medical therapy (SMT) and included as controls. No liver transplantation.

Results: Thirty five analysed and 21(60%) received CRRT. Baseline characteristics were comparable apart from ammonia, which was higher in the CRRT (p=0.001). Seven (33.3%) in CRRT and 3 (21.4%) in SMT group fulfilled Kings College Criteria for LT (p=0.445). In

CRRT, 13 (61.9%) survived while in SMT group 7 (50%) survived (p=0.486). The survival time was 6.3 days in CRRT vs 7.29 days in the SMT group (p=0.769). On risk predictive analysis, failure to reduce ammonia by 30% by day 3 of therapy (p=0.001), inotrope requirement at day 3 (p=0.001), bilirubin at day 3 (p=0.001) and ammonia at day 3 (p=0.023) were associated with mortality. On Model 1 of Cox regression analysis, which included ammonia at day 3, bilirubin at day 3 and inotrope requirement at day 3, only bilirubin levels were associated with mortality (HR 1.157, p=0.04). Since bilirubin is reduced by CRRT, analysis performed again by including CRRT and inotrope in model 2. Inotrope requirement associated with 9.5 folds increase in mortality (HR 9.569, p=0.001), however CRRT was not significant

Conclusion: Increased survival in children who received CRRT, however it did not reach statistical significance. High bilirubin and persisting inotrope requirement at day 3 were associated with mortality.

Abstract Submission No. 100476

O-0828

Outpatient intensive nutrition therapy improves survival and frailty in ACLF: Randomized trial

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Background: Improvement in the nutritional status of Acute on Chronic Liver Failure (ACLF) patients may lead to reduction in the disease related morbidity and mortality. This study assessed the impact of dietician supported outpatient intensive nutrition therapy (OINT) on survival and frailty in patients with acute on chronic liver failure.

Methods: Seventy adult patients with ACLF by Asia Pacific Association for Study of liver (APASL) definition and frailty assessed by Liver frailty Index (LFI) at baseline were randomized 1:1 to receive standard medical therapy (SMT) plus OINT (intervention) versus SMT (control) alone. The primary outcome was an improvement in survival at 3 months. Secondary outcome measures included improvement in frailty, prognostic scores (Model of End stage Liver Disease, MELD, Model of End stage Liver Disease- Sodium, MELD Na, Asia Pacific APASL Research Consortium, AARC score) and hospitalization.

Results: There was a significant improvement in overall survival in the intervention group as compared to controls. After a period of 3 months follow up, the survival in OINT group was much better than the SMT group, 91.4% (Standard error (SE): 4.7%) vs. 57.1% (SE: 8.4%), p<0.001). On cox regression model adjusted for age and comorbidities, inclusion in the intervention arm, baseline SMI, and AARC score were the independent predictors of survival at end of 3-months (p<0.05 each). The LFI score significantly improved in the OINT as compared to SMT, Δ -0.93 (-0.71-1.13) vs. Δ -0.33 (-0.44-0.72) (p<0.001). On cox regression analysis adjusted for age, CTP, MELD, AARC score, and allocation to treatment group, to assess the predictors of improvement in frailty, enrolment in intervention arm and AARC score were independent predictors, p<0.001 for improvement in frailty. The disease severity as assessed by MELD, MELD-Na, and AARC score showed a significant improvement in the OINT group

than the SMT arm ($p < 0.05$, each). The patients in OINT group had lesser number of hospitalizations 6 (17%) versus 16 (45.7%) ($p = 0.010$) over the course of 3 months as compared to SMT group.

Conclusion: Outpatient intensive nutrition therapy has a significant impact on improving survival, frailty and disease severity of ACLF patients with a reduction in number of hospitalizations and supports the key role of nutrition in addition to standard medical treatment in ACLF patients.

Abstract Submission No. 100525

O-0829

ALTA: a simple nutritional prognostic score for patients with HBV-ACLF

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Background & Aims: Malnutrition, as a common but usually neglected complication, can increase the mortality in patients with hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF). The aim of this study was to develop a simple nutritional prognostic score to accurately predict the mortality in HBV-ACLF patients.

Methods: In this multicenter retrospective study, clinical data from 195 HBV-ACLF patients were used to develop a new prognostic score, and then was validated in two external cohorts.

Results: Four independent factors were significantly associated with 28-day mortality of HBV-ACLF patients and constituted a new prognostic score (ALTA score = $2.216 \times \text{age} - 2.283 \times \text{lymphocyte count} - 1.902 \times \text{total cholesterol} - 0.152 \times \text{albumin} - 1.629$). Notably, the AUROC of ALTA score for 28/90-day mortality (0.955/0.947) were significantly higher than those of three other ACLF prognostic scores (COSSH-ACLF II, 0.848/0.791; MELD, 0.607/0.596; MELD-Na, 0.602/0.582; all $P < 0.001$), and three known nutritional scores (CONUT, 0.746/0.816; OPNI, 0.256/0.200; NRS-2002, 0.313/0.330; all $P < 0.001$). Further classified ALTA score into three strata, the hazard ratios of mortality at 28/90 days were obviously increased in the intermediate-risk and high-risk groups than low-risk group (19.0/8.0 and 67.9/29.7). The negative predictive values of low-risk group and positive predictive values of high-risk group for 28/90-day mortality were 97%/78% and 94%/100%, respectively. Further optimized ALTA score into a scoring sheet (ALTA 2.0), it still exhibited excellent predictive ability. These results were then validated in two external cohorts.

Conclusion: ALTA, as a simpler and easier to use nutritional prognostic score for clinicians, can accurately predict short-term mortality of HBV-ACLF patients, hence, it might be used to guide clinical management.

Abstract Submission No. 100576

O-0830

Forecasting Initial 15-Day Mortality in Alcohol Related Acute On Chronic Liver Failure (ACLF)

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Background and Aim: The initial 15 days study in alcohol related ACLF is scarce, a period significant for mortality and liver transplantation feasibility. This study aims to fill this gap by conducting a detailed analysis of this timeframe.

Methods: Clinical and biochemical blood parameters of 227 alcoholic ACLF patients were collected. Patients were followed till 90 days or death with observations on 0, 4, 7, 15, 30, 45, 60, and 90 days. Statistical analysis was focused on 15 day mortality.

Results: Of 227 patients, 41% (94) died within 15 days. Baseline means of 15 day mortality versus survived showed significant difference in alcohol intake (198g/day v 144g/day), serum creatinine (2.2mg/dl v 1.6mg/dl), lactate (2.8mmol/l v 1.8mmol/l) and AARC score (10.7 v 9.4).

Significant hazard ratios (HR) on multivariate cox regression of categorical blood parameters were creatinine ($< 0.7\text{mg/dl}$ v $> 1.5\text{mg/dl}$, HR-0.44), INR (< 1.8 v > 1.8 , HR-0.47), lactate ($< 1.8\text{mmol/L}$ v $> 1.8\text{mmol/L}$, HR-0.42), neutrophil counts ($< 80\%$ v $> 80\%$, HR-0.43). Those consuming $< 200\text{g/day}$ of alcohol had 70% less mortality to those with $> 300\text{g/day}$. Among the prognostic scores, AARC (score ≤ 7 v > 10 , HR-0.10) and SIRS (present v absent, HR-9.5) were key determinants. In decision tree analysis SIRS presence alone leads to 65% mortality, SIRS with lactate $> 1.4\text{mmol/l}$ resulted in 75% deaths, and trio combination of SIRS, lactate $> 1.4\text{mmol/l}$, and alcohol intake $> 200\text{g/day}$ leads to 100% mortality.

Conclusions: Alcoholic ACLF have 41% initial 15 Day mortality. The combination of SIRS presence, lactate level $> 1.4\text{mmol/L}$, and alcohol intake $> 200\text{g/day}$ was linked to 100% deaths.

Abstract Submission No. 100656

O-0831

XBP1 mediating NFκBp65 promotes macrophage derived inflammation via MT2 transcript in liver IRI

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Background: XBP1, the most conserved transcription factor of endoplasmic reticulum stress, plays important roles in physiological and pathological settings. Its activity has profound effects on disease progression and prognosis. We aimed to investigate the role of XBP1 in macrophage-originated sterile inflammation during liver ischemia/reperfusion injury (IRI).

Methods: Macrophage XBP1 expression and liver injury were analyzed in patients undergoing ischemia-related hepatectomy. Then, we created a myeloid-specific XBP1-knockout (XBP1M-KO) strain to study function and mechanism of XBP1 on macrophage-derived sterile inflammation in murine liver IRI model with In-vitro parallel research. Macrophages co-cultured with hypoxia-treated hepatocytes were applied to investigate impact of XBP1 in vitro. We also analyzed RNA sequencing and databases for potential XBP1 target gene by CUT&RUN and luciferase reporter assay.

Results: Clinically, macrophage XBP1 expression significantly increased in ischemic liver tissues and positively correlated with liver injury after hepatectomy. Less hepatocellular damage was presented in XBP1M-KO mice than XBP1-proficient controls based on serum biochemistry, pathology, ROS and inflammation. In vitro, XBP1 deficiency inhibited sterile inflammation and migration in macrophages co-cultured with hypoxia-treated hepatocytes. Analysis of RNA sequencing and databases determined Metallothionein 2 (MT2) as an XBP1 target gene, negatively regulated by binding with its promoter. XBP1 deficiency increased MT2 expression and IKB α expression, but inhibited NF- κ B-p65 phosphorylation. MT2 inhibition and NF- κ B activation markedly neutralized XBP1M-KO-related benefits by promoting sterile inflammation during liver IRI.

Conclusion: XBP1 promotes macrophage-originated sterile inflammation, increases liver IRI by binding to the MT2 promoter, and regulates MT2/NF- κ B pathway, providing a potential therapeutic target for liver IRI.

Abstract Submission No. 100697

O-0832

Biomarker discovery, validation & pathways in infection related acute-on-chronic liver failure

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Objective: Evaluating infections in the context of acute-on-chronic liver failure (ACLF) presents a formidable challenge. This study employs untargeted proteomics to uncover protein signatures and pathway perturbations associated with infections in ACLF.

Design: We prospectively enrolled 231 ACLF patients (92.6% males, mean age 42.1 years, 65% alcoholic hepatitis), both with and without bacterial/fungal infections. Untargeted proteomics was performed on plasma samples from 84 patients (discovery cohort), followed by biomarker discovery and validation using differential expression, discriminant analysis, machine learning, and ELISA in 147 patients. Perturbed pathways between infected and non-infected groups were analyzed.

Results: Infection-positive patients exhibited elevated leucocyte count, procalcitonin, organ failures, severity scores, and a 30-day mortality of 81.4% vs. 6.6% ($p < 0.001$ each). Among the 516 identified proteins, 27 were upregulated and 38 downregulated in infections (adjusted- $p < 0.05$). Validation yielded a four-protein panel (LGALS3BP, PLTP, CFP, GPX3) classifying infections with AUC 0.854 (0.787-0.922), retaining significance after adjusting for disease severity and inflammation. A PACIFY model, integrating three proteins (LGALS3BP, PLTP, GPX3), procalcitonin, CLIF-C OF, and leucocytosis/leucopenia, yielded AUC 0.957 (0.927-0.986), accuracy 89.1%, sensitivity 90.2%, and specificity 99.7% for infection diagnosis. PACIFY outperformed procalcitonin, SIRS, WBC, NLR, neutrophil%, and composite models ($p < 0.001$). Pathway analysis unveiled diverse perturbations including impaired pathogen-response, reduced-phagocytosis, neutrophilic extracellular traps, complement functions, hypocoagulation and hypofibrinolysis, dysregulated carbohydrate metabolism and autophagy, with heightened cell death and proteolysis.

Conclusion: The PACIFY model emerges as a robust tool for identifying infections in ACLF, surpassing existing markers. Pathway disruptions provide insights for innovative therapies and infection prevention in ACLF.

Abstract Submission No. 100743

O-0833

Predictive model based on PNI for infection in acute-on-chronic liver failure

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Objective Prognostic Nutritional Index (PNI) is an index that can reflect nutritional status and immune function of patients and calculated from the serum albumin concentration and the total number of peripheral lymphocytes. This study aims to explore the predictive value of PNI on infectious complication in patients with acute-on-chronic liver failure (ACLF).

Methods Two hundred and twenty patients with ACLF hospitalized in the First Affiliated Hospital of Xi'an Jiaotong University were selected, who were divided into infection group and non-infection group based on whether they were infected in hospital. Differences in clinical data and laboratory indicators were compared between the two groups. Logistic regression analysis was used to select the influencing factors related to infectious complication. Receiver operating characteristic curve (ROC) was applied to evaluate the predictive value of PNI on infection.

Results: (1) In patients with ACLF, there were 152 and 68 patients in infection group and non-infection group respectively. Ascites, hepatorenal syndrome, PNI, ALB and so on were statistical differences between the two groups ($P < 0.05$). (2) Among 152 infectious patients, the common sites of infection were abdominal infection and pulmonary infection, with an incidence of (113/198, 57.07%) and (58/198, 29.29%). (3) The results of logistic multivariate analysis showed that low PNI, ascites and hepatorenal syndrome were risk factors for infectious complication. When $PNI \leq 40.625$, it has a better prediction effect on infectious complication in patients with ACLF, with sensitivity of 0.842 and specificity of 0.412.

Conclusion The low PNI is an independent risk factor for developing infection in patients with ACLF. When $PNI \leq 40.625$, it can predict infectious complication in patients with ACLF.

Abstract Submission No. 100799

O-0834

Hepatitis E virus infection portends high mortality in patients with acute-on-chronic liver failure

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Background: Hepatitis E virus (HEV) is one of the top causes of viral hepatitis worldwide, but limited data exist on its impact in acute-on-chronic liver failure. We evaluated the outcomes of HEV in patients with ACLF in a multinational cohort of APASL ACLF Research Consortium (AARC).

Methods: Prospectively collected data of 5612 ACLF patients from 25 countries in the AARC database between 2007 and 2021 was studied. The data analysed included demographic profile, severity of liver disease (MELD, AARC score), chronology of organ failure development, treatments and outcomes. Statistical analyses were carried out using RStudio version 2023.09.01 and OpenEpi version 3.01.

Results: The study included 340 HEV IgM-positive patients (6.06% of total cohort) and 5272 non-HEV patients who were hospitalised for ACLF. Compared with non-HEV patients, HEV-positive patients have similar demographic profile (age, gender, and chronic liver disease) and disease severity at baseline (MELD 29.9 and AARC score 9.62). However, HEV patients have significantly higher 90-day mortality (54.7% vs. 48.1%, $p=0.019$), number of organ failures by day 4 (median of 2 vs. 1, $p<0.001$) and progression (time to death: 11 vs. 13 days, $p=0.012$).

Conclusions: HEV infection is associated with higher mortality rate and number of organ failures in ACLF patients. This may be related to the lack of specific therapy for HEV infection.

Abstract Submission No. 100843
O-0835

Syndecan-1 improves ACLF by promoting liver regeneration and attenuating hepatocytes apoptosis

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Background and Aims: Acute-on-chronic liver failure (ACLF) has a high short-term mortality rate. Syndecan-1 (SDC-1) is a major molecule of heparan sulfate proteoglycans present on healthy liver tissue, which can be shed from the cell surface. The core proteins of SDC-1 carry heparan sulfate (HS) chains, and sulodexide (SDX) is a heparinoid compound. Thus, we aimed to assess diagnostic, prognostic and therapeutic efficacy of SDC-1 and its side chains in ACLF patients.

Methods: Serum SDC-1 was examined in 26 healthy controls, 34 patients with chronic hepatitis, 38 with liver cirrhosis, and 101 ACLF patients by ELISA. And a prospective cohort of 101 ACLF patients was followed up to develop a novel prognostic score. Furthermore, we established an ACLF mouse model treated with SDX and HS.

Results: Serum levels of SDC-1 in ACLF patients were obviously increased compared to healthy controls ($P < 0.0001$). According to our 90 days of clinical observations, non-survived ACLF had markedly higher baseline serum SDC-1 levels than survivors ($P < 0.05$). A novel

prognostic model (UIAS= $0.076 \times \text{Age} + 0.001 \times \text{SDC-1} + 1.454 \times \text{INR} + 2.854 \times \text{UGIB} - 12.165$) was developed for ACLF. In a cell model of acute liver injury, overexpression of SDC-1 significantly increases expression of proliferating cell nuclear antigen (PCNA) and cyclinD1. Furthermore, in a mouse model, we found that SDX and HS significantly attenuated ACLF, which may be promoting liver regeneration and restraining caspase3-related apoptosis. Furthermore, **Conclusion:** Collectively, our findings suggest that SDC-1 can potentially serve as a predictive biomarker for ACLF prognosis and may represent a promising therapeutic target for relieving severe liver injury.

Abstract Submission No. 100848
O-0836

Activating cholinergic pathway attenuates Liver injury by inhibiting MLKL-mediated necroptosis

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Background: The function of cholinergic anti-inflammatory pathway (CAP) in acute liver failure (ALF) with inflammatory storm remains indefinite. Mixed lineage kinase domain-like pseudokinase (MLKL), a key terminal effector of necroptosis, plays a crucial role in regulating liver inflammation. Investigation about CAP regulation on necroptosis would enrich our understanding over cholinergic anti-inflammatory mechanism.

Approach and Results: Co-injection of Lipopolysaccharide and D-galactosamine were used to establish the model of ALF. PNU-282987 was used to activate the CAP. Liver biopsy specimens and patients' serum from liver failure patients were also analyzed.

We confirmed that activating the CAP alleviated hepatocyte destruction, accompanied by a significant decrease in hepatocyte apoptosis, pro-inflammatory cytokines, and NLRP3 inflammasome activation. Moreover, hepatic necroptosis and serum MLKL levels were induced in ALF and MLKL levels were positively correlated with the extent of liver damage and the expression of proinflammatory markers (IL-6, IL-1 β , TNF- α). MLKL was colocalized with macrophage marker F4/80 in livers. Mechanistically, MLKL deletion also remarkably decreased pro-inflammatory cytokines and inhibited polarity shift toward inflammatory macrophages. Furthermore, Activating the CAP inhibits MLKL-mediated necroptosis and downregulated markers of inflammatory macrophages in vivo and in vitro. Finally, we revealed that the levels of serum MLKL were elevated in patients with liver failure and closely correlated with clinical course. Increasing hepatic MLKL were also confirmed in patients.

Conclusion: Together, these data indicated that activation of the CAP attenuates Liver injury by inhibiting macrophage-derived MLKL-mediated necroptosis and regulating macrophage polarization and function. Targeting MLKL might be a potential therapeutic way to treat ALF.

Abstract Submission No. 100929
O-0837

Niclodamide inhibits Macrophage Ferroptosis against LPS/D-GalN-induced Acute Liver Failure

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Acute liver failure (ALF) is a life-threatening liver disease with a high mortality rate, and the identification of specific therapeutic agents represents a crucial clinical challenge. Although oxidative stress and inflammatory responses within the liver play pivotal roles in the pathogenesis of ALF, the precise regulatory mechanisms remain elusive. Ferroptosis, a form of programmed cell death, is closely associated with oxidative stress and inflammation. Applying the strategy of “old drugs with new uses” and bioinformatics analysis, we screened for potential agents and identified niclosamide, an anthelmintic drug. Niclosamide dose-dependently improved survival rates and protected mice from LPS/D-galactosamine-induced liver injury. In vitro, niclosamide affected macrophage proliferation and the production of inflammatory mediators in response to LPS without exerting a direct protective effect on hepatocytes. Subsequent studies revealed that niclosamide could inhibit macrophage ferroptosis, particularly M2 macrophage ferroptosis, in vivo. Consistently, niclosamide suppressed macrophage ferroptosis without affecting hepatocytes. Based on these findings, we propose the scientific hypothesis that niclosamide targets hepatic macrophage ferroptosis to inhibit the development and progression of ALF.

Abstract Submission No. 101039
O-0838

Comparison of 28 Day Survival of Patients with ALF and ACLF treated with DPMAS

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Objectives: The study aims to determine the clinical outcomes of patients who underwent DPMAS.

Methods: This is a cross-sectional analytic study that retrospectively analyzed 36 adult patients, 14 with ALF and 22 with ACLF who received DPMAS in 2 Tertiary Hospitals in the Philippines.

Results: A total of 36 adult patients on DPMAS were included, 30 were on DPMAS and 6 were on DPMAS + Plasma Exchange (PE). Of the 30 patients who underwent DPMAS, 14 have ALF and 16 have ACLF. All Six patients who underwent DPMAS and PE have ACLF. The median age was 59 (IQR 17.25) and majority are males (78%). The most common etiologies for ALF were hypoperfusion, 4 (11%), and Drug-induced, 4 (11%), while hepatocellular carcinoma, 10 (28%), followed by Chronic Hepatitis B, 9 (25%) are common etiologies for ACLF. Majority had Child Pugh Class C and Grade 3 Hepatic Encephalopathy. Total bilirubin declined after DPMAS for both ALF (17.845 to 11.485, $p=0.646$) and ACLF (16.685 to 12.02, $p=0.118$). 28-day Survival rate in ALF on DPMAS is 18%, while ACLF patients on DPMAS is 30% ($p=0.854$). There was no difference between survival distributions of ALF+DPMAS, ACLF+DPMAS and ACLF+DPMAS+PE ($p=0.844$) using the Kaplan Meier method.

Conclusion: DPMAS and DPMAS+ PE improved the clinical and laboratory parameters in both ALF and ACLF. A larger cohort of patients, however, is needed to ascertain its clinical significance.

Abstract Submission No. 101122
O-0839

TPO promotes hepatocyte regeneration by elevating platelets in rats with acute liver failure

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Aim: To investigate the role of platelets and recombinant human thrombopoietin (rhTPO) on liver regeneration in rats of acute liver failure (ALF).

Methods: A rat model of acute liver failure was constructed by injection of D-amino galactose (D-GalN). The experimental rats were randomly divided into rhTPO group ($n=20$) and control group ($n=20$), which were given rhTPO 15 $\mu\text{g}/\text{kg}$ or saline for 5 days before D-GalN injection respectively. Liver tissue and blood samples were taken from rats at 6, 24 and 72 hours after the construction of an acute liver failure model after D-galactose injection in both groups. Hepatic histopathological changes and Ki67 were observed in both groups. The survival, liver function, serum HGF level were compared between the two groups after injection of D-GalN. Cell proliferation and cell apoptosis were analyzed by BrdU and TUNEL.

Results: Before D-GalN injection, the PLT counts and liver weight of rhTPO group were remarkably higher than that in the control group ($P < 0.01$). After injection of D-GalN, the rhTPO group had significantly lower ALT levels at 6 and 24 hours and significantly lower TBil levels at 72 hours as well than the control group ($P < 0.05$). The proportion of TUNEL-positive cells in liver tissues in the rhTPO group was lower than that in the control group ($P < 0.01$), the serum HGF levels and the proliferation index of Ki67 and the proportion of BrdU-positive cells were significantly higher than that in the control group ($P < 0.05$).

Conclusion: TPO significantly elevated PLT counts in D-amino galactose induced ALF rats. Platelet elevation induced by rhTPO promoted recovery of liver function, reduced hepatocyte apoptosis and increased liver regeneration in ALF rats.

Abstract Submission No. 101255
O-0840

Exosomes from senescent hepatocytes activate HSCs and protect against acute liver failure by ITGA5

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Background: Our group previously found that hepatic stellate cells (HSCs) activation is a physiological and potentially beneficial response to serve as the architecture to prevent liver collapse during acute liver failure (ALF). Acute hepatocyte senescence occurs in acute injury and senescent cells influence the microenvironment by senescence-associated secretory phenotype, such as exosomes. However, the crosstalk between the secretome of senescent hepatocytes and HSC activation in ALF remains unclear.

Methods: Lipopolysaccharide (LPS) and D-galactosamine (D-GalN) were used to induce ALF. Human hepatocyte line LO2 and HSCs cell line LX2 were used in vitro experiments. Exosomes were isolated from the conditional media of senescent (Sen) or non-senescent (NSen) hepatocytes by differential ultracentrifugation and identified by electron microscope and western blots.

Results: Cellular senescence markers, such as p21, P16, and p53, were increased in mice with acute liver failure. Senescent hepatocytes, induced by etoposide, secreted more exosomes than non-senescent cells. Exosomes derived from Sen-hepatocytes promote migration, proliferation, and activation of HSCs. Proteomic characterization of exosomes

revealed that ITGA5 was overexpressed in exosomes derived from Sen-hepatocytes. ITGA5 was also increased in Sen-hepatocytes and liver with ALF mice, which was regulated by mTORC1 in cellular senescence condition. ITGA5 silencing in HSCs reduced HSC activation and migration by inhibiting Smad2 phosphorylation. Pharmacologic inhibition of ITGA5 using ATN-161 exacerbated liver failure by inhibiting HSC activation and impairing liver structure.

Conclusion: ITGA5-enriched exosomes derived from senescent hepatocytes activate hepatic stellate cells via regulation of Smad2 signaling, which maintains the liver architecture to prevent collapse during acute liver failure.

Abstract Submission No. 101397
O-0841

DPMAS Therapy in Patients with Liver Failure: A Non-randomized Cluster-controlled Study (PADSTONE)

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Background: Liver failure is a life-threatening syndrome and cause high short-term mortality. Double plasma molecular adsorption system (DPMAS) is one of the available artificial liver support systems which its efficiency for chronic liver disease (CLD) patients with liver failure remains controversial.

Methods: A prospective, multicenter and cluster-controlled study was conducted (NCT05129904) and 57 tertiary hospitals were recruited and allocated to the DPMAS treatment clusters (n=28) and standard medical treatment (SMT) clusters (n=29). Outcomes included disease progression, survival, death and liver transplantation and safety of DPMAS therapy. Twelve-months is required for each participant to complete post-discharge follow-up.

Results: In total, 648 liver failure patients were enrolled in DPMAS group and 615 patients in SMT group. MELD score was comparable between these two groups (24±5 vs. 24±6, p=0.984). For the DPMAS group, 31.9% patients had 2 DPMAS treatment sessions and 77.1% of the initial DPMAS treatment was with subsequent plasma exchange. Unfractionated heparin was the most common anticoagulants used in DPMAS treatment. The total bilirubin, ALT and CRP levels were all significantly improved after the initial DPMAS therapy. The 28-day transplant-free mortality was much lower in DPMAS group than SMT group (15.7% vs. 20.0%, p=0.048). Allergy (3.7%) and dialyzer coagulation (3.2%) as well as the arterial hypotension (2.9%) were the common adverse events during DPMAS treatment.

Conclusions: DPMAS treatment for CLD patients with liver failure can significantly improve the liver function markers and the 28-day mortality. DPMAS therapy was associated with few adverse events and its safety is confirmed.

Abstract Submission No. 101409
O-0842

Clinical Characteristics and Risk Factors of End-Stage Liver Disease Complicated by Infections

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Background: Bacterial or fungal infection is one of the most frequent complications for end-stage liver disease (ESLD) patients. However, clinical characteristics and risk factors in ESLD with bacterial or fungal infection have not been fully elucidated.

Methods: ESLD patients from 14 tertiary hospitals were involved in this retrospective cohort study from January 2012 to December 2018 in central China. The clinical characteristics and risk factors in ESLD with bacterial or fungal infection were analyzed.

Results: Out of all 1208 ESLD patients, 565 (46.8%) were complicated by bacterial infection and 16 (1.3%) were complicated by fungal infection. Spontaneous bacterial peritonitis was the most common type of infection (51.5%), followed by pneumonia (43.7%), urinary tract infection (7.9%) and bacteremia (2.8%). Seventy-two samples showed positive culture results, among which 28 (38.9%) were gram-positive bacteria, 28 (38.9%) were gram-negative bacteria and 16 (22.2%) were fungus. ESLD patients with bacterial or fungal infection both showed higher level of white blood cell and procalcitonin, severer liver and coagulation dysfunction, and more likely to develop ascites, hepatorenal syndrome, hepatic encephalopathy, upper gastrointestinal bleeding, and hepatopulmonary syndrome than those without. Bacterial infection was a mortality risk factor for patients with ESLD and acute on chronic liver failure (ACLF) was an independent predictor for poor outcomes in ESLD with bacterial or fungal infection.

Conclusions: Bacterial infection was an independent risk factor of mortality of ESLD. Homogeneity and heterogeneity in epidemiology, clinical characteristics and risks of mortality were shown among different entities of ESLD with bacterial or fungal infections.

Abstract Submission No. 101425
O-0843

Fulminant Hepatic Failure In Pregnancy Challenges, Etiology, Management And Its Associated Mortality

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Background: FHF in pregnancy negatively maternal affects and fetal outcomes, which depend on the etiology, timely diagnosis, prompt management, and early referral equipped medically to a center for managing obstetric complications.

The study aimed to determine the challenges, etiology, management, and associated mortality in pregnant Fulminant hepatic failure (FHF) patients.

Methodology: A cross-sectional study at the Department of Gastroenterology, JPMC, Karachi, Pakistan All pregnant patients with FHF, age ≥ 16 years recruited were investigated for acute viral serology, complete blood count, function function tests, tests, liver renal serum MELD creatinine, score parameters and King's college criteria (KCC) parameters

Results: We have enrolled 47 patients up till now with a mean age of 25.14 ± 8.32 years. The KCC criteria cut-off point was reached in a total of 40 (85.10%) patients (out of 47) of which 30 (75%) patients died.

Conclusion: We conclude that for pregnant women, diagnosis should consider early hepatitis E as the usual cause of FHF in our case with consultation termination of pregnancy. The Management protocols need to be individualized for each case keeping in mind the risk versus benefit to both the mother and the fetus

Abstract Submission No. 101524

O-0844

Role of plasma-derived exosomal lncRNA in regulating the systemic inflammatory response in HBV-ACLF

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This study investigated the RNA characteristics related to disease progression in hepatitis B virus (HBV)-related acute-on-chronic liver failure (ACLF) and the molecular mechanisms involved in immune regulation. Plasma exosomal long noncoding RNA (lncRNA) of 5 healthy volunteers, 5 patients with chronic hepatitis B (CHB) flares, and 8 patients with HBV-ACLF was characterized using RNA sequencing analysis. Exosomal differentially expressed lncRNA (DELncRNA) was screened using differential analysis and protein-protein interaction, and competing endogenous RNA network maps were constructed. Immune-related mRNAs mediated by DELncRNA regulation were identified using immunology databases. Their expression levels were verified by RNA sequencing samples of 5 patients with CHB flares, and 5 patients with HBV-ACLF. Bioinformatics analysis was used to predict the potential biological functions of the DELncRNA. A newly identified lncRNA, MSTRG.38026, was differentially expressed in HBV-ACLF plasma exosomes. We predicted that MSTRG.38026 binds to hsa-miR-22-3p to regulate 107 immune-associated mRNAs. GO enrichment and KEGG pathway analysis suggested possible biological functions associated with immune-related mRNAs mediated by MSTRG.38026. The expression of TFKC(DAK), TGFBR1, and NFAT5 was significantly downregulated in high-throughput sequencing validation. This work is the first to characterize the lncRNA profile of exosomes generated from the plasma of patients with HBV-ACLF.

Abstract Submission No. 101538

O-0845

LPS promotes inflammation via proteasomal degradation of Atg13 in HSCs during ACLF

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Background: Inflammation plays a critical role in the progression of ACLF. Atg13 is a vital regulatory component of ULK1 complex. Hepatic stellate cells (HSCs) were considered non-inflammatory cells and contributed only to hepatic fibrosis in the past. Recently, some studies found that HSCs can secrete inflammatory cytokines. Autophagy has been shown to regulate inflammation, it is unclear whether ubiquitin (Ub)-proteasome system (UPS) is involved in inflammatory responses in HSCs during ACLF.

Methods: Clinical data were collected from ACLF patients. The expression of Atg13 was assessed by rt-PCR and western blotting. Atg13 was knocked down by si-RNA in LX2 cells. A co-immunoprecipitation assay was used to detect protein binding and poly-ubiquitination of Atg13. In vitro tests with LX2 cells were performed to explore the effects and regulation of p38 MAPK, Atg13, UPS, autophagy, and inflammation.

Results: We evaluated the role of Atg13 in HSCs inflammation and explored the underlying mechanisms. Inflammatory factors are up-regulated via activation of p38 MAPK and inhibition of autophagy in LX-2 cells. Expression of Atg13 was decreased in LPS-incubated LX2 cells. Atg13 knockdown markedly inhibited autophagy and promoted LPS-induced inflammation in LX2 cells. Our results also showed that LPS induced depletion of Atg13 via UPS, which was p38 MAPK dependent.

Conclusions: LPS induces proteasomal degradation of Atg13 via p38 MAPK, participating in the aggravation of LPS-induced autophagy inhibition and inflammatory responses in LX2 cells. Atg13 serves as a mediator between autophagy and proteasome. Modulating Atg13 or proteasome activity might be a novel strategy for treating HSCs inflammation.

Abstract Submission No. 101574

O-0846

The role of L3-PMI in the prognostic evaluation of patients with acute-on-chronic liver failure

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BACKGROUND: Sarcopenia is closely related to the prognosis of the patients with end-stage liver disease. However, there are still lack of simple and practical evaluation indicators in clinical practice. The purpose of this study is to explore the applicable value of the third lumbar psoas muscle index (L3-PMI).

METHODS: We retrospectively studied the data of 140 patients who met the ACLF diagnostic criteria for hepatitis B cirrhosis. Analyze the patient's L3-PMI and clinical characteristics and prognosis.

RESULTS: The 140 patients were divided into the survival group with 102 cases and the death group with 38 cases according to their 90-day survival status. The L3-PMI value of patients in the death group was $4.89 \pm 1.42 \text{ cm}^2/\text{m}^2$, significantly lower than that in the survival group ($5.94 \pm 1.24 \text{ cm}^2/\text{m}^2$) ($P < 0.001$). In addition, 33 ACLF patients with hepatic encephalopathy (HE) had an L3-PMI value of $5.17 \pm 1.49 \text{ cm}^2/\text{m}^2$ which was significantly lower than that of 107 patients without

HE ($P = 0.020$). Draw the ROC curve of L3-PMI predicting death by gender. The area under the ROC curve for males was 0.726, the cut-off value was 5.02, the sensitivity and specificity were 85% and 50% respectively. The area under the ROC curve for females was 0.774, and the cut-off value was 4.60. The sensitivity and specificity were 50% and 100% respectively.

CONCLUSION: L3-PMI has important clinical application value for evaluating the prognosis of ACLF patients related to hepatitis B liver cirrhosis.

Abstract Submission No. 101620

O-0847

Activation of hepatocyte p53 triggers acute liver failure with multiple organ injury.

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p53 is the major cellular regulator, which controls proliferation and cell death. Meanwhile, its impact on acute liver failure (ALF) remains unknown. This work aims to study the role of p53 on ALF. In Gene Expression Omnibus database, human hepatic p21, a p53 target, was up-regulated in fulminant hepatitis liver compared with normal liver. C57B6J mice administered with acetaminophen or concanavalin A showed upregulation of p53 protein in the liver. We knocked out Mdm2, a negative regulator of p53, inducibly and hepatocyte-specifically by tamoxifen administration in mice (Mdm2Δhep mice). Mdm2Δhep mice showed activation of p53 signaling with extensive cell death in hepatocyte, and elevated serum ALT and bilirubin. Also multiple organ injury was noted as the increase of TUNEL-positive cells and inflammatory cells in the kidney, heart, colon, and lung, and elevation of serum Cystatin C. All of the Mdm2Δhep mice died within 168 hours after tamoxifen injection. Of note, further deletion of hepatocyte p53 negated all of these findings. Multiplex cytokine assay and liver RNA-seq in Mdm2Δhep mice showed the elevation of multiple inflammatory cytokines. Among them, leukemia inhibitory factor (LIF) was the most elevated cytokine. LIF increased with nutlin-3, an inhibitor of Mdm2, in CL2 and HepG2 (hepatocyte cells). LIF up-regulated inflammatory cytokines including LIF itself in LX-2 (hepatic stellate cell) and HK2 (renal tubule epithelial cell). LIF was elevated in multiple organs and serum in Mdm2Δhep mice, suggesting the possibility of LIF-mediated systemic inflammatory reaction. Collectively, acute activation of hepatocyte p53 is suggested to trigger ALF with multiple organ injury.

Abstract Submission No. 101635

O-0848

Evaluating the Life-Saving Potential of Liver Transplants for ACLF with Circulatory Failure

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Background & Aims: Circulatory failure (CF) is a severe type of extrahepatic organ failure in acute-on-chronic liver failure (ACLF). This study aimed to clarify the clinical characteristics and survival benefit of liver transplantation (LT) in hepatitis B virus-related ACLF (HBV-ACLF) patients with CF.

Methods: The clinical data of 2247 hospitalized HBV-ACLF patients with and without CF from the Chinese Group on the Study of Severe Hepatitis B open cohort were enrolled to evaluate the survival benefit of LT.

Results: A total of 222 HBV-ACLF patients were diagnosed with CF, and 2025 patients were diagnosed with non-CF. Patients with CF were older, had worse laboratory indicators, and had a higher proportion of complications, prognostic scores and mortality (28/90/360-day: 93.6%/95.2%/95.7% vs. 26.9%/37.7%/43.1%, $p < 0.001$) than those with non-CF. Septic and haemorrhagic shock were the main causes of CF. Age, white blood cell counts and international normalized ratio were identified as independent risk factors for CF development during hospitalization. The survival rate in HBV-ACLF patients with CF undergoing LT was significantly higher than that in those without LT (28-/90-/360-day: 62.9%/54.3%/54.3% vs. 6.4%/4.8%/4.8%, $p < 0.001$). Propensity score matching analysis confirmed these results (28-/90-/360-day: 62.9%/54.3%/54.3% vs. 7.1%/7.1%/7.1%, $p < 0.001$). Stratification analysis further showed that CF patients with INR < 3.5 had a higher 360-day post-LT survival rate.

Conclusions: HBV-ACLF patients with CF exhibited a poor prognosis, and LT significantly improved their survival. Patients with INR < 3.5 had a higher survival benefit from LT. These findings can help refine candidate selection for LT in clinical practice.

Abstract Submission No. 101647

O-0849

Longitudinal single-cell profiling unveils distinct immune traits linked to ACLF progression

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Background: Acute-on-chronic liver failure (ACLF) is a life-threatening syndrome involving dysfunction in multiple immune cells. This study aims to comprehensively profile the dynamic immune responses along the progression of ACLF.

Methods: We conducted single-cell RNA-sequencing (scRNA-seq) of 379,132 individual cells from 45 samples of 32 subjects using peripheral blood mononuclear cells (PBMCs). This included 17 hospitalized hepatitis B virus-related ACLF and early stage non-ACLF patients exhibiting a progressive, stable or recovering course of ACLF. Bulk RNA-Seq, flow cytometry and histological assays were employed in other ACLF cohorts for validation.

Results: The single-cell transcriptome landscape identified forty-one immune cell clusters, including 4 low-density neutrophil clusters, revealing cell-type-specific changes in ACLF progression. We discovered that IL1R2⁺-macrophage and FCGR4B⁺-neutrophil are hallmarks of the progressive course of ACLF, especially in the end stage. We also found the intensified interactions of ANNEXIN and VISFATIN signaling within these two cell clusters, showing an anti-inflammation effect in the end stage of ACLF. Upregulation of hypoxia, inflammatory response, TNF a signaling via NFkB in CD24⁺ neutrophil was observed. Highly activated T cells, including GZMK⁺CD4⁺- and GZMK⁺-COTL1⁺-CD8⁺- T cells with increased cytotoxic function, gradually decreased in severe ACLF patients. The patients were stratified into six subtypes with specific features, significantly associated with ACLF outcome. External validation of cell cluster signatures confirmed their specificity in ACLF progression.

Conclusions: Our comprehensive immune profiling reveals dynamic changes in the innate and adaptive immune responses in progressive ACLF, highlights anti-inflammatory functions of macrophage and provides diverse immune subtypes for ACLF stratified medicine.

Abstract Submission No. 101687

O-0850

Hypomethylation of TL1A predicts the prognosis of ACHBLF

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In Asia, chronic acute hepatitis B liver failure (ACHBLF) accounts for more than 70% of ACLF. ACHBLF has a short - to medium-term mortality rate of about 50-90%. The purpose of this study was to investigate the clinical significance of TL1A and DR3 in development of ACHBLF. In a total of 270 subjects, RT-PCR, Methylation and Western -blot were used to detect the expression levels of TL1A and its receptor DR3 in PBMCs and serum. The results showed that the expression of TL1A and DR3 mRNA in ACHBLF was higher than that in chronic hepatitis patients or healthy control group. In addition, the methylation frequency of TL1A promoter in patients with ACHBLF was significantly lower than that in other groups. Moreover, at the protein level, western blot assay results showed that TL1A expression in patients with ACHBLF was higher than that in other patients. The results indicate that TL1A and its receptor DR3 can predict disease progression in ACHBLF and the methylation of TL1A gene promoter can be used as a useful biomarker for prognosis of chronic acute hepatitis B failure.

Abstract Submission No. 101691

O-0851

Hypermethylation of glutathione peroxidase 4 promoter predicts poor prognosis of HBV-ACLF

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Background: Hepatitis B virus-associated acute-on-chronic liver failure (HBV-ACLF) is a syndrome with a high short-term mortality rate, and its prognosis is critical in clinical management.

Methods: A total of 289 participants including 84 patients with HBV-ACLF, 61 patients with non-HBV ACLF, 94 patients with CHB and 50 HCs were recruited. We detected the expression of *GPX4* in peripheral blood mononuclear cells (PBMCs) by real-time quantitative polymerase chain reaction (RT-qPCR). The methylation level of *GPX4* gene promoter in PBMCs was detected by TaqMan probe-based quantitative methylation-specific PCR (MethyLight). Receiver operating characteristic (ROC) curves were generated to estimate the discriminations.

Results: The expression levels of *GPX4* in PBMCs and serum of HBV-ACLF patients were lower while the methylation level of *GPX4* promoter was higher than that of non-HBV-associated acute-on-chronic liver failure (non-HBV ACLF) patients, chronic hepatitis B (CHB) patients and healthy controls (HCs). The methylation level of *GPX4* promoter yielded a larger area under the receiver operating characteristic curve (AUROC) than the model for end-stage liver disease (MELD) score in predicting 90-day mortality.

Conclusions: *GPX4* promoter methylation level has promising potential as a predictor of 90-day mortality in patients with HBV-ACLF.

Abstract Submission No. 101727

O-0852

Single-cell landscape of immunological responses in acute-on-chronic hepatitis B liver failure

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Aim: Acute-on-chronic liver failure (ACLF) is a syndrome that manifests as systemic inflammation and organ failure, which preferentially affects patients with chronic liver disease. In Asia, hepatitis B virus (HBV) is the main etiology. Here we combined the transcriptional profiles of immune cells with assembled T cell receptor (TCR) and B cell receptor (BCR) sequences to suggest dynamic changes in patients with hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF) and provide a basis for finding immunotherapy targets.

Methods: We performed single-cell RNA sequencing in peripheral blood samples of 3 patients with chronic hepatitis B(CHB) and 8 patients with HBV-ACLF. Single-cell RNA sequencing was used to analyzed the functional properties of immune cells. We compared the transcriptional profiles of immune cells and their feature of TCR and BCR between the two groups.

Results: We sequenced a total of 121,096 single cells from two groups. Compared with the patients with CHB, the proportion of NK cells and T cells was significantly downregulated in the patients with HBV-ACLF. In patients with HBV-ACLF, the immune landscape showed immune exhaustion with skewed T cell receptor repertoire and B cell receptor repertoire.

Conclusion: These results suggest the clonal expansion in T cells and B cells of liver failure from chronic HBV infection.

Abstract Submission No. 101835

O-0853

Esophageal varices stratification as early sign of portal hypertension in ACLF: APASL-AARC Study

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Background: Acute on chronic liver failure (ACLF) is a new clinical entity which has a high mortality rate. The presence of esophageal varices (EV) is the hallmark of early sign of PHT in CLD patients. However, study about the presence of EV in ACLF patients is still lacking. **Aim:** To know the association of the presence EV and its clinical stratification in ACLF patients.

Method: APASL-ACLF Research Consortium (AARC) database registry was retrospectively reviewed. The data analysis was performed using SPSS version 25.

Results: Of 426 patients, no EV found in 192 patients, whereas small EV was found in 201 patients, and large EV found in 33 patients. Based on ACLF severity grade, small EV was found more in ACLF grade 3 patients (40.8%) when compared to large EV which only found in 18.2%. The presence of high-risk stigmata EV was found to be lower in ACLF grade 3 patients when compared to low-risk EV (17.1% vs. 40.3%). The presence of low-risk EV was more significantly associated with mortality when compared to the presence of high-risk EV ($p = .032$). In ACLF patients, mortality rate was found to be higher in patients without significant PHT when compared to significant PHT ($p = .000$). However, there was no statistically significant in ACLF patients with multi-organ failure ($p = .100$).

Conclusion: The presence of high-risk EV is not really associated with the prognosis of ACLF patients, however, it still needs to be included in the patient's management to improve the prognosis.

Abstract Submission No. 101918
O-0854

Rifaximin has no beneficial role in ACLF patients admitted to ICU - a double blind RCT

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Background: Patients with acute-on-chronic liver failure (ACLF) often receive antibiotics when admitted to the intensive care unit (ICU). It is unclear if additional rifaximin has any synergistic effect with broad-spectrum antibiotics in ICU patients with acute overt hepatic encephalopathy (OHE).

Methods: In this double-blind trial, APASL-defined ACLF patients admitted to ICU for OHE were randomized to antibiotics alone (ab) or antibiotics with rifaximin (ab+r). HE resolution (or 2-grade reduction), time to resolution, in-hospital mortality, nosocomial infection, and endotoxin level changes were compared.

Results: Of 96 patients with ACLF, 46 received ab alone, and 50 received ab+r. On Kaplan Meier analysis, 41.3% in the antibiotics arm compared to 32% in the antibiotics+rifaximin arm achieved the primary objective ($P=0.34$), and the time taken was comparable ($P=0.6$). In-hospital mortality was 67.4% in the control arm and 64% in ACLF patients receiving rifaximin ($P=0.98$). The proportion of patients achieving infection resolution was comparable ($P=0.71$). Nine percent in the ab group and 18% in the ab+r group developed nosocomial

infections ($P=0.23$). All patients with nosocomial infection died in-hospital. Both groups showed comparable rise in endotoxin levels ($P=0.3$).

Conclusion: Rifaximin has no beneficial role in patients with ACLF admitted to ICU.

Abstract Submission No. 101948
O-0855

Plasma multi-omics reveals gut dysregulated metaproteome and metabolites as poor outcomes in ALF

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Background and Aims: Acute liver failure (ALF) has high mortality and identification of microbial/metabolic signatures in plasma could stratify ALF patients predisposed to early mortality.

Method: Plasma multi-omics was performed on 40 ALF patients and 5 controls (training-cohort). Multi-omics signatures differentiating ALF Non-survivor (ALF-NS) from ALF Survivor (ALF-S) were validated in 270 ALF patients (TC-1; plasma and paired one drop blood ($n=160$); TC-2; external validation ($n=70$)) and Diseases control (TC-3 ($n=70$)), using High Resolution Mass Spectrometry (HRMS), Machine-Learning (ML) and correlated with clinical parameters and outcome.

Results: Multi-omics signature were distinct for ALF, more so for ALF-NS. Non-survivors showed increased metabolites; bile-acids, tryptophan, tyrosine linked to inflammation, cell death, stress and proteins linked to hyper-inflammation ($p < 0.01$, $FDR < 0.01$, $FC > 1.5$). Bacterial-peptide based alpha/beta diversity was higher in ALF-NS corresponding to Proteobacteria, Firmicutes, Actinobacteria functionally associated to energy, amino-acid and xenobiotic metabolism ($p < 0.05$). ALF-NS specific metaproteomic modules/functionality directly correlated with metabolic modules/ functions and clinical parameters ($R^2 > 0.7$, $p < 0.05$). Metabolomic signature directly correlated with clinical parameters and bacterial-peptides e.g., (chenodeoxycholic acid-Firmicutes: alkaliphilus oremlandii and Proteobacteria: phyllobacteriaceae; ($R^2 > 0.75$)). Probability of detection (POD) of Non-survival built on top five metabolites, namely, chenodeoxycholic acid, 4-(2-Amino phenyl)-2, 4-dioxobutanoate, L-Tyrosine, carnosine and alanyl-tyrosine showed diagnostic accuracy of 98% ($AUC = 0.98(0.92-1.0)$) and distinguish ALF predisposed to early mortality ($\log\text{-rank} < 0.05$). Validation using HRMS on TC-1, TC-2 and TC-3 and 5 ML-algorithm on (ALF=270) the metabolome panel showed >98% accuracy/sensitivity and specificity for prediction of mortality.

Conclusion: Plasma multi-omics outlines hyper-inflammation and hydrophobic bile acid accumulation as characteristic features for ALF-NS. Baseline plasma metabolite signatures could segregate ALF predisposed to early mortality.

Abstract Submission No. 101976
O-0856

Plasma exchange improves 30-day but not 90-day survival of alcohol-related ACLF: A meta-analysis

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Background: Alcohol-related acute-on-chronic liver failure (ACLF) is characterized by high mortality rates in the absence of liver transplantation. Plasma exchange (PLEX) has emerged as a potential therapeutic intervention for patients with ACLF of various etiologies. This meta-analysis investigates the short-term and long-term efficacy of PLEX in patients with alcohol-related ACLF compared to standard medical therapy (SMT).

Methods: A comprehensive search was conducted across PubMed, Embase, Scopus, and the Cochrane databases to identify studies comparing PLEX to SMT in patients with alcohol-related ACLF. Pooled odds ratios (OR) with corresponding 95% confidence intervals (CIs) were calculated using the Mantel-Haenszel method within a fixed-effects model. The primary outcome assessed was 30-day survival, with secondary outcomes including 90-day survival.

Results: Our analysis incorporated data from five studies, encompassing 249 patients (119 in the PLEX group vs. 130 in the SMT group). Three studies were retrospective, while two studies were prospective non-randomized trials. Compared to SMT, PLEX was significantly associated with higher 30-day survival (OR 0.48, 95% CI 0.28-0.84, $p = 0.01$). However, the pooled odds ratio for 90-day survival with PLEX did not reach statistical significance (OR 0.75, 95% CI 0.44-1.26, $p = 0.27$). Low heterogeneity was observed between the studies ($I^2 = 24\%$).

Conclusion: PLEX effectively improves short-term survival, as evidenced by a significant improvement in 30-day survival for patients with alcohol-related ACLF. However, its impact on 90-day survival remains inconclusive. Further research, especially randomized controlled trials, is needed to clarify the long-term implications of PLEX in this patient population.

Abstract Submission No. 102006

O-0857

Patients with decompensated cirrhosis have poorer physical functioning than patients with ACLF

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Background: Acute-on-chronic liver failure (ACLF) is characterized by rapid deterioration of liver function, while cirrhosis is a slowly progressive disease. Liver transplantation (LT) remains the treatment of choice for these patients with advanced disease. There are no studies evaluating the health-related quality of life (HRQoL) of patients with APASL-defined ACLF, which we aimed to assess.

Methods: In this cross-sectional study, consecutive patients with ACLF and decompensated cirrhosis attending the AIG Hospitals, Hyderabad, were included and assessed for SF-36 HRQoL scoring. The primary outcome was HRQoL among patients with decompensated cirrhosis and ACLF after matching for age and severity scores.

Results: A total of 350 patients were included in the study. Thirty-two percent ($n=113$) were ACLF, and 68% ($n=237$) were cirrhosis. On propensity-matched analysis (matched for age and MELD Na score), 102 patients with ACLF were matched with 35 patients with cirrhosis. Cumulative score of general health was lower in both groups

(41.45%±16.4% vs. 44.3%±17.45%; $P=0.4$). Both groups performed poorly on energy levels scale (49.3% vs. 53%; $P=0.41$). On other scales, including emotional (70% vs. 72%), social (68.24% vs. 73%), and pain (84.37% vs. 85.22%), were adequate in both groups. Interestingly, despite matching, the physical functioning of patients with cirrhosis (46.31%±27.2%) was much lower than those with ACLF (60%±24.7%; $P=0.007$). Transplant-free survival was 19% (19/101) among patients with ACLF compared to 14.3% (5/35) at day 30 ($P=0.54$).

Conclusions: Patients with decompensated cirrhosis have worse physical functioning than patients with ACLF. Further research aimed at interventions to improve the QoL is required.

Abstract Submission No. 102007

O-0858

High serum bile acids drive AKI progression and terlipressin non-response in patients with ACLF

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Background and aim: Acute-on-chronic liver failure (ACLF) patients frequently have cholemic nephropathy. The association of serum bile acids (BA) with AKI progression, organ dysfunction, and mortality has not been studied.

Methods: In a prospective cohort of ACLF patients ($n=242$) with AKI, serum BA and urine neutrophil-gelatinase-associated lipocalin (NGAL) were measured at enrolment. Logistic regression was performed to identify predictors of AKI progression.

Results: ACLF patients, aged 43.2 ± 9.8 years, 91.2% males, 73% with alcohol etiology, 87% with sepsis, AKI stages (1:2:3) (40%:31%:29%), 61% with HRS-AKI, the mean serum BAs were 154.2 ± 45.8 mg/dl, and NGAL of 1881 ± 1714 ng/ml. AKI progression at day 4 was observed in 42.6%, 26% required dialysis and 48% died at 28 days. On multivariable analysis, higher BA (OR 1.008, 1.001-1.016), AARC score (OR 1.72, 1.37-2.15), NGAL (OR 1.56, 1.01-2.46), and number of organ failures (OR 1.89, 1.27-2.83) predicted AKI progression which was an independent predictor of 28-day mortality (HR 1.98, 1.25-3.16). The BA correlated with circulatory failure (OR 1.008, 1.001-1.015) but not with brain and pulmonary failure ($p>0.05$). BA >175 mg/dl predicted non-response in HRS-AKI (3.25, 1.38-7.67) and the presence of bilirubin crystals/bile acid casts on urine microscopy ($p=0.005$) but not 28-day mortality (HR 1.33, 0.84-2.11).

Conclusion: Serum BA correlates with circulatory failure, and predicts AKI progression and non-response in HRS-AKI but not mortality. High serum BA (>175 mg/dl), NGAL, and the presence of bile casts could signify structural AKI and limited response to vasoconstrictors. AKI progression determines worse clinical outcomes therefore therapeutic modalities targeting reduction of BA may improve outcomes in ACLF patients with AKI.

Abstract Submission No. 102031

O-0859

Second hit acute insult increases mortality in patients of Acute-On-Chronic Liver Failure

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Background and Aims: ACLF is due to underlying chronic liver disease with super-added acute hepatic insult leading to high short term mortality. We analysed the impact of second hit acute insult to a primary chronic liver disease (CLD) presenting as ACLF.

Patients and Methods: We analyzed the prospective collected data from AARC registry. Clinical data, laboratory parameters, complications and survival were serially noted. Acute insult is considered second hit if its of different i.e. ACLF in ethanol related or HBV related CLD in absence of alcoholic hepatitis or HBV reactivation.

Results: Total of 8684 patients [mean age 44.6 ±11.6 years, 86.2% male] with alcohol (5648,65%) followed by HBV (1621, 18.7%), AILD (787,9.1%), Cryptogenic/NASH (407,4.7%), and HCV (177,2%). Similarly the acute insult in majority was SAH (4933, 56.8%), HBV reactivation (1069,12.3%), DILI (475,5.5%) followed by AVH(462, 5.3%). The alcohol CLD presented with ACLF due to SAH in 66.2% cases, where as AVH (4.6%) and DILI(5.3%) accounted for nearly one third. Similarly in patients with HBV CLD, the HBV reactivation was seen only in 26.4%, but the majority were due to alcoholic hepatitis (45.1%), AVH(6.5%), DILI (5.9%) and others in rest. Interestingly the second hit i.e another insult was seen in 50.2% (4398) cases. The single hit i.e ALD with SAH or HBV reactivation in HBV CLD or AIH flare associated with a better younger age, lower bilirubin, albumin, INR, AARC score, less organ failure, lower incidence of HE, sepsis, variceal bleed, need of RRT, ICU care and ventilatory support than those having another second hit etiology ($p<0.001$). A higher 90 days mortality [53.9% versus 46.4%,OR=1.37(95CI 1.15-1.67), $p<0.001$] with shorter median survival [48.1 days versus 54.8 days, $p<0.001$] noted with second hit acute insult.

Conclusion: In this large cohort, the ACLF cohort had a different acute insult than the primary chronic liver disease in nearly half of the cases. This innovative concept of second hit leading to ACLF had a different natural course and is associated with a poor outcome. A search for the acute insult and consideration of necessary definitive therapy, may guide the mangement decision to improve outcome.

Abstract Submission No. 200144

O-0860

LPCAT3/LPLAT12 deficiency in the liver ameliorates acetaminophen-induced acute liver injury.

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Acetaminophen (APAP) is a double-edged sword, mainly depending on the dosage. A moderate dose of APAP is effective for fever and pain relief; however, an overdose induces acute liver injury. The mechanism underlying APAP-induced acute liver failure is unclear, and its treatment is limited. A recent report has shown that several oxidized phospholipids are associated with APAP-induced acute liver failure. Lysophosphatidylcholine acyltransferase 3 (*Lpcat3*, *Lplat12*), which is highly expressed in the liver, preferentially catalyzes the incorporation of arachidonate into lysophospholipids (PLs). In the present study, we investigated the roles of *Lpcat3* on APAP-induced acute liver injury using liver-specific *Lpcat3*-knockout mice. Hepatic *Lpcat3* deficiency reduced the degree of APAP-induced necrosis of hepatocytes around zone 3 and ameliorated the elevation of hepatic injury serum marker levels, and prolonged survival. Lipidomic analysis showed that the accumulation of oxidized and hydroperoxidized phospholipids was

suppressed in *Lpcat3*-knockout mice. The amelioration of APAP-induced acute liver injury was due not only to the reduction in the lipid synthesis of arachidonic acid PLs because of *Lpcat3* deficiency, but also to the promotion of the APAP detoxification pathway by facilitating the conjugation of glutathione and N-acetyl-p-benzoquinone imine. Our findings suggest that *Lpcat3* is a potential therapeutic target for treating APAP-induced acute liver injury.

Abstract Submission No. 100086

O-0861

Noninvasive proteomic biomarkers for HEV-related acute liver failure

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Background: Timely and effective prognostic biomarkers for hepatitis E virus (HEV)-related acute liver failure (ALF) are urgently needed. **Methods** We performed four tandem mass tag (TMT)-labeled quantitative proteomic and targeted proteomics parallel reaction monitoring (PRM) studies on cross-sectional cohort 1 and 2 including 20 acute hepatitis E and 20 HEV-ALF patients respectively.

Results: Pregnancy zone protein (PZP) is a potential prognostic biomarker for HEV-ALF. PZP was identified by TMT and PRM quantitative proteomics. In the derivation cohort, PZP levels of the HEV-ALF patients in survival group were significantly higher than those of the dead group. According to the median level of PZP, HEV-ALF patients in the retrospective cohort 1 were divided into the high PZP (> 1316.18 ng/L) and low PZP (≤ 1316.18 ng/L) groups. the survival time of the high PZP group was significantly longer than that of the low PZP group. Compared with PZP levels at admission, levels at discharge increased significantly in the improvement group, and decreased significantly in both the fluctuation and deterioration groups. Besides, multivariate logistic regression showed that laminin, hepatic encephalopathy, TBil, and PZP were independent factors affecting the prognosis of HEV-ALF patients, which were used to establish a novel prognostic model (ePLT). The assessment in the derivation and validation cohorts showed that the ePLT score was significantly superior to the MELD, KCH and Child-Pugh scores.

Conclusions: PZP is a promising prognostic biomarker, and ePLT is a high-performance prognostic score for HEV-ALF patients, which contribute to clinical decision-making in the management of HEV-ALF.

Abstract Submission No. 100469

O-0862

Outcomes and Risk Factors of Early Liver Injury after Transjugular Intrahepatic Portosystemic Shunt

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Backgrounds: Transjugular intrahepatic portosystemic shunt (TIPS) reduces the portal vein blood flow into the liver while declining portal venous pressure, resulting in liver ischemia injury and even liver

failure. This study aimed to verify the impact of post-TIPS early liver injury on survival through large sample retrospective analysis and explore the risk factors of post-TIPS liver injury.

Methods: The data of patients undergoing TIPS in West China Hospital from November 2009 to March 2021 were collected. We analyzed the predictive ability of end-stage liver disease model score (MELD) on the 90-day, 1-year, and 3-year survival rates after TIPS and screened out the independent predictive factors of post-TIPS liver injury by regression analysis.

Results: A total of 1108 patients were included. The post-TIPS MELD score was superior to other scoring systems, with a better predictive effect on the 90-day survival rate and 1-year survival rate. The 90-day survival rate (98.3% vs. 87.2%, HR 15.9, 95% CI 7.9-31.9, $P < 0.001$), 1-year survival rate (95.1% vs. 79.2%, HR 8.3, 95% CI 5.0-13.7, $P < 0.001$) and 3-year survival rate (86.5% vs. 68.8%, HR 4.0, 95% CI 2.8-5.7, $P < 0.001$) were significantly higher in patients with a post-MELD score less than 15. Preoperative total bilirubin, serum creatinine, INR, and change of portosystemic pressure gradient were independent predictors of early liver injury after TIPS.

Conclusion: Baseline liver function and pressure reduction contribute to the occurrence of early liver injury after TIPS. Post-TIPS MELD score can accurately predict short-term and long-term survival.

Abstract Submission No. 100495

O-0863

Prospective study of the effect of TPO on platelets and prognosis in patients with ACLF

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Objective: To evaluate the dynamic changes in platelet and liver function in ACLF patients complicated with severe thrombocytopenia with recombinant human thrombopoietin (rhTPO) in a prospective cohort to observe the effects of elevated platelets on bleeding events and 90-day mortality in patients with ACLF.

Methods: Seventy patients with ACLF complicated with severe thrombocytopenia were prospectively enrolled and divided into a TPO group and a control group, with 35 patients in each group. The TPO group was given rhTPO for 7 days. The baseline, 7-day and 14-day PLT counts and liver function indices were compared and 90-day mortality and incidence of bleeding events were observed.

Results: There was no significant difference in 90-day mortality between the TPO group and the control group (8.6% vs. 17.1%, $P=0.284$). The incidence of bleeding events within 90 days was 11.4% in TPO group and 22.9% in the control group ($P=0.205$). The PLT count in the TPO group was significantly higher than that at baseline at 7 and 14 days after treatment ($28 \times 10^9/L$ vs. $64 \times 10^9/L$ vs. $73 \times 10^9/L$, $P=0.001$), and the PLT count peaked at 14 days. The serum HGF and TPO levels were significantly higher than those at baseline (serum HGF: 130.4 pg/ml vs. 195.4 pg/ml, $P=0.000$) and (serum TPO: 41.8 pg/ml vs. 143.7 pg/ml, $P=0.000$) in the TPO group at 7 days after treatment. The serum albumin level, INR and MELD score in the TPO group at 14 days after treatment were significantly improved compared with those before treatment (ALB 34.5 g/L vs. 28.2 g/L, $P<0.05$; INR 1.6 vs. 1.7, $P<0.05$; MELD 14.7 vs. 16.0, $P<0.05$).

Conclusion: rhTPO can significantly increase the PLT count in ACLF patients with thrombocytopenia, reduce the occurrence of bleeding events, and promote the improvement of liver function, and it has no significant effect on 90-day mortality.

Abstract Submission No. 100573

O-0864

A case report of hepatic amyloidosis presenting as Acute-on-Chronic Liver Failure

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Amyloidosis encompasses a heterogeneity of disorders characterized by the extracellular deposition of abnormal fibrillar proteins, which frequently involves the liver but hepatic failure rarely occurs. Herein, we present a case of a 54-year-old female with no significant liver history, use of unknown herbal medicine 3 months prior, presented with progressive jaundice for 2 months, abdominal distension for 6 weeks, associated with hepatosplenomegaly, ascites, and stable hemodynamics. The initial laboratory findings showed serum alanine aminotransferase of 24 IU/L, serum aspartate aminotransferase of 127 IU/L, total bilirubin of 12.26 mg/dL, INR of 1.55 with negative viral hepatitis, autoimmune profiles and no significant findings on abdominal computed tomography. A transjugular liver biopsy was performed and revealed extensive deposition of extracellular hyaline material, which is not typical for sinusoidal obstruction syndrome caused by alkaloid toxins. The patient's condition deteriorated rapidly and was managed symptomatically with a transjugular intrahepatic portosystemic shunt, however, the patient passed away one month later before making a definitive diagnosis. The patient's liver biopsy result was sent to the abroad center and showed Salmon-pink color material with birefringence under polarized light on Congo Red stain, which indicates amyloidosis. The diagnostic challenge in this case occurred in the etiological work-up for progressive jaundice and acute on chronic liver failure. We urge clinicians not to be satisfied with a diagnosis that could not explain fully the lab results and to have high clinical suspicion to make an early diagnosis and initiate prompt treatment, particularly in limited-resourced countries

Abstract Submission No. 100723

O-0865

Investigating factors involved in the rate of the examination success of transjugular liver biopsy.

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Background: Performing percutaneous liver biopsies could be impossible or difficult in patients with ascites or coagulation abnormality. Transjugular liver biopsy (TJLB) is a relatively safe alternative technique in such cases. There are limited studies on the factors involved in its technical success of TJLB. This study aimed to investigate the factors that influence the technical success of TJLB.

Methods: We enrolled fifty patients who underwent TJLB at our hospital between August 2020 and April 2023. We retrospectively measured the angle between the inferior vena cava (IVC) and the hepatic vein (HV) using CT or MRI coronal sections. In cases where TJLB was successful, we measured the angle between the IVC and the HV at the biopsy site. In cases where TJLB was unsuccessful, we measured the angle between the IVC and the right hepatic vein (RHV).

Results: TJLB was successfully performed in 42 cases (84.0%). Among these successful TJLB procedures, 38 cases (90.5%) were

performed on the RHV, and 4 cases (9.5%) on the middle hepatic vein (MHV). We were able to measure the angles between the IVC and the HV in 31 cases. The mean angles between the IVC and the HV in the successful (n=24) and unsuccessful (n=7) groups were $46.7 \pm 10.0^\circ$ and $59.9 \pm 13.6^\circ$, respectively, and were significantly smaller in the successful group ($p=0.042$).

Conclusion: We are more likely to perform TJLB successfully in cases in which the angle between the IVC and the HV is small.

Abstract Submission No. 100847

O-0866

Association of Coexistent HBsAg and anti-HBs with Prognosis of HBV-ACLF Patients

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Objectives: Coexistence of hepatitis B surface antigen (HBsAg) and antibody against HBsAg (anti-HBs) constitutes an atypical serological profile in chronic hepatitis B infection. The characteristics and impact of this serological pattern in the critically ill population of HBV-ACLF remain unclear.

Methods: Clinical data from 561 HBV-related ACLF patients were retrospectively collected. Flow cytometry was used to detect the peripheral blood lymphocyte subsets. The outcome was recorded as surviving or non-surviving in a 90-day follow-up.

Results: Among 561 HBV-ACLF patients, 31 cases exhibited the double-positive pattern for HBsAg and anti-HBs, resulting in a coexistence rate of 5.5%. Compared with patients without anti-HBs, those with anti-HBs had higher HBV DNA levels ($4.9 [2.8-5.4 \log_{10}]$ IU/mL vs $4.5 [3.4-5.6 \log_{10}]$ IU/mL; $p = 0.017$) and serum core antibody titers but lower HBsAg levels ($47.5 [7.6-169.3]$ IU/mL vs $163.2 [30.2-1601.2]$ IU/mL; $p = 0.034$). Patients with the coexistence of HBsAg and anti-HBs were older ($50.0 [30.0-73.25]$ vs $42.0 [33.0-51.0]$ years, $p = 0.010$), had a higher proportion of cirrhosis (87.1% vs 69.6% , $p = 0.038$), and higher total bilirubin levels ($329.2 [213.3-456.8]$ U/L vs $280.0 [180.6-393.4]$ U/L; $p = 0.022$). Lymphocyte subset analysis suggests that peripheral CD3⁺, CD4⁺, and CD8⁺ T-cell counts were lower in HBsAg and anti-HBs coexisting patients. Survival analysis indicated poorer short-term prognosis for patients with anti-HBs, with a significantly higher mortality rate compared to those without anti-HBs (58.1% vs. 38.9% , $p = 0.034$).

Conclusion: Coexistence of HBsAg and anti-HBs may be associated with a more severe disease state in HBV-ACLF.

Abstract Submission No. 100969

O-0867

Long-term prognosis of HBV-ACLF patients with extremely low-level viremia

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Background: High viral load is closely associated with outcomes of chronic hepatitis B. However, for patients with viral loads lower the limit of quantification (LLOQ), especially those who have survived liver failure, the long-term outcomes remain unclear.

Methods: 80 HBV-ACLF patients who survived more than 48 weeks without liver transplantation and received NUCs therapy were enrolled. Based on HBV-DNA loads after 48 weeks treatment, patients were categorized into the UD (undetectable), extremely low-level viremia (eLLV, detectable but LLOQ 20 IU/mL), LLV (20-2000 IU/mL), and partial virological response (PVR, > 2000IU/mL) groups.

Results: 1. 80 HBV-ACLF patients were followed for 228.09 ± 97.01 weeks, with most in the eLLV group (n=43, 53.75%), followed by LLV (n=25, 31.25%), UD (n=10, 12.5%), and PVR (n=2, 2.5%) group.

2. In the eLLV group, HBsAg levels were significantly higher than UD group [$1804.66 (325.67, 3130.58)$ vs. $35.17 (0.00, 989.79)$ IU/mL, $P=0.004$], while anti-HBs levels were significantly lower [$0.15 (0, 0.57)$ vs. $98.96 (3.40, 276.05)$ mIU/mL, $P=0.003$]. Additionally, eLLV group exhibited significantly higher anti-HBe levels compared to the LLV group [$0.84 (0.16, 1.52)$ vs $1.60 (1.00, 2.28)$ S/CO, $P=0.042$, Table 1].

3. Kaplan-Meier survival analysis indicated superior overall survival in the eLLV group compared to the LLV group ($P=0.029$, Figure 1).

4. Moreover, eLLV group had lower cumulative incidences of recurrent decompensation events than the LLV group ($P=0.013$, Figure 2).

Conclusions: HBV-ACLF patients with eLLV demonstrated superior long-term outcomes compared to the LLV group. Adjusting antiviral regimens for LLV patients to achieve eLLV levels may enhance long-term prognosis.

Abstract Submission No. 101021

O-0868

Diabetes Mellitus Linked to Higher Mortality in Alcohol-related Acute-on-Chronic Liver Failure

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Background: Acute-on-Chronic Liver Failure (ACLF) is characterized by acute deterioration in patients with chronic liver disease, leading to multiple organ failures and a high mortality. Alcohol is the most common cause of ACLF. While diabetes mellitus is a risk factor for adverse outcomes in liver disease, its specific impact on outcomes in alcohol-related ACLF remains elusive.

Aims: This study aims to assess the impact of diabetes mellitus on the mortality of patients with alcohol-related ACLF.

Methods: We recruited patients with alcohol-related ACLF from the AARC registry. The diagnosis of alcohol-related ACLF was established when the treating unit identified alcohol as both the etiology of

chronic liver disease (CLD) and the acute precipitant. Patients with coexisting other etiologies of CLD or other precipitants (such as HBV, HCV, HEV, DILI etc.) were excluded. Patients were categorized based on the presence or absence of diabetes. The primary outcome was 90-day mortality, with the analysis considering only baseline clinical, laboratory features, and severity scores.

Results: The study included a total of 2,096 patients with alcohol-related ACLF, comprising 109 diabetic (91.7% male, median age 45 years) and 1,987 non-diabetic individuals (90.9% male, median age 42 years). The median MELD-Na score was 31.0 (IQR 27.0-36.0) while the median CTP score was 12 (IQR 11.0-12.0) for both groups. By 90 days, 979 (47%) patients had died, and 109 (5%) patients had received liver transplantation (LT); 12 patients died even after LT. The 90-day mortality was significantly higher in diabetics compared to non-diabetics (67.9% vs 45.5%, $p < 0.05$). A log-rank test demonstrated a statistically significant difference in survival between patients with and without diabetes mellitus in both overall survival ($p < 0.01$) and transplant-free survival analyses ($p < 0.01$), indicating a substantial impact of diabetes on outcomes in alcohol-related ACLF (Figure).

Conclusions: The presence of diabetes mellitus in patients with alcohol-related ACLF markedly increases the risk of mortality, highlighting the particularly dangerous nature of this condition in diabetic individuals. This underscores the urgency for further research to elucidate the underlying mechanisms of this association.

Abstract Submission No. 101154
O-0869

EXPERIENCE ON USE OF DPMAS AMONG PATIENTS WITH ACLF AND DECOMPENSATED LIVER CIRRHOSIS - CASE SERIES

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Liver transplantation is the definitive management for acute liver (ALF) and end-stage liver disease (ESLD). This is limited by accessibility, lack of potential donors, and cost. At present, as a bridge for liver transplantation, artificial liver support systems (ALSS) such as double plasma molecular adsorption system (DPMAS) are being utilized.

This case series aimed to review outcomes of patients who had DPMAS from 2018 to 2023. This case series included patients from a tertiary referral center in the Philippines. Records of patients who had acute-on-chronic liver failure, acute liver failure, and decompensated liver cirrhosis who underwent DPMAS were reviewed.

Six patients were included in this series. Four out of the six patients were discharged after DPMAS, while two died from multi-organ failure. Prothrombin time and INR improved post-DPMAS. Consequently, prognostic scores, specifically MELD-Na, was lower. Likewise, Hepatic Encephalopathy (HE) grade and degree of ascites improved. Two of these patients underwent successful liver transplantation eventually. Patients who underwent DPMAS in this series showed improvement in laboratory parameters measuring hepatic synthetic function, and MELD-Na. DPMAS is a promising modality for bridging ALF and end-stage liver disease to transplantation, and in some cases, recovery to compensated state.

Abstract Submission No. 101280
O-0870

Antibiotics and steroids for 4-weeks in ACLF-AH with steroid response showed reduction of infections

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Introduction: In this retrospective analysis we analysed whether oral antibiotics (cefixime) at discharge given for 1-week vs. 4-weeks in combination with steroids reduced infections in ACLF (alcoholic hepatitis).

Patient and methods: Retrospective database of APASL-AARC consortium was taken from April 2021- April 2022 and prospectively data was followed up for 6-months with patients of ACLF and having alcoholic hepatitis (steroid eligible) and received steroids for 28 days. Primary objective was to study infections at day 28. Secondary objectives were to study mortality at 28-day and 90 days; incidence of HRS; HE; AKI.

Results: 1124 patients with ACLF collected during the period, 534 patients (47.5%) having alcoholic hepatitis were screened; 110 (20.59%) patients had received steroids (prednisolone 40mg for 4 weeks) of which 28 patients (25.4%) received oral cefixime (200mg/Bid for 4 weeks) while 82 patients (74.5%) received oral cefixime (200mg/Bid 7 days) along steroids. Incidence of AKI {6/28 (21.42%) vs. 19/82 (23.17%), $P = 1.00$ }; UGIB {2/28 (7.1%) vs. 9/82 (10.9%), $P = 0.72$ } were comparable. Incidence of infections at 28 days {5/28 (17.8%) vs. 35/82 (42.6%), $P = 0.02$ }, repeated hospitalizations {3/28 (10.7%) vs. 26/82 (31.7%), $P = 0.04$ }, mean number of hospitalized days (90-days) { 10 ± 3.4 vs 18 ± 6.7 }, $P = 0.001$ was lower in the 4-week arm. Incidence of pneumonia {7.1% (2/28) vs 21.9% (18/82), $P = 0.09$ }, cellulitis {10.7% (3/28) vs 14.6% (12/82), $P = 0.75$ }, SBP {7.1% (2/28) vs 23.1% (19/82), $P = 0.09$ } was lower in the 4-week arm, not significant. Of steroid non responders {30/82 (36.5%)}; 13/30 were continued on antibiotics suspecting subclinical infection showed lower infection rate requiring hospitalization {2/13 (15.3%) vs. 9/17 (52.9%), $P = 0.04$ }. Lower 28-day mortality was also noted in 4-week arm {2/28 (7.1%) vs. 18/82 (21.9%), $P = 0.09$ }.

Conclusions: 4-week antibiotic-steroid therapy in steroid responder AH helped in reduction of severity of infections; duration of hospitalization; improved 4-week mortality.

Abstract Submission No. 101331
O-0871

Ascites in Hepatitis A-induced liver failure: Does it impact outcome?

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Introduction: Hepatitis A virus (HAV) in developing nations is one of the leading causes of acute liver failure (ALF) in children. Survival with native liver (SNL) is guarded. We aimed to study the factors that are associated with outcome in this condition.

Methods: A prospectively maintained database registered all ALF admitted between 2017-2022. Poor outcome (PO) was defined as death or requirement of liver transplantation. Underlying chronic liver disease was excluded.

Results: Comparison of HAV-ALF (n=55) vs non-HAV-ALF (n=44) [hepatitis B (n=12), hepatitis E (n=2), Epstein-Barr (n=7), parvovirus (n=6) and indeterminate (n=19)] showed age (7 ± 4.0 vs 9.9 ± 4.6 y, $p=0.002$), duration of illness (33.9 ± 23.8 vs 21 ± 6.8 days, $p=0.04$), PELD score (31.4 ± 14.1 vs 27.4 ± 20.1 , $p=0.07$) and SNL (51% vs 38%, $p=0.1$). Among HAV-ALF, 61% had ascites (35% at presentation, 26% during admission; jaundice to ascites duration 17 ± 22 days) and 65% had encephalopathy (55% at presentation, 10% during admission; jaundice to encephalopathy duration 15.5 ± 19 days). PO was seen in 90% of those who developed ascites prior to encephalopathy (41%) and required large volume paracentesis (33%). Violin plots (Figure 1) shows comparison of liver function with final outcome. On multiple step-wise logistic regression, ascites preceding encephalopathy [OR 2.1 (1.6-3.3), $p=0.002$], spontaneous bacterial peritonitis [OR 1.8 (1.2-2.3), $p=0.02$] and PELD score [OR 4.3 (2.3-4.8), $p=0.001$] were independent predictors of PO. At presentation, PELD score cutoff <23.5 (AUROC 0.86) and serum albumin >3.1 g/dL (AUROC 0.77) were associated with SNL.

Conclusions: Ascites preceding encephalopathy and spontaneous bacterial peritonitis are associated with poor outcomes in acute liver failure. Universal vaccination policies need to be reinforced.

Abstract Submission No. 101442

O-0872

Recent trend of acute hepatitis and acute liver failure in our hospital

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Background/aim: The etiologies of acute hepatitis (AH) and acute liver failure (ALF) are various. This study aimed to clarify recent trends and the prognosis for each cause.

Methods: Patients with AH and ALF admitted to our department from January 2001 to October 2023 were included. Patients were classified as having ALF if PT fell below 40% within 8 weeks of onset.

Results: There were 238 eligible patients (100 males and 138 females) with a median age of 45 years; the highest T-bil, AST, and ALT (median) were 7.8 mg/dL, 770 U/L, and 1128 U/L, respectively, and the lowest PT was 64.1%. The number of cases averaged 8.6 cases/year in 2015-2021, but increased to 14 cases/year after 2022. As for the etiologies, unknown, HBV, and drug-related were the most common, at 25/20/21%, respectively. HBV showed a decreasing trend, while an increasing trend in unknown and drug-related. Cases with COVID-19 infection were included among the unknown causes since 2021. The proportion of women increased significantly from 58/124 (47%) in 2001-2011 to 80/114 (70%) in 2012-2023. ALF occurred in 73 patients (30.7%) overall. Unknown/HBV was the most common causes of ALF. The prognosis for unknown and HBV was poor, with liver transplantation/death rates of 79% and 71%, respectively. Among comatose ALF patients with and without transplantation, 2/12 (17%) and 28/30 (93%) died, respectively.

Conclusions: Recently, HBV-related AH and ALF have decreased, while unknown and drug-related cases tended to increase. The overall number of cases also showed an increasing trend, as for the proportion of women.

Abstract Submission No. 101483

O-0873

Isoproterenol attenuates LPS/D-GalN-induced liver injury through β arrestin2 exerts anti-inflammatory

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Background and Aims: Previous studies have shown that stimulating B2-adrenergic receptors inhibits lipopolysaccharide (LPS)-induced macrophage production of inflammatory factors. The aim of the study was to explore the mechanisms by which the SNS alleviates liver inflammatory harm during acute liver failure (ALF).

Methods: C57BL/6J mice were administered isoproterenol (ISO) in an ALF model established using LPS and D-galactosamine (D-GalN). THP-1 cells were pretreated with ISO before LPS administration. β -arrestin2 expression in THP-1 cells was knocked down by siRNAs *in vitro*.

Results: In LPS/D-GalN-induced ALF mice, ISO administration led to a decrease in serum levels of proinflammatory cytokines (TNF- α , IL-1 β , and IL-6), mitigating liver damage and reducing the mortality of mice. Furthermore, ISO reduced the infiltration of M1-type macrophages in the liver of ALF mice. Proteomic enrichment analysis suggested that ISO mainly affected the function of liver macrophages, especially the inflammation signaling, such as the MAPK and NF- κ B pathways. Pretreatment with ISO resulted in a reduction of LPS-stimulated inflammatory factors (TNF- α , IL-1 β , and IL-6) in THP-1 cells. Additionally, ISO treatment attenuated the phosphorylation levels of MAPK P38 and NF- κ B P65 by LPS in activated macrophages. Subsequently, β arrestin2 was knocked down in THP-1 cells. Interestingly, the *in vitro* results showed that the deficiency of β arrestin2 dramatically repealed anti-inflammation of adrenergic and inhibited the phosphorylation activity of NF- κ B and MAPK signals.

Conclusion: Pretreatment with ISO could potentially exert anti-inflammatory effects through β -arrestin2 and may serve as an innovative pharmacotherapy for the purpose of delaying the pathogenesis and progression of ALF.

Abstract Submission No. 101509

O-0874

Cost-effectiveness analysis of two non-biological artificial liver modes in early HBV-ACLF

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Objective: This study aimed to evaluate the cost-effectiveness of two artificial liver support systems, double plasma molecular adsorption system with sequential low-dose plasma exchange (DPMAS+LPE) and plasma exchange (PE), in early hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF).

Methods: 95 patients treated with DPMAS+LPE and 95 with PE at the Third Affiliated Hospital of Sun Yat-sen University were retrospectively analyzed with a 90-day follow-up. Cost-effectiveness analysis of 90-day survival rates and direct medical costs from the healthcare system perspective was conducted, incorporating probabilistic sensitivity analysis.

Results: The average total costs over 90 days were ¥91,661 [95%CI:85,284 - 99,879] for DPMAS+LPE and ¥86,853 [95%CI:78,001 - 98,822] for PE, with mean survival rates of 91.59% [95%CI:82.11% - 94.74%] and 83.12% [95%CI:73.68% - 89.47%], respectively. Cost-effectiveness ratios were ¥100,078 and ¥104,491 for the two groups. The incremental cost-effectiveness ratio of DPMAS+LPE versus PE was ¥56,765, below China's per capita GDP in 2022. Probabilistic sensitivity analysis indicated an 85% probability of DPMAS+LPE being economically favorable compared to PE when the willingness-to-pay threshold was set at 3 times the per capita GDP.

Conclusion: DPMAS+LPE treatment improves the 90-day survival rate in early HBV-ACLF patients. Despite increased direct medical costs, the additional cost required per incremental survival rate is deemed acceptable, suggesting the economic viability of DPMAS+LPE therapy.

Abstract Submission No. 101550

O-0875

Prognostic Value of Plasma Level of Superoxide Dismutase in HBV-related ACLF

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Background: HBV-ACLF is the major type of ACLF in China. The mortality rate has decreased in recent years; however, it is still above 50%. Many cases of HBV-ACLF are caused by HBV reactivation due to discontinuation of nucleoside analog treatment. The present study focused on plasma levels of superoxide dismutase (SOD) in HBV-ACLF patients and investigated whether the SOD level is a useful biomarker in assessing disease severity and predicting outcomes of HBV-ACLF patients, including patients treated with entecavir (ETV) and patients who were withdrawn from ETV.

Methods: Plasma samples and clinical data from 200 HBV-ACLF patients and from age- and sex-matched cirrhotic and healthy controls were collected. Plasma levels of SOD were measured using an ELISA commercial kit.

Results: In the ETV withdrawal group HBV-ACLF patients, the mortality rate was higher than in the ETV group (69.95% vs. 46.71%). Moreover, HBV-DNA and SOD plasma levels were higher in the ETV withdrawal group than in the ETV group (log10(HBV-DNA): 6.49±0.24 vs. 4.79±0.14; SOD: 463.1±27.61 vs. 397.2±10.97). The mortality and liver transplantation rates were significantly higher in HBV-ACLF patients with SOD plasma levels of > 428 U/mL than in patients with SOD plasma levels of ≤ 428 U/mL.

Conclusions: Reactivation of HBV and elevated oxidative stress caused by discontinuation of ETV treatment are crucial factors in the pathogenesis of HBV-ACLF. The SOD plasma level may serve as a useful biomarker in estimating disease severity and predicting outcomes of HBV-ACLF patients who stop ETV treatment.

Abstract Submission No. 200005

O-0876

Fulminant Hepatic Failure Etiology, Manifestation and Outcomes: Experience of Tertiary Care Hospital.

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Objective: To determine etiologies, clinical manifestation and outcomes of adults with fulminant hepatic failure in Tertiary Care Hospital of Karachi, Pakistan. **INTRODUCTION:** FHF is influenced by a multitude of causal factors, with the primary underlying cause differing worldwide depending on age and geographical conditions. The myriad of manifestations includes jaundice, abdominal pain, fever, fatigue, malaise, nausea and anorexia. The progression itself is characterized by severe coagulopathy followed by encephalopathy, which is the hallmark of FHF, eventually leading to coma and death. Therefore, this study was aimed at assessing the etiological factors, clinical manifestation and outcomes in patients suffering with FHF. **Methodology:** This cross-sectional study was conducted in the Department of Gastroenterology, JPMC, Karachi, from January 2018 until the present. A total of 102 male and Female patients, referred to this hospital, with confirmed diagnosis of FHF were included in the study. Evaluation of such patients was based on history, examination and investigations, including liver function tests, prothrombin time, renal parameters, serum albumin and viral serology. Chi square test was applied to evaluate the effects of socioeconomic status, residency, and age on outcome.

Conclusion: This study highlights higher mortality rate in adults by revealing the association between clinical manifestations, viral serology, and mortality in patients with FHF and concludes that that HEV infection was significantly higher in patients with clinically manifested Jaundice, nausea/vomiting, fatigue and fever. While survival rate revealed that hepatitis E virus IgM antibody, hepatic encephalopathy, sepsis, jaundice, fatigue, abdominal pain, and dyspepsia were significantly associated with mortality rate ($p < 0.05$).

Abstract Submission No. 100747

O-0877

Expression Pattern and Clinical Significance of Myeloid Checkpoint VISTA in Cholangiocarcinoma

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Background: Intrahepatic cholangiocarcinoma (iCCA) is a prevalent and life-threatening disease characterized by a grim prognosis and limited therapeutic options. The presence of immunosuppressive cells, including tumor-associated macrophages (TAM) and myeloid-derived suppressor cells (MDSC), has hindered the effectiveness of current immune checkpoint inhibitor (ICI) therapies. This study focuses on VISTA, an emerging myeloid immune checkpoint, with the objective

of assessing its clinical significance in iCCA and exploring its potential synergy with anti-PD-1/CTLA-4 therapy.

Methods: We leveraged bulk and single-cell RNAseq data to investigate VISTA abundance and distribution within iCCA. VISTA expression levels were utilized to construct patient stratification and prognostic models in a cohort comprising 113 patients. Cell communication analysis, in conjunction with multiple immune markers, shed light on the role of VISTA in shaping the iCCA tumor microenvironment. Ex vivo treatment experiments were conducted to probe the potential synergy between VISTA blockade and anti-PD-1/CTLA-4 therapy.

Results: Our findings revealed that VISTA expression significantly exceeded that of common checkpoint molecules and was predominantly localized in tumor-infiltrating myeloid cells. High infiltration of VISTA+ cells in the patient cohort exhibited strong correlations with adverse pathological characteristics and poorer prognosis. Analysis of the tumor microenvironment indicated a substantial connection between VISTA and the immunosuppressive phenotype of myeloid cells. Ex vivo treatment experiments suggested that VISTA blockade mitigated immune exhaustion and enhanced responsiveness to ICIs.

Conclusions: Targeting the myeloid checkpoint VISTA holds promise as a strategy to augment the efficacy of anti-PD-1/CTLA-4 therapy in iCCA, offering potential advancements in the treatment of this challenging disease.

Abstract Submission No. 101048

O-0878

Reducing Gamma Glutamyl Transferase after Steroid Administration in Biliary Atresia

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Background: Biliary atresia is the leading cause of liver transplantation in children. Recent literature suggests that immune mechanisms are responsible for the pathogenesis of biliary atresia. This study aims to evaluate the effect of steroid therapy on Gamma Glutamyl Transferase (GGT) levels in biliary atresia.

Methods: A randomized control trial study was conducted on infants with biliary atresia. Methylprednisolone was administered at 2 mg/kg BW/day two times a day and Gamma Glutamyl Transferase was evaluated 2 weeks after the treatment. This study was analysed using SPSS ver 25.00.

Results: A total of 40 infants with biliary atresia between the ages of 2 weeks to 3 months (20 infants in the placebo group and 20 infants in the methylprednisolone group). There were no differences in bilirubin and liver function tests in the two groups (Methylprednisolone vs placebo: direct bilirubin 9.87 (6.11 - 14.20) mg/dl vs 6.68 ± 2.44 mg/dl; SGOT 176.54 ± 96.09 U/L vs 205.00 (135.25 - 280.25) U/L; p>0.05, but GGT level was lower in the methylprednisolone (160.50 (107.25 - 300.50) U/L) than placebo group (437 (157 - 1755.40) U/L; p = 0.028).

Conclusion: There is a reduction in GGT levels following administration of methylprednisolone. Methylprednisolone may have an effect in suppressing the inflammatory process in biliary atresia.

Abstract Submission No. 101066

O-0879

Methylprednisolone Reduces MMP-7 as a Marker of Fibrosis Progression in Biliary Atresia

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Background: Chronic inflammation leads to fibrotic obliteration of the extrahepatic biliary tree in biliary atresia. Developing new therapies is necessary to reduce reliance on surgical intervention and liver transplantation. This study aims to evaluate the effectiveness of methylprednisolone (MP) versus placebo in reducing Matrix Metalloproteinase-7 (MMP-7) levels in biliary atresia.

Methods: Randomized, double-blind, placebo-controlled trial, 40 infants with biliary atresia received methylprednisolone (20) and placebo (20). An oral methylprednisolone (2 mg/kg/day) was given for 14 days. Laboratory measurements and MMP-7 levels were evaluated at weeks 0 and 2. Data analysis was performed using SPSS (Version 25).

Results: A total of 22 boys (55%) and 18 girls (45%) were involved in this study at a median age of 10 weeks (8 - 12 weeks). There were no differences in direct bilirubin and MMP-7 levels between the MP and placebo groups before treatment (9.87 [6.11 - 14.20] mg/dL vs. 6.68 ± 2.44 mg/dL; p=0.69 and 1.52 [1.12 - 1.67] ng/ml vs. 1.28 ± 0.54 ng/ml, p=0.394). MMP-7 levels after treatment were lower in the MP group (1.07 ± 0.48 ng/ml, p = 0.002) compared to the placebo group (1.55 ± 0.74 ng/ml, p = 0.040). The MP group has a higher level of reducing MMP-7 than the placebo group (Δ = 0.463 ± 0.592 ng/ml vs. 0.267 ± 0.624 ng/ml, p = 0.040).

Conclusion: Methylprednisolone showed a significant reduction in MMP-7 levels. Anti-inflammatory drug may be effective in suppressing the inflammatory process resulting in fibro-obliteration in biliary atresia.

Abstract Submission No. 101143

O-0880

RCT Study in Biliary Atresia: Effect of methylprednisolone on liver function tests

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Background: Biliary atresia is a fibrotic biliary obstruction. Although Kasai surgery has been performed, the need for Liver transplantation is still high. Pharmacologic treatment may be an alternative for the suppression of biliary fibrosis. This study aims to investigate the effect of steroids in liver function test in biliary atresia.

Methods: This study is a randomized controlled trial in infants with biliary atresia under three months. Subjects were divided into placebo and methylprednisolone. Methylprednisolone was given at a dose of 2 mg/kg/day for two weeks. A liver function test was performed prior to treatment and two weeks after treatment. The data were analyzed using SPSS.

Result: A total of 40 infants aged 9.5 (8-11.75) weeks were enrolled in the study, with 20 receiving placebo and 20 receiving methyl prednisolone. The AST level was not different between placebo and MP before treatment (205.00 (135.25-280.25) vs 176.54 ± 96.09 U/L; p=0.99), but ALT level in the placebo group was higher than in the MP group (168 (113.75 - 313.25) U/L vs 83 (58.50 - 185.50) U/L; p=0.023). There was no difference in the reduction of AST and ALT levels between placebo and methylprednisolone groups (36.50 (-58 - 83.75) vs 18.5 ± 142.38 U/L; p=0.90 vs -91.64 ± 180 vs -14 (-133.5 - 5.25) U/L; p=0.38).

Conclusions: The administration of methylprednisolone did not have an effect on the reduction of AST and ALT levels. Liver function test may not be specified regarding biliary inflammation.

Keyword: Biliary atresia, Methylprednisolone, AST, ALT

Abstract Submission No. 101175

O-0881

Clinical utility of comprehensive genomic profiling tests for advanced biliary tract cancer.

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Comprehensive genomic profiling (CGP) tests have become widespread in Japan since 2019. The range of treatment options for biliary tract cancer and other cancers is expanding. We report on the current status of CGP tests for biliary tract cancer at our hospital which is designated hospital, and another hospital which is cooperative hospital, for cancer genomic medicine in JAPAN. We retrospectively analyzed 71 patients who underwent CGP tests at our hospitals for biliary tract cancer by April 2023. Types of biliary tract cancers are as follows: intrahepatic cholangiocarcinoma 53.5%, extrahepatic cholangiocarcinoma 28.2% and gallbladder cancer 18.3%. In 71.8% of biliary tract cancers, treatment or clinical trials based on genetic mutations were recommended. Major genetic mutations in intrahepatic cholangiocarcinoma were as follows: *KRAS* mutation 21.1%, *FGFR2* fusion 15.8%, *IDH1* mutation 10.5%, extrahepatic cholangiocarcinoma were as follows: *KRAS* mutation 30.0%, *TP53* mutation 25.0%, *BRC42* mutation 10.0% and gallbladder cancer were as follows: *KRAS* mutation 15.4%, *MDM2* amplification 15.4%, *ERBB2* mutation 15.4%. On the basis of the CGP testing, 11 patients (15.5%) received targeted therapy. Among them, five patients (45.5%) received pemigatinib therapy for *FGFR2* fusion gene. The overall response rate of pemigatinib therapy was 60%, with 3 patients having a partial response. These conducting CGP tests at a more appropriate time could provide patients with greater benefit from treatments based on their specific gene mutations in biliary tract cancer.

Abstract Submission No. 200004

O-0882

Diagnostic and prognostic significance of the PTEN gene in periampullary carcinoma.

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Objective: Periampullary Adeno Carcinoma is a heterogeneous carcinoma and is identified in its advanced stages. In periampullary tumours, the influence of a PTEN (phosphatase and tensin homolog) gene mutation on prognosis is unknown. The effect of PTEN downregulation and hypermethylation on the survival of periampullary cancer patients has yet to be investigated. As a result, we aimed to look into the expressional value of PTEN gene as a potential biomarker.

Materials and Methods: One hundred and one tumour tissues from the patients were investigated for the mutational and expressional of the PTEN gene. Sanger sequencing was used for molecular profiling, immunohistochemistry for protein expression, methylation specific PCR for methylation status, and a- terminaldeoxynucleotidyltransferase biotin-dUTP nick end labelling test for programmed cell death

(apoptosis). The changes were linked to clinicopathological features, overall survival and recurrence-free survival.

Results: In ampullary tumours, the clinicopathological relationship was significantly downregulated ($p=0.06$), although hypermethylation ($p=0.08$) and apoptosis loss ($p=0.06$) were dramatically elevated in patients under 50 years of age. The ampullary tumour had a higher survival rate than the bile duct, duodenum, and pancreatic head cancers ($p=0.00$). Furthermore, early stage T1 patients have a better prognosis than later stage T1 patients ($p=0.017$). Patients who got adjuvant CTRT had a greater survival rate than those who did not ($p=0.010$).

Conclusion: The absence of PTEN gene expression is detected in the ampullary subgroup of periampullary tumours. Those who have positive hypermethylation but modest expression has a poor overall survival. PTEN apoptosis-negative patients, on the other hand, had a higher survival rate.

Abstract Submission No. 200105

O-0883

TNFRSF14 and LIGHT are upregulated in biliary epithelia of primary sclerosing cholangitis

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Background and aims: Recent genome-wide association studies (GWAS) identified more than 20 disease susceptibility genes of PSC. However, little is known about the tissue expression profiles of these genes. This study aims to identify specific GWAS risk genes expressed in the biliary epithelia (BE) of patients with PSC.

Methods: We analyzed the expression levels of the GWAS risk genes in liver tissues of patients with PSC ($N = 45$) and healthy controls ($N = 12$) by quantitative polymerase chain reaction. Subsequently, we validated the expression levels in the BE by immunohistochemistry. Liver samples of patients with primary biliary cholangitis (PBC) were also used as disease controls ($N = 20$). We further investigated the correlations between gene expression levels and histological findings in PSC group.

Results: We found that the hepatic expression levels of several GWAS risk genes were significantly altered in PSC group. Among these candidates, we focused on *TNFRSF14*, which encodes immune-related receptor. Immunohistochemical analysis revealed that 42% of BE in PSC group showed *TNFRSF14*-high expression, while no elevated expression was observed in the control and PBC groups. We additionally evaluated the expression of LIGHT, an activating ligand for *TNFRSF14*. LIGHT-high expression was observed in 53% of BE in PSC group, which was significantly higher than in the control (0% , $P < 0.001$) and PBC (15% , $P = 0.006$) groups. In addition, LIGHT expression was positively correlated with the fibrotic stage of PSC.

Conclusions: We demonstrated that *TNFRSF14* and LIGHT is specifically expressed in the BE of patients with PSC.

Abstract Submission No. 200223

O-0884

Gemcitabine and cisplatin plus PD-L1 inhibitors with lenvatinib in advanced biliary tract cancer

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Background: Gemcitabine and cisplatin (GemCis) plus durvalumab, a PD-L1 inhibitor, is the latest standard first-line therapy of advanced biliary tract cancers (BTCs). The efficacy and safety of GemCis chemotherapy and PD-L1 inhibitors, in combination with lenvatinib have not been reported.

Methods: In this retrospective, single-center, single-arm study, patients with advanced BTCs who received GemCis plus PD-L1 inhibitors, durvalumab or envafoleumab, with lenvatinib as first-line treatment were screened. The progression-free survival (PFS), overall survival (OS), objective response rate (ORR), disease control rate (DCR) and safety were evaluated.

Results: From December 2021 to July 2023, 43 advanced BTC patients with a median age of 60 years (range 35-79) were enrolled. Fifteen (34.9%) patients were over 65 years-old. The median duration of treatment was 5.0 months (IQR: 3.2 to 5.9), and the median duration of follow-up was 10.1 months (IQR: 6.6 to 12.2). According to mRECIST, the median PFS was 11.29 months and the median OS was 14.8 months. The 1-year PFS and OS rates were 45.9% and 61.4%, respectively. ORR and DCR were 48.8% and 95.3%, respectively. Any grade adverse events (AEs) occurred in all patients (100%) throughout the treatment. 60.46% (26/43) of the patients experienced grade 3 or 4 AEs. The most common grade 3 or 4 AEs were myelosuppression (37.2%) and hyponatremia (18.6%). No grade 5 AE occurred.

Conclusions: GemCis plus PD-L1 inhibitors with lenvatinib represents an effective and tolerable treatment option in advanced BTC patients, including the elderly patients. Further follow-up is ongoing.

Abstract Submission No. 100144
O-0885

HAIC, lenvatinib, and PD-1 inhibitors versus GC chemotherapy for advanced biliary tract cancer

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Background: Recently, hepatic arterial infusion chemotherapy (HAIC) combined with/without lenvatinib and PD-1 inhibitors has shown good efficacy and safety in hepatobiliary cancers. The present study aimed to compare the efficacy and safety of FOLFOX-HAIC combined with lenvatinib and PD-1 inhibitors versus gemcitabine and cisplatin (GC) for advanced biliary tract cancer (ABTC).

Methods: From January 2020 to December 2022, 26 patients with ABTC were classified into the HAIC-lenvatinib-PD1 group (H-L-P, n = 16) and GC group (GC, n = 10). The quality of life assessment was conducted every 2 months for a cycle by the EORTC QLQ-C30 Scale. The objective response rate (ORR) and disease control rate (DCR) were evaluated according to the Response Evaluation Criteria in Solid Tumours 1.1 (RECIST 1.1). Overall survival (OS), progression-free survival (PFS) and adverse events (AEs) were analysed by the Kaplan-Meier method.

Results: However, the H-L-P group had a higher performance status (PS) score than the GC group (median, 1.85 vs. 1). The H-L-P group achieved longer PFS (median, 13.7 vs. 8.2 months), prolonged OS (median, 15.8 vs. 11.5 months), and a higher ORR (32.5% vs. 18.7%) than the GC group. The incidence of serious AEs in the H-L-P group was comparable to that in the GC group (grade 3-4, 56.3% vs. 60%). Compared with the GC group at the fifth cycle, the H-L-P group had significantly better scores in quality of life and physical function, while the symptom score was significantly lower.

Conclusion: The combination therapy of FOLFOX-HAIC plus lenvatinib and PD-1 inhibitors has promising survival benefits in the management of patients with ABTC and provides a new treatment option for ABTC.

Abstract Submission No. 100400
O-0886

Choledochal Cysts in Children- Clinical Spectrum

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OBJECTIVE: To study clinical spectrum of choledochal cyst (CDC) in children

METHODS: Records from January 2017 to May 2023 reviewed for children undergoing CDC excision with hepaticojejunostomy

Results: Ninety two included with 34.8% males. Median age 36 (20-60) months. Type IVa (34.8%) most common, followed by Type Ia (33.7%), Type Ic (16.3%), Type IVb (5.4%), Type Ib (3.3%), Type II (3.3%) and forme fruste (3.3%). Recurrent pain abdomen (60.9%), vomiting (52.2%), jaundice (35.9%) were common symptoms, lump was in only 5 (5.4%). Fever in 28.3%. No difference in symptoms amongst the subtypes. Neonatal cholestasis was in 17 (18.5%), with 10 children of Type Ia, 5 of Type IVa, 1 each of Type IVb and forme fruste, however, its incidence was not different amongst the subtypes (p=0.158). GB stone in 20 (21.7%) with no association with any subtype (p=0.590). CBD stone was in 33 (35.9%). It was more common with forme fruste subtype (100%) and Type IVb (60%) as compared to other (Type Ia-25.8% vs Type Ic-45.7% vs Type II-33.3% vs Type IVa-34.4%), difference was not significant (p=0.106). CDC rupture in 15.2% with no association with any subtype (p=0.795). Pancreatitis in 25%, no difference amongst subtypes (p=0.429). LCC was in 27.2% and more common in forme fruste (100%) and Type Ib, Type Ic, Type II (33.3% each) than in Type Ia (16.1%) and Type IVb (0%), but difference not significant (p=0.052).

CONCLUSION: Type IVa is the most common subtype with pain and jaundice most frequent symptoms. Neonatal cholestasis is a common presentation and pancreatitis and LCC must be looked for in all. Rupture is frequent (15%)

Abstract Submission No. 100776
O-0887

CA19-9, CA19-9/CRP and CA19-9/Bilirubin in Differentiating Benign and Malignant Obstructive Jaundice

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Background: CA19-9 is a tumour marker which is significantly elevated in biliary and pancreatic malignancy. Many strategies have been recommended to improve the power of CA 19-9 to differentiate benign and malignant obstructive jaundice. Aims and objective: This study was carried out to explore the role of CA19-9, CA19-9/CRP ratio and CA19-9/total bilirubin ratio in differentiating benign and malignant obstructive jaundice.

Materials and Methods: The present study was conducted at GHPD, BIRDEM Hospital, Bangladesh. It included 60 patients with obstructive jaundice. They were divided into two groups; benign (n=29) and malignant (n=31). The nature of obstructive jaundice was obtained by ultrasonography, CT scan, MRCP, ERCP, tumour marker and histopathology. All patients were tested for CA19-9, CRP and serum bilirubin.

Results: The mean±SD age (years) of the benign group was 56.90±15.80 and malignant group was 56.97±12.60. The ROC analysis for CA19-9 yielded sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy at cut-off value 70 U/ml were 71%, 49%, 60%, 61% and 61% respectively and area under the curve (AUC) was 0.625. The CA19-9/CRP ratio showed sensitivity, specificity, PPV, NPV and accuracy at cutoff value 5.2 were 80%, 97%, 96%, 82% and 88% respectively and AUC was 0.910. The CA19-9/total bilirubin ratio showed sensitivity, specificity, PPV, NPV and accuracy at cut-off value 14 were 58%, 48%, 54%, 51% and 54% respectively and AUC was 0.509.

Conclusion: CA 19-9/CRP ratio had high diagnostic value in differentiating benign and malignant obstructive jaundice than CA19-9 alone and CA19-9/total bilirubin ratio.

Abstract Submission No. 100885

O-0888

Etiological spectrum of Paucity of intrahepatic bile duct (PIHBD) in infants

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Background and objectives: Ductal paucity is one of the important differential diagnosis of infants presenting with cholestasis. PIHBD is defined as bile duct to portal tract ratio < 0.6. In the study we aimed to identify all the causes of ductal paucity in infants.

Methods: from June 2021 to June 2023 all the liver biopsies done in children <1 year old were screened. Of the total 150 liver biopsies, 100 were of infants, out of them 13 had ductal paucity.

Results: Out of total 13 liver biopsies, 6 were of females. Median age (days, IQR) at the time of biopsy was 75 (55-156). Median bilirubin, GGT, albumin (Median, IQR) was 9 (5-13), 178 (156-202), 3.5 (3-3.9) respectively. Of the total 13 biopsies with PIHBD, 5 were of progressive familial intrahepatic cholestasis, 1 was of hypopituitarism, 1 was of cystic fibrosis, 1 was of Alagille syndrome, 1 was of Zellweger syndrome and 4 were of prematurity related in which sepsis and respiratory distress was indication of admission. Out of 13 patients, 3 showed poor outcomes (Zellweger syndrome, Alagille syndrome and one infant with prematurity).

Conclusion: Ductal paucity encompassed 13% of etiology of infantile cholestasis. It generally had favourable outcomes, so, timely diagnosis and intervention is necessary. Liver biopsy is confirmatory diagnostic modality.

Abstract Submission No. 101063

O-0889

Effect of Methylprednisolone on Bilirubin Ratio and Pro-Inflammatory Cytokines in Biliary Atresia

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Background: Biliary atresia lead to progressive hepatic fibrosis due to progressive immune-mediated cholangiopathy. Interleukin (IL)-18 and IL-17 have been shown to play important roles in immunologic processes. This study aims to evaluate the effect of methylprednisolone on bilirubin ratio, IL-18 and IL-17 expression in biliary atresia.

Methods: A double-blind randomized controlled trial was conducted in infants with biliary atresia at the age of 2-12 weeks at the Dr. Soetomo General Hospital, Surabaya, Indonesia. Group 1 received methylprednisolone (2 mg/kg/day, twice daily) and group 2 received placebo for 2 weeks. Laboratory, IL-18 and IL-17 were evaluated before and after treatment between groups.

Results: A total of 40 infants aged 9.5 (8-11.75) weeks were double-blind randomized to receive methylprednisolone (n=20) vs placebo (n=20). After two weeks of evaluation, the ratio of direct bilirubin (DB)/total bilirubin (TB) was a statistically significant decrease after treatment compared to placebo ($\Delta = -0.35$ (-2.25 - 0.40) vs. $\Delta = 0.60$ (-0.55 - 0.70)) $p=0.018$. There was no difference between IL-17 and IL-18 ratio in both groups, but the reduction of IL-17 and IL-18 levels after the administration of methylprednisolone was higher compared with placebo (IL-17 $\Delta = 29,325$ (-54,282 - 94,844) vs 26,754 (-32,535 - 86,848) pg/ml, $p=0.882$); (IL-18 $\Delta = 1,330$ (-4537 - 6,423) vs 0,405 (-3,224 - 6,546) pg/ml, $p=0.850$)).

Conclusions: Administered methylprednisolone was effective in reducing IL-17 and IL-18 in biliary atresia. The lowering of DB/TB ratio may be associated with the reduction of atresia process in bile duct, further study is necessary.

Abstract Submission No. 101144

O-0890

Biochemical and Clinical Factors in Pediatric Cholestasis: Liver Biopsy Study

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Background: Cholestasis in children, whether intrahepatic or extrahepatic, presents a complex array of clinical manifestations and biochemical markers that require in-depth evaluation. Biopsy is an important diagnostic tool for determining the underlying pathophysiologic mechanisms and suggesting appropriate management strategies.

Methods: The retrospective cohort study was obtained from the medical records of pediatric cholestatic patients. Total sampling was used in this study. Clinical and laboratory biomarker were analyzed. The data were analyzed using the SPSS 21.0 version.

Results: A total of 119 children were included in this study, consisting of 31 intrahepatic and 88 extrahepatic cholestatic. Liver biopsy was performed, and differences were found between intrahepatic and extrahepatic cholestatic children in age ($p=0.001$), duration of disease

($p=0.048$), portal hypertension ($p=0.007$), Hb ($p=0.009$), WBC ($p=0.016$), PPT ($p=0.026$), and GGT level ($p=0.009$). Meanwhile, no differences were found in the onset of jaundice (0.111), birth weight ($p=0.144$), ascites ($p=0.067$), MMP-7 ($p=0.677$), Plt ($p=0.13$), albumin ($p=0.400$), direct bilirubin ($p=0.178$), total bilirubin ($p=0.152$), APTT ($p=0.419$), AST ($p=0.637$), and ALT level ($p=0.949$).

Conclusions: This study emphasizes the central role of liver biopsy in unraveling the complex web of biochemical and clinical factors in children with intrahepatic and extrahepatic cholestasis.

Keywords: cholestasis, intrahepatic, extrahepatic, liver biopsy

Abstract Submission No. 101359

O-0891

Genomic profile characteristics of pancreaticobiliary maljunction, including cancer patients

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Background: Pancreaticobiliary maljunction (PBM) is known to be a high-risk factor for biliary tract cancer (BTC). It has been reported that TP53 and KRAS mutations are found not only in the cancerous area but also in the noncancerous area. However, genetic studies on PBM have been insufficient.

Methods: Patients who underwent surgical resection for PBM and BTC between 1990 and 2023 at our hospital and affiliated hospitals were included in this study. FFPE tissue samples were sampled from different histological types (normal mucosa, hyperplasia, dysplasia, and carcinoma) by laser microdissection, and targeted sequencing was performed using the panel targeting 60 genes frequently identified in BTC, and compared with clinicopathological features.

Results: PBM patients with BTC showed various functional gene abnormalities, including driver mutations such as TP53 and ARID2, not only in the carcinoma but also in the non-cancerous areas including hyperplasia and normal cholangiocarcinoma mucosa. On the other hand, driver mutations were also found in some areas in patients who did not develop gallbladder cancer (prophylactic resection), but were rare. In addition, driver mutations were rarely found in non-cancerous areas in patients with BTC without PBM.

Conclusions: PBM patients with BTC showed a great variety of genetic abnormalities in both cancerous and noncancerous areas. On the other hand, in patients of prophylactic resection without cancer, driver mutations were almost completely absent despite the presence of mucosal changes. We believe that these findings can develop better strategies in patients with PBM.

Abstract Submission No. 101444

O-0892

Carcinosarcoma, A Rare Malignant Neoplasm of the Biliary Duct: A case report

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Carcinosarcoma is a rare malignant biphasic tumor with both carcinoma component and a spindle cell sarcomatous component intimately intermingled. As published by the World Journal of Gastrointestinal Oncology, there are only 12 cases reported worldwide. We report a case of a 63-year-old Filipino presenting with 10-day history of jaundice, right upper quadrant pain, and weight loss. Preliminary work-up showed, transaminitis, hyperbilirubinemia, negative hepatitis profile, and elevated CA19-9 (1007.70 U/mL). Whole abdomen MRI showed high-grade hepatic hilar obstructive process with marked intrahepatic ductal dilatation secondary to poorly defined soft tissue in the common hepatic duct region measuring 1.2 cm with small (<1.0 cm) porta hepatis & periportal as well as retroperitoneal & bilateral inguinal lymph nodes and normal common bile duct. He underwent Endoscopic retrograde cholangiopancreatography with Spyglass cholangioscopy, with the following findings: nodular and hyperemic lumen with a stricture seen in the said area. Multiple biopsies were taken. Histopathology of proximal common bile duct and common hepatic tissue (diagnosis concurred with 3 other pathologists) revealed: biphasic neoplasm suggestive of a carcinosarcoma. Since R0 resection was not feasible, patient underwent systemic chemotherapy (gemcitabine-based) targeting both lineages (carcinoma and sarcoma). Currently, patient is on his 12th cycle of chemotherapy and for re-evaluation for resectability.

Abstract Submission No. 101449

O-0893

Correlation of Serum Matrix Metalloproteinase-7 and Liver Function Test in Biliary Atresia

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Background: Biliary atresia (BA) is a rare progressive infant cholangiopathy characterized by cholestasis. BA is a leading cause of pediatric liver transplantation. Early diagnosis using sensitive biomarkers is crucial for good outcomes. However, at present, there is no certain non-invasive diagnostic method to diagnose and differentiate it from other cause of cholestasis. The aim of this study was to evaluate the correlation of serum matrix metalloproteinase-7 (MMP-7) levels with laboratory parameters.

Material and Methods: This cross-sectional study included infants with biliary atresia who were admitted to Soetomo General Academic Hospital, Surabaya. Blood samples as well as baseline clinical and demographic data were collected when admitted. Serum MMP-7 levels were determined by enzyme-linked immunosorbent assay.

Result: There were 85 infants with biliary atresia, mean age 11 (1 - 35) weeks, 46 (54.1%) boys, with onset of jaundice at 2 (1 - 20) weeks. The MMP-7 levels were 1.91 (0.39 - 9.95) pg/dl, 4.06 (1.41 - 4.79) g/dl, AST 235.37 ± 130.48 U/L, ALT 143.2 (30 - 641) U/L, 361 (23.9 - 3746) U/L, direct bilirubin 8.75 ± 4.28 mg/dl, and total bilirubin 12.34 ± 6.36 mg/dl. MMP-7 showed a positive correlation with albumin levels ($r=0.232$; $p=0.033$), but correlated negatively with AST ($r=-0.252$; $p=0.020$) and ALT ($r=-0.275$; $p=0.011$) levels. Direct or total bilirubin, hemoglobin, leukocyte or platelet levels were not associated with MMP-7 ($p>0.05$).

Conclusion: There is positive correlation between MMP7 and albumin, but the relationship between MMP and serum transaminases is reversed. MMP-7 may be used as a prognostic marker for liver damage.

Abstract Submission No. 101530
O-0894

A two-stage anticancer strategy targeting ECM stiffness in primary li

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Background: Intrahepatic cholangiocarcinoma(ICC) has a stiffer extracellular matrix(ECM), higher malignancy, and worse prognosis compared to hepatocellular carcinoma(HCC). This study aimed to explore relationships between ECM stiffness and primary liver cancers(PLC, including HCC and ICC) and develop anticancer strategies targeting ECM stiffness in PLC(ICC especially).

Methods: We first explored relationships between ECM stiffness and malignant phenotypes of PLC through in-vitro and in-vivo experiments. Next, we took functional molecules related to ECM stiffness in ICC as examples to explore specific mechanisms of the intracellular response of cancer cells to ECM mechanical signals. Finally, we newly constructed nanoparticles(NPs) and extracted ICC membrane(ICCM) to camouflage cationic polymers for siRNA and BAPN (ICCM@NPs-siRNA@BAPN) to achieve ICC-specific targeted delivery.

Results: The immunofluorescence results of 181 PLC tissue chips(HCC=90, ICC=91), in-vitro and in-vivo experiments showed that ECM stiffness could affect malignant phenotypes of PLC(ICC especially). The new transcript of ABHD11-AS1, a functional lncRNA related to ECM stiffness in ICC, regulated malignant phenotypes of ICC cells and their response to ECM mechanical signals through the YAP1/ABHD11-AS1/STAU2/ZYX/YAP1 loop signaling pathway. ICCM@NPs-siABHD11-AS1@BAPN could be a two-stage anticancer strategy targeting ECM stiffness in ICC.

Conclusions: This study demonstrated that ECM stiffness could affect malignant phenotypes of PLC(ICC especially) and took the YAP1/ABHD11-AS1/STAU2/ZYX/YAP1 loop signaling pathway as the entry point to explore specific mechanisms of mechanical signals conduction from ECM in ICC cells and their impact on cancer progression. Moreover, ICCM@NPs-siABHD11-AS1@BAPN was a spatially selective delivery system integrating ECM softening and blockade of intracellular mechanical signal transduction in ICC.

Abstract Submission No. 101669
O-0895

Bleeding Ducts - Hemobilia, A Rare Presentation of Intraductal Papillary Neoplasm Of The Bile Duct

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Intraductal papillary neoplasm of the bile duct (IPNB) is a rare premalignant neoplasm accounting for 7-30% of bile duct tumors. Common clinical manifestations include abdominal pain, cholangitis and jaundice.

A 70-year old woman with history of gallbladder intracholecystic papillary neoplasm (ICPN) presented with persistent melena with anemia (hemoglobin 6.2g/L). Prior endoscopies did not show any actively bleeding lesions. On admission, patient presented with melena, mild epigastric pain, and pallor.

A second look EGD revealed hemobilia. Patient underwent mesenteric angiogram, particle embolization of selected arteries and intraoperative ultrasound revealed multiple hepatic heterogeneous foci. Whole abdominal CT scan revealed no hepatic mass lesions, common bile duct (CBD) and intrahepatic duct (IHD) dilatation and a 1cm nodular enhancing focus in the proximal CBD. Spyglass cholangioscopy revealed a lobulated polypoid lesion with villous surface at the main right IHD. Patient underwent choledochoscopy with laser ablation of multiple IHD tumors, excision of IHD mass, and t-tube choledochostomy. Frozen section revealed mucinous IPNB, predominantly low grade with focal high-grade dysplasia. Due to persistence of melena, patient underwent angiogram with embolization of hepatic arteries; percutaneous transhepatic biliary drainage (PTBD). Although with initial improvement, patient eventually expired after 6 months.

In our case, the hemobilia may be due to the diffuse and infiltrative nature of the tumor into adjacent liver parenchyma and vasculature. The co-occurrence with ICPN may be contributory. IPNB has relatively good prognosis hence need for early surgical management. Apart from surgery, other treatment options such as laser ablation, PTBD and embolization need to be explored further.

Abstract Submission No. 102032
O-0896

Extra-hepatic bile duct resection in cases with intrahepatic cholangiocarcinoma

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Abstract

Objective: To evaluate the significance of combined extra-hepatic bile duct resection (EHBDR) in cases with intrahepatic cholangiocarcinoma (IHCC) in terms of clinic-pathological features and long-term survival.

Methods: Radically-resected cases with IHCC from 2000 to 2020 were identified from Surveillance, Epidemiology, and End Results (SEER) database. Comparative analyses were performed between resected IHCC patients who received EHBDR and those without EHBDR.

Results: A total of 1521 radically-resected cases with IHCC (189 cases received EHBDR) were included. Comparable age, sex, race, marital status, liver cirrhosis, differentiation status, and adjuvant chemotherapy were acquired between two groups. EHBDR achieved a greater lymph node yield ($P<0.001$). The incidence of cases with T3-4 or N+ disease was significantly higher in the EHBDR group ($P<0.001$). Adjuvant radiotherapy was more frequently performed in cases with EHBDR ($P<0.001$). Even various independent prognostic factors have been matched between two groups, cases in the EHBDR group still shared a much worse prognosis than those without EHBDR. For early-staged cases, combined EHBDR was even harmful. However, for more advanced cases, EHBDR achieved equivalent survival versus those without EHBDR.

Conclusion: Combined EHBDR was not associated with any survival benefit in radically-resected cases with IHCC and was even harmful for some early-staged cases. However, a greater lymph yield was achieved via EHBDR. Future well-designed studies with more detailed data, such as recurrence rate within 6 months after surgery and the time from the date of surgery to the date of the occurrence of obstructive jaundice, are warranted for further exploration.

Abstract Submission No. 200013

O-0897

Cholangiocarcinoma (Bismuth Corlette Class I) secondary to Choledochal Cyst (Todani Type II)

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Cholangiocarcinoma is the most common bile duct tumor and is the 2nd most common primary hepatic malignancy, accounting for 15% to 20% of all hepatobiliary malignancy. One of the definite risk factors for cholangiocarcinogenesis is the presence of choledochal cyst, especially types I (common), IV (multiple intrahepatic and extrahepatic cysts) and V (Caroli disease). Pathophysiology is due to chronic bile stasis within the cysts, causing chronic inflammation. The incidence of choledochal cysts types I and IV, comparing to types II (diverticulum) and III (choledocoele), are approximately 1:10,000 and 1:1,000,000, respectively.

To date, there are only 4 reported cases of cholangiocarcinoma arising from type II choledochal cysts.

We report herein a case of a previously healthy 33-year-old Filipino male who complained of a 1-month history of colicky abdominal pain, and 2-weeks history of jaundice, icteric sclera, tea-colored urine and acholic stools. Patient was initially diagnosed as obstructive jaundice probably secondary to choledocholithiasis through ultrasonography. ERCP revealed multiple filling defects within of what seems to be the gallbladder, a narrowing at the proximal CBD with preferential flow of contrast to the gallbladder, and a cystic structure beside the gallbladder. Upper abdominal MRI with MRCP revealed a choledochal cyst type II with intraluminal stones and a contracted gallbladder. Patient underwent biliary exploration which revealed a CBD tumor and a choledochal cyst with multiple intraluminal stones. Core needle biopsy of the tumor revealed poorly-differentiated adenocarcinoma. Patient was diagnosed as Perihilar Cholangiocarcinoma (Bismuth Corlette Class I) secondary to Choledochal Cyst (Todani Type II) with Lithiasis.

Abstract Submission No. 200014

O-0898

Clinical impact of bile cytology and surgical site complication on locoregional recurrence in eCCA.

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Background: Cholangiocarcinoma is a lethal malignancy with a poor prognosis because of its high rate of recurrence after radical resection. In terms of prevention of recurrence, the intraductal irrigation of the remnant rectum prior to anastomosis decreased local recurrence in rectal cancer. The presence of surgical site complications (SSC) is regarded as a risk factor for the recurrence in other cancers. However, there have been few studies similar to this in extrahepatic cholangiocarcinoma (eCCA). We here investigated whether preoperative positive bile cytology and postoperative complications were associated with recurrence in eCCA.

Method: Ninety-six patients who underwent R0 resection for eCCA in our hospital were investigated. The relationship between clinicopathological factors and long-term outcomes was evaluated.

Result: 42 patients had SSC including bile leakage. Preoperative bile cytology was positive (Class IV, V) in 50 patients except for 13 patients who had not undergone bile cytology. Recurrence at the peritoneum and local site was significantly more frequent in the SSC group than in the non-SSC group (42.8%:11.1%, $p=0.0003$). While the occurrence of SSC was not associated with preoperative bile cytology-positive cases ($p=0.4980$), bile cytology-positive patients with SSC had a higher rate of peritoneum and local recurrence than the other patients (72.2%:13.9%, $p<0.0001$). Both preoperative positive bile cytology and the presence of SSC were significant factors of recurrence-free survival (RFS) ($p=0.0096, 0.0175$).

Conclusion: Preoperative positive bile cytology is a risk factor for recurrence in eCCA. Furthermore, adding the factor of SSC, the peritoneum or local recurrence was more frequently observed.

Abstract Submission No. 200035

O-0899

ADC values predict prognosis and Ki67 expression in intrahepatic cholangiocarcinoma on DW-MRI

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Background:

Ki67 is a marker of cell proliferation and key in cancer treatment because it reflects the grade and prognosis of malignant tumors.

Apparent diffusion coefficient (ADC) values are derived from DWI and are a common imaging metric used to quantify the biological behavior of tumors and evaluate curative response. ADC values have been associated with Ki67 expression in breast cancer and pancreatic neuroendocrine tumors, but information about the relationship between Ki67 expression and ADC values in ICC is lacking.

Method: We investigated the ability of ADC values to predict Ki67 expression, using retrospective analysis of 39 cases of ICC confirmed by surgical pathology. All patients had undergone MRI, and ADC values (mean, minimum, maximum) were calculated. Ki67 expression was assessed by immunohistochemistry, and patients were divided into groups of high ($n = 13$) and low Ki67 expression ($n = 26$). To assess the diagnostic performance of the ADC values for Ki67 expression, we used the receiver operating characteristic curve and compared the areas under the curve (AUCs).

Results: The high Ki67 expression group had a significantly poorer prognosis than the low group. The minimum ADC values were significantly lower in the group with high Ki67 expression. For predicting high Ki67 expression, the AUC values were 0.7189 for minimum ADC values. The diagnostic sensitivity and specificity of the minimum ADC values were 84.6% and 73.1%, respectively. In addition, with ADC values combined, the AUC increased to 0.760.

Conclusion: ADC values can non-invasively predict ICC associated with high Ki67 expression.

Abstract Submission No. 100050

O-0900

A case of cystic pseudo-tumor as a complication of radiofrequency ablation therapy

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Radiofrequency ablation (RFA) therapy is a curative treatment for small-sized hepatocellular carcinoma (HCC) tumors. It is widely performed at many institutions worldwide, and its complications have been well discussed in previous studies. Here, we report a highly rare case of cystic pseudo-tumor as a complication of RFA treatment. The patient was a 71-year-old individual with HCC who had an etiology of non-alcoholic steatohepatitis. He also had hypertension, type 2 diabetes, chronic renal failure on dialysis, prostatic cancer, and a history of hepatectomy for HCC. We performed RFA therapy for HCC recurrence in the left lobe near the stomach. Four months later, we identified the formation of a cystic lesion in the treated area of the liver without any symptoms. This cystic lesion was surrounded by a thick wall. Cyto-diagnosis of the fluid within the cystic lesion revealed that the fluid was serous and not purulent. Total bilirubin levels of the fluid were not elevated, and no evidence of malignancy was found. Computed tomography examination at 16 months after RFA showed a collapse of the cystic lesion, and small amounts of gas were detected in the RFA-treated lesion, indicating that penetration of the stomach had occurred. Artificial ascites could not completely prevent gastrointestinal tract injury, but would be necessary to keep thermal injury to minimum in ablation therapy.

Abstract Submission No. 100317
O-0901

GAED resected by ESD: a case report of the patient with cirrhosis and previous liver cancer

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Gastric adenocarcinoma with enteroblastic differentiation (GAED) is a rare special type of gastrointestinal tumor. Our patient had a history of CHB with cirrhosis for more than 25 years and underwent 13 years combination therapy for HCC, like RFA and TACE, besides targeted drugs for 4 years. GAED was found in the greater curvature of upper segment of gastric body. The gastric and duodenal background mucosa was slightly edematous with regular dilation of microvessels. We suspect it's caused by targeted drugs. The lesion consists of two parts, 0-IIa+IIb. Fine villous white fur epithelium showed a distinctive

appearance in Faded flat area. Biopsy specimens taken from the lesion in the 0-IIa reddish position revealed to low-differentiated adenocarcinoma. The lesion removed by using endoscopic submucosal dissection. The lesion located in the mucosal layer, and the small infiltrated the submucosa to 196um. The irregular carcinomatous adenoids are tubular and cystadenoid, similar in shape to common intestinal adenocarcinoma components. Part of the region was solid, the epithelial cells were cubic, the atypia was significant, and the cytoplasm was transparent and vacuole-like. The patient survived with high quality at the fourth month after surgery. Through comprehensive and diverse treatment methods, the survival of patients is prolonged. Multidisciplinary collaborative treatment significantly improves the quality of life of patients.

Abstract Submission No. 100318
O-0902

Acute liver failure by scrub typhus; a rare presentation

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Acute liver failure (ALF) can be due to numerous causes and result mostly in mortality if liver transplantation cannot be offered. Scrub typhus is an acute febrile disease caused by *Orientia tsutsugamushi* transmitted by mites. Liver injury in scrub typhus is common but reversible. However, there are reported cases of ALF due to scrub typhus, mainly in conjunction with other clinical conditions.

Herein we report a case who presented with scrub typhus complicated by ALF and treated successfully without transplantation in our institute. A 27-years-old lady was admitted with complaints of jaundice and fever. LFT showed bilirubin of 10.2/8.4 mg/dL with ALT/AST of 1058/2134 IU/mL. A working diagnosis of acute viral hepatitis was made. Viral serology for HAV, HEV, HBV, HCV, TORCH were negative. Patient developed seizure followed by encephalopathy and INR came out to be 3. Patient was transferred to ICU and counselled for liver transplantation. Due to non-availability of donor, transplantation was not carried out. Patient slowly improved with conservative management but her fever was persistent. Fever panel test was sent and scrub typhus IgM came to be positive. Patient was put on doxycycline. Fever came down but liver enzymes worsened. Antibiotics changed to Azithromycin and patient improved. After a hospital stay for 29 days she was discharged.

Due to the non-specificity and diversity of the initial presenting symptoms, scrub typhus causing ALF can easily be missed. A lack of awareness about the disease and its role in causing ALF, there is always a chance of misdiagnosis.

Abstract Submission No. 100320
O-0903

A Case Report of durable HBs Ag Loss after Peg-Interferon Alpha and Nucleotide Analog finite Therapy

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Introduction: The main goal of therapy for patients with chronic HBV infection is to improve survival and quality of life by preventing disease progression and consequently Hepatocellular Carcinoma (HCC) development.

Case Report: A 28-year-old gentleman visited the outpatient clinic because of recently known HBV infection 8 years ago. He had history of HBV Vaccinations 10 years ago, but no immune response of HBs Ab detected.

His serological testing were positive for HBs Ag, HBe Ab, and HBs Ab, HBe Ag and HBe Ab (both IgM and IgG) were negative. HCV Ab and HIV Ab were also negative. HBV DNA - $1.19E + 04$ IU/mL and qHBs Ag 584 IU/mL. ALT - 66 IU/mL, AST 70 IU/mL, AFP - 3.5 IU/mL.

Ultrasound Abdomen showed chronic hepatitis.

Fibroscan showed F3 fibrosis and moderate steatosis.

He was started Tenofovir (TDF) 300 mg daily on December 2015.

Three months after TDF, HBV DNA was not detected and qHBs Ag was reduced to 467 IU/mL.

One year after TDF, qHBs Ag was 352.6 IU/mL and started Peg-IFN 100 ug weekly.

HBs Ag became negative after 24 weeks of Peg-IFN. Then, stopped Peg-IFN and continue TDF for one year. Follow up HBs Ag and HCC screening was done yearly. Still HBs Ag was negative to date and no features of HCC.

Conclusion: In some CHB cases, durable HBs Ag loss can rarely be achieved even with a finite therapy of Peg-IFN and TDF, as a functional cure.

Abstract Submission No. 100331

O-0904

Cytokine release syndrome caused by the durvalumab plus tremelimumab combination therapy for HCC

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Background: Cytokine release syndrome (CRS) is a systemic inflammatory syndrome that can lead to life-threatening, caused by elevated levels of cytokines and the activation of immune cells. It can be triggered by systemic therapies mainly immune activating treatments, pathogens, malignancies, or autoimmune diseases. In recent years, CRS has been reported as an immune-related adverse event associated with immune checkpoint inhibitor. We report a case of severe CRS that occurred following the initiation of durvalumab plus tremelimumab combination therapy for advanced hepatocellular carcinoma (HCC).

Case Report: A combination therapy of durvalumab plus tremelimumab was initiated in a 35-year-old female with stage IV metastatic HCC. A few weeks later, she visited our department due to a fever. She had low blood pressure and a body temperature of 39°C. Blood tests revealed signs of inflammation, elevated transaminases, and renal impairment. Suspecting sepsis, broad-spectrum antibiotics and vasopressors were initiated. While the vasopressors could be promptly discontinued, the high fever persisted, and liver enzymes continued to rise, leading to a tendency toward disseminated intravascular coagulation. Given the elevated IL-6 levels, we considered the possibility of CRS and administered steroid pulse therapy. The patient's overall condition began to improve and we began tapering the steroids. However, a few days later, with the re-elevation of IL-6 and CRP levels, we suspected a recurrence of CRS and administered tocilizumab. Subsequently, her condition showed improvement and she was discharged on the 22nd day of hospitalization.

Conclusion: Severe CRS has the potential to become life-threatening, so appropriate therapeutic interventions are necessary.

Abstract Submission No. 100370

O-0905

Gastric Bleeding in Sorafenib for HCC Drop Metastases

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Case Report: A 66-year-old male patient had hepatitis B with undetectable HBV DNA and negative anti-HCV without follow-up in 2012. He was found to have one 9.6 cm pedunculated HCC over the left lobe and received a left lobectomy. He was found one left abdominal 10 cm mass, another small right lobe tumor, and the third small one with external compression in 2018 and the former was done percutaneous biopsy which was reported HCC. He began sorafenib therapy with low AFP in 2018. His AFP showed mild elevation in 2020 and we did one TACE to his intrahepatic tumor without good embolized effect. Though the floating drop metastasis differed in size in the CT, it was reported stable disease and he kept sorafenib from reimbursement. Finally, he suffered from UGI bleeding in 2021 and was found with gastric invasion by the drop metastasis. The surgeon resectioned the three lesions after discussing about his bleeding. He was found active hepatitis C but S-seroconversion of hepatitis B and one L-spinal metastases, and he began his radiation therapy, regorafenib and epclusa. Now he still has good life quality in regorafenib and elevated PIVKA-II.

Conclusion: Aggressive treatment for advanced HCC patients should be considered for the stable disease.

Abstract Submission No. 100455

O-0906

Recovery of Severe Acute Hepatic Graft-versus-Host Disease in a Recently Transplanted Pre-B Cell ALL

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Introduction: Acute Graft-versus-Host Disease (GVHD) is a complication among hematopoietic cell transplant recipients within 100 days. But only around 9% involve both the liver and the gastrointestinal tract. Diagnosing hepatic GVHD is quite challenging, since it is indistinguishable from other disorders such as infection and drug-induced liver injury.

Clinical Significance: Hepatic GVHD has a higher non-relapse mortality rate than non-hepatic. However, early recognition and management even without a liver biopsy can help prevent the development of permanent organ damage.

Case Report: Here we present a case of a 57 year-old female, with pre-B cell acute lymphoblastic leukemia and with no known liver disease, who underwent allogeneic HSCT (mismatched/haploidentical) two months prior to admission. Patient was managed as a case of pneumonia in an immunocompromised host. At Day +83 post-transplant, she presented with high grade fever, diarrhea, generalized jaundice, and vomiting. She was diagnosed with acute hepatic graft-versus-host-disease through elevated bilirubins and late increase in transaminases (Grade 0). This eventually progressed to Grade 4 in a span of 17 days with the highest total bilirubin and direct bilirubin recorded to be 33

mg/dL and 24 mg/dL, respectively. Patient was then started on high dose steroids and liver supportive therapy, such as minophagen drip, transtemetil, udcacid, and silymarin. Her liver profile started to down-trend after 25 days, and noted clinical improvement of symptoms.

Conclusion: Elevated bilirubins, rather than increase in transaminases, is the best diagnostic marker for Hepatic GVHD. Prompt administration of steroids can help improve the patient's overall survival.

Abstract Submission No. 100456
O-0907

Unmasking Hepatoid Adenocarcinoma of the Stomach Mimicking as Hepatocellular Carcinoma: A Case Report

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Hepatoid adenocarcinoma of the stomach (HAS) is a rare malignancy characterized by its hepatocellular differentiation and aggressive nature. Due to its scarcity and vague clinical presentation, diagnosing HAS poses significant challenges, often leading to its misidentification as hepatocellular carcinoma due to their indistinguishable radiologic and clinical parameters.

We report a 68-year-old male who initially sought consult for a perplexing symptom: a persistent three-week history of hiccups. During an abdominal ultrasound, solid hepatic nodules were incidentally discovered, triggering further investigations. Subsequent tests unveiled a dramatic elevation in alpha-fetoprotein (AFP) levels (~60,000 ng/mL) and the presence of hypovascular hepatic masses, accompanied by portal vein thrombosis, as evident on a 4-phased dynamic liver scan. The initial suspicion was hepatocellular carcinoma, primarily due to an atypical enhancement pattern observed. To explore the anomaly further, a fine needle aspiration biopsy of the liver mass was performed. Notably, given the unusual initial symptom of hiccups and anemia, gastro-duodenoscopy was done revealing an unexpected gastric mass located in cardia up to the esophagus.

Histopathological analyses of both the liver and gastric masses, supplemented by immunohistochemical stains, ultimately confirmed the diagnosis of gastric adenocarcinoma with liver metastasis. This case emphasizes the significance of a comprehensive diagnostic approach for rare conditions such as HAS with liver metastasis, highlighting the need for integrating clinical, radiological, and histopathological findings. It underscores the importance of considering HAS as a potential differential diagnosis in cases of AFP-producing liver lesions that exhibit atypical hepatocellular carcinoma imaging characteristics.

Abstract Submission No. 100539
O-0908

A case of neuroendocrine carcinoma caused obstructive jaundice by extensive hepatic infiltration.

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A 74-year-old man was found to have obstructive jaundice (T-Bil 18.6 mg/dl). He had a history of total gastrectomy and Roux-en-Y

anastomosis for upper gastrointestinal bleeding in his 20s. Imaging findings showed that the tumor was 80mm which extensively infiltrated to both lobes of liver, gallbladder, duodenum, and main portal vein and caused biliary stricture classed Type3A in Bismuth classification. Biliary drainage was attempted using a balloon endoscopy, but it could not reach Vater papilla. Next, percutaneous transhepatic bile duct drainage was performed to posterior segmental branch, but jaundice did not improve. An endoscopic ultrasound-guided hepatic jejunal anastomosis (EUS-HJS) was performed on B3, and a self-expandable metal stent was implanted from B3 to the anterior segment using the fistula formed by the EUS-HJS, and T-bil was reduced to 1.3 mg/dl. Since bile cytology and bile duct biopsy did not yield a pathological diagnosis, a liver tumor biopsy was performed. Pathology findings showed that synaptophysin and chromogranin A were positive for immunostaining, and the Ki-67 index was over 90%. Finally, considering the extensive necrosis and rapid growth rate of this tumor, this patient was diagnosed as a neuroendocrine carcinoma (NEC). The patient had poor performance status, so the best supportive care was selected and the patient was discharged. The cases of NEC caused obstructive jaundice by rapid hepatic infiltration are rare. And in this patient, there was difficulty on biliary drainage for reconstructed intestinal tract. However, we finally succeeded in improving jaundice by combination of percutaneous procedure and interventional EUS.

Abstract Submission No. 100541
O-0909

A case of cholangitis as immune-related adverse events with biliary infection after cholangiography.

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Background: Immune checkpoint inhibitors possibly cause immune-related adverse events (irAE). The rate of sclerosing cholangitis in irAE is small, but it is reported difficult to cure immune checkpoint inhibitor-induced cholangitis because steroid therapy has no efficacy for them.

Case: 75-year-old-man had had a history of subtotal esophagectomy for esophageal cancer at age 71. He was performed multidisciplinary treatment involving Nivolumab therapy for lung metastasis from age 73. During hospitalization of treatment for ulcer in a reconstructed gastric tube perforating the pericardium, he was found to have jaundice (T-Bil 13.7 mg/dl) on day 46. Imaging findings showed that non-continuous strictures of wide part of bile tract with dilation of upper bile duct. It was suspected sclerosing cholangitis, so an endoscopic retrograde cholangiopancreatography (ERCP) was performed. It showed that pruned-tree appearance by cholangiography and circular homogeneous wall thickening of parts of bile duct with stricture by intraductal ultrasound. Bile cytology and brush cytology from stricture were not malignant. After balloon dilation of stricture, an endoscopic nasobiliary drainage tube was put, but it was removed soon. This patient was diagnosed as an immune checkpoint inhibitor-induced cholangitis, and introduced steroid therapy on day 50. But severe acute cholangitis occurred, then ERCP with biliary stenting was performed. However, jaundice did not improve and he died from sepsis caused by biliary infection on day 55.

Discussion: ERCP in the cases of cholangitis as irAEs possibly causes severe biliary infection from cholestasis in these cases, so its indication should be carefully considered.

Abstract Submission No. 100589

O-0910

Corticosteroid therapy for prolonged jaundice and pruritus in HIV patients with acute hepatitis A

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Background: Recent years have seen global outbreaks of acute hepatitis A (HA), particularly affecting men who have sex with men (MSM). In Tokyo in 2018, an outbreak primarily impacted MSM, including some individuals living with HIV (PLWH). Two PLWH experiencing prolonged jaundice and severe pruritus were treated with corticosteroids, demonstrating successful responses. This marks the first report use of corticosteroids for prolonged cholestatic HA in PLWH.

Cases: The first case involved a 34-year-old male, on antiretroviral therapy (ART) for six years. Despite CD4 count of 527/ μ l and suppressed HIV-RNA viral load, he faced elevated peak ALT 3494 IU/l and total bilirubin (T-Bil) 31.9 mg/dl. Severe itching and fatigue led to the initiation of 25 mg/day (0.5 mg/kg) of prednisolone (PSL) on day 62. T-Bil levels gradually normalized by day 142.

In the second case, a 36-year-old male, 11 years on ART with CD4 count 620/ μ l and suppressed HIV-RNA viral load, encountered peak ALT 2690 IU/l and T-Bil 22.8 mg/dl. Despite well-managed HIV, he too experienced itching and fatigue. Initiation of 30 mg/day (0.5 mg/kg) of PSL on day 32 resulted in a T-Bil decrease of 2.1 mg/dl by day 71.

Discussion: Around 1% of HA cases may lead to prolonged jaundice and severe itching. Cholestasis might arise from various bilirubin metabolism defects. This study suggests that corticosteroid therapy could be an effective option for well-controlled PLWH on ART.

Abstract Submission No. 100611

O-0911

Detection of ETV-associated drug resistance mutation S202G in a case of HBV/HIV coinfection

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Background: Entecavir (ETV) resistance is often acquired following lamivudine (3TC) resistance but is rarely proven by clinical specimen analyses over time. A case study outlines the gradual acquisition of the S202G mutation spanning approximately 8 months.

Case: A man in his 40s, diagnosed with HIV/AIDS and chronic hepatitis B eight years ago, initially received tenofovir /emtricitabine (FTC)/darunavir/ritonavir. Subsequently, HIV-RNA and HBV-DNA were suppressed, and CD4 counts increased. Later, due to renal issues, he was switched to 3TC/abacavir/dolutegravir (DTG) and ETV. Upon transfer to our clinic three years ago, he exhibited suppressed HIV-RNA, CD4 count 635/ μ l, normal transaminases, HBsAg 245.38IU/ml,

HBV-DNA 2.6 log IU/ml, and HBV genotype A2. Subsequently, reaching AST 40U/L, ALT 70U/L, HBsAg exceeding 99999.99IU/ml, and HBV-DNA rising to 7.9 log IU/ml after one year. Stored specimens revealed L180M and M204V mutations, 3TC resistance, at our clinic's initial visit, and a gradual shift from AGC to GGC nucleotides, indicating S202G acquisition over 8 months. Because of no other mutations, TAF/FTC and ETV were initiated, resulting in normalized liver function and declining HBV-DNA levels. Analysis of GenBank HBV/HIV coinfection samples revealed few reports of ETV resistance mutations and no reports of S202G.

Discussion: It is reported the acquisition of HBV multidrug resistance during HBV/HIV coinfection treatment, specifically marking the initial report of S202G acquisition. The reasons for the low number of registrations of ETV resistance of coinfection in GenBank were that coinfection was not specified and that many registrations were from Asia and Africa where ETV has not been used.

Abstract Submission No. 100621

O-0912

A Rare Case of Advanced Hepatocellular Carcinoma in Acute Intermittent Porphyria without Cirrhosis

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Introduction: Acute hepatic porphyrias (AHP) are associated with an increased risk of hepatocellular carcinoma (HCC). Traditionally, patients with AHP and HCC are more likely to be women, be ≥ 50 years old, and have liver fibrosis or cirrhosis. However, recent data has shown that AHP patients can have HCC in the absence of liver fibrosis or cirrhosis. We present a case of a patient with acute intermittent porphyria (AIP) without liver fibrosis who was diagnosed with advanced HCC.

Case: A 73 year old lady with a history of AIP diagnosed in 1981 and last AIP flare in 1991 developed new onset severe abdominal pain and outside imaging revealed findings of multiple liver lesions. She was referred to our center and MRI with IV Gadavist demonstrated a 11.4 x 9.7 x 15.x cm invasive HCC involving with right portal vein with multiple intrahepatic metastases and a bone lesion. Ultrasound guided liver lesion biopsy and liver parenchymal biopsy was performed. Pathology demonstrated sinusoidal dilatation and focal minimal non-specific portal inflammation. Cytology was positive for hepatocellular carcinoma. She was referred to oncology and initiated systemic chemotherapy.

Discussion: Our patient with longstanding AIP despite having no liver fibrosis still developed HCC with metastatic disease. This case supports the 2023 American Gastroenterological Association (AGA) Clinical Practice Update on AHP management that recommends HCC surveillance for patients with AHP starting at age 50 regardless of their symptom severity.

Abstract Submission No. 100651

O-0913

PERITONITIS TUBERCULOSIS - A DIAGNOSIS CHALLENGE: CASE REPORT

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Background: Peritoneal tuberculosis (TB) is one of the most challenging forms of extra-pulmonary tuberculosis to diagnose, most common in the developing world because the symptoms and signs of peritoneal TB are nonspecific.

CASE: A 31-year-old female patient presented to the ER with a chief complaint of abdominal pain for the last 2 months, VAS 8/10, associated with lethargic, body weight loss, fever, nausea, vomiting, for 1 months. Her vital sign was stable with the temperature 38.5 C. The laboratory showed Hb 8.6 g/dL, WBC 12,800/mm³. The blood smear showed microcytic hypochromic anemia caused by chronic disease anemia. Abdominal CT with contrast was performed and showed suggestive peritonitis tuberculosis with peritoneum thickening and minimal ascites. Anti-tuberculosis drugs were planned to be given for 9 months. After 2 months therapy, the symptoms were gradually improving and body weight increases by at least 10 kilograms.

DISCUSSION: Female patients with complaints of abdominal pain can be caused by various diseases, determined based on the symptoms that occur, medical history, and epidemiological data. Peritonitis tuberculosis is one of the differential diagnoses with the most common complaints being abdominal pain (73%) and fever (58%). The complaints are difficult to differentiate from other intra-abdominal diseases, and the major diagnostic unavailable. In this patient, radiologic imaging techniques were the diagnostic basis, and abdominal CT with contrast showed peritoneal thickening. Treatment of peritoneal TB is primarily the anti-TB regimen.

CONCLUSION: Peritoneal tuberculosis has non-specific symptoms and complaints, making diagnosis difficult. A correct diagnosis is desirable.

KEYWORDS: Diagnosis, Peritonitis, Tuberculosis

Abstract Submission No. 100658

O-0914

A RARE CASE OF HIRSCHPRUNG'S DISEASE IN AN ADULT PATIENT: CASE REPORT

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Background: Hirschsprung's disease is considered a newborn disease, occurs in 1:5000 births, but in adults it is rarely considered and often undiagnosed. A variety of diagnostic tests including contrast enema and anorectal manometry may be used as diagnostic screens, but diagnosis ultimately rests upon histopathological evaluation of a rectal biopsy.

CASE: A 25-year-old male patient presented to the outpatient clinic with chief complaints of abdominal pain for the last 3 months, associated with bloating, nausea, and constipation. He has no similar complaints since birth. Abdominal computed tomography with contrast showed dilatation of the colon, colitis with fat stranding and multiple periodic lymphadenopathy (mainly sigmoid, descending, and transverse colon), fecal material, and minimal ascites was found. The final diagnosis at our hospital was adult hirschsprung, diagnosed by the history taking and abdominal computed tomography. The patient was referred to a digestive surgeon for further treatment.

DISCUSSION: Constipation is a common disorder that usually refers to persistent, infrequent defecation, difficult stool passage. This condition can deteriorate into distal colon obstruction, worsening constipation or even acute intestinal obstruction. Barium enema and biopsy are the gold standard. Surgical procedure to removal of the aganglionic segment remains the definitive treatment for this disease.

CONCLUSION: Adult Hirschsprung's disease should be considered in any young patient presenting with a long-standing history of

constipation, although it is rare. Abdominal computed tomography examination is recommended as a useful tool in the suspected diagnosis. Definitive treatment is surgical removal of the aganglionic segment.

KEYWORDS: Abdominal, Adult, Constipation, Hirschsprung

Abstract Submission No. 100715

O-0915

A Case of HCC with Inferior Vena Cava and Right Atrium Tumor Thrombus in a Patient with COVID-19

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Advanced hepatocellular carcinoma (HCC) presents with extensive vascularity and frequently spreads to the portal and hepatic veins while extension to the inferior vena cava (IVC) and right atrium (RA) is rare. Patients with RA thrombus have poor prognosis, with a median survival of 2 months due to increased risk of heart failure, pulmonary embolism or sudden cardiac death.

This is a case of a 50-year old female with liver cirrhosis secondary to Chronic Hepatitis B who presented with a two month history of progressive dyspnea and abdominal discomfort. Triphasic abdominal CT scan showed a cirrhotic liver with a large heterogeneously enhancing mass with enhancement pattern of HCC and elevated alpha-fetoprotein. Tumor thrombus was noted in the IVC and RA. Chest CT scan showed filling defects in the left lower lobar pulmonary artery, medial segmental artery and distal lobar artery as well as pulmonary metastases. She was treated with 5 fractions of external beam radiation therapy, targeting the venous thrombus in the RA and IVC, along with lenvatinib, tenofovir and apixaban. Patient reported only fatigue after initiation of treatment. At 3 years post treatment, patient remains stable with minimal abdominal discomfort and improvement of dyspnea. She is maintained on Lenvatinib and serial CT scan monitoring shows stable thrombus with decrease in size of the hepatic mass.

This case study presents a patient with HCC with tumor thrombus in the IVC and RA that was treated with radiotherapy, oral anticoagulation and lenvatinib with good treatment response and tolerability, prolonging survival.

Abstract Submission No. 100769

O-0916

A Case of Hemobilia Secondary to Polyarteritis Nodosa with Underlying Gallbladder Hemangioma

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Polyarteritis Nodosa (PAN), a rare autoimmune disorder characterized by inflammation of small and medium-sized arteries leading to the development of multifocal aneurysms, carries the potential for rupture and hemorrhage. We report a 25-year-old female who presented with epigastric pain, coffee ground vomitus and melena. Liver enzymes, total bilirubin and lipase exceeded tenfold the normal limit. Abdominal computed tomography showed hyperdensities within the biliary tree, suggestive of hemobilia, with acute acalculous cholecystitis. Upper endoscopy was unremarkable, and due to persistent bleeding, cholecystectomy was performed. Intraoperatively, blood clots were noted

within the gallbladder and common bile duct, with intermittent bleeding proximal to the choledochotomy. Histopathology noted varicized blood vessels in the serosa and muscularis layer of the gallbladder, consistent with hemangioma. Six days post operative, hematochezia recurred with sanguinous T-tube output. Angiogram of the right hepatic artery revealed multifocal stenosis with outpouching in the distal A8 branch and embolization was performed. Based on the seven-item diagnostic criteria for PAN and the presence of characteristic beading pattern on angiogram, a diagnosis of PAN was established and hydrocortisone was started.

This case underscores the intricate clinical scenario of PAN presenting as hemobilia, necessitating a heightened level of clinical suspicion and a collaborative medical approach. Early diagnosis and appropriate management are pivotal in mitigating the potentially severe consequences of this unique and significant complication associated with PAN.

This case report highlights the rare co-occurrence of PAN and gallbladder hemangioma, which manifested in a rare manner, not previously reported in scientific literature.

Abstract Submission No. 100790
O-0917

Combine hepatectomy and flow modulation surgery for patient with HCC and gastroesophageal varices

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Gastroesophageal varices (GEV) bleeding is a complication of portal hypertension, and usually a contraindication of liver resection. Flow modulation surgery include portosystemic shunt and devascularization combined with splenectomy has been proved to be effective in treat GEB and decrease portal vein pressure in liver transplantation. We present 2 cases HCC with gastroesophageal varices treated by liver resection combined with flow modulation surgery.

Case 1: Patient female, 71 years old, diagnosis: HCC, cirrhosis with fundal gastric varices (GOV 2) and large gastrosplenic shunt, thrombocytopenia. We have performed dorsal subsegmentectomy combined with Fundectomy and Periesophagogastric devascularization. She recovered well and was discharged after 14 days.

Case 2: Patient male 47 years old with diagnosis of HCC, recurrent esophageal bleeding (6 times in 2 years despite of NSBB treatment), thrombocytopenia. We have performed dorsal subsegmentectomy combined with Warren shunt. His esophageal varices rebled at POD 9 and treated by EBL. He recovered well and was discharged at POD 20.

Conclusion: Liver resection can combine with flow modulation surgery to treat for patient with HCC and GEV

Abstract Submission No. 100815
O-0918

Patients with Hepatosplenic Schistosomiasis who underwent Modified Sugiura Procedure: A Case Series

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Approximately 5% with schistosomiasis develop Hepatosplenic Schistosomiasis (HSS). It encompasses periportal fibrosis, portal hypertension, upper gastrointestinal bleeding (UGIB) due to variceal bleed, and

varying degrees of cytopenia and splenomegaly due to hypersplenism that poses significant morbidity and mortality.

From 2019 to 2023, four cases previously diagnosed and managed for Schistosomiasis presented with sudden onset hematemesis. Abdominal imaging studies showed splenomegaly with splenic index ranging from 1358 to 5184, with mass effect and displacement of bowels and left kidney. Laboratories revealed anemia, thrombocytopenia, and prolonged coagulation studies. UGIE showed Esophago-Gastric Varices and then started on Propranolol. Rectal biopsies showed Schistosomiasis ova. The patients underwent the Modified Sugiura procedure where post-procedure, all had rebound thrombocytosis controlled with hydroxyurea. Monitoring revealed resolution of anemia, thrombocytopenia and coagulation studies. Only one patient had recurrence of hematemesis controlled with rubber band ligation, and all subsequently had no recurrence of hematemesis.

HSS currently has no established guidelines for management. Available data suggest an interplay between medical therapy, variceal interventions, and surgical procedures. Medical management includes praziquantel especially in communities with high levels of transmission to prevent reinfection and Propranolol as primary and secondary prophylaxis for variceal bleeding. For patients with bleeding varices, treatment considerations include rubber band ligation, sclerotherapy, shunt surgical procedures, or devascularization with splenectomy. For patients with secondary hypersplenism, distal splenorenal shunt surgery or esophageal and gastric devascularization with splenectomy are surgical options. Potential benefits with carvedilol, transjugular intrahepatic portosystemic shunt, and spleen preserving procedures are options to be explored for future trials.

Abstract Submission No. 100851
O-0919

Atypical Nutcracker's Syndrome in Polycystic Liver Disease: A Case Report

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Background: The formation of esophago-gastric varices is a rare complication of polycystic liver disease (PLD) where the multiplicity of cysts leads to pseudo-cirrhosis and portal hypertension. However, these cysts may also lead to extrinsic vascular compression, wherein the nutcracker syndrome (NCS) is one of the rarest. We report an unusual case of a PLD patient who presented with bleeding gastric varices due to NCS.

Case Presentation: A 67-year-old female with innumerable large hepatic cysts due to PLD presented with a 3-day history of melena. An esophagogastroduodenoscopy revealed a large isolated gastric fundal varix with stigmata of recent bleeding. A total of 1.5 ml. of cyanoacrylate was injected with hemostasis adequately achieved. The patient was sent home with carvedilol. However, patient had recurrence of melena after 1 month. Repeat esophagogastroduodenoscopy showed the same findings with no diminution of the size of the varices. Repeat 2.5 ml. cyanoacrylate injection was successfully performed. A triphasic computed tomography scan of the abdomen showed a non-dilated portal vein but with extrinsic compression of the left renal vein by the superior mesenteric artery, caused by downward pressure from the cysts, leading to the formation of a gastro-renal shunt and gastric varices. A multidisciplinary conference was convened where a comprehensive strategy involving the placement of coils with subsequent

balloon-occluded retrograde transvenous obliteration was offered to the patient.

Conclusion: The rare coexistence of PLD and NCS presents substantial challenges in diagnosis and management. An effective multidisciplinary collaboration underscores the significance of a comprehensive approach when addressing this condition.

Abstract Submission No. 100861

O-0920

Mother to child transmission of HBV - Role of birth-dose and HBIG for prevention

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We report a case of vertical transmission of HBV from the mother to 3/4 of her children and how the child who received neonatal immunoprophylaxis escaped infection.

A 26-year-old housewife gave birth to her first child "A" via emergency C-section. She was tested for HBV and HCV as a part of pre-operative screening where she tested negative.

During routine antenatal visit to the hospital for her second pregnancy, she tested positive for HBV. The child "S" was given Hepatitis B Birth-dose and Hepatitis B Immunoglobulin (IVIG) right after normal vaginal delivery.

She gave birth to the third child "I", 4 years ago at the hospital. No postpartum intervention for preventing the vertical transmission was done.

Her youngest child "M" was born at home 6 months ago. She was prescribed Tenofovir disoproxil 350mg during pregnancy. No postpartum intervention for protecting the child was done.

Frontline workers screened the family and found the mother positive for HBV as well as 3 of the 4 children.

Conclusion: The probable source of the mother and the first child "A" acquiring HBV is the C-section surgery. Mother gave birth to 3 more children. The only child who did not acquire the infection was the one who received neonatal immunoprophylaxis.

Although during one of the pregnancies, the mother received antiviral tenofovir, it did not prevent the vertical transmission to that child in absence of birth-dose and HBIG.

This highlights the value of antenatal screening and at-birth intervention for preventing the vertical transmission of HBV.

Abstract Submission No. 100896

O-0921

SUCCESSFUL DOWNSTAGING OF HEPATOCELLULAR CARCINOMA WITH IMMUNOTHERAPY

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A 63-year-old businessman, from Tamil Nadu, with comorbidities of **Diabetes Mellitus, Systemic Hypertension** for 20 years and had history of **NASH related cirrhosis for 10 years** with preserved liver

synthetic function (Child A). Patient underwent prophylactic endoscopic variceal ligation twice and has been on beta blockers.

In Dec 2021, he presented with mild **right upper quadrant pain, excessive fatigue and weight loss of 10 kgs** over two months. On clinical examination, he was stable with no signs of decompensation and performance status of 0.

On evaluation, AFP was elevated- 16345 IU/L. CT abdomen revealed ill-defined, **9.2 x 7.5 x 6.3 cm** enhancing lesion- **Suggestive of HCC.**

Right and main portal venous thrombosis, Cirrhosis of liver with portal hypertension.

After multidisciplinary team discussion, he underwent Trans arterial chemo embolization and was started on Lenvatinib. Follow up imaging showed stable disease and patient was continued on Lenvatinib.

In May 2022, PET CT revealed uptake along the edges of the lesion and patient underwent second TACE. Lenvatinib could not be continued further due to intolerance.

Patient was switched over to immunotherapy with atezolizumab 1200mg and bevacizumab 900mg for 11 cycles once in every three weeks. Following initiation of immunotherapy, AFP reduced gradually from 10820 IU/L to 834 IU/L.

Thus, successful downstaging was achieved in this patient with overall survival till date being 487 days. Patient is continued on immunotherapy and recent PET CT showed no active lesions and no uptake within portal vein thrombus.

Abstract Submission No. 100924

O-0922

Malignant Hepatic Solitary Fibrous Tumor in a 28- year old Filipino male : A Case Report

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Background: Hepatic Solitary fibrous tumor (HSFT) is a rare mesenchymal tumor with few cases reported in literature. Malignant cases of HSFT are even rarer occurrence, and information regarding the optimal management of the disease is currently limited. We present a case of an unresectable malignant giant HSFT in a 28-year old male.

Case Presentation: A 28-year old Filipino male with no known comorbidities sought consult for right upper quadrant pain and weight loss for three months. Whole abdomen ultrasound showed a large predominantly solid mass. Dynamic CT showed a large heterogeneously enhancing mass almost occupying the entire liver with incomplete washout on portovenous and delayed phases.

Serum AFP and CA 19-9 were unremarkable. Liver biopsy revealed a poorly differentiated malignancy with epithelioid features. Immunohistochemical staining were positive for CD34 and STAT6 clinching the diagnosis of solitary fibrous tumor. Multidisciplinary approach with referrals to hepatobiliary surgeon and oncologist was done. Tumor was deemed unresectable and patient was offered tyrosine kinase inhibitor for possible downstaging.

Conclusion: HSFT is a rare tumor and should be included in the differential diagnosis of liver lesions with atypical imaging findings. The best choice for treatment is complete surgical resection but for massive HSFT with limited hepatic residual volume, strategies to increase the resectability of the tumor is deemed important. More data are needed for unresectable HSFT and long-term follow-up is critical.

Keywords: case report; hepatic solitary fibrous tumor;

Abstract Submission No. 101090

O-0923

AN UNUSUAL SYNERGY WITH DEPLETING ENERGY**Deepa Janakiraman¹, Nirmala Dheivamani¹, Sindhuja TA¹, Senthil Kumar R¹, Winston Thomas¹**¹Department of Paediatric Gastroenterology, MADRAS MEDICAL COLLEGE, INSTITUTE OF CHILD HEALTH, CHENNAI, TAMIL NADU, INDIA CHENNAI India**Introduction:** Cryptogenic cirrhosis is now replaced by various genetic diagnoses, considerably bringing down the percentage of cryptogenic cirrhosis from 30% to 9%. Genetic basis should be suspected in multisystem involvement.**CASE REPORT:** 12year old, 3rdborn male child of 3rddegree consanguinity, presented with abdominal distension for one month, jaundice and easy fatigability for 10days. Child had ascites, mild hepatic encephalopathy, INR 2.5, high SAAG low protein ascites and oesophageal varices on endoscopy suggestive of DCLD with portal-hypertension. Workup for Wilson, autoimmune and infective aetiologies were negative. Child was registered for liver transplantation(LT). But within 15days of discharge, readmitted with Right Hemiparesis, left UMN facial palsy and bilateral ptosis suggesting nonvascular territory metabolic stroke. MRI showed diffuse diffusion restriction suggesting mitochondrial leuko-encephalopathy. Lactate was also elevated, hence diagnosis of Mitochondrial DNA Depletion syndrome (MPV17 related) was suspected, further confirmed with exome sequencing and managed with mitochondrial cocktail.**DISCUSSION AND CLINICAL SIGNIFICANCE:** Of the 100 MPV17 related hepatoencephalopathy cases reported till date, 96% has infantile onset, while only 4% had childhood onset. None of the childhood onset had liver failure. To our knowledge ours is the 1stcase of childhood onset Mitochondrial DNA depletion syndrome-6 with DCLD. Onset of neurological involvement precludes the option of LT for this child.In the era of genomics, **thorough evaluation including genetic testing for definitive aetiology of cryptogenic cirrhosis is warranted before proceeding for LT.** In multi-system involvement, especially metabolic stroke with DCLD mitochondrial disease should be considered even in childhood.

Abstract Submission No. 101218

O-0924

EBV+ lymphoepithelioma-like cholangiocarcinoma in a woman with HBV treated by MWA: A case report**Lanxia Zhang¹, Qingjing Zeng¹, Xuqi He¹, Yuxuan Wu¹, Guanghui Guo¹, Kai Li¹**¹Department of Ultrasound, The Third Affiliated Hospital of Sun Yat-sen University Guangzhou China**Background:** Lymphoepithelioma-like cholangiocarcinoma (LELCC), a rare subtype of carcinoma, has the same immunophenotype as intrahepatic cholangiocarcinoma. Some are associated with EBV infection. It cannot be diagnosed without pathology because of its atypical image feature. The main treatment method is surgery.**Methods:** A 28-year-old HBV+ Asian female was found to have a 12*8 mm hypoechoic lesion with no obvious blood flow signals in her liver during a health checkup at our hospital. She had no signs or symptoms. Contrast-enhanced ultrasonography (CEUS) revealed hyperenhancement in the arterial phase, and hypoenhancement in the portal and delayed phases. She underwent ultrasound-guided radiofrequency ablation without biopsy at another hospital. CEUS revealed a 10*10 mm hyperenhanced lesion next to the ablation zone in the arterial phase 8 months later. The portal and delayed phases showed

hypoenhancement. Imaging fusion of the MRI scans before and after the first ablation revealed a residual tumor, for the latter lesion completely overlapped with the primary. Ultrasound-guided Microwave ablation (MWA) was performed.

Results: The biopsy specimen examination showed EBV+ LELCC. No recurrence was found during one and a half years follow-up.**Conclusions:** Imaging fusion is useful to diagnose residual tumor or local tumor progression. MWA may play a role in the treatment of LELCC.

Abstract Submission No. 101235

O-0925

A Case Report of Giant Cavernous Hepatic Hemangioma with Kasabach-Merritt Syndrome**Areangela Angeles¹, Jose Gullain E. Cataluna¹, Jemimah P. Fajardo¹**¹St. Luke's Medical Center, Quezon City Quezon City Philippines

Cavernous hepatic hemangiomas are hypervascular, venous malformations which is considered as the most common benign mesenchymal lesions of the liver. The rate of spontaneous rupture ranges from 1% to 4%, occurring mostly in giant hemangiomas (6-25 cm), with a mortality rate that can reach up to 75%. The operative mortality rate of this complication is around 36.4%.

This is a case of a 22-year-old male with no known co-morbid illness with unremarkable family history and personal social history who presented for progressive sharp and stabbing abdominal pain. Laboratory examination showed anemia (Hgb 8.8), leukocytosis (WBC 10930), thrombocytopenia (58k). Whole Abdominal CT scan with intravenous contrast revealed a large heterogeneously predominantly hypodense exophytic right hepatic lobe mass (14x11.8x16.8cm) considering hemangioma with intratumoral bleed.

Patient underwent Hepatic Angiogram with Gel and particle embolization of the branches of the right hepatic artery to control the bleeding, and blood transfusion. However, repeat Dynamic CT scan of the liver showed liver enlargement and progression of heterogenous non-enhancing lobulated exophytic mass lesion (15.3x12.6x19.8cm previously 14x11.8x16.8cm) with signs of bleeding and increase in hyperdense fluid collection relating to hemoperitoneum. Thus, the patient underwent Exploratory laparotomy with Evacuation of Intraperitoneal Hematoma, Right Hepatectomy with Cholecystectomy on the background of adequate Functional Liver Reserve by Liver Volumetric Study.

On the third day post operatively, patient developed Pneumonia and recurrent Pleural Effusion with subsequent thoracentesis and pigtail drainage. Medical management resulted to marked improvement of the signs and symptoms and was subsequently discharged well.

Abstract Submission No. 101259

O-0926

A case of HCC with a remarkable response following of durvalumab/tremelimumab after systemic therapy**TAKAYOSHI OIKAWA¹, Hidekatsu Kuroda¹, Asami Ito¹, Ippeki Nakaya¹, Hiroaki Abe¹, Tamami Abe¹, Akiko Suzuki¹, Kei Endo¹, Yuichi Yoshida¹, Keisuke Kakisaka¹, Akio Miyasaka¹, Takayuki Matsumoto¹**¹Division of Gastroenterology and Hepatology, Department of Internal Medicine, Iwate Medical University Yahaba-cho Japan

Introduction: Durvalumab plus tremelimumab (DUR/TRE) is a new first-line treatment that combines immune checkpoint inhibitors for hepatocellular carcinoma (HCC) and is available worldwide. We herein report a case of HCC with a remarkable response to DUR/TRE as fourth-line treatment.

Case: A 76-year-old woman with chronic hepatitis B underwent radiofrequency ablation for HCC in 201X. In December 2021, a metastatic nodule was found on the subxiphoid process of the puncture route for ablation therapy. The patient underwent a computed tomography (CT)-guided tumor biopsy for a pathological examination and surgical treatment in February 2022. Subsequently, multiple lung metastases and peritoneal dissemination appeared, and she received sequential treatment with atezolizumab plus bevacizumab, lenvatinib, and sorafenib; however, disease progression was observed. The patient underwent DUR/TRE in April 2023. After three courses of DUR/TRE, a prominent tumor reduction was observed on CT. No adverse events were observed.

DISCUSSION: This patient did not respond to anti-PD-L1 antibody or a VEGF inhibitor but did respond to post-treatment DUR/TRE, suggesting that the anti-tumor effect of anti-CTLA-4 antibody was a possible response factor. In addition, the behavior of AFP suggests that tumor shrinkage may have been achieved early in the treatment period.

Conclusion: Combination therapy with anti-CTLA-4 antibody may be effective in the post-treatment of patients who have failed systemic treatment with anti-PD-L1 antibody or a multi-tyrosine kinase inhibitor.

Abstract Submission No. 101285

O-0927

A Case of Hepatocellular Carcinoma 37 Years after Surgery for Truncus Arteriosus

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Background: Patients who have undergone the Fontan procedure have been reported to develop Fontan-associated liver disease (FALD). However, reports of liver disease following other pediatric congenital heart disease surgeries are relatively rare.

Case Presentation: The patient is a 38-year-old male diagnosed with truncus arteriosus at 8 months of age and underwent the Rastelli procedure which connects the right ventricle to the pulmonary artery and patches the ventricular septal defect. At 38 years of age, he developed a 5 cm hepatocellular carcinoma (HCC) located in segment 3(S3) of the liver diagnosed by several contrast enhanced examination. Consequently, the patient underwent left hepatic lobectomy. However, he developed recurrent HCC six months after the surgery, followed by a total of six recurrences within two years post-surgery.

Conclusion: In patients with FALD, liver disease is thought to arise from chronic congestion due to elevated central venous pressure (CVP), a condition not typically seen after the Rastelli procedure, where CVP is managed through periodic right ventricular outflow tract reconstructions. In this case, although there was no noticeable elevation of liver enzymes, multiple HCC recurrences suggest a high potential for carcinogenesis, similar to FALD. A 1-year survival rate for

HCC associated with FALD has been reported as 50% (Int J Cardiol 2021). It implies that HCC surveillance might be necessary not only for FALD patients but also for certain other types of postoperative congenital heart disease cases.

Abstract Submission No. 101315

O-0928

Recurrence Of Myopathy After Liver Transplantation For Patients With End-Stage GSD Type IIIa

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Glycogen storage disease (GSD) is a hereditary metabolic disorder of glycogen metabolism. The total incidence of GSD is 1/20,000-43,000. Based on enzyme deficiency and affected tissues, GSD is divided into 12 types. Most patients with Type III GSD present disease in both the liver and muscles (referred to as Type IIIa), and 15% of patients have the disease restricted to just the liver (referred to as Type IIIb). We report here a case of a 28-year-old female patient with Type IIIa GSD. As the disease progressed to decompensated cirrhosis, she had a rupture of esophageal varicose veins with bleeding and a large amount of ascites. She underwent orthotopic liver transplantation (DCD) in our hospital at the age of 23. After the treatment, the patient's signs of cirrhosis completely disappeared. However, six months ago, she presented with elevations in creatine kinase and occasional weakness in both lower limbs after exertion. Therefore, we improved coronary CTA, echocardiography, electromyography and other examinations, no obvious exception is displayed. Although cases of recurrence of myopathy due to cyclosporine administration have been reported internationally, this patient was on long-term oral tacrolimus. Creatine kinase showed a downward trend after oral administration of Coenzyme Q12. Our center will continue to follow this patient. This case warns us that a liver transplant cannot completely cure patients with type IIIa, and close follow-up is still needed after the operation.

Abstract Submission No. 101468

O-0929

A Thirteen-years-old Child with Acute Pancreatitis and STEMI Mimics - A Diagnostic Dilemma

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Background: Infection is a very rare cause of acute pancreatitis (AP). AP may cause various ECG changes and simulating acute STEMI (pseudo-MI) is a very rare presentation. To our knowledge, simultaneous acute pancreatitis and acute myocarditis due to infection is seldomly reported in the literature.

Case synopsis: A 13 years child without any co-morbidity presented with fever, abdominal pain and chest pain. Severe AP was diagnosed on the background of typical abdominal pain, raised lipase and CT scan of abdomen. She was transferred to Coronary Care Unit due to acute severe chest pain. Examination revealed pulse- 180/min, cold periphery, B.P- 80/50 mm Hg, diffuse abdominal tenderness, bilateral basal crepitations. ECG showed STEMI, and she had raised troponin-I, NT ProBNP. Echocardiogram revealed regional wall motion abnormality with LVEF- 35%. She was treated conservatively and coronary

angiogram revealed normal epicardial coronary arteries. Her follow-up echocardiography showed reduced ejection fraction and no further attack of AP. Her common etiology for pancreatitis was negative. As she had both pancreatitis and myocarditis, we thought the cause was infection as she had fever, leukocytosis and raised inflammatory markers. (Though we could not prove the infective etiology of AP by serology/ PCR due to limited resource).

Discussion: AP may cause ST elevation mimicking STEMI. Myocarditis also causes chest pain, arrhythmia, myocardial injury and ECG changes mimicking acute MI. This was a very rare case simultaneous acute pancreatitis and myocarditis, hepatitis and multi organ failure.

Conclusion: Clinicians should be aware that AP can mimic acute myocardial infarction/myocarditis.

Abstract Submission No. 101539

O-0930

Long-term follow up of patient with occurrence of autoimmune hepatitis post-COVID-19 vaccination

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Case: 50S, male. Chief complaint: general fatigue, dark urine. History: He regularly went to the local doctor for his allergic dermatitis. He also had allergy to contrast media and alcohol. He did not receive any transfusion or surgery. He does not have any tattoos or drug abuse. Present illness: He never had abnormal liver function tests before. After one or 2 weeks of 2nd-COVID-19 vaccination (COMIRNATY), he felt fatigue or admitted dark urine, respectively, and visited his local doctor. He was then introduced and admitted to our department for the examination of his abnormal liver function tests. Laboratory data on admission were: AST, 150 IU/L; ALT, 831 IU/L; total bilirubin, 9.81 mg/dL; PT 77%; INR 1.16; ESR 31 mm/hr; IgG, 2200 mg/dL; and anti-nuclear, 40-fold. Viral hepatitis markers and autoantibodies were negative. After 9 days of admission, liver biopsy was performed and liver histology indicated the compatible to autoimmune hepatitis (AIH), acute form. Despite of negative drug lymphocyte stimulation test to COVID-19 vaccine, AIH was confirmed by 16 points based on the international scoring system (1999). After 13 days, 60 mg daily of prednisolone was started and his liver function tests returned to within normal limits. After 2 years of onset, AST, 15 IU/L; ALT, 14 IU/L and IgG, 1451 mg/dL without any medication.

Conclusion: Patient with occurrence of AIH post-COVID-19 vaccination was followed up for almost two years and seems to have better prognosis with transient prednisolone administration. Further studies on this regard will be needed.

Abstract Submission No. 101549

O-0931

Walled-off Necrosis after Total Aortic Arch Replacement Treated Successfully by EUS-guided Drainage

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Background: Acute pancreatitis and walled-off necrosis (WON) are rare and fatal complications of thoracic and thoracoabdominal aortic aneurysm surgery. Considering the poor general condition of the post-operative patient, less invasive treatments are favorable. We experienced a case of WON secondary to a total arch replacement successfully treated with endoscopic ultrasound (EUS)-guided drainage.

Case Report: A 67-year-old man was referred to our hospital for the treatment of WON after acute pancreatitis. He had undergone total aortic arch replacement due to aortic arch aneurysm and coronary artery bypass grafting due to angina pectoris 6 weeks ago in a previous hospital. On the second postoperative day, he had developed acute pancreatitis. Although conservative management (antibiotics, hydration, etc.) relieved the symptoms of acute pancreatitis, the peripancreatic fluid collection remained, accompanied by duodenal obstruction and vomiting. Contrast-enhanced computed tomography showed that heterogeneous enhancement and fluid collection in the pancreatic body and tail had increased, consistent with WON. Even after 6 weeks of conservative management, the WON was not resolved, so we performed EUS-guided transluminal drainage with a 19-gauge EUS-FNA needle (EZ Shot3 Plus; Olympus) and a 7-Fr 4-cm double pigtail plastic stent (Zimmon; COOK MEDICAL), and a 6-Fr pigtail nasal drainage tube (Flexima; Boston Scientific). Then, CRP improved, however, his upper abdominal pain remained. Together with additional stents, the WON resolved gradually and his pain and oral intake had improved.

Conclusions: To the best of our knowledge, this is the first case of WON after aortic surgery treated with EUS-guided transluminal drainage for WON.

Abstract Submission No. 101566

O-0932

Acute liver injury and bilateral pulmonary artery thrombosis due to Hypereosinophilic syndrome

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Background: Hypereosinophilic syndrome (HES) is a leukoproliferative disorder characterized by marked eosinophilia of unknown origin and organ damage due to tissue eosinophilia. Organ infiltration of eosinophils includes lymph nodes, skin, gastrointestinal tract, lungs, and liver, and acute hepatitis may occur if the liver is infiltrated. Venous thromboembolism (VTE) is a complication of HES, affecting approximately 25% of patients with HES and with a mortality rate of 5-10%. We herein report a case of HES with acute liver injury and bilateral PE associated with DVT.

Case presentation: A 46-year-old Japanese man was referred to our hospital because of a marked increase in eosinophils (22,870/ μ L) and elevated liver enzymes. A decrease in platelets and prothrombin time (PT, %) and an increase in fibrin were noted. Computed tomography (CT) showed thrombi of approximately 8 cm in both femoral veins. A bone marrow puncture examination revealed normal morphology of the eosinophilia with slightly hyperplastic bone marrow. A liver biopsy revealed eosinophilic infiltration, hepatocyte necrosis, fibrosis and multiple thrombi. We suspected acute liver injury and DVT associated with HES, and started treatment with steroids and heparin. Four days

after the start of treatment, sudden chest pain and cardiopulmonary arrest occurred. CT revealed bilateral pulmonary artery thrombosis, and though tissue plasminogen activator was administered, the patient died. **Discussion/Conclusion:** In the treatment of HES, it is important to examine for liver injury and DVT, and it is suggested that thrombi may lead to PE and should be evaluated and treated immediately and appropriately.

Abstract Submission No. 101892
O-0933

How to manage HCC patients with high-risk PE and high-risk bleeding: can we perform thrombolysis?

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Background: Acute pulmonary embolism (PE) as the first sign of hepatocellular carcinoma (HCC) is a rare condition with high morbidity and mortality. Thrombus formation in hepatic vein is a marker of an advanced stage. Patients with high-risk PE require immediate reperfusion. Thrombolysis can be done quickly and easily, but it can also cause serious complications, especially with a high risk of bleeding.

Case Illustration: A 45-year-old man went to a private hospital's ER with sudden shortness of breath (SOB). He was desaturated and shocked. Acute PE was diagnosed after bedside TTE in the ER revealed RV dysfunction. We continued with the CT examination and found a thrombus in the PA, and we discovered a mass in the liver. We assessed patients with high-risk PE and high-risk bleeding. Advanced liver disease is a contraindication to thrombolysis. The treatment options for this patient are surgical or CDT, but these are not available. We had to do thrombolysis under careful supervision and consider the risks and benefits. Thrombolysis was successful in stabilizing hemodynamics, but severe bleeding occurred after 24 hours. We treated the bleeding, and finally, the patient survived.

Conclusion: High-risk PE requires aggressive therapy, and advanced liver disease is a condition with a high risk of bleeding. If the bleeding risk is acceptable or we know how to treat bleeding complications, systemic thrombolysis should be considered. Patients treated with thrombolytic therapy show rapid improvement, which may lead to a lower rate of mortality and morbidity.

Abstract Submission No. 101934
O-0934

A case of type 1 diabetes complicated with nonalcoholic steatohepatitis and glycogenic hepatopathy

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Background: Nonalcoholic steatohepatitis (NASH) is a well-known complication of type 2 diabetes. By contrast, we report here a marked steatohepatitis patient who has a history of type 1 diabetes.

Case report: A 29-year-old male with liver damage was referred to our hospital. Six years ago, he started injecting insulin after suffering from acute onset type 1 diabetes. However, he could not continue his diet therapy and his HbA1c level was elevated by over 10%. One year later, the levels of liver enzymes were elevated. The ultrasound examination revealed fatty change of the liver. His alcohol intake was scarce and discontinuation of the drugs did not restore the data, and adversely the levels of liver enzymes were worsened. He was finally admitted to our hospital and both diet therapy and blood sugar control were strengthened. After his body weight fell by 3 kg from 90 (body mass index, 26), the liver enzyme levels started to decrease. The biopsy specimen of the liver showed the findings of NASH with mild fibrosis. In addition, the hepatocytes were strongly stained with PAS indicating massive glycogen deposit. Comprehensively, both NASH and glycogenic hepatopathy were thought to contribute to his liver damage. Five months later, the blood sugar level was well-controlled and the levels of liver enzymes were normalized.

Conclusions: If liver damage is seen in type 1 diabetes patients, both NASH and glycogenic hepatopathy should be considered.

Abstract Submission No. 101996
O-0935

Fibrolamellar Hepatocellular Carcinoma Treated with ALPPS: A Case Report

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Background: Fibrolamellar hepatocellular carcinoma (FL-HCC) is a rare subtype of HCC accounting for 1% of primary liver cancers. It occurs mostly in young adults without underlying liver disease and complete resection is the preferred treatment. However, most are greater than 10 cm at the time of diagnosis, making resection challenging. Associating Liver Partition and Portal Vein Ligation For Staged Hepatectomy (ALPPS), which involves deportalization and in-situ parenchymal transection to induce rapid liver growth, allows resection of extensive tumors within a shorter period of 1-2 weeks making it an attractive surgical option for FL-HCC.

Case Presentation: A 25-year-old male was admitted in our institution for planned hepatectomy. Nineteen months prior, patient presented with recurrent epigastric pain. CT scan showed a mass in liver segments 4B, 5 and 8 confirmed by biopsy to be Fibrolamellar HCC. He was optimized for surgery; underwent coil embolization, selective internal radiation therapy, and was maintained on Lenvatinib. However, surveillance imaging showed increase in the size of the mass hence salvage ALPPS surgery was contemplated. After stage 1 of ALPPS, he developed Ischemic Reperfusion Injury and Acute Kidney Injury. However, he was able to recover and successfully completed stage 2 of ALPPS.

Conclusions: Given the rarity of FL-HCC, efficacy of treatments aside from surgery has not been established yet. Therefore, early diagnosis and meticulous planning for surgical resection are imperative in its treatment. ALPPS can be considered in select FL-HCC patients, keeping in mind the risk of higher morbidity weighed against the higher completion rate for hepatectomy.

Abstract Submission No. 102069
O-0936

A20 haploinsufficiency complicated by autoimmune hepatitis

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Aim: A20 haploinsufficiency (HA20) is a recently described autoimmune-inflammatory disease that manifests symptoms similar to those of Bechet's disease. However, little is known about the involvement of the liver in HA20. Herein, we report a case of HA20 complicated by autoimmune hepatitis (AIH).

Case presentation: A 33-year-old woman was previously diagnosed with HA20 and chronic thyroiditis and was treated with prednisolone (PSL) (7.5 mg/day) and levothyroxine sodium hydrate (125 µg/day). She experienced general malaise and jaundice, and biochemical evaluation revealed elevated liver function with an aspartate aminotransferase level of 817 U/L, an alanine aminotransferase level of 833 U/L, and a total bilirubin of 8.3 mg/dL. Pathological evaluation of the liver biopsy revealed interface hepatitis and the patient was diagnosed with acute exacerbation of AIH. Upon increasing the PSL dose to 60 mg/day, the liver enzyme levels rapidly decreased. During tapering of PSL, azathioprine 50 mg/day was added, and there was no relapse of AIH with combination therapy of PSL 7 mg/day and azathioprine 50 mg/day.

Conclusion: This is the first report of biopsy-proven AIH in an Asian patient with HA20. This case has significant implications for the pathogenesis and treatment of AIH in patients with HA20.

Abstract Submission No. 200086
O-0937

Hematemesis Unveiling Gastric Tuberculosis: Emphasizing Diagnostic Value of Endoscopic Ultrasound

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In 2021, the Philippines ranked fourth globally in tuberculosis cases, with 650 individuals affected per 100,000, designating it as a high TB burden country. Gastric tuberculosis, though rare, poses diagnostic challenges due to clinical manifestations resembling more prevalent gastric pathologies. Gastrointestinal bleeding, typically associated with peptic ulcers, esophageal varices, or gastric malignancies, can occasionally indicate infectious processes like tuberculosis, especially in high-prevalence regions.

This report details the diagnostic journey of a 35-year-old male with recurrent hematemesis. Initial investigations, including upper gastrointestinal (GI) endoscopy and CT scans, failed to yield a definitive diagnosis. Subsequent GI endoscopy revealed a 2.0cm mucosal protrusion with a clean-based ulcer, emphasizing the importance of advanced diagnostic techniques like endoscopic ultrasound (EUS). EUS identified a hypoechoic lesion at the muscularis mucosa, with multiple hypoechoic lymph nodes. The fine-needle biopsy during EUS confirmed *Mycobacterium tuberculosis* (MTB) infection.

This case underscores the critical need for heightened clinical suspicion for gastric tuberculosis in patients with gastrointestinal bleeding when conventional diagnostic approaches fall short. It also highlights the significance of advanced diagnostic techniques like EUS for precise identification of submucosal lesions, potentially averting the need for more invasive measures such as resection. This report contributes to existing literature by emphasizing the value of a comprehensive diagnostic approach and the role of advanced imaging in accurately diagnosing gastric tuberculosis.

Abstract Submission No. 200113
O-0938

Eosinophilic Duodenitis with Concomitant Eosinophilic Esophagitis

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Eosinophilic esophagitis (EoE) and eosinophilic duodenitis, distinct inflammatory disorders affecting the esophagus and duodenum, present diagnostic challenge. This complexity is heightened when endoscopic findings in the duodenum are apparent while the esophagus remains visually unremarkable. Few reports discuss eosinophilic gastroenteritis with esophageal involvement, and esophageal lesions in eosinophilic gastroenteritis are relatively uncommon. Identifiable endoscopic features exist for eosinophilic gastroenteritis, yet a definitive diagnosis based solely on these are insufficient. This case underscores diagnostic intricacies and advocates for a comprehensive approach to accurately identify these conditions.

We present a 29-year-old male with asthma, experiencing episodic epigastric pain and tenderness with loose stools post-travel from Japan. Initial diagnostics revealed marked leucocytosis (19000/uL) and peripheral eosinophilia (18%) and normal fecalysis result. Ciprofloxacin and Metronidazole started yet symptoms persisted. Upper gastrointestinal endoscopy done, esophagus was unremarkable with multiple superficial duodenal ulcers seen. Biopsies confirmed severe eosinophilic infiltration in the duodenum (>100/hpf) and tissue eosinophilia in the esophagus (>70/hpf). Patient was prescribed with Fluticasone inhaler as swallow, 220mcg, 2 puffs twice a day with noted improvement on symptoms upon follow-up.

This clinical case highlights diagnostic challenges with eosinophilic gastrointestinal disorders. The unexpected finding of eosinophilic esophagitis in a patient primarily presenting with eosinophilic duodenitis emphasizes the importance of meticulous evaluation and targeted biopsies when clinical suspicion remains high. The successful response to inhaled corticosteroids further supports the eosinophilic nature of the observed mucosal pathology, contributing to the evolving understanding of these disorders and guiding clinicians toward a detailed diagnostic approach for improved patient management.

Abstract Submission No. 200126
O-0939

Salmonella Infection Manifesting as Typhoid Hepatitis: An Uncommon Presentation of Common Disease

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Background: Typhoid is an infection caused by *Salmonella typhi* which is transmitted through fecal-oral route, hence the high number of incidence in developing countries. As an enteric infection, typhoid typically manifests as fever with enterocolitis symptoms. Here we present an unusual case of typhoid infection with prominent acute hepatitis manifestations.

Case presentation: A 50-year-old man had been experiencing fever for one week with a right upper quadrant abdominal pain which worsened one day before admission. He reported no complaints of enterocolitis symptoms other than nausea and abdominal pain which were

misinterpreted with probable cholecystitis. Laboratory tests showed elevated liver enzymes $>3\times$ the upper limit of normal, slightly elevated bilirubin levels, and elevated alkaline phosphatase and gamma-glutamyl transferase level, demonstrating an R factor for mixed type liver injury. Empirical antibiotic was given, abdominal ultrasound and computed tomography were performed yet revealed no signs of biliary abnormality. However, periportal edema suggesting parenchymal liver disease was seen. Further tests showed negative results for hepatitis A, B, C and other causes of liver injury were excluded. After two days, fever was still relapsing and other possible causes of infections were investigated, in which IgM for Salmonella was tested positive, confirmed with a blood culture. Patient was then treated with the drug of choice for Salmonella and responded well to the treatment.

Conclusion: Typhoid hepatitis is an unusual presentation of typhoid infection, but still a matter to be considered especially in developing countries. Early recognition and prompt treatment should be done to prevent further complications.

Abstract Submission No. 100306

O-0940

Drug eluting nanoyarn integrated biliary metallic stents to prevent stent occlusion

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Background: Bile duct occlusion presents a significant therapeutic challenge and has serious clinical consequences including cholangitis and death. Biliary stenting using self-expanding metal stent (SEMS) is the current clinical practice to alleviate the obstruction in patients with malignant biliary obstruction (MBO). However, stent occlusion due to tumour in-growth or biliary sludge formation within the stent poses a significant challenge in maintaining stent patency. To achieve sustained palliative benefit of biliary stenting, both biliary sludge formation and tumour in-growth need to be addressed. In this study, we report the potential of a nanotechnology-driven strategy to provide localized drug elution for sustained durations on heparinized SEMS.

Methodology: Gemcitabine hydrochloride was incorporated within nanofibrous polymeric yarns of Polycaprolactone (PCL) and integrated with the heparinized SEMS. This Gemcitabine-laden nanoyarn integrated heparinized SEMS [Nanostent] was functional, akin to bare SEMS, when tested as per ASTM standards. In vivo safety and feasibility of Nanostents was evaluated by fluoroscopy guided endoscopic implantation in porcine bile ducts.

Results: In vitro drug release studies demonstrated its potential to elute Gemcitabine for a period of six months. Histological analysis proved stent patency up to six months, with minimal inflammation. The presence of Gemcitabine in blood was not detected, while remnant drug was present in the yarns on explanted stents even at 5 months, confirming sustained drug elution. Cholangitis was also not a significant issue in the animals with Nanostents.

Conclusion: This novel Nanostent could offer dual benefits of sustained drug elution and prolonged stent patency in MBO.

Abstract Submission No. 101035

O-0941

Sucralfate vs proton pump inhibitor(PPI) vs combination post esophageal variceal band ligation

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Background: Proton pump inhibitor (PPI) and sucralfate are commonly used for prophylaxis of post-endoscopic variceal band ligation (EVL) ulcer bleed. This study compares the outcomes of a combination of sucralfate and PPI vs sucralfate alone vs PPI alone post EVL. **Method:** This was a single-centre, single-blind randomized trial involving 300 patients undergoing EVL using a multiband ligation device (VGRIPP). Prior use of PPI or sucralfate, anticoagulation, renal insufficiency, pregnancy, and pre-existing esophageal ulcers on endoscopy were excluded. Patients were randomized in 3 arms (100 each): PPI (pantoprazole 40 mg bd) alone, and sucralfate (1 g qid) alone or sucralfate plus PPI combination. The endoscopy was repeated after 14 days of medications. The primary endpoint was post-EVL ulcer bleed. Secondary endpoints were chest pain and post-EVL ulcer.

Results: The mean age was 43.56 ± 13.14 years. 218 (72.6%) were males. The cause of portal hypertension was cirrhosis in 246 patients and non-cirrhotic portal hypertension in 54 patients. The mean number of bands applied per patient was 3. Post-EVL ulcer bleeding occurred in 9(3%) patients with no difference amongst the three arms. There was 1 (0.3%) ulcer bleed-related mortality. Post-EVL ulcers and chest pain were seen in 59(19.7%) and 45(15%) patients respectively which was similar in three arms.

Conclusion: There was no significant difference in post-EVL outcomes in the three arms.

Abstract Submission No. 101131

O-0942

Outcome of upper Gastrointestinal bleeding secondary to PUD : Experience from Karachi, Paskitan

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Objective: To determine the outcome of upper Gastrointestinal bleeding (UGIB) secondary to Peptic ulcer disease (PUD).

Study Significance: This study will provide the outcome of PUD causing UGIB.

Method: This was a Retrospective, cohort study conducted at Gastroenterology department of JPMC, Karachi from Jan. 2022 till Dec. 2022. All patients with UGIB were included in the study. The data obtained was analyzed on the statistical software SPSS version 23.

Result: Total 1098 patients with UGIB were evaluated, out of which 142(13%) patients had PUD. The mean age of patients was 53 ± 19 years, 97(68.3%) were male. Most common presenting symptom was hematemesis 117 (82.4%). Among risk factors, the most frequent association was found to be with use of Non-steroidal anti-inflammatory drugs (NSAIDS) 113 (79.6%). The most common endoscopic finding was of Forrest class (FC)-III ulcer.

Most commonly done endoscopic intervention was adrenaline sclerotherapy 19 (13.4%).

Rebleed occur in 20(14.1%). However, 6 (4.2%) presented with recurrent bleed. 15(12.6%), died at first week and one month mortality was 7 (4.9%).

Conclusion: PUD if not diagnosed and treated promptly can lead to serious complication like UGIB. Due to advent of interventional

endoscopy, UGIB Can be managed quite efficiently as compared to the past and mortality is expected to reduce.

Abstract Submission No. 101326
O-0943

A Large Stone in Neglected CBD Stent Treated with Single-Operator Cholangioscopy Guided Lithotripsy

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Biliary stent placement has become standard of care while facing benign biliary stricture after bile duct stone removal. Neglecting biliary stents prompts worries about enduring consequences. This report delivers prolonged impact, highlights clinical presentations, diagnostics and management. The goal is to remind clinician regarding complication of long term stent placement and the management needed to underwrent this condition.

A 69-year-old male presented to the Emergency Department with complaints of abdominal bloating, nausea, and vomiting persisting for the last 2 months. The patient had a history of post-cholecystectomy with a retained biliary stent for the past 2 years. The patient missed follow-up appointments, resulting in the stent remaining in place without scheduled removal. Vital signs were within normal limits, with slight tachycardia. Physical examination revealed icteric sclerae and epigastric tenderness. Pancreatic amylase was elevated at 169 U/L, lipase at 359 U/L, and bilirubin at 4.83 mg/dL. Ultrasound revealed proximal choledocholithiasis sized 2 cm in the common bile duct, resulting in intra- and extrahepatic bile duct dilation. A CBD stent was identified during the ultrasound examination. The patient underwent stent removal and lithotripsy using the single-operator cholangioscopy guided lithotripsy (SpyGlass system). Post-procedure, the patient's condition gradually improved, accompanied by a decline in pancreatic amylase and lipase levels (pancreatic amylase 100 U/L and lipase 214 U/L).

Conclusion: The removal of the stent and lithotripsy using the Spy-Glass system proved effective in managing choledocholithiasis in this patient with neglected biliary stent. This case highlights the importance of timely intervention to prevent ongoing complications.

Abstract Submission No. 101457
O-0944

Comparison of severity of pancreatitis with and without diclofenac sodium in post ERCP patients

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Objective: To compare the severity of pancreatitis after ERCP.

methods: Randomized controlled trial in which we enrolled 160 patients of either gender between age 20-70 years who presented with obstructive jaundice. Patients were divided into 2 groups. Group A was administered 75 mg of diclofenac sodium intramuscularly as an add on prophylactic therapy along with the standard treatment and Group B was administered with standard treatment alone. Patients were monitored for 48 hours for any complaint of abdominal pain and measurements of serum lipase and amylase at 4 and 24 hours after the procedure.

Results: At 4 hours : in group A patients mean serum amylase was 266.8 U/L $\pm$ 57.9 SD and it was 261.6 U/L $\pm$ 57.6 SD in group B patients (p=0.566). Mean serum lipase was 1061.1 U/L $\pm$ 279.3 SD in group A and it was 1018.6 U/L $\pm$ 281.5 SD in group B patients (p=0.345). At 24 hours: in group A patients mean serum amylase was 137.7 U/L $\pm$ 84.6 SD and it was 170.3 U/L $\pm$ 132.1 SD in group B patients (p=0.065). Mean serum lipase was 326.1 U/L $\pm$ 116.4 SD in group A and it was 362.1 U/L $\pm$ 137.2 SD in group B patients (p=0.071). PEP was 3.8% (n=3/80) in group A patients while it was 13.8% (n=11/80) patients in group B (p=0.025).

Conclusions: Efficacy of intramuscular diclofenac sodium for prophylaxis of post-ERCP pancreatitis was significantly better when compared with control group

Keywords: Diclofenac sodium, ERCP, post ERCP pancreatitis

Abstract Submission No. 200221
O-0945

A novel Hemostatic spray to tackle post-EVBL and post-Glue ulcer bleed patients

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Introduction: Post-EVBL ulcer bleed remains a dreaded complication with a high mortality rate (upto 50%). There have been usage of haemostatic techniques in various parts of the world, but none report high efficacy. We have formulated a novel technique of endoscopically delivering collagen powder to achieve haemostasis and wound healing in post-EVBL and post-Glue ulcer bleed patients

Aim:

Primary: To assess efficacy of collagen spray in achieving immediate haemostasis

Secondary: To assess efficacy of collagen spray in achieving ulcer resolution at week 3

Method: This is an interventional prospective single-centre study conducted over a 2-year period at VGM Hospital, India. Post -EVBL ulcers were graded as per the Jamwal and Sarin classification. We used endoscopically delivered collagen powder as the haemostatic agent. 37 patients were enrolled in a case-based manner. (21 post-EVBL ulcer, 16 post-glue ulcer). Endoscopic spraying of collagen powder was done and re-assessed in 48 hours. Surveillance endoscopy was done at week 3.

Results: We found that 92% of patients with the post- EVBL ulcer bleed and all patients with post-Glue therapy ulcers achieved complete haemostasis and ulcer resolution. Grades B, C and D of post- EVBL ulcers showed complete ulcer resolution, whereas Grade A ulcers showed no resolution. The spray did not show any side effects across the patient population.

Conclusion: The collagen spray offers a novel, safe and highly effective intervention to tackle post- EVBL and post-Glue ulcer bleed patients resulting in haemostasis and ulcer resolution in these otherwise difficult to tackle patient cohorts.

Abstract Submission No. 200267
O-0946

Risk Factor of severe adverse events with EUS-HGS

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Background: Although EUS-HGS is an effective alternative treatment to ERCP, there is a risk of severe adverse events. In this study, we evaluated the risk factors of severe adverse events with EUS-HGS. **Methods:** We retrospectively investigated the patients receiving with EUS-HGS from April 2017 to July 2023 at our hospital. The patients were divided into two groups, Group A; the patients with adverse events of Clavien-Dindo classification grade over III and Group B; the others. [Result] There are 192 cases in total, of which 24 are allocated into Group A and 168 into Group B. In patient factors, the ratio of male in group A is higher than group B. However, there is no significant difference with age, malignancy, performance status, ascites, antithrombotic drug, age adjusted Charlson Comorbidity Index (AA-CCI), Prognostic Nutritional Index (PNI). In procedural factors, the number of device replacements is higher in Group A than Group B. However, there is no significant difference with dilation of puncture needle, procedure time, metallic stent, diathermic sheath. Also, there are no difference in technical and clinical success rates. In multivariate analysis, high AA-CCI ($p=0.02$) and high number of device replacement ($p=0.01$) is revealed in risk factors.

Conclusion: We found that AA-CCI and device replacement were associated with severe adverse events. As many of the patients underwent EUS-HGS are elderly people with comorbidity, it is important to reduce the number of device replacement. In addition, for elderly patients with multiple comorbidities, sufficient preoperative explanation and postoperative management are necessary.

Abstract Submission No. 101485
O-0947

PRECUT PAPILLOTOMY vs. STANDARD SPHINCTEROTOMY REGARDING THE DURATION OF HOSPITALIZATION

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Background: Our aim in this study is to compare the ERCP procedures performed with the standard sphincterotomy or pre-cut incision techniques in terms of patients' hospitalization periods.

Methods: In this study, patients who applied to Ankara Training and Research Hospital internal medicine or gastroenterology outpatient clinic, or emergency service and who were referred to the ERCP unit with an ERCP indication after physical examination, biochemical and non-invasive examinations and who had underwent ERCP were retrospectively evaluated. The patients who were hospitalized after ERCP procedure were included in the study.

Results: In order to achieve standardization, 133 patients with naive papillae and normal biliary anatomy were included in the study. Successful cannulation was achieved in all patients. For cannulation, standard sphincterotomy was used in 109 (81.9%) cases, and pre-incision techniques were used in 24 (18.0%) cases. The total ERCP procedure time was significantly longer in pre-cut incision group compared with the standard sphincterotomy group. When the mean length of stay after the procedure of all cases with ERCP was evaluated, the hospitalization period of patients who underwent standard sphincterotomy was found to be statistically significantly lower than those who underwent pre-cut incision.

Conclusions: We believe that standard sphincterotomy should be preferred rather than pre-cut incision, if possible, and close follow-up would be beneficial in patients who underwent ERCP with the

diagnosis of choledocholithiasis in difficult cannulation situations. Elongated hospitalization periods and increased complication rates and antibiotic requirements should be kept in mind in patients if pre-cut incision is required.

Abstract Submission No. 101909
O-0948

Thromboelastography and the risk of major bleeding after endoscopic variceal treatment in cirrhosis

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Background: Gastroesophageal variceal bleeding (EGVB), a common complication of cirrhosis, is often treated by endoscopy. Thromboelastography (TEG) is a global viscoelastic test to evaluate the hemostatic status of cirrhotic patients. However, it is unclear about whether TEG can predict the risk of major bleeding after endoscopic variceal treatment in cirrhotic patients.

Methods: All cirrhotic patients who were consecutively admitted to the General Hospital of Northern Theater Command from August 2018 to August 2022 and underwent endoscopic variceal treatment and TEG test were retrospectively screened. According to the development of major bleeding after endoscopic variceal treatment, patients were divided into major bleeding group and non-major bleeding group. Logistic regression analyses were conducted to explore whether TEG parameters were significantly associated with the risk of major bleeding after endoscopic variceal treatment. Odds ratios (ORs) with their 95% confidence intervals (95% CIs) were calculated.

Results: Overall, 108 cirrhotic patients were included. Multivariate logistic regression analyses showed that only Child-Pugh class (A/B vs. C) ($OR=0.053$; $95\%CI=0.006-0.441$, $p=0.007$) was independently associated with the risk of major bleeding after endoscopic variceal treatment. However, reaction time (R) (6.38 minutes vs. 6.35 minutes, $p=0.180$), coagulation time (K) (2.77 minutes vs. 3.16 minutes, $p=0.778$), angle (α) (63.07 degrees vs. 59.67 degrees, $p=0.328$), and maximum amplitude (MA) (51.70 mm vs. 49.00 mm, $p=0.459$) were not significantly different between major and non-major bleeding groups.

Conclusions: Major bleeding after endoscopic variceal treatment cannot be predicted by TEG parameters, but the severity of cirrhosis.

Abstract Submission No. 200238

O-0949

Experience with intraductal RFA for neoplasms of the major duodenal papilla with intraductal spread.

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Relevance: Due to the high risk of malignancy, all adenomas of the major duodenal papilla(MDP) must be removed. Currently, the method of choice for adenomas of the MDP is intraluminal endoscopic interventions, while neoplasms of the MDP with intraductal spread (types III and IV according to the classification typing of adenomas of the MDP) are particularly difficult for endoscopic techniques. The introduction of intraductal radiofrequency ablation into clinical practice

provides new opportunities for minimally invasive treatment of patients with adenomas of the MDP, including those with extensive spread to the bile ducts.

Material and methods: From 2022 to 2023, 11 patients with adenomas of the MDP with extension to the CBD and/or MPD underwent intraductal radiofrequency ablation. The extent of spread to the CBD ranged from 10 to 30mm, to the MPD-from 5 to 11mm.

Results: Technical success was achieved in all observations. Complications after performing intraductal RFA were noted in 4 cases: in 2 cases, post-manipulation pancreatitis developed, and in another 2 cases, during control cholangioscopy, residual adenomatous growths were revealed, and therefore these patients required a repeat session of intraductal RFA. Technical implementation of stenting of the MPD and CBD was achieved in all cases.

Conclusion: The use of intraductal RFA in the treatment of patients with adenomas of the MDP, characterized by extensive spread to the ducts, made it possible in all cases to ensure complete destruction of the intraductal component of the tumor with a lasting clinical effect without the need for highly traumatic surgical intervention.

Abstract Submission No. 200239

O-0950

Results of endoscopic operations for adenomas of the major duodenal papilla

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Relevance: With the widespread introduction into clinical practice of modern highly informative methods of endoscopic examination, the incidence of neoplasms of the major duodenal papilla (MDP) has increased compared to the previous decade. Regardless of the presence of clinical manifestations, according to the majority of authors, adenomas of the MDP must be removed due to possible malignant transformation.

Material and methods: From 2005 to 2023 in the surgical endoscopic department of the National Medical Research Center of Surgery named after A.V. Vishnevsky comprehensively examined and operated on 149 patients with neoplasms of the major duodenal papilla. Of these, 134 patients underwent endoscopic interventions to remove tumors of the MDP.

Results: Radical removal of the adenoma of the major duodenal papilla was achieved in 90.5% of cases. Complications after endoscopic removal of adenomas were noted in 16.6% of cases: post-manipulation pancreatitis developed in 10 (7.9%) cases, bleeding developed in the postoperative period in 7 (5.5%) cases, and bleeding in another 4 (3.1%) cases. observations of perforation of the duodenal wall. During dynamic examination from 1 to 3 years, residual adenomatous growths were identified in 9.5% of cases.

Conclusion: The endoscopic classification of adenomas of the major duodenal papilla (Table 1) that we have developed allows us to determine the most effective and safe method of surgical intervention for each type of tumor by clearly defining the boundaries of the use of endoscopic technologies, as well as to unify the endoscopic description of the tumor to achieve continuity in monitoring patients by various specialists.

Abstract Submission No. 200240

O-0951

Endoscopic classification of neoplasms of the major duodenal papilla.

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Aim: Demonstrate the developed endoscopic classification of papillary tumors.

Material: at the surgical endoscopic department of the Surgical Endoscopy Department of the Vishnevsky National Research Medical Center for Surgery examined and treated 149 patients with papillary tumors.

Classification: Based on the analysis of research data from 149 patients, we have developed an endoscopic classification of papillary tumors, which consists of 4 types (table):

Type I (ExtraPapillary): a tumor with extrapapillary growth, localized within the papilla, without signs of spread to the duodenum and ducts.

Type II (ExtraPapillary+Duodenum): a tumor with extrapapillary growth and spread along the walls of the duodenum. Depending on the direction of tumor growth, 4 subtypes are distinguished: SP (Suprapapillary)-proximal from the papilla, IP (Intrapapillary)-distal from the papilla, LPR (LateroPapillary Right)-to the right of the papilla, LPL (LateroPapillary Left)-to the left of the papilla. There are also 2 additional subtypes: PD (Peri/Parapapillary Diverticulum)-on the walls of the para/peripapillary diverticulum, and IM (Invasion Muscle)-invasion into the muscular layer of the duodenal wall.

Type III (IntraDuctal): tumor with intraductal spread. Depending on the involvement of the ducts in the tumor process, 4 subtypes are distinguished: CBD-on the common bile duct, MPD-on the main pancreatic duct, IA-localized exclusively within the ampulla, subtype CBD+MPD-on both ducts.

Type IV (ExtraPapillary+IntraDuctal): tumors with mixed extrapapillary and intraductal growth, that is, a combination of types I and III, or II and III.

Conclusion: Endoscopic classification of papillary tumors allows us to determine the most effective and safe method of surgical intervention for each type of tumor.

Abstract Submission No. 100451

O-0952

Gut-Bone-Liver Axis: Interplay of Gut Microbiome and Myeloid Cells in MASLD

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Metabolic dysfunction-associated steatotic liver disease (MASLD) is a prevalent chronic liver condition affecting 32% of adults globally. Recent research suggests a link between disrupted gut microbiome and MASLD, but the exact causal relationship remains unclear. In this study, we hypothesize that gut microbiome mediates the progression of MASLD through its effects on bone marrow haematopoiesis.

A novel mouse model of MASLD utilising a refined diet, known as the Liver Disease Progression Aggravation Diet (LIDPAD), coupled with thermoneutral housing conditions was used. To deplete gut bacteria,

drinking water supplemented with a mixture of antibiotics were given ad libitum in one of the groups. Three groups of C57BL/6J mice were fed on regular chow diet, LIDPAD diet, and LIDPAD diet with antibiotics respectively, for a duration of 4 and 12 weeks. Liver disease severity was assessed using liver histology grading and plasma alanine transaminase (ALT) level. Immune cells in bone marrow, spleen and blood were profiled using flow cytometry.

The antibiotic-treated group exhibited reduced body weight, liver and visceral fat percentages compared to LIDPAD mice. Improved glucose and insulin tolerance, along with a decrease in MASLD severity, were observed in the antibiotic-treated group. These improvements associated with a reduction in bone marrow monocytes and their progenitors. In summary, we found that the gut microbiome accelerated the progression of MASLD partially through the mediation of bone marrow monocyte production. Targeting the gut microbiome has the potential to control chronic inflammation and become a new treatment approach for MASLD.

Abstract Submission No. 100636

O-0953

Compensatory metabolic regulation of gut microbiome by host immunity

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Background: Metabolites from bowel microbiota regulate both host immunity and metabolism. Short chain fatty acids, tryptophan, and bile acids are well-known examples. However, it is uncertain whether host immunity regulates the gut microbiome to benefit the metabolic needs of the host.

Methods: We employed mice with varying immunocompetence and exposed them to different diets to explore how these factors interact. Compositions of gut microbiome were examined with ribosomal 16S sequencing, and metagenomic functions were inferred and quantified from 16S-derived operational taxonomic units. Biochemical reactions and pathways were compared between different mouse strain-diet combinations.

Results: Although the fatty liver phenotype was exacerbated by host immunity, we found evidence of metabolic compensation occurring only in the gut microbiome of wild-type mice fed high-fat diet (HFD). A metabolic reaction involving S-adenosyl-L-methionine, a glutathione precursor and methyl donor for the host, is especially affected without host immunity. By integrating reactions into pathways, we further demonstrate metabolic compensation at the pathway level, which presents a distinctive profile in line with that observed in mice fed normal chow.

Conclusion: In brief, host immunity actively regulates the gut microbiome to compensate, manifesting gradually after continuous HFD exposure and causing results distinct from the steatosis-inducing effects in the liver.

Abstract Submission No. 100685

O-0954

Gut microbiota and metabolites dysbiosis of NASH-HCC and related neuropsychiatric disorders in mice

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Background: NASH-HCC and related neuropsychiatric disorders are crucial causes of impaired health quality of life and mortality of liver disease. This study focused on the role of gut-liver-brain axis in NASH-HCC and related anxiety-/depression-like behavior.

Methods: The NASH-HCC mice were established dynamically with Western diet plus CCl₄ intervention for 12 and 24 weeks. Body weight, liver enzymes, pro-inflammatory factors and degree of liver fibrosis /cancer were recorded in detail. Meanwhile, behavioral changes were tested by OFT, TST and RPT. Dynamic changes in gut microbiota and serum metabolites were further detected through 16S rRNA and untargeted metabolomics.

Results: NASH with stage 2.2 (± 0.4) fibrosis occurred at 12 weeks, and indicators such as TC, TG, AST, ALT, and pro-inflammatory factors (IL-6, IL-1 β , TNF- α) increased significantly. At 24 weeks, the degree of fibrosis worsened to stage 3 and 83% of mice had multiple tumors, with maximal size greater than 6 mm. Anxiety-/depression-like behaviors emerged at 12 weeks and pronounced at 24 weeks. Multi-omics analysis suggested *Faecalibaculum rodentium* significantly surged at 12 and 24 weeks, accompanied with increased serum Arachidonic acid, bile acids, DL-Carnitine, FAHFA (10:0/16:1), LPC (18:5), Uric acid, and decreased Linoleic Acid, Acetyl-L-carnitine, LPC (20:4) etc., which enriched in lipid metabolism and carbon metabolism. Spearman correlation analysis showed that microbiota and related metabolites was significantly correlated with the concentration of pro-inflammatory factors.

Conclusion: *Faecalibaculum rodentium* and related metabolites including Arachidonic acid, bile acids, FAHFA (10:0/16:1), Acetyl-L-carnitine etc. induced inflammation might be gut-liver-brain axis mechanism in NASH-HCC and related neuropsychiatric disorders.

Abstract Submission No. 100750

O-0955

Targeted Dietary Modulation of Gut Microbiome in An Animal Model of MASLD

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With a 32% global prevalence, metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease. Studies have highlighted gut microbial dysbiosis as an etiological factor of MASLD. Conversely, butyrate, a microbial-derived metabolite produced upon fibre fermentation, demonstrates ability to ameliorate MASLD. We hypothesize that specific dietary fibre supplementation can alleviate MASLD by targeted expansion of butyrate-producing gut bacteria.

We used a MASLD mouse model, housed in thermoneutral conditions and fed a defined Liver Disease Progression Aggravation Diet (LIDPAD). C57BL/6J mice received LIDPAD supplemented with 10% of different fibres - glucomannan, galactomannan, arabinoxylan and amylopectin, over 12 weeks. Cellulose, as a non-fermentable fibre control, and a calorie-matched control diet were also included. Disease severity was evaluated via liver histology and microbiome composition was analysed through 16S rRNA sequencing.

At 12 weeks, arabinoxylan- (25.07g vs 30.91g; $p < 0.0001$) and glucomannan-fed (28.16g vs 30.91g; $p = 0.0017$) mice had significantly lower body weights than those fed cellulose (Fig 1). Mice receiving arabinoxylan also showed significantly lower liver weight (0.86g vs

1.70g; $p < 0.0001$) and higher cecum weight (0.83g vs 0.3g; $p = 0.020$). Although no significant differences in overall liver histological scores were observed, the groups showed differences in gut microbiome composition, with the arabinoxylan group showing distinct β -diversity in principal component analysis (Fig 2). Fibre supplementation enriched butyrate-producing genera like *Clostridium* and *Bacteroides*, along with commensal bacteria like *Parabacteroides* (Fig 3). In conclusion, despite having negligible effect on MASLD, fibre supplementation changed the gut microbiome considerably, highlighting diet as an effective strategy for targeted microbiome modulation.

Abstract Submission No. 100844
O-0956

Dietary impact on gut permeability in MASLD

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Background: A breach in the gut barrier influences the progression of metabolic dysfunction-associated steatotic liver disease (MASLD), highlighting perturbed gut-liver communication. With no FDA-approved treatments, many dietary management strategies are recommended for MASLD patients. Yet, how these interventions affect gut and liver health remains unclear.

Methods: Male C57BL/6J mice (8 weeks) were subjected to either a diet reversion or inulin-supplemented MASH-inducing Liver Disease Progression Aggravation Diet (LIDPAD) regimen. Mice on diet reversion were initially fed LIDPAD for 4 weeks and then switched to control diet for another 4 weeks (MAFL_R). Mice in inulin group received the LIDPAD along with 8% inulin-supplemented water. Both interventions were evaluated against their cognate LIDPAD and control groups. Following these dietary regimens, intestinal mucosal and liver samples underwent RNA-sequencing.

Results: MAFL_R mice lost an average of 12% in weight and showed improved glucose tolerance compared to mice that adhered to LIDPAD. While LIDPAD mice exhibited increased gut permeability and resulting hepatic steatosis, diet reversion diminished these effects, leading to decreased gut permeability and a reduction in hepatic lipid accumulation. Conversely, 8% inulin-supplemented diet did not lead to any weight loss or enhanced glucose tolerance. It also failed to improve gut permeability and no observable improvements in MASH compared with the LIDPAD-fed mice. Transcriptomic analyses of the intestinal mucosa and liver further supported these experimental findings on gut and liver health.

Conclusion: Our study indicates that improvement in gut barrier function correspond with enhanced liver health. Conversely, a disrupted gut barrier aligns with worsening liver conditions.

Abstract Submission No. 101207
O-0957

Multi-omics reveal microbial determinant impacting treatment response in primary biliary cholangitis

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Primary biliary cholangitis (PBC) is a chronic autoimmune liver disease, and inadequate response to ursodeoxycholic acid (UDCA) poses a high risk of progression towards liver cirrhosis. Alterations of gut microbiota has been implicated in PBC, but the functional changes and their clinical implications remain largely enigmatic. In this study, we performed integrated analyses of gut metagenomics, serum and fecal metabolomics in UDCA treatment-naïve PBC (n=132) compared with healthy controls (n=131). We defined compositional and functional dysbiosis in the PBC gut microbiome, including a characteristic decrease in Clostridia taxa and concordant changes in microbial enzymes and metabolite pools (e.g., cholesterol derivatives). Notably, PBC metagenomes clustered into two community types represented by varying abundances of Clostridia taxa. The *Clostridia*^{low} metacommunity indicated an unfavorable response to UDCA compared to the *Clostridia*^{high} metacommunity. Integrative analysis of metagenome and metabolome demonstrated a significant decrease of anti-inflammatory microbial activities (e.g., tryptophan metabolism and secondary bile acids) and a shift from fermentation to respiratory metabolism in the *Clostridia*^{low} metacommunity, indicating dysregulated immune responses and impaired intestinal barrier integrity. Furthermore, the *Clostridia*^{high} microbiome showed a more complex microbial co-abundance network and more pronounced microbe-host interactions. Finally, the association of microbial metacommunities and treatment response was validated in an independent cohort. Our study suggests that inter-individual variations in PBC gut microbiome may impact heterogeneity in therapeutic efficacy, highlighting the potential of using microbiota-based approach for personalized interventions.

Abstract Submission No. 101339
O-0958

The association of H Pylori infection with Minimal Hepatic Encephalopathy in Child A and B Cirrhosis

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INTRODUCTION: Hepatic encephalopathy includes a spectrum of transient and reversible neurological and psychiatric manifestations found in patients with chronic liver disease and portal hypertension. The least severe form of Hepatic Encephalopathy (HE), which is not recognized on clinical examination is Minimal hepatic encephalopathy (MHE) that profoundly impairs Health Related Quality of Life (HRQoL). This study aimed to estimate the proportion of MHE in patients with Child A & B Cirrhosis, the factors associated with MHE and the prevalence of H. pylori infection among them

METHODS: Cross-sectional study done among the patients diagnosed to have Child A & B cirrhosis. After baseline investigations and endoscopy, MHE was diagnosed by psychometric tests. H. pylori infection was identified by gastric biopsy.

RESULTS: Out of 260 patients included in our study, the prevalence of MHE in Child A & B cirrhotics was 60% (n=156). H pylori infection was found in 131 out of 260 patients. In patients with MHE, 98 patients (74.8%) had H pylori infection ($p < 0.001$), whereas 53 patients (51.5%) had H pylori infection in non-MHE group, which is statistically significant. MHE was more among Child B patients ($p = 0.01$). Among the factors influencing MHE, Frailty was found in 79% (n=83) with MHE ($p < 0.001$).

CONCLUSION: The burden of MHE is substantial in patients with cirrhosis with no apparent cognitive defect. This study proves that the prevalence of H pylori is significant in patients with MHE. Therefore, an additional benefit of H pylori eradication in the treatment of MHE in patients with Child A & B cirrhosis needs to be explored to identify the causative role of Hpylori in MHE.

Abstract Submission No. 101343

O-0959

Knowledge and awareness of probiotics dietary sources assessments: gut-liver axis in focus.

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Background & aims: Gut Microbiome (GM) dysbiosis is well known by their alternated compositions and activities that have been shown strong association to different human health problems such as chronic liver diseases (CLD). However, maintain a healthy gut could be achieved by healthy dietary pattern including prebiotics and probiotics dietary sources. This study aimed to measure the awareness and knowledge levels of probiotics dietary sources between Hepatology and Gastroenterology specialties comparing to chronic liver diseases patients (CLDP) visiting the national liver institute (NLI), Egypt additionally to CLDP nutritional assessment in association to their healthy gut.

Methods: A cross-sectional study in 4-armed questionnaires applied between 22 CLDP including anthropometric, Social-economic, health status and nutritional assessment (foods, dietary habits history & 24 hour recall) forms additionally to 42 doctors within their awareness & knowledge for probiotics dietary sources.

Results: Data illustrated lack of understanding and usage of probiotics dietary sources consumptions between CLDP and doctors whom do not fully understood the differences between the probiotics dietary sources thus increasing probiotic dietary sources awareness are needed not only for CLDP but also for doctors.

Conclusions: Educational awareness program with probiotics dietary sources should be raised at least once a month to the NLI visitors and the Egyptian healthcare experts/doctors with different photos additionally to clarifying their sources and roles within the GM association (gut-liver axis). However, much more probiotics dietary interventions are needed.

Abstract Submission No. 101405

O-0960

Intestinal permeability in cirrhosis: Correlation of biomarkers and urine polyethylene glycol

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Introduction: Increased intestinal permeability (IP) is the gateway to a cascade of events in cirrhosis. Polyethylene glycol (PEG) is an upcoming tool to assess IP. Zonulin and intestinal fatty acid binding protein (IFABP) are biomarkers of tight-junctions and epithelial damage. We aimed to evaluate and interrelate the biomarkers of gut integrity and PEG in cirrhosis.

Methodology: Cirrhotic children and controls (extrahepatic portal-venous obstruction) were prospectively enrolled. Five hours after ingestion of 1 gm/kg of PEG3350, urine was collected and processed by proton-nuclear magnetic resonance (¹H-NMR) spectroscopy to derive the integrated-PEG (I-PEG) value (area under the peak-curve). Serum intestinal fatty acid binding protein (IFABP) and zonulin were assessed on the same day. With the risk factors, a model was created to predict outcome in cirrhotics.

Results: Cirrhotic children (n=56) versus controls (n=35), aged (13.7±3.5 vs. 10.6±2.9 years, p=0.6) had I-PEG (12.9±5.1 vs 3.8±4.2, p=0.02), zonulin (96.6±24 vs 16.3±5.1 ng/mL, p<0.01) and IFABP (4.9±3.3 vs. 1.8±1.2 ng/mL, p<0.01). Among cirrhotics, I-PEG was significantly higher in decompensated (n=20) vs. recompensated (n=36) patients (11.8±7.1 vs 4.9±3.9, p=0.03) and large vs. small esophageal varices (12.4±4.8 vs 6.3±2.2, p=0.03). I-PEG correlated with IFABP (r=0.77, p<0.01), zonulin (r=0.88, p<0.01) and pediatric end-stage liver disease (PELD) score (r=0.67, p=0.03). Zonulin >25ng/mL (OR:3.08, CI:1.05-4.12, p< 0.01) and I-PEG>5 (OR:3.19, CI:2.2-7.73, p=0.01) were independent predictors of hospital readmissions over next 6 months. The risk factor model (AUROC:0.87, p<0.001, 92% sensitivity;60% specificity) predicted morbidity better than isolated PELD or Child-Turcotte-Pugh scores.

Conclusions: I-PEG and zonulin risk factor model predicts short-term morbidity in cirrhotic patients.

Abstract Submission No. 101602

O-0961

Antagonism of Gut *R. gnavus* and *A. muciniphila* Modulates the Clinical Course of Chronic Hepatitis B

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Delayed HBeAg seroconversion (HBe-SC) in patients with chronic hepatitis B (CHB) increases risk of progression to severe liver diseases. HBe-SC is mainly due to immune interaction between HBV and the host, but the details remain elusive. We hypothesized gut microbiota trigger the immune reactions to lead to HBe-SC through gut-liver axis. Patients with CHB (n=102) in different disease phases were recruited. HBV-hydrodynamic injection (HDI) mouse model was established. Multi-platform metabolomics assays were performed to explore the role of gut microbiota. *Ruminococcus gnavus* was found to be the most abundant in patients with immune-tolerance (IT) and poor response to antiviral treatments. *Akkemansia muciniphila* was highly enriched in patients who underwent HBe-SC in an immune-active (IA) state. This observation was proven by HBV-HDI mouse models in BALB/c, C57BL/6J, C3H/HeN and germ-free mice. Patients of IT phase demonstrated a higher level of cholesterol to bile acids (BAs) metabolism than those of IA phase. Outgrowth of *R. gnavus* prolonged HBV persistence via increasing BAs metabolism in mouse models. *R. gnavus* encoded bile salt hydrolase to deconjugate the primary BAs and control the total pool of BAs. *A. muciniphila* counteracted *R. gnavus* through *A. muciniphila*'s secretome metabolites, which comprised of small molecules structurally similar to apigenin, lovastatin, ribavirin etc., and their cholesterol-lowering, antibacterial and antiviral properties may finally lead to HBV elimination. In conclusion, *R. gnavus* and *A. muciniphila* play opposite roles in HBe-SC and the bacterial metabolites of *A. muciniphila* highlight the targets of future anti-HBV therapy.

Abstract Submission No. 101753
O-0962

The Novel Findings in Liver Ischemia-Reperfusion Injury - Fasting and Short-Chain Fatty Acids-

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Background: Liver ischemia-reperfusion injury (IRI) is an important issue to overcome in liver surgery and transplantation. Diet restriction has demonstrated the protective effects against several organs. Additionally, short-chain fatty acids (SCFAs), which are produced in intestinal environment by dietary fibers, have anti-inflammatory effects. This study aimed to reveal the impact of fasting and SCFAs in liver IRI.

Methods: We performed two different approaches to control liver IRI in mice by applying partial warm hepatic IRI model. Firstly, the 12-hour fasting was performed before IR setting. The control IR group was given food and water ad libitum, while the fasting IR group was only water for 12-hour before the IR insult. We also performed another experiment evaluating the impact of diet with SCFAs on liver IRI. Mice were fed either a control ordinary diet (CD) or an inulin diet (ID) for two weeks before the IR insult. We assessed for their impact on immune responses, liver damage and histological changes.

Results: IR induced-liver damage was significantly ameliorated in both the fasting IR group and ID group. Short-term fasting significantly upregulated Forkhead Box O1, induced by increased β -hydroxybutyric acid, leading to remarkable mitigation. In ID group, bacteroides acidifaciens was increased in feces, which resulted in the elevation of SCFAs such as propionate in the portal vein. Propionate administration before IR onset markedly improved liver IRI.

Conclusion: The changes of intestinal environment by preoperative short-term fasting or SCFAs might have significant influence in mitigation liver IRI. Our trials may offer potential clinical benefits.

Abstract Submission No. 100091
O-0963

Dysphagia impairs health-related quality of life in patients with chronic liver disease

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Aim: This study aimed to reveal the prevalence and characteristic of dysphagia, and its association with health-related quality of life (HRQOL) in patients with chronic liver disease (CLD).

Methods: This cross-sectional study included 335 outpatients with CLD in Gifu University Hospital. Dysphagia, sarcopenia risk, malnutrition risk, and HRQOL were assessed using the Eating Assessment

tool-10 (EAT-10), SARC-F, Royal Free Hospital-Nutrition Prioritizing Tool (RFH-NPT), and Chronic Liver Disease Questionnaire (CLDQ), respectively. Dysphagia and low HRQOL were based on EAT-10 ≥ 3 and CLDQ overall score < 5 , respectively. Factors associated with dysphagia and low HRQOL were assessed using the logistic regression model.

Results: The median age was 66 years, and 50% were male. Dysphagia and low HRQOL were observed in 10% and 31%, respectively. Patients with dysphagia were notably older, cirrhosis, had higher risk of sarcopenia and malnutrition, and demonstrated lower CLDQ overall score (median, 4.41 vs. 5.69; $p < 0.001$) than those without dysphagia. After adjustment, SARC-F (odds ratio [OR], 1.21; 95% confidence interval [CI], 1.00-1.46; $p = 0.048$) and RFH-NPT (OR, 1.72; 95% CI, 1.06-2.80; $p = 0.030$) were independently associated with dysphagia. As for HRQOL, EAT-10 (OR, 1.14; 95% CI, 1.03-1.27; $p = 0.012$) and SARC-F (OR, 1.39; 95% CI, 1.19-1.61; $p < 0.001$) were independently associated with low HRQOL.

Conclusion: Dysphagia was prevalent in approximately 10% of patients with CLD and associated with a risk of sarcopenia and malnutrition. Dysphagia screening is essential in daily practice as dysphagia impairs HRQOL in patients with CLD.

Abstract Submission No. 100105
O-0964

Mapping trends and hotspots in clinical research on bacterial infections in cirrhosis

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Background: Bacterial infection is the most common complication in cirrhosis patients. This study evaluated the research hotspots and trends of bacterial infections in cirrhosis through bibliometric analysis, and provides guidance for future research on bacterial infection in cirrhosis.

Methods: We extracted publications on bacterial infections associated with cirrhosis from the Web of Science Core Collection and Scopus databases, covering the period from inception to 2022. CiteSpace and VOSviewer were used for bibliometric analysis.

Results: Publications on bacterial infections in cirrhosis reflect an upward trend, with 60 countries/territories contributing to research, of which the U.S. ranks first with 151 publications. The Journal of Hepatology is the prime publication on liver cirrhosis associated with bacterial infections, Fernandez Javier being the most-cited author. Cirrhosis with bacterial infection is the most popular research topic regarding mortality, infection, ascites, spontaneous bacterial peritonitis and sepsis. The research hotspots of the future are systemic inflammation, acute decompensation of cirrhosis, acute-on-chronic liver failure and model.

Conclusion: The hotspots and trends of related research are discussed, and the research results are presented objectively through knowledge maps. The research directions in this field are analyzed to provide a reference for subsequent clinical research.

Abstract Submission No. 100159
O-0965

TREATMENT OF GI BLEEDING DUE TO PORTAL HYPERTENSION IN VIETNAM

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Introduction: Bleeding from esophageal varices still carries a significant mortality risk. Aim: Evaluate the treatment effectiveness of three treatment method: Endoscopic band ligation, transjugular intrahepatic portosystemic shunt (TIPS) and liver transplantation for cirrhotic patients with GI bleeding due to portal hypertension.

Patients & methods: Cirrhotic patients with GI bleeding were divided into three groups. Patients has complete records, clinical examination, rate of hemostasis and complications after treatment.

Results: * **Group of endoscopic band ligation (n = 178):** Age: 46.8; male/female: 3.9. Child-Pugh: 92%. Severe GI bleeding: 48.8%. Rate of hemostasis: 92.6%. Eradication of varices: 76.3%. Rate of rebleeding after 6 and 12 months, respectively 12.9% and 17.4%. * **Group of TIPS (n = 64):** Age: 49.5; male/female: 8/1. Child-Pugh: 92%. Number of GI bleeding: 4.3 (1-20 times). Rate of hemostasis: 98.5%; Rate of bleeding: 25%. Hepatic encephalopathy: 35.9%. Mortality: 20.3%. * **Group of liver transplantation (n = 17):** Age: 43.4; Male/female: 13/4. History: Number of ligation endoscopy: 3.9 times (3-6 times). Successful liver transplant: 17/17 (100%). No serious complication.

Conclusion: Liver transplantation is the ideal method for cirrhotic patients with GI bleeding due to portal hypertension.

Abstract Submission No. 100174
O-0966

Predictors of liver-related readmissions in cirrhotic patients: a retrospective study

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Background: Cirrhosis leads to a high risk of death and readmission as well as severe complications.

Methods: To research the predictors influencing cirrhotic patients' readmission, we conducted a retrospective study. Collecting sociodemographic, clinical, and hospitalization characteristics and defined the primary endpoint as the first liver-related readmission occurring within 30 and 90 days following the initial hospitalization. Adult patients admitted with cirrhosis in our hospital spanned from January 2009 to December 2022. Differences between groups were analyzed using the Student's t-test and chi-square test. Logistic regression analysis and multiple linear regression analysis were performed to identify predictors associated with readmission and the length of the first hospitalization.

Results: A total of 1285 patients were admitted with cirrhosis. Among these patients, 767 (59.7%) were males and the mean age was 58.9 ± 12.3 years. 72 (5.6%) and 154 (12.0%) individuals were readmitted within 30 and 90 days. Compared with those not readmitted, patients readmitted in 30-day and 90-day had a higher proportion of males, ascites, spontaneous bacterial peritonitis and electrolyte abnormalities, Child-Pugh-Turcotte scores, as well as a higher prevalence of longer initial hospital stays and initial hospitalization costs. The logistic regression analysis saw hepatic encephalopathy, spontaneous bacterial peritonitis are predictors within 30-day readmission, and diabetes, hepatic encephalopathy, ascites, and spontaneous bacterial peritonitis within 90-day readmission. The cost for the first admission, hypertension and spontaneous bacterial peritonitis were significant predictors of the length of hospitalization.

Conclusions: Cirrhotic patients who presented with hepatic encephalopathy, ascites, and spontaneous bacterial peritonitis were at a higher risk of rehospitalization.

Abstract Submission No. 100266
O-0967

Outcomes during hospitalization in cirrhotic patients with multidrug-resistant bacterial infection

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Background: This study aimed to investigate the clinical impact of multidrug-resistant (MDR) bacterial infection and outcomes in hospitalized patients with cirrhosis.

Methods: We consecutively enrolled hospitalized cirrhotic patients with bacterial infections admitted to the Chulalongkorn University Hospital, Bangkok, Thailand, from 2018 to 2021. Clinical outcomes during hospitalization in patients with MDR and non-MDR infection were evaluated.

Results: Overall, 323 patients (aged 65.1 ± 15.2 years) had bacterial infection, with a mean Child-Pugh score of 8.8 ± 2.1 . Nosocomial and healthcare-associated infection was identified in 88 (27.2%) and 100 (31.0%) patients. MDR bacterial infections were found in 27.9% of patients (n=90). In patients with MDR infection, the most isolated bacteria were *E. coli* (60%, n=54), *Acinetobacter sp.* (18%, n=20), *Klebsiella sp.* (13.8%, n=12), and *Enterococci* (8.9%, n=8). Urinary tract infection (31.1%, n=287), pneumonia (8.9%, n=28), and spontaneous bacterial peritonitis (11.1%, n=10) were the most frequent MDR infections. Patients with MDR infection had higher rates of septic shock (52.2% vs. 19.7%, $p < 0.001$), organ failure (67.8% vs. 42.9%, $p < 0.001$), invasive ventilator use (56.7% vs 23.6%, $p < 0.001$), and ICU admission (41.1% vs. 19.3%, $p < 0.001$) than those with non-MDR infection. Moreover, patients with MDR infection had a higher in-hospital mortality than non-MDR bacterial infection. (44.4% vs. 30%; $p = 0.014$). Multivariate analysis showed that nosocomial infection (OR=3.75; 95%CI: 2.17-6.48, $p < 0.001$), chronic kidney disease (OR=2.62, 95%CI: 1.22-5.64, $p = 0.01$), and hospitalization in previous three months (OR=1.80, 95%CI: 1.06-3.04, $p = 0.03$) were independent predictors of MDR infection.

Conclusion: MDR infection was found in 27.9% of cirrhotic patients and was associated with high mortality and poor outcomes during hospitalization. Nosocomial infection, chronic kidney disease, and recent hospitalization are risk factors for MDR infection.

Abstract Submission No. 100275
O-0968

High disease burden of significant portal hypertension in diabetic chronic hepatitis B

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Objective: Antiviral therapy with oral nucleos(t)ide analogues (NAs) is effective in suppressing serum hepatitis B virus (HBV) DNA and

reducing the risk of portal hypertension. Yet, NA treatment cannot completely abolish the risk of portal hypertension, especially in those with diabetes mellitus (DM). We aimed to evaluate the disease burden of significant portal hypertension in patients with chronic hepatitis B (CHB) and DM (CHB-DM) who have been receiving NAs.

Methods: Consecutive NA-treated CHB-DM patients were recruited for transient elastography examination to measure the spleen stiffness measurement (SSM). Significant portal hypertension was defined as a SSM > 41.3 kPa, and/or presence any clinical sign of portal hypertension (e.g., splenomegaly, ascites, varices).

Results: We recruited 260 CHB-DM patients with successful SSM; their mean age was 64±11 years; 66.2% were male. The median (interquartile range) of SSM was 17.0 (22.7-21.1) kPa. The prevalence of significant portal hypertension was 29.2%, defined with SSM > 41.3 kPa in 11.9%, splenomegaly in 22.7%, ascites in 13.5% and varices in 26.9%. Patients with significant portal hypertension had less satisfactory control of DM (HbA1c 7.8% vs. 6.7%, $p=0.017$).

Conclusion: Significant portal hypertension is common in CHB-DM patients. Suboptimal glycaemic control associated with significant portal hypertension. New generations of antidiabetic agents, namely sodium-glucose co-transporter-2 inhibitors (SGLT2i) are promising in improving glycaemic control and potentially helpful in reducing complications from portal hypertension in CHB-DM patients with cACLD. **Financial support:** This work was supported by the General Research Fund from the Research Grant Council grant to Grace Wong (Reference: 14106922).

Abstract Submission No. 100391

O-0969

Comparison between predictors of mortality in patients of chronic liver disease, barring ACLF

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Background: Complications of Chronic liver disease carries high mortality risk. Available scoring systems are used for predicting short and long-term mortality. There is lack of data comparing different scoring systems with outcome in chronic liver disease barring ACLF.

Aims and objectives: The aim of present study was comparison between these scoring systems in predicting mortality risk in chronic liver disease.

Methods: This was prospective, observational study including consecutive 400 admitted patients of chronic liver disease barring ACLF. The primary endpoint of study was comparison of different scoring systems in predicting outcome during hospitalization. The secondary endpoint was development of in hospital complications of chronic liver disease and its impact on outcome.

Results: Among 400 patients, the male: female ratio was 3:1. Commonest aetiology of chronic liver disease was NASH (48.8%) and alcohol (32.8%). The mortality rate was 25.08% during hospitalization. The comparison among prognostic scores, AUROC of Child-Pugh was 0.778, MELD Na was 0.859, SOFA score was 0.985 and APACHE II was 0.995.

Conclusion: Among different scoring systems, the APACHE II score predicted best in-hospital mortality in patients with chronic liver disease barring ACLF.

Abstract Submission No. 100605

O-0970

A RFH-NPT-based Nomogram to predict the long-term survivals of liver carlesis : a multicenter study

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Background & Aims: Malnutrition risk is an important predictor of outcomes in cirrhosis patients. The Royal Free Hospital-Nutritional Prioritizing Tool (RFH-NPT) is recommended for identifying malnutrition risk in liver disease patients. We aimed to develop and validate a RFH-NPT-based nutrition screening model to predict outcomes of cirrhosis.

Methods: Cirrhotic inpatients from February 2016 to July 2016 were included as training cohort, and patients from 6 clinical medical centers were enrolled as validation cohort. A nomogram was established based on the prognostic variables determined by COX, BSR and LASSO regression, and assessed by concordance index, calibration curves, decision curve analysis (DCA) and brier curve. Its performance was compared with Child-Pugh score, the model for end-stage liver disease (MELD) and MELD-Na, and validated by an external dataset.

Results: 152 patients with cirrhosis were enrolled into training cohort. During the 5-year follow-up, 53 (34.9%) patients died. Age, albumin, total bilirubin, blood urea nitrogen, and RFH-NPT classification were identified as prognostic factors in Cox regression and conducted the RFH-NPT based nomogram which showed valuable consistency with actual observations. The DCA achieved great utility. In a comparison of the areas under the ROCs, the nomogram had superior performance than Child-Pugh, MELD and MELD-Na in predicting the timing course of survival, respectively. Besides, another 320 cirrhotic patients were enrolled as validation cohort, and confirmed the superiority of nomogram in prognosing the survival outcomes.

Conclusion: A novel RFH-NPT-based malnutrition screening nomogram provides better accuracy of predictions for long-term outcomes in cirrhosis patients.

Abstract Submission No. 100664

O-0971

Comparison of mortality prediction of MELD, MELD-La, and MELD-3.0 on Korean Liver Cirrhosis patients

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Background & Aims: The Model for End-Stage Liver Disease (MELD) score has widely been used for mortality prediction of Liver cirrhosis (LC) patients and for transplantation allocation. There had been recent modifications such as MELD-Lactate (MELD-La) and MELD-3.0, which has integrated the factors that the original MELD score had not.

The goal of this study is to compare MELD, MELD-La, and MELD-3.0 in the mortality prediction of LC patients in Korea.

Methods: This is a retrospective, single-centered study in which LC patients who were admitted to Konkuk University Hospital via emergency department between January 2011 and December 2022 were enrolled and reviewed. Predictive values for 1-month and 3-month mortality of MELD, MELD-La, and MELD-3.0 were calculated using area under the receiver operating characteristics (AUROC) curve and their difference are statistically analyzed using DeLong's test.

Results: Total of 1,152 patients were included in this study. Among them, 165(14.3%) patients died in one month and 211(19.7%) died within three months. The AUROCs for 1-month mortality of MELD, MELD-La, MELD-3.0 were 0.808, 0.79, 0.807, and for 3-month mortality of MELD, MELD-La, MELD-3.0 were 0.805, 0.753, 0.817, respectively. Multiple comparison of ROC curves demonstrated that MELD and MELD-3.0 have reflected the 3-month mortality prediction of LC patients better than MELD-La ($p=0.0018$, $p=0.0003$ respectively).

Conclusion: This study has shown that either MELD or MELD-3.0 is better tool compared to MELD-La in predicting 3-month mortality of LC patients, whereas the comparison of MELD and MELD-3.0 have shown no significant difference in predicting mortality of LC patients.

Abstract Submission No. 100709

O-0972

Diagnostic accuracy of microRNAs as non-invasive biomarkers for the diagnosis of liver cirrhosis

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Background: This study evaluates the diagnostic accuracy of circulating microRNAs(miRNAs) as non-invasive biomarkers to identify patients with early liver cirrhosis in a large prospective cohort of patients with chronic liver disease.

Materials and Methods: The ELEGANCE Study is a prospective, multi-centre, cohort study enrolling patients at increased risk of HCC in Singapore (ClinicalTrials.gov: NCT04965259). Patients were enrolled if they had compensated liver cirrhosis or non-cirrhotic chronic liver disease due to hepatitis B (HBV), hepatitis C (HCV) or non-alcoholic fatty liver disease (NAFLD). Plasma from subjects were profiled through high-throughput qPCR to identify candidate miRNAs. Student's t-test was used to identify differentially expressed (DE) miRNAs between groups. A ridge model was trained from the training cohort and validated in the validation cohort.

Results: Plasma from 1318 subjects (464 cirrhosis, 643 HBV, 14 HCV, 197 NAFLD) were divided into a training cohort (617 subjects) and a validation cohort (701 subjects). In training, 35 miRNAs exhibited DE between cirrhotic and non-cirrhotic groups (fold change<0.81 or >1.23, FDR<0.05). Among these, 12/20 were significantly up-regulated and 6/15 were significantly down-regulated in validation. The consistency of miRNA DE is significant ($p < 0.0001$). Employing ridge model in training, a panel of 36 miRNAs achieved an AUROC of 0.77 to differentiate cirrhosis from non-cirrhosis patients. The panel performed consistently with an AUROC of 0.76 in the validation.

Conclusion: Circulating miRNAs demonstrated potential as a non-invasive biomarker to identify patients with early liver cirrhosis among patients with chronic liver disease and track the progression of chronic liver disease.

Abstract Submission No. 100741

O-0973

ROLE OF INFLAMMATORY BASED MARKERS IN THE DIAGNOSIS OF BACTERIAL INFECTION AMONG CIRRHOTIC PATIENTS

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Bacterial infection is common and accounts for morbidity and mortality in cirrhosis. It has been reported that 30 to 60% of cirrhotic patients acquire a bacterial infection with an incidence of 4-5-fold higher compared to the general population. This study aimed to describe the potential use of inflammatory markers as predictive factors of bacterial infections in cirrhotic population.

A retrospective analytical study of 272 patients with liver cirrhosis from 2015 to 2022 at Chong Hua Hospital was done. Cirrhotic patients were classified based on their presence and absence of infection. MELD score, Child-Pugh score and inflammatory based markers (RDW, MPV, NLR, LMR) were analyzed. To find the significant predictors of bacterial infection, univariate and multivariate regression analyses were performed. The area under the curve (AUC) was used to assess the markers' diagnostic efficacy.

The most common infections identified in patients with cirrhosis were pneumonia (40.12%), urinary tract infection (24.42 %) and SBP (13.95 %). The most common bacteria isolated from patients with cirrhosis were *Klebsiella*, *Escherichia coli*, and Methicillin resistant staphylococcus aureus (MRSA). Furthermore, among the different inflammatory based markers, neutrophil lymphocyte ratio (NLR) and lymphocyte monocyte ratio (LMR) were significant predictors of bacterial infection in cirrhotic patients with cut off ≥ 4.7 and ≤ 2.26 respectively.

Bacterial infection prevalence is relatively high in patients with liver cirrhosis. Our study demonstrated that baseline NLR and LMR are predictors of bacterial infection in patients with cirrhosis. These tests may provide a simple method of identifying patients susceptible to infection.

Abstract Submission No. 100753

O-0974

Serum ammonia level predicts complications and mortality in clinically stable outpatient cirrhotics

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Background: Ammonia has long been established as a neurotoxin involved in the pathogenesis of hepatic encephalopathy (HE). The Child-Turcotte-Pugh (CTP) score has factored in HE to prognosticate patients with cirrhosis but is limited by observers' subjectivity. This study

was aimed to test the hypothesis that serum ammonia level predicts complications and mortality in clinically stable outpatient cirrhotics

Methods: In this ongoing study to predict the decompensation, ACLF and mortality in cirrhosis (Solidarity-DAM), stable out-patients were recruited according to the declaration on Helsinki. The primary end-point was all non-elective admission for cirrhotic decompensation, ACLF or death. Ammonia measurements were carried out in fasting blood in accordance with international standards.

Results: A total of 197 outpatients with median age of 68.0 years [IQR: 60.0-74.0], BMI of 25.2 [IQR:22.9-28.6]), majority males (61%) were recruited. Patients with CTP classes A/B/C were 64.5%, 13.7%, 4.6% respectively. The median MELD was 7[IQR: 6-10]. The median serum ammonia[N=162] in patients who achieved and did not achieve predefined clinical outcomes (CO) were 55 [IQR: 45-91] and 25 [IQR: 17-42] respectively. The CO was not dependent on age, BMI, etiology of cirrhosis or concomitant diabetes mellitus. However, MELD, CTP, history of HE and presence of ascites predicted CO in univariate analysis [$p < 0.05$ for all]. In the multivariate analysis only serum ammonia was a predictor of defined CO, HR:1.016[1.001-1.032; $p = 0.037$]. Kaplan-Meier curve is attached as figure 1.

Conclusion: Serum ammonia can predict complications and mortality in clinically stable cirrhotics. Ammonia may be a potential target of therapy to prevent future decompensating events.

Abstract Submission No. 100798

O-0975

Serum BNP levels and 90 day mortality in patients of decompensated liver cirrhosis

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Background: Patients with decompensated cirrhosis usually have excess of fluid as do patients of heart failure. Elevated B-type natriuretic peptide (BNP) level is a marker of increased blood volume in heart failure and is also increased in patients with decompensated liver disease.

Methods: We conducted a prospective study of 150 patients with decompensated cirrhosis without evidence of cardiac systolic dysfunction to evaluate the role of BNP levels in predicting prognosis and deterioration of ascites in patients with decompensated cirrhosis. Patients with heart failure, arrhythmias, coronary artery disease, rheumatic heart disease, pulmonary hypertension, chronic kidney disease and liver cancer were excluded.

The primary outcome was correlation between BNP levels and 90-day mortality in these patients.

The secondary outcome was deterioration in ascites determined by the need for therapeutic paracentesis in the follow up period.

Results: During the study period 45 patients of 150 (30%) died. Median BNP levels in those who survived was 94 pg/mL (range 53-177) and in those who died was 263 pg/mL (range 134-315). Patients with higher BNP had significantly higher mortality rates (HR 2.45; $p < 0.03$) A BNP ≥ 180 pg/mL had specificity of 80% in predicting 90-day mortality. Patients with BNP ≥ 235 pg/ml were more likely to require therapeutic paracentesis in the next 90 days (HR 1.73; $p < 0.06$).

Conclusion: BNP is useful prognostic marker in patients with decompensated cirrhosis without systolic dysfunction. It could be also be used to predict requirement of therapeutic paracentesis in these patients.

Abstract Submission No. 100804

O-0976

Efficacy of Continuous Terlipressin Infusion in HRS-AKI in a Transplant-Enriched Population

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Background: Hepatorenal syndrome-acute kidney injury (HRS-AKI) is a serious complication of decompensated cirrhosis and is associated with significant morbidity and mortality. Terlipressin is approved as a bolus administration in the US and there is a need for US-based data on continuous terlipressin infusion, particularly its impact on access to liver transplant (LT).

Methods: Open label study of continuous terlipressin infusion (INFUSE; NCT04460560) in 50 patients with HRS-AKI, was conducted. ACLF grade 3, serum criteria (SCr) > 5.0 mg/dL, or MELD ≥ 35 were exclusions; cohort was enriched with patients listed/in evaluation/eligible for liver transplant. Patients were followed for 90 days post-treatment.

Results: (Table) Median EOT SCr values, MELD and MELD-Na scores were lower than median baseline value respectively (2.6 vs 1.4; MELD: 24, 28; MELD-Na: 19, 24). Nineteen of the 40 (47.5%) transplant candidates underwent LT or SLKT by day 90 of follow up; 16 of those had LT-alone. Most of the patients who received a transplant by day 90 were complete responders. One patient had hypoxic respiratory failure due to fluid overload and responded to diuretics.

Conclusions: In patients with HRS-AKI, treatment with continuous terlipressin infusion facilitated high response rates and had a favorable safety profile. Transplant candidates who received terlipressin underwent LT at a comparable rate to US transplant candidates who received a deceased donor liver within 1-year, and none of complete responders required SLKT. The high transplant rate following terlipressin mitigates concerns over impacted organ access due to improved MELD scores, and offers an effective bridge to LT.

Abstract Submission No. 100840

O-0977

Secular trend of disease burden of hydrothorax in patients with liver cirrhosis

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Objective: Hydrothorax is one of the most debilitating complications in patient with liver cirrhosis. We aimed to evaluate the secular trend

of the disease burden of hydrothorax over the last two decades in Hong Kong.

Methods: This was a territory-wide cohort study of consecutive patients with liver cirrhosis retrieved from the Clinical Data Analysis and Reporting System (CDARS) from Hospital Authority in 2000-2020. Hydrothorax was defined by the diagnosis codes and retrieved from January 2000 to June 2023.

Results: Among the 31,542 patients with liver cirrhosis, 3,251 (10.3%) patients suffered from hydrothorax; their mean age was 58.4 ± 14.2 years; 65.4% were male; mostly due to chronic hepatitis B (72.5%). The disease burden of first incident hydrothorax increased from 109-133 annually in 2000-2008, to 194 annually in 2009, peaked at 210 annually in 2010, then gradually decreased to 60-72 annually in 2021-2022 (Figure). Recurrent episodes also peaked in 2011 (636 episodes annually) and decreased to 249-286 episodes annually in 2021-2022 (Figure).

Conclusion: The disease burden of hydrothorax peaked a decade ago and gradually decreased over the last decade. This is likely related to the improved treatment for the underlying aetiologies of liver cirrhosis, particularly chronic hepatitis B and C. The findings highlight the importance of treating the underlying aetiologies of liver cirrhosis in order to prevent debilitating cirrhotic complications.

Abstract Submission No. 100879

O-0978

Anticoagulants and antiplatelet agents are commonly used in patients with cirrhosis

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Background: Patients with cirrhosis are more susceptible to both thrombosis and bleeding. Using anticoagulant and antiplatelet agents is often a double-edged sword - reducing thrombotic risk on one hand while increasing bleeding risk on the other hand. This study aims to evaluate the prevalence of anticoagulant and antiplatelet usage and the clinical profile of a territory-wide cohort of patients with cirrhosis.

Method: This was a territory-wide retrospective cohort study of 31,542 cirrhotic patients diagnosed between 2000 and 2020 in Hong Kong. The clinical, laboratory, and medication data were collected. Anticoagulant and/or antiplatelet users were defined as those with prescription of these medications for 4 weeks or more.

Results: 9,373 (29.7%) patients were identified as anticoagulant and/or antiplatelet users; their mean age was 67.5 ± 12.1 years; 63.4% were men; 2,761 (29.5%) had MELD score >10 ; most of them (70.7%) suffered from chronic hepatitis B. Aspirin was the most commonly used medication ($N=8337$), with the longest duration (37.6 IQR: $6.1-94.5$ months). Among antiplatelet users, aspirin users and clopidogrel users had similar age and clinical characteristics. Among anticoagulant users, direct oral anticoagulants (DOAC) users were older than warfarin users (age 72.7 ± 11.1 vs. 63.8 ± 13.5 years, $p < 0.001$), but had better renal function and lower MELD score (Table).

Conclusion: Anticoagulants and antiplatelet agents are commonly used in patients with liver cirrhosis, even in some patients with hepatic decompensation. DOACs are preferentially prescribed to younger patients with better renal and liver function. Studies to evaluate the

efficacy and safety of these medications in the presence of cirrhosis are warranted.

Abstract Submission No. 100891

O-0979

Role of Spot urine sodium/potassium ratio in predicting Acute Kidney Injury in cirrhosis

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Introduction: Acute kidney injury (AKI) is a common complication in decompensated cirrhosis and serves as an independent predictor of prognosis. Hence, early identification of AKI can play a pivotal role in managing these patients with a better outcome in terms of survival. The main objective of this study was to determine the role of spot urine sodium to potassium (Na/K) ratio in decompensated cirrhosis in predicting short term mortality in these patients.

Methodology: A prospective observational study was conducted at our institution between October 2021 and September 2022 in 102 inpatients, admitted for complication/s related to cirrhosis liver. Patients admitted for reasons unrelated to cirrhosis like elective procedures were excluded. Spot urine samples were analyzed for sodium, potassium, protein and creatinine; urine Na/K ratio, fractional excretion of sodium (FeNa) and protein creatinine ratio were calculated. All patients were followed up for one month and new onset AKI, MELD Na and 30-day mortality were noted. Statistically analysis was done using SPSS software. Descriptive statistics, linear correlation, receiver operating curve (ROC) and Kaplan Meier survival plot were used.

Results: 39 patients (38.2%) had AKI at admission and 16 patients (15.7%) developed AKI during followup. Urine Na/K ratio ± 1.3 correlated statistically with AKI at admission, new onset AKI during hospital stay and on one month follow up (p value < 0.001), with a sensitivity and specificity of 78.2% and 81% respectively. Also, the ratio had a significant inverse correlation with MELD - Na score and 30-day mortality (p value < 0.001).

Conclusion: Spot urine Na/K ratio has a significant inverse correlation with the onset of AKI and 30-day mortality and seems to be a good prognostic tool in day-to-day practice in decompensated cirrhosis.

Abstract Submission No. 100973

O-0980

Change in Rotational Thromboelastometry Parameters in Patients with Cirrhosis After Transfusion

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Introduction: Conventional coagulation tests (CCT) are often used to assess bleeding risk and guide transfusion in patients with cirrhosis. However, due to rebalanced hemostasis the actual bleeding risk may be lower. Emerging data suggests that use of rotational thromboelastometry (ROTEM), a whole blood viscoelastic test, predicts bleeding risk more accurately.

In this study, we describe CCT and ROTEM parameter changes post transfusion of platelets or fresh frozen plasma (FFP).

Method: Patients described here were part of a randomized control trial (REduCe). All patients were duly consented according to Declaration of Helsinki. 40 patients were randomized, of which 70% (N=28) received transfusion based on pre-defined trigger points described elsewhere. (NCT:05698134). CCT and ROTEM were carried out before and within 2 hours after transfusion.

Results: There were 25 males and 3 females. Mean age was 57.1 ± 7.9 years. All patients had abnormal CCT. Median MELD was 18 (IQR 10-21). 14% had Child A, 25% Child B and 61% (n=17) Child C cirrhosis.

Patients who received platelet transfusion showed significant changes in INTEM and EXTEM for clot formation time (CFT), clot propagation (A5) and maximum clot firmness (MCF); and significant increase in platelet count (mean 39 to 51, $p=0.01$).

Patients who received FFP had significant change in INTEMCT (mean 231 to 204, $p=0.02$); no change in INR (mean 1.76 to 1.68, $p=0.162$).

Conclusion: Patients who received FFP showed no significant changes in INR/PT, but changes in ROTEM parameters were significant. ROTEM parameter changes were also significant after platelet transfusion.

Abstract Submission No. 101123

O-0981

Mortality of cirrhotic patients with hydrothorax over the last two decades

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Objective: Hydrothorax is an independent risk factor for mortality in patient with liver cirrhosis. We aimed to evaluate the secular trend of the disease burden and death of cirrhotic patients with hydrothorax over the last two decades in Hong Kong.

Methods: This was a territory-wide cohort study of consecutive patients with liver cirrhosis retrieved from the Clinical Data Analysis and Reporting System (CDARS) from Hospital Authority in 2000-2020. Hydrothorax was defined with the diagnosis codes and retrieved from January 2000 to June 2023.

Results: Among the 31,542 patients with liver cirrhosis, 3,251 (10.3%) patients suffered from hydrothorax; their mean age was 58.4 ± 14.2 years; 65.4% were male; mostly due to chronic hepatitis B (72.5%). The disease burden of first incident hydrothorax increased from 2000 and peaked in 2010, then gradually decreased in 2011-2022 (Figure). There was a delayed in the peak of death of these patients, which only peaked in 2015 (183 deaths annually) and decreased to 115-119 deaths annually in 2021-2022 (Figure).

Conclusion: The disease burdens of hydrothorax peaked in 2010 whereas the deaths peaked 5 years after that. This is likely related to the improved treatment for the underlying aetiologies of liver cirrhosis, particularly chronic hepatitis B and C. The findings highlight the importance of early treatment for the underlying aetiologies of liver cirrhosis in order to minimise the deaths from this important cirrhotic complication.

Abstract Submission No. 101253

O-0982

STING activation hampers HBV replication but promotes liver injury in CHB concurrent with NAFLD

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Object/Background: Concomitant NAFLD is common in patients with chronic hepatitis B (CHB), but the implications on liver-related outcomes remains controversial. STING plays a central role in innate immune activation. Here, we aim to investigate the role of STING in CHB patients concurrent with NAFLD.

Methods: HBV transgenic mice and pAAV-1.2 HBV hydrodynamic injection mice fed with a high-fat diet were used to establish CHB concurrent with NAFLD models. THP1 and HepG2/HepG2.2.15 cells were stimulated with palmitic acid *in vitro*. The liver tissues obtained from healthy controls and patients with CHB, NAFLD, CHB concurrent with NAFLD were used for clinical validation.

Results: Compared with CHB or NAFLD mice, the concurrent presence of CHB and NAFLD resulted in significantly upregulated in liver inflammation and fibrosis, despite decreases in HBV DNA levels. Concomitant with disease progression, CHB mice concurrent with NAFLD exhibited upregulated hepatic STING expression and impaired autophagic flux. We found that macrophage STING enhanced hepatocyte inflammation and HSC activation by upregulating the expression of IFN- β , IL-1 β , IL-18 and TGF- β 1. STING stimulation resulted in the production of P-TBK1, which impaired the function of RAB7, thereby preventing STING from entering autophagic lysosomes for degradation and subsequently exacerbating disease progression. STING deficiency restored RAB7 function, enhanced autophagic flux, and mitigated liver inflammation and fibrosis. The expression of STING and RAB7 was confirmed in liver samples from patients.

Conclusion: STING activation hampers HBV replication but exacerbates liver inflammation and fibrosis in CHB concurrent with NAFLD by impairing RAB7 function and disrupting autophagic flux.

Abstract Submission No. 101305

O-0983

Understanding the Current Status of Zinc Deficiency in Patients with Chronic Liver Disease

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Background: Since sarcopenia in chronic liver disease is a poor prognostic factor and there is no fundamental cure, prevention of sarcopenia is critical. Zinc deficiency, which is common in chronic liver disease, exacerbates sarcopenia by decreasing muscle mass and worsening the condition in association with increased ammonia levels.

Aim: In the present study, we sought to determine the status of zinc deficiency and identify associated risks using clinical parameters collected from patients with chronic liver disease in a prospective study.

Method: We analyzed clinical data from our extensive prospective study on chronic liver disease, examining patient backgrounds, zinc correlations, and risk factors. Zinc deficiency was defined by Japan Clinical Nutrition Society criteria (less than 60 $\mu\text{g/mL}$: deficiency, 60-80 $\mu\text{g/mL}$: latent deficiency).

Result: Excluding 40 cases with missing data, 1168 chronic liver disease cases were analyzed. Median age was 68, with 678 males. Zinc measurements were available for 40.7%. Median serum zinc was 74 µg/mL, significantly lower in alcoholic liver disease (62 µg/mL). Serum zinc correlated positively with albumin and negatively with ALBI, FIB4, M2BPGi, and NH3. Logistic regression analysis identified albumin <4.0 mg/dL as a risk factor for zinc <60 µg/mL. ROC analysis, using Alb 3.8 mg/mL, showed 82.3% sensitivity and 81.7% specificity for zinc deficiency.

Conclusion: In chronic liver disease, although serum albumin levels of 3.8 mg/mL may signal early zinc deficiency, fewer than half of the cases underwent zinc measurements. This highlights clinicians' limited awareness. Early diagnosis and supplementation of zinc deficiency may prevent the onset and progression of sarcopenia.

Abstract Submission No. 101321

O-0984

Classification of 5,102 Mongolian patients with liver cirrhosis by causes

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Background: Liver cirrhosis is number one cause of mortality within GI related causes of death in Mongolia. But there are no large scale studies that assesses all causes of cirrhosis in Mongolia. Methodology: Total of 16,324 people underwent elastography testing during the 5-year period from October 31, 2017 to December 6, 2022 were analyzed in detail by the anamnesis-synthesis method, and the correlation between them was summarized.

Results: Out of 5,102 eligible patients with F4 level fibrosis (liver cirrhosis) 1,493 people had HCV Ab positive or 33%, 890 people with HBV infection or 20%; 1479 (32%) patients had HBV and HDV co-infection; 73 or 2% had HBV, HDV and HCV triple infection; 99 patients or 2% were co-infected with HBV and HCV. 427 people or 9% had NAFLD only. Out of "NAFLD only" patients we surveyed for alcohol consumption level: 115 (27%) patients had moderate to severe alcohol consumption while, 312 (73%) were abstainers. 80 people or 2% had cirrhosis unknown causes.

Conclusion: Viral cause of liver cirrhosis still represented 89% of all causes, while NAFLD was 7% and ALD related 2% respectively.

Abstract Submission No. 101322

O-0985

The RCT Study of JianPiHuaZhaoXingNao formula in Treatment of Cirrhosis Mild Hepatic Encephalopathy

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Background: This study aimed to observe the clinical efficacy of JianPiHuaZhaoXingNao formula (JPHZXN) in the treatment of mild hepatic encephalopathy (MHE) caused by hepatitis B virus (HBV) related cirrhosis, providing new perspectives and strategies for the treatment of MHE.

Methods: A total of 60 patients with HBV related cirrhosis of MHE, treated at Dongzhimen Hospital from September 2020 to August 2022, were randomly divided into a treatment group and a control group, with 30 patients in each group. Both groups received routine basic treatment, and the treatment group additionally received oral JPHZXN, while the control group received oral placebo. Neurological and psychological tests, liver function, and traditional Chinese medicine syndrome scores were recorded at the time of enrollment and after 24 weeks to evaluate the clinical efficacy.

Results: There were no statistically significant differences in gender, age, education level, neurological and psychological test, liver function, and syndrome scores between the two groups, indicating comparability. After 24 weeks of treatment, the number connection test A (NCT-A) time and Digital symbol test (DST) scores, AST, and syndrome scores in the treatment group showed significant improvement compared to baseline ($P < 0.05$). The total effective rate in the treatment group (86.67%) was significantly higher than that in the control group (33.33%) ($P < 0.05$).

Conclusions: JPHZXN has a favorable effect on the neurological and psychological tests and cognitive function of patients with HBV related cirrhosis of MHE. It can improve AST within the normal reference range, effectively reduce syndrome scores, and ameliorate clinical symptoms.

Abstract Submission No. 101502

O-0986

Friality Correlates With Greater Odds of hepatic encephalopathy, Ascites, & SBP: a study from Pakistan

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Introduction: Frailty is associated with morbidity & mortality in advanced cirrhosis. However, the information on correlation between frailty & complications in decompensated cirrhosis is scarce. We aim to evaluate the impact of Frailty on risk of hepatic encephalopathy (HE), ascites, & spontaneous bacterial peritonitis (SBP) & impact of multidomain implementation on these outcomes.

Methods: We prospectively evaluated the impact of Frailty on prevalence of ascites, HE, & SBP among cirrhotic adults. Frailty was defined by the Liver Frailty Index (LFI) & a level of > 4.4 termed as frail. Development of complications (worsening ascites, HE or SBP) & unplanned hospitalization were recorded. In this study one arm of frail continued with their normal diet & was taken as control & the other arm (intervention) was given training of taking 5 meals/day, containing appropriate protein & fat contents. Additional Branched chain amino acids were also given to these patients. Physical exercise (both cardiac & resistance) advised. They were evaluated for a period of 6 months for the complication rates. Between-group comparisons used chi-squared methods & adjusted multivariate logistic regression.

Results: 179 patients were included (MELD 13.2 ± 3.4 , Child-Pugh A/B/C 34.9%/35.1%/30%), & 74.3% were frail. Compared to the robust group, pre-frail & frail patients had significantly higher cumulative 1-year probabilities of worsening ascites (0% vs. 8.5% vs. 18.4%, $p = .009$), & SBP (0% vs. 13.5% vs. 34.2%, $p < .001$), encephalopathy (0% vs. 28.9% vs. 71.1%, $p = 0.02$) & unplanned hospitalizations (100% vs. 90.8% vs. 80.4%, $p = .014$). Two models of multivariable Cox regression analysis were done adjusted with MELD-

Na&Child-PughC, frailty was associated with developing decompensation (HR 3.01, $p=.04$; & 2.98, $p=.04$, respectively) & unplanned hospitalization (HR 2.46, $p=.02$; & 2.39, $p=.03$, respectively).

Control arm with frailty were significantly more likely to have ascites, HE, & SBP. (Control arm Vs. interventional arm: ascites, 66% vs. 93%; HE, 81% vs. 49%; SBP, 4% vs. 16%, $p<0.001$ for all).

Conclusion: Frailty is associated with higher odds of cirrhosis complications including ascites, PSE, & SBP, which was observed across all liver disease etiologies. With the implementation & mitigating the knowledge regarding proper diet & exercise we can improve condition of patient & can avoid complications

Abstract Submission No. 101525
O-0987

Predictive performance concerning distinct SMI cut-offs of sarcopenia for mortality among cirrhosis

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Background: Although the clinical relevance of sarcopenia has been verified in the context of cirrhosis, there are insufficient data concerning cut-offs of CT-demarcated skeletal muscle index (SMI) in different ethnicities. We aimed to clarify the predictive performance of distinct SMI values-defined sarcopenia for prognostication among cirrhosis.

Methods: We prospectively enrolled 341 inpatients due to cirrhosis-associated acute deterioration. A wealth of cut-offs concerning SMI (TJ, northern China, southern China, Japan and Turkey criteria) were testified to determine 2-year all-cause mortality according to Kaplan-Meier survival curve with log-rank test and multivariate Cox regression.

Results: Sarcopenia was present in 26.4%, 7.9%, 22%, 29.6% and 7.9%, respectively, according to TJ, northern China, southern China, Japan and Turkey criteria. Survival curve showed significant differences between patients with and without sarcopenia defined by all criteria (P for log-rank test <0.05). Univariate Cox regression indicated age, BMI, CTP class, MELD-Na, creatinine, total bilirubin, sodium, albumin and sarcopenia were significantly associated with long-term mortality. Further multivariate Cox regression by adjusting age, BMI and MELD-Na revealed that northern China-defined sarcopenia was independently associated with mortality (HR = 1.99, $P = 0.0431$), while TJ criteria-defined sarcopenia exhibited marginally significant association (HR = 1.62, $P = 0.0595$). Moreover, sarcopenia defined by northern China (HR = 1.93, $P = 0.0453$), TJ (HR = 1.73, $P = 0.0280$), and southern China criteria (HR = 1.73, $P = 0.0368$) was significantly associated with mortality by adjusting age, BMI and CTP class.

Conclusions: Our findings provide strong evidence to develop continent-based SMI cut-offs to identify sarcopenic cirrhotic patients, considering its prognostic importance.

Abstract Submission No. 101577
O-0988

Value of Thromboelastography in Prognosis Evaluation of Hospitalized Patients with Liver Cirrhosis

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Objective We sought to evaluate associations between Thromboelastography (TEG) parameters and 1-year prognosis in patients with cirrhosis.

Methods: A prospective clinical study was conducted on cirrhotic patients hospitalized in our hospital from May 2020 to October 2020. The relationship between TEG index, routine coagulation index, biochemical examination, complication rate and 1-year prognosis were statistically analyzed.

Results A total of 144 patients with liver cirrhosis were enrolled. 42.4% of patients had α Angle decreased, K value prolonged in 48.2% of patients, and MA value decreased in 59.0% of patients. R value is low correlated with D-Dimer ($r = -0.28$), and INR has no strong correlation with TEG measurement value ($r < 0.4$). D-dimer was not correlated with α angle and Ma value ($r < 0.2$). K value, α Angle and Ma values are moderately to strongly correlated with PLT and FIB (r value is between 0.45-0.67). Fibrinogen was negatively correlated with gastrointestinal bleeding, and D-dimer was negatively correlated with PVT. MA is an independent risk factor for 1-year prognosis.

Conclusion TEG can more comprehensively reflect the coagulation status of patients with liver cirrhosis. TEG is related to the 1-year prognosis of patients with liver cirrhosis.

Keywords Thromboelastography, Coagulopathy, Cirrhosis, Prognosis.

Abstract Submission No. 101711
O-0989

Prognostic factor which can predict esophageal varices aggravation after PARTO

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Background: Plug-assisted retrograde transvenous obliteration (PARTO) is known to be an effective treatment for gastric varices. However, it is also known to worsen esophageal varices after PARTO. The aim of this study is to identify prognostic factors which can predict the worsening of esophageal varices after PARTO in patients with gastric varices.

Methods: Ninety-nine patients who underwent PARTO between Jun 2015 and Jan 2023 were enrolled in this study. Esophageal varices and their exacerbation were evaluated by gastroduodenoscopy. Twenty-five patients who did not undergo follow up endoscopy after PARTO were excluded.

Results: The mean age of patients were 57.9 ± 9.9 years and 64.9% were male. Most common etiology of liver cirrhosis was alcoholic liver disease (40.5%) followed by hepatitis B virus (28.4%). The cumulative worsening rate of esophageal varices at 1, 2, and 3 years were 32.4%, 48.6% and 50.0%. In the univariate logistic regression analysis, left gastric vein (LGV) dilatation which LGV diameter more than 3.5mm, total bilirubin, aspartate aminotransferase, albumin, prothrombin time, international normalized ratio, hepatic vein pressure gradient (HVPG), MELD score, Child-Pugh class were associated with worsening of esophageal varices after PARTO. In multivariate logistic regression analysis, LGV dilatation (OR 3.272; 95% CI 1.016-10.534; $p = 0.047$) and HVPG (OR 1.182; 95% CI 1.017-1.375; $p = 0.030$) were independent risk factor of worsening of esophageal varices.

Conclusion: LGV dilatation and HVPG are associated with esophageal varices aggravation after PARTO.

Keywords: Plug-assisted retrograde transvenous obliteration (PARTO), Esophageal varices, Gastric varices

Abstract Submission No. 101926

O-0990

Usefulness of retinol-binding protein to predict mortality in patients with chronic liver disease

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Background: Rapid turnover proteins (RTP), including retinol binding protein (RBP), transthyretin (TTR), transferrin (Tf), are useful in evaluating dynamic nutritional status. This study aimed to investigate the relationship between RTP and mortality in patients with chronic liver disease.

Methods: We included 341 patients with chronic liver disease who had RTP measurements taken between October 2011 and December 2021. Low RBP group was defined as RBP below 2.7 mg/dL for men and 1.9 mg/dL for women. Survival curves were estimated using the Kaplan-Meier method and the survival between two groups were compared using the log-rank test.

Results: Of the patients included, the median age was 67 years and 48% were male. The prevalence of chronic hepatitis, Child-Pugh A, B, and C were 84, 116, 77, and 64, respectively, and the median MELD score was 8 points. The median RBP, TTR, and Tf were 1.5 mg/dL, 11 mg/dL, and 227 mg/dL, respectively. During the median observational period of years, 23% patients died. Multivariate analysis showed that RBP (hazard ratio, 2.98; 95% CI, 1.47-6.04; $p = 0.002$) was independently associated with mortality independent of MELD score and sodium, while TTR and Tf were not significant.

The low RBP group had significantly worse mortality than the normal RBP group (survival rate: 1 year 83% vs. 95%, 3 years 72% vs. 93%, 5 years 91% vs. 67%; $p < 0.001$).

Conclusions: Our study revealed that RBP is associated with mortality in patients with chronic liver disease independent of liver functional reserves.

Abstract Submission No. 101969

O-0991

Interleukin-6 as Predictor of Hepatic Encephalopathy Incidence in Hepatic Cirrhosis Patients

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Background: Systemic inflammation is known as the driving force for the development of hepatic encephalopathy (HE) and recent studies demonstrated that elevated Interleukin-6 (IL-6) are associated with the presence and progression of HE in patients with liver cirrhosis.

Methods: 200 hepatic cirrhosis outpatients were included in the study and were followed for a mean time of 305 days. Baseline clinical assessment and laboratory data were recorded. HE grade was diagnosed with West-Haven criteria and portosystemic encephalopathy test.

Outcomes included incidence of HE covert and overt and death rates, during the follow-up.

Results: Elevated IL-6 group showed a significantly higher overt HE (41%) than the normal IL-6 group (1%), covert HE (47%) to Normal Group (6%), ($P < 0.0001$), non HE was higher in the normal IL-6 group (93%). Moreover, the death rate was significantly greater in the elevated IL-6 group (16%) than in the normal IL-6 group (1%) ($P = 0.033$). The cutoff value of IL-6 levels in the prediction of hepatic encephalopathy incidence was assessed. Our receiver operating characteristic results revealed that IL-6 cutoff value higher than 50.27 for covert HE and the cutoff value is greater than 120.83 for overt HE. The sensitivity values of IL-6 for severity and mortality were 93.3 and 90.5%, respectively, and the specificity values were 90.0 and 86.7%, respectively.

Conclusion: Elevated levels of serum IL-6 in cirrhosis patients were related to the HE event. In predicting the incidence of covert HE and overt HE in cirrhosis patients, the optimum IL-6 cutoff levels were 50.27 and 120.83 pg/ml, respectively.

Abstract Submission No. 102002

O-0992

Prognostic Markers for Improved Survival Estimation in spontaneous bacterial peritonitis (PROMISE)

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Introduction: Spontaneous Bacterial Peritonitis (SBP) has high in-hospital mortality. Survival is dependent on early recognition, antibiotics, and albumin infusion. We investigated the predictors of mortality in patients with SBP.

Methods: In this retrospective study we analysed electronic records of adult patients with SBP to determine the clinical outcomes. From an initial review of 1611 patient records, 1303 were included. Role of ALBI in predicting long-term outcomes and mortality was assessed.

Results: 1303 patients [mean age 48.56 ± 13.85 years, males 84.5%, etiology being ethanol 41% and MAFLD, 38%] with SBP having serial follow-ups and outcomes from the date of diagnosis were studied. At one year from SBP diagnosis, 436 patients (33.46%) expired, whereas 867 (66.5%) survived. On multivariate analysis AST, total bilirubin, total protein, blood urea, serum creatinine, serum potassium and chloride levels, total leucocyte count, neutrophil to lymphocyte ratio (NLR), INR, ascitic fluid lymphocyte count, MELD score and ALBI score were independent predictors of survival at 1 year. ALBI score: grade 1 with score ≤ -2.60 had 13/15 (86.7%), grade 2 > -2.60 and ≤ -1.39 had 219/296 (74%) and grade 3 > -1.39 had 635/992 (64%) survival at 1 yr of SBP diagnosis. AUC for predicting mortality by ALBI and MELD score is 59.6% (p -value < 0.001) and 69.7% (p -value < 0.001). AUC for predicting AKI by ALBI and MELD score is 49.6% (p -value 0.78) and 84% (p -value < 0.001).

Conclusion: This study highlighted parameters such as serum AST, bilirubin, renal markers, NLR, MELD, and ALBI score as key one-year survival predictors.

Abstract Submission No. 102008

O-0994

THE INCREASING BURDEN OF AKI AND HRS IN HOSPITALIZED PATIENT WITH CIRRHOSIS

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Background: Acute kidney injury (AKI) and specifically hepatorenal syndrome (HRS) are complications that occur in hospitalized patients with cirrhosis that results in significant morbidity and mortality. However, the burden and changing epidemiology of AKI and HRS are not well described in Canada.

Methods: Data from 04/2015 to 03/2020 obtained from 29 hospitals in Ontario, the most populated province in Canada, participating in the GEMINI collaborative. Using data from hospital information systems linked to administrative data, we included patients admitted with cirrhosis, defined by having ICD-10-CA discharge diagnosis, and similarly identified admissions for AKI and HRS. We used logistic regression with cluster robust standard errors to estimate the trends over time.

Results: A total of 26,221 admissions for 12,288 patients with cirrhosis were included (64% male, mean age 63). AKI was present in 6,997 (26.7%) episodes and HRS in 1,433 (5.4%). AKI was associated with significantly worse outcomes, with higher need for ICU and mechanical ventilation, longer length of hospitalization and higher in-hospital mortality. The latter was 33.6% in those with AKI vs 8.4% in those without. We found that the odds of having AKI rose over time among hospitalized patients with cirrhosis (OR 1.06, 95%CI [1.04-1.07], $p < 0.001$), as did the odds of having HRS (OR 1.08, 95%CI [1.04-1.11], $p < 0.001$). Meanwhile, over the 6 years of observation, the mean age of patients admitted with AKI remained stable, as did their risk of in-hospital death. Finally, the odds of female patients being affected by HRS also increased over time (OR 1.07, 95%CI [1.00-1.15], $p = 0.042$).

Conclusion: The burden of AKI and HRS in patients admitted with cirrhosis in Ontario is increasing, and the proportion of female patients affected by HRS is as well.

Abstract Submission No. 102014
O-0995

Determinants of survival in a large cohort of cirrhosis in a tertiary care centre in India

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Introduction: The prognosis of cirrhosis is dependent on decompensation as the presenting feature and the severity of hepatic dysfunction as assessed using the Child-Turcotte-Pugh (CTP) and the Model for End-Stage Liver Disease (MELD) scores. We evaluated the survival and its determinants.

Methods: Prospective study in a 2640 patients with liver cirrhosis. Data were collected on age, sex, presentation at first visit, ascites, Child-Pugh and Model for End-Stage Liver Disease (MELD) and MELD Na score. Subjects were recruited and followed up from 2013 May till 2023 September for events of decompensation. Cox regression model with hazard ratios (HR) were computed using SPSS version 22.0.

Results: The mean age of the study participants were observed as 56.22 ± 9.79 years. 78% were males. 87.4% were with compensated cirrhosis (CC) and 12.6% had decompensated cirrhosis (DC) disease. 61% were with alcoholic liver disease (ALD); 8% had Hepatitis B viral infection; 2.5% HCV; 0.5% autoimmune hepatitis and 28% had non-alcoholic steatohepatitis (NASH). Alcohol abuse with hepatitis was observed in 32% with decompensation. Mortality was higher in the DC compared to CC (72.8% Vs 15.4%; $p < 0.001$). Mortality was higher in encephalopathy, ascites, acute kidney injury and spontaneous bacterial peritonitis. Survival HR (95% CI): CHILD B and C: 2.73

(95% CI 1.44 -5.12) $p = 0.041$; MELD Na > 12: HR 2.22 (95% 1.12-4.22) $p = 0.010$. The cox regression model, Chi-square statistics showed that overall model has -2 Log Likelihood of 414.6 with 4 degrees of freedom (df) has a p-value of 0.001. CTP class B and C have 2.4 times more risk for mortality than CTP class A ($p = 0.01$). Etiology was independently associated with mortality ($p < 0.05$).

Conclusion: Higher CTP class and higher MELDNa were associated with 2 to 3 fold higher mortality and early diagnosis is needed to reduce the mortality

Abstract Submission No. 102080
O-0996

Assessing the causal association between human blood metabolites and the risk of cirrhosis

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Background: The development of cirrhosis is intricately linked to metabolism, but there remains insufficient evidence regarding the definitive causal role of metabolites in either promoting or preventing cirrhosis.

Methods: We applied Mendelian randomization (MR) analysis to assess the association between serum metabolites and cirrhosis using genome-wide association study statistics. The inverse variance weighting method was used to generate the main results. To ensure the robustness and reliability of the findings, sensitivity analyses, including MR-Egger, weighted median, Cochran's Q test, Egger intercept test, and leave-one-out analysis, were performed. Additionally, we conducted a metabolic pathway analysis to identify potential pathways associated with the observed outcomes.

Results: Following a meticulous screening, we retained 1091 metabolites and 309 metabolite ratios for Mendelian randomization (MR) analysis. After screening by IVW and sensitivity analysis, 9 metabolites and 3 metabolite ratios were identified with a causal association on cirrhosis ($P < 0.05$). In particular, high levels of glutamine degradant were associated with a low risk of cirrhosis (odds ratio = 0.88, 95% confidence interval: 0.78-0.98, $p = 0.0218$). Furthermore, the metabolic pathway analysis identified aminoacyl-tRNA biosynthesis and arginine biosynthesis that may be associated with the disease.

Conclusion: These findings indicated that glutamine degradant has a protective impact on cirrhosis, thus offering a novel perspective on the metabolite-mediated development mechanism of cirrhosis via integrating genomics with metabolomics.

Abstract Submission No. 200158
O-0997

Adipose Tissue Cell Signaling is Dysregulated in Liver Cirrhosis

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In the APASL-2023 presentation, we reported the overexpression of angiogenic factors and accelerated proliferation of adipose tissue mesenchymal cells (ADMSC) in the adipose tissue of cirrhosis patients compared to healthy subjects. This study is aimed to investigate potential dysregulation in cell signaling pathways in adipose tissue of cirrhosis patients. Adipose tissue samples were collected from liver

donors (healthy) and liver transplant recipients with cirrhosis. Analysis involved real-time PCR, western blots, DCFDA dye for reactive oxygen species (ROS) estimation, and RNA-Seq. Results revealed elevated levels of phosphorylated Akt, JNK, and beta catenin in both cirrhotic adipose tissue and cultured ADMSC, indicating increased cell growth signaling. The tumor suppressor gene PTEN, a negative regulator of Akt, exhibited lower levels in cirrhotic adipose tissue, potentially contributing to enhanced Akt/PKB signaling. This pathway is associated with cell cycle regulation and inhibition of cell proliferation. Additionally, microRNA analysis demonstrated heightened levels of pro-growth microRNA 181-a and reduced levels of anti-tumor microRNAs 21 and 22 in cirrhotic adipose tissue. The reactive oxygen species production in ADMSC did not significantly differ between cirrhosis and healthy groups. The findings collectively suggest that the elevated levels of growth factors, cytokines, bile acids, xenobiotics, and inflammatory mediators in cirrhosis contribute to the hyperactivation of pro-growth signaling pathways in adipose tissue, ultimately leading to adipose tissue dysfunction.

Abstract Submission No. 200188
O-0998

Mesenchymal stem cells for the treatment of decompensated cirrhosis (MSC-DLC-1): A phase I trial

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Background: Decompensated cirrhosis (DLC) is a global burden with limited therapeutic options. Human umbilical cord-derived MSCs (UC-MSCs) have shown their potential for treating DLC, but the dose and related mechanisms are still unclear. We designed an investigator-initiated, single-arm, dose-escalation clinical trial to evaluate the safety and identify the suitable dose of UC-MSCs in treating patients with DLC(NCT05227846).

Methods: A single injection of UC-MSCs was administered in a pre-determined dose in each cohort (cohort 1 with 5.0×10^7 cells, cohort 2 with 1.0×10^8 cells, cohort 3 with 1.5×10^8 cells, and cohort 4 with 2.0×10^8 cells) according to the “3+3” rule. The primary evaluation measures included the incidence of adverse events and the change in the Model for End-stage Liver Disease (MELD) score from baseline to the 28th day. Secondary evaluation measures included: the change in the MELD score, the incidence of each complication associated with DLC, liver transplant-free survival, and the incidence of liver failure, among other relevant measures. All patients will be followed up for 24 months.

Results: Fifteen patients with Child-Pugh scores ranging from 7 to 12 with DLC were enrolled (3 patients in cohort 1, 3 patients in cohort 2, 6 patients in cohort 3, 3 patients in cohort 4). All 4 cohorts showed no signs of dose-limiting toxicities at 28 days after treatment with 4 adverse events (1 rash in cohort 2, 1 rash and 1 kidney calculi in cohort 3, 1 influenza-like symptoms in cohort 4). No serious adverse event and suspicious and unexpected serious adverse reactions occurred.

Conclusion: Up to maximum dose of 2.0×10^8 cells, the safety and tolerability of UC-MSCs have been demonstrated in patients with DLC.

Abstract Submission No. 200194
O-0999

The most common etiology, complication, and mortality of LC at the Gastroenterology Center FCHM

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Background: According to the World Gastroenterology Association report, 112 million people are suffering from LC, and it is one of the top mortality causes within gastroenterology-related diseases in Mongolia, the LC rate was 70.1% per 10,000 people on average over the last ten years. However, it reached 73.1% (23402 cases) in 2022 and 55% for gastroenterology-related death.

Method: We conducted a retrospective study of 5464 patient histories from the FCHM who were diagnosed with Gastroenterological disease between 2018 and 2022. Later, we pointed out 1965 patient histories that were diagnosed with LC.

Result: There were 945 males and 1020 females. Patients between ages 36 and 45 had the highest LC. The most common etiology of LC was HBV and HDV infection, which was 82%. For the severity of LC, CTP-A, B, and C were 440, 957, and 568, respectively. MELD scores <9, 10-19, 20-29, and 30+ were 494, 1037, 363, and 71, respectively. The severe complications were EV bleeding for 450 cases (22.9% of total EV cases), SBP for 435 cases (22.1% of ascites cases), HRS for 58 cases, hepatopulmonary syndrome for 37 cases, liver failure for 931 cases, and HCC for 180 cases.

Conclusion:

LC is diagnosed within 36-80 years old people more. Hepatitis virus (B, D, and C) is the most common etiology of LC. The main life-threatening complications were EV bleeding and SBP, which were counted in more than 22% of total patients.

Abstract Submission No. 200215
O-1000

The efficacy and safety of NOACs in cirrhosis and portal vein thrombosis patients: a meta-analysis

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Background: The imbalance of pro- and anticoagulant factors increases the risk for both bleeding and thrombosis in patients with cirrhosis. This study was to identify the efficacy and safety of novel oral anticoagulants (NOACs) in portal venous thrombosis (PVT).

Methods: We performed searches in PubMed, Embase, CNKI, Wanfang data, and CQVIP, up to Nov, 2023, using the key words “liver cirrhosis”, “cirrhotic”, “Portal Vein Thrombosis”, “New oral

anticoagulants”, “anticoagulants” in English or Chinese. The meta-analysis was performed by Revman 5.4.1.

Results: We enrolled 11 studies, 2 RCT and 9 cohort studies, with a total of 899 PVT patients. The PV recanalization rate after NOACs anticoagulation therapy was better than that in the traditional therapy group. [RR=2.59, 95%CI(1.33,5.01),Z=2.81, P=0.005]. Meanwhile, the risk of bleeding was lower in the NOACs group than that of traditional group. [RR=0.47, 95%CI(0.31,0.72),Z= 3.52, P=0.0004].

Conclusions: Anticoagulant therapy is necessary for patients with cirrhosis complicated with portal vein thrombosis, and it is safe and effective to use new oral anticoagulant. due to the lack of large sample randomized controlled trials, the accuracy of the results needs to be further verified.

Abstract Submission No. 100095

O-1001

Insulin and glucagon levels in relationship with plasma amino acid imbalance in liver cirrhosis

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Alteration in insulin and glucagon levels might account for the plasma amino acid imbalance in cirrhotics. In order to verify this hypothesis we evaluated basal insulin, glucagon, branched chain amino acids and aromatic amino acids in 10 controls and 17 cirrhotics. Tyrosine and aromatic amino acids significantly correlated with I/G ratio. On the other hand, insulin did not correlate with any of the plasma amino acids. Our data suggest that the catabolic state associated with increased glucagon levels may account for some of the alterations in the plasma amino acid profiles in cirrhotics.

Abstract Submission No. 100173

O-1002

MELD-sarcopenia Score Predicts Short-term Readmission of Patients with Hepatic Encephalopathy

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Purpose: To investigate whether the quality of skeletal muscle mass could predict short-term readmission in patients with hepatic encephalopathy (HE).

Method: Patients with HE were enrolled from 2018 to 2022. Sarcopenia and myosteatosis were defined using the L3 skeletal muscle index (SMI) and skeletal muscle density (SMD) obtained from CT imaging. MELD-Sarcopenia score was calculated. Multivariable analysis and multiple linear regression were applied to identify predictors of 30-day readmission and length of hospitalization.

Results: 123 patients with HE were included. 55 (44.7%) and 87 (70.7%) patients were identified with sarcopenia and myosteatosis. Patients with sarcopenia exhibited a higher prevalence of myosteatosis, lower SMI and SMD ($p < 0.05$). Patients with myosteatosis were older, had a lower body mass index, a higher neutrophil-to-lymphocyte ratio and MELD-sarcopenia scores ($p < 0.05$). 10 (8.1%) patients were readmitted within 30 days. The readmitted group had a higher MELD-sarcopenia score (25.0 ± 6.6 vs. 19.5 ± 7.8 , $p = 0.034$) and lower L3 SMD (28.3 ± 5.9 vs. 33.8 ± 6.9 , $p = 0.015$). In the multivariable analysis, MELD-sarcopenia score (95% CI 1.388 [1.074-1.793], $p = 0.012$) and SMD (95% CI 0.778 [0.610-0.991], $p = 0.042$) were found to be significantly associated with the 30-day readmission of patients with

HE. Age ($p = 0.028$), alcohol liver disease ($p = 0.025$), and hypertension ($p = 0.003$) were associated with the length of hospitalization for patients with HE.

Conclusions: The MELD-sarcopenia score and SMD were identified as predictive factors for short-term readmission in patients diagnosed as HE.

Abstract Submission No. 100192

O-1003

serum-ascites Vitamin D Gradient: A Diagnostic Marker for SBPin Egyptian Cirrhotic Patients

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The most prevalent infectious consequence of liver cirrhosis is spontaneous bacterial peritonitis. Ascitic fluid PMN counts more than 250 cells/microL are used as the gold standard for diagnosing SBP. Patients with decompensated cirrhosis also had significantly decreased serum 25-OH vitamin D levels compared to controls.

Aim: to investigate the role of (serum ascites vitamin D gradient) as a diagnostic factor for diagnosis of SBP.

Patients and Method: This cross-sectional study included 80 cirrhotic ascitic patients from Egypt who were treated at the hospitals affiliated with the Tropical Medicine and Infectious Diseases Department at Tanta University.

Group 1: 40 ascitic patients with SBP.

Group 2: 40 ascitic patients without SBP

Results: Child-Pugh score was significant in both groups as child C was significantly higher in group 1 than group 2. Total leucocyte count and differential neutrophil were significantly higher in group 1 than group 2 while child B was higher in group 2 than group 1. Differential lymphocyte was significantly lower in group 1 than group 2 .SADG was significantly lower in group 1 than group 2 .SADG ratio can significantly predict SBP ($P = 0.036$ and AUC = 0.632) at cut-off ≤ 25.8 with 37.50% sensitivity, 95.00% specificity, 88.2% PPV and 60.3% NPV

Conclusion: Patients with cirrhotic ascites had decreased SADG and higher SBP. In these cases, it might be used as a diagnostic and prognostic marker for SBP. Patients with decompensated cirrhosis, independent of SBP, have a decreased prevalence of vitamin D insufficiency.

Abstract Submission No. 100440

O-1004

Inflammatory status in portal vein is not associated with the PVT in patients with cirrhosis

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Background: Cirrhotic patients have particular proinflammatory or hypercoagulable characteristics, which may contribute to portal vein thrombosis (PVT) development. However, it remains unclear whether proinflammatory characteristics either in porta veins or peripheral veins are associated with the presence of PVT.

Method: This was a retrospective case-control study and we enrolled cirrhotic patients with PVT and portal hypertensive complications who underwent the transjugular intrahepatic portosystemic shunt (TIPS) and consented to get the blood sample between November 2018 and September 2020. Cirrhotic patient receiving TIPS without PVT was matched based on Child-Pugh class during the same period.

Results: A total of 15 patients with PVT who underwent TIPS due to portal hypertensive complications were included in this study. Hence, 15 patients receiving TIPS without PVT during the same period were matched based on the Child-Pugh class. We found plasma levels of these factors were similar between the two groups either in portal vein or jugular vein. In addition, no significant differences were observed regarding levels of these proinflammatory factors between the jugular and portal vein in our cohort.

Conclusion: We found no elevated inflammatory status in the portal vein. Additionally, when matched by the Child-Pugh class, no significant difference in portal and peripheral inflammatory status was observed between patients with PVT and patients without in our study. However, relatively few patients were enrolled and only several inflammatory factors were measured in our study. Hence, a large cohort and comprehensive procoagulant and inflammatory profiles are needed to assess the role of inflammation and hypercoagulability in PVT.

Abstract Submission No. 100604

O-1005

NPAR in liver cirrhosis: Novel prediction model of 90-days mortality and rehospitalization risk

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Background: Specific prediction model for liver cirrhosis (LC) patients to determine 90-days mortality and 90-days rehospitalization risk were scarce in literature. Previous studies found that neutrophil percentage-to-albumin ratio (NPAR) was a potential predictor of mortality in several diseases. This study aimed to develop a prediction model of 90-days mortality and 90-days rehospitalization risk in LC patients.

Methods: We retrospectively recruited LC patients from a tertiary grade hospital. Demographical data, history and physical examination, laboratory tests (complete blood counts, liver and kidney function), complications, and outcomes were recorded. NPAR was calculated through the ratio of neutrophil percentage (%) / serum albumin concentration (g/dL) at admission to the hospital. Prediction models were performed with logistic regression analysis.

Results: A total of 100 LC patients were enrolled. NPAR was significantly higher in dead patients within 90 days, but lower in hospitalized within 90 days patients. NPAR, hepatic encephalopathy (HE) grade, and creatinine serum were predictor of 90 days mortality ($y = -11.616 + 0.822 \times \text{HE grade} + 0.202 \times \text{NPAR} + 1.617 \times \text{creatinine}$). For 90 days rehospitalization, NPAR, HE grade, thrombocyte levels, and albumin levels were the predictors ($y = -6.321 - 0.813 \times \text{HE grade} + 0.005 \times \text{thrombocytes} + 0.043 \times \text{NPAR} + 1.487 \times \text{albumin}$). The risk could be calculated with $1/1 + \exp[-(y)]$. The new prediction models have higher discriminative value compared to CTP score.

Conclusion: The new prediction models have shown great accuracy in predicting 90 days mortality and hospitalization, hence potential for further evaluation of LC patients at admission.

Abstract Submission No. 100749

O-1006

Identifying small varices in patients with compensated cirrhosis

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Background: This study aims to investigate whether patients with pure small varices have different clinical outcomes compared to those with high-risk varices. Predictive value of serum-based non-invasive index for small varices was also analysed.

Methods: Adult patients with compensated cirrhosis who underwent esophagogastroduodenoscopy (EGD) at our center from January 2016 to October 2017 were enrolled and followed up until July 2023.

Results: A hundred and forty-two compensated cirrhosis patients, with a median age of 53 (23-83) years, were included. Of them, 60.6% were male patients (n=86) and chronic hepatitis B was the most common cause of cirrhosis (50.7%). According to the EGD findings, 58, 60, and 24 patients were respectively divided into three groups: none, small only (varices < 5 mm in diameter), or high-risk varices (varices ≥ 5 mm or small varices with red signs). Of these, 134 patients completed follow-up with a median time of 75.2 months and an overall cumulative variceal bleeding rate of 14.2%. The respective cumulative bleeding rate was 1.7% (n=1), 15% (n=9), and 41.7% (n=10) (Figure 1). Survival analysis indicated a significant difference in patients with different baseline varices status ($P < 0.001$) (Figure 2). ROC analysis showed that the P2MS model based on the platelet count, monocyte and neutrophil fraction had the highest but moderate diagnostic value for pure small varices (AUC=0.737).

Conclusion: Small varices is an important early event in compensated cirrhosis and should be paid attention. Exploring new serum markers for predicting varices are still needed.

Abstract Submission No. 100914

O-1007

Long-term efficacy of rifaximin treatment in Japanese patients with hepatic encephalopathy

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Background: Rifaximin, a non-absorbable antibiotic, is one of the major treatment options for hepatic encephalopathy (HE). However, the data about the efficacy and safety of long-term administration for Japanese patients with decompensated cirrhosis are still limited.

Methods: The patients who received rifaximin for more than 48 weeks in our institute between November 2016 and June 2022 were enrolled. Laboratory data including serum ammonia level, Child-Pugh score (CPS), Albumin-Bilirubin (ALBI) score, at pre-treatment and post-treatment (12, 24 and 48 weeks after rifaximin administration) were analyzed. The hospitalization rate due to overt HE during 24 weeks before and after rifaximin administration was investigated. The adverse events caused by rifaximin treatment was also evaluated.

Results: A total of 27 patients with decompensated cirrhosis were enrolled in this study. Ammonia levels were significantly decreased at 12, 24 and 48 weeks of rifaximin administration. The CPS was improved after 24 weeks of rifaximin administration. Furthermore, the ALBI scores were also improved after 12 weeks of rifaximin administration. The hospitalization rate was significantly decreased after treatment compared to before treatment (44.4% vs. 11.1%, $p=0.006$). There were

no serious adverse events after rifaximin usage. Renal function was not impaired after rifaximin administration by 48 weeks.

Conclusions: The long-term rifaximin treatment was effective and safe for patients with HE. Our results suggest that rifaximin may improve liver function in patients with decompensated cirrhosis.

Abstract Submission No. 100942

O-1008

Prediction of Mortality in Liver Cirrhosis Patients with AKI using NLR, CTP score and Infection

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Background: Acute kidney injury complicates liver cirrhosis and is associated with increased mortality. Systemic inflammation, liver dysfunction and infection are associated with higher mortality in cirrhotic patients with AKI. We aimed to evaluate the utility of a novel scoring system which combined neutrophil-lymphocyte ratio (NLR), Child-Turcotte-Pugh (CTP) score and presence of infection in predicting in-hospital mortality in liver cirrhosis patients with AKI.

Methods: A total of 141 cirrhotic patients with AKI was included in the study. Clinical and biochemical characteristics were obtained. Bivariate and multivariate analyses were done to identify independent predictors of in-hospital mortality. Odds-ratio (OR) was measured using multiple logistic regression. A scoring system was made using the OR of independent predictors. Receiver operating characteristic (ROC) curve analysis was done to assess the accuracy of the novel combined scoring system.

Results: NLR, CTP score and presence of infection were identified as independent predictors of outcome. A score of ≥ 2.4 was associated with increased mortality with area under ROC curve (AUROC) of 0.791, 85.9% sensitivity, 61.9% specificity and 84.1% positive predictive value, with an OR of 10.8 (95% CI 4.6 to 25.2). This scoring system is more superior to NLR and non-inferior to CTP score in predicting in-hospital mortality upon comparison of AUROC curves.

Conclusions: NLR, CTP score and infection are associated with increased mortality in cirrhotic patients with AKI and a scoring system combining these three variables can be used to identify cirrhotic patients with AKI with an increased risk for in-hospital mortality.

Abstract Submission No. 101012

O-1009

Improvement in Frailty with Nutrition in Patients with Cirrhosis - a Randomized Controlled Trial

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Background and Aims: There is limited data on nutritional intervention on frailty status in cirrhosis. Aim was to assess the effects of nutritional therapy on changes in frailty status in cirrhotic patients.

Material and Methods: A randomized controlled trial conducted in a tertiary care centre on patients with cirrhosis, who were randomized to assigned to nutritional therapy (group A: 30-35 kcal/kg/day, 1.0-1.5 g protein/kg/day;) and no nutritional therapy (group B: patients continued on their same diet) for 6 months. Frailty status was assessed by liver frailty index (LFI) and gait velocity(GV). Primary endpoints were improvement or worsening in frailty status. Secondary endpoints were improvement of other nutritional parameters and liver functions.

Results: Till date 34 patients were randomized to group -A (n=18, age 43.4 $\pm$ 9.8 yr, 14 men) and group-B (n=16, age 42.7 $\pm$ 10.1 yr, 12 men). Alcohol was most common (64%) etiology. Baseline characteristics including age, body mass index (BMI), hemoglobin, MELD score, mid arm circumference (MAC), hand grip (HG), GV and LFI were comparable in both the groups. Improvement in GV (Δ GV 0.99 $\pm$ 0.32 vs -0.82 $\pm$ 0.28, p=0.001), LFI (Δ LFI -0.62 $\pm$ 0.24 vs 0.3 $\pm$ 0.32, P= 0.001) HG strength (Δ HG 4.2 $\pm$ 1.3 vs -2.9 $\pm$ 1.2, p=0.001), MAC (Δ MAC 2.69 $\pm$ 0.28 vs -2.15 $\pm$ 0.26, p= 0.01) was observed in group A compared to group B at the end of study. Liver functions assessed by Child Turcotte Pugh and Model for end stage liver disease also significantly improved in group A compared to group B, p<0.001.

Conclusion: Nutritional therapy is effective in the improving the frailty status, nutritional parameters and liver functions in cirrhotic patients.

Abstract Submission No. 101080

O-1010

Poor monitoring reduces survival in patients with delta viral cirrhosis

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Background: Regular monitoring of liver complications is crucial to reduce morbidity and mortality in patients with delta viral liver cirrhosis. **Aim:** To determine the factors associated with liver decompensation in patients with delta viral liver cirrhosis.

Methods: We analyzed the factors associated with reduced survival in 144 patients with delta viral liver cirrhosis, followed over a period of 4 years.

Results: mean age 52 years, 58% men; 73% come from the south and center of Moldova. Only 20.8% (n=30) of patients had surveillance for HCC and 27.08% (n=39) for liver decompensation throughout the study period. On multivariable regression, age 53.3 years (OR 1.64, p<0.005), decompensated cirrhosis (OR 1.91, p<0.001) were associated with significantly higher odds of undergoing surveillance every 6 months for liver decompensation and every 14 months for HCC. Close monitoring every 4 months (p=0.001) versus every 14 months was associated with reduced risk of decompensation.

Conclusion: Our study suggests that monitored patients were more likely to prevent decompensation and had significantly better survival. More efforts are needed to optimize the surveillance of patients with delta liver cirrhosis.

Abstract Submission No. 101093

O-1011

Spectrum of Clinical Presentation In Patients With Chronic Liver Disease Secondary To NAFLD

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Non-Alcoholic Fatty Liver Disease (NAFLD) is the most common chronic liver disease (CLD). NAFLD is recognized as an important public health problem nowadays and it encompasses a variety of liver pathologies including steatosis, Nonalcoholic steatohepatitis (NASH), cirrhosis and finally hepatoma. The overall prevalence of NAFLD in

Asia is now estimated to be 29.6% and in Pakistan about 15% of general population.

It is a descriptive cross-sectional study in which all patients with CLD NAFLD were enrolled from March 2021 till date presenting in Gastroenterology Department Jinnah postgraduate medical center Karachi. After informed consent all patients were evaluated for the spectrum of presenting symptoms and the data were recorded on preformed proforma.

134 patients were enrolled with the mean age of the patients 42.96 ± 13.98 . Males 94 (70%) and females 40 (30%). Mean Body mass index (BMI) were 25.84 ± 3.50 . Child Pugh Score and MELD Na was calculated of all patients. Risk factors were evaluated 100(74%) of patients had diabetes, 114(85%) had sedentary lifestyle, 80(60%) had dyslipidemia, 64(48%) were smokers and 67(50%) had hypertension. Most common clinical presentation was ascites 81 (60%), followed by upper gastrointestinal bleeding 50 (37%), hepatic encephalopathy 40 (30%), jaundice 31 (23%), coagulopathy 21 (16%) and hepatorenal syndrome 19 (14%).

Ascites was the most common presenting clinical feature followed by the upper gastrointestinal bleed and hepatic encephalopathy and affecting males more than females. NAFLD is typically a chronic lifelong condition, that may get worse over time and produces debilitating outcomes. Management requires a multidisciplinary approach with clear risk stratification.

Abstract Submission No. 101164
O-1012

Prediction of the severity of liver cirrhosis with esophageal varices determined by iv-GTT

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To judge the severity of liver cirrhosis, Ozawa have studied blood glucose curves of 50g OGTT and described the relationship between glucose tolerance and severity. There is a disadvantage with OGTT in that only the blood glucose curves types can be classified. OGTT is influenced by gastric emptying time. We have studied in-GTT and OGTT in 18 cases of liver cirrhosis complicated with esophageal varix and studied the prognosis. The OGTT pattern was of the parabolic type in all cases, whereas K-glucose in ivGTT was 1.26-3.46, showing variations depending on the case. Where a major operation was performed in cases <2.0, there was a significant tendency to die of hepatic failure. From this it appears that K-glucose in iv-GTT clearly reflects the severity of liver cirrhosis.

Abstract Submission No. 101170
O-1013

Comparison of LMR with CPS and MELD Score Determining Severity and Outcome in Cirrhotic Patient

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Background: Lymphocyte/Monocyte ratio (LMR) is a simple and effective marker that has potential to predict the severity of hepatic dysfunction in cirrhotic patient like Model for end-stage liver disease (MELD) score and Child-Pugh (CP) score. Comparison of LMR with CP Score and MELD Score in the determination of hepatic dysfunction severity in patients with cirrhosis was the objective of the study.

Method: This Cross-sectional analytical study was conducted in the Dept. of Gastroenterology, BSMMU from Sept 2019 to Aug 2020. Total 40 compensated cases and 82 decompensated cases were included and information regarding clinical profile, laboratory parameters was collected. LMR, MELD score and CP score were calculated both in compensated and decompensated cirrhotic patient. Correlation between LMR and CP/MELD score were established and cut-off values of LMR were obtained. Bland-Altman plot and Helley MacNeil test were used for comparison of measurement techniques. Data were analyzed by SPSS 20. $p < .05$ was considered as a level of significance.

Results: Mean values for LMR and MELD and CP scores were 7.93 ± 3.08 , 5.25 ± 0.43 & 7.10 ± 1.19 , respectively. Average LMR was significantly higher in compensated group while CP and MELD Score was lower in that group ($p < 0.001$). MELD and CP were positively correlated with each other ($p < 0.001$). LMR was negatively correlated to both MELD and CP scores ($p < 0.001$). Cut-off value of LMR, CP and MELD were $LMR \leq 2.18$ (sensitivity: 75%, specificity: 87.3%), $CPS \geq 13.5$ (sensitivity: 75%, specificity: 98.3%) & $MELD \geq 30.5$ (sensitivity: 75%, specificity: 94.9%) respectively. Patients in the low LMR group showed decreased survival than those of high LMR group ($p = 0.000$). Non survived group had lower LMR and higher MELD and CP scores than those of the survived group ($p < 0.001$).

Conclusion: In comparison with CP Score and MELD Score in the determination of hepatic dysfunction severity and outcome in cirrhotic patients, LMR is a useful tool.

Keywords: Liver cirrhosis, lymphocyte count, LMR, CP Score, Meld Score, chronic Hepatitis C, ROC analysis, inflammation mediators, hepatic dysfunction

Abstract Submission No. 101327
O-1014

Severity of liver cirrhosis is negatively correlated to serum levels of FT3.

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Introduction: Chronic liver disease (CLD) is a leading cause of morbidity and mortality in Pakistan. The liver plays a dominant role in the metabolism of thyroid hormones. Type I deiodinase, which converts part of thyroxine (T4) to triiodothyronine (T3), is the major liver enzyme responsible for approximately 30%-40% of extra thyroidal production of T3. Patients with chronic liver disease may have aberrant functioning of Type I deiodinase causing thyroiditis, hyperthyroidism, or hypothyroidism.

Aims: To determine the levels of FT3 in liver cirrhosis patients.

Methods: It is a cross-sectional study in which patients with liver cirrhosis were enrolled from April 2022 till date at Gastroenterology department Jinnah postgraduate medical center Karachi.

Results: A total of 246 patients (mean age 49 ± 14 years, 160 males and 86 females) with liver cirrhosis were selected. Most common etiology of liver cirrhosis was HCV in 177(72%) patients, 50(20%) had HBV, 10(4.2%) had HBV/HDV and 9(4%) had Non hepatitis B & C related cirrhosis. Among CLD patients, most had CTP score B 158(64%). Among all, 24(10%) patients were found to have hypothyroidism, 12(5.6%) had subclinical hypothyroidism, 2(2%) patients had hyperthyroidism. On bivariate analysis, we found that as the severity of cirrhosis increases, indicated by Child Pugh A to C and increasing MELD, serum levels of FT3 reduces significantly (p value 0.001).

Conclusion: According to this study, we recommend that all cirrhotic patients should undergo thyroid function evaluation as a significant proportion of these patients developed hypothyroidism due to reduced serum levels of FT3.

Abstract Submission No. 101547

O-1015

INDICATIONS OF SYNCHRONOUS SPLENECTOMY FOR TREATMENT OF HCC WITH HYPERSPLENISM AND LIVER CIRRHOSIS

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Hepatocellular carcinoma (HCC) frequently occurs in cirrhotic patients with concurrent hypersplenism, posing challenges in their management. This review article explores the indications of synchronous splenectomy for HCC with hypersplenism due to cirrhosis. Hypersplenism in cirrhosis leads to thrombocytopenia, leukopenia, and erythrocytopenia, impacting interventions. Synchronous splenectomy offers potential benefits. It addresses hypersplenism-related complications, improving platelet count and coagulation function, reducing bleeding risk and improving hemostasis. Splenectomy also alleviates hypersplenism-related symptoms, enhancing patients' quality of life. Additionally, it aids surgical management by providing better liver exposure, facilitating tumor identification and resection, resulting in improved surgical outcomes and reduced bleeding. Moreover, splenectomy may have immunomodulatory effects. It counteracts the immunosuppressive influence of an enlarged spleen, potentially enhancing tumor control and improving long-term outcomes. However, patient characteristics and careful assessment guide splenectomy decisions. Factors include cirrhosis severity, portal hypertension, comorbidities, and overall health. Evaluation of potential risks and complications, such as infection and thrombosis, is also necessary. In conclusion, synchronous splenectomy is considered for HCC with hypersplenism due to cirrhosis. It addresses complications, aids surgical management, and potentially modulates the immune response. Individual patient assessment and further research are needed to establish clear indications, refine protocols, and determine long-term outcomes of splenectomy in HCC treatment.

Key-words: HCC, Hypersplenism, Synchronous splenectomy, hepatectomy, cirrhosis, portal hypertension

Abstract Submission No. 101856

O-1016

The signatures and interlinks of gut bacteria, fungi and metabolites in cirrhotic patients

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Abstract

Background: A growing studies have been demonstrated a complex and multifaceted relationship between the liver cirrhosis and gut microbiome community. However, most microbial analyses focused on the role of the gut bacterial component in cirrhosis progression, while the impacts of fungi are still unclear.

Methods: A total 45 cirrhotic patients and 30 healthy participants were recruited. Stool samples were collected for 16S rRNA sequencing,

ITS2 DNA sequencing, and untargeted metabolomic detection to confirm intestinal bacteria, fungi and metabolomic signatures respectively. Bioinformatics analyses were performed to characterize the alterations and associations among gut bacteria, fungi, metabolite and the clinical features.

Results: The composition, abundance and diversity of intestinal bacteria and fungi in patients with cirrhosis was significantly different compared with that in healthy individuals. As for the gut microbial composition in cirrhotic patients, an decrease abundance bacteria producing short-chain fatty acids and unsaturated fatty acid was observed, including *Blautia*, *Anaerobutyricum*, *Ruminococcus*, *Gemmiger*, and *Dorea*, while intestinal fungi composition exhibited an elevation expression of opportunistic pathogens, such as *Candida* and *Saccharomyces*. Gut bacterial, fungal abundance, metabolite and clinical characteristics (WBC, ALB, CTP, HGB, PLT, PTA and MELD) were significantly linked. Furthermore, based on or differential bacteria, fungi,metabolites, we constructed a diagnostic model for cirrhosis (AUC= 0.804).

Conclusions: Our findings characterized the connections among the gut bacteria, fungi, metabolite and the clinical features, providing an experimental basis and theoretical support for using specific gut microbiome to achieve early noninvasive clinical diagnosis and assess the effect of clinical treatment for patients with cirrhosis.

Abstract Submission No. 101955

O-1017

Tolvaptan is safe and effective in management of hyponatremia in acute on chronic liver failure

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Introduction:There are therefore no treatment options for managing hyponatremia in patients with APASL-ACLF. We retrospectively analyzed our experience of using Tolvaptan in ACLF patients over the past 2 years.

Patients and Methods: 61 patients with ACLF(with serum sodium < 125 mEq/l non-responsive to free water restriction and plasma volume expansion with albumin were started on tolvaptan on a dose of 7.5 mg OD, (maximum of 15mg/day). The maximum duration of therapy was restricted to 7 days. Primary end-point was rise in serum Na to >130 Meq/L.

Results: Mean CTP and MELD scores were 11.07 ± 1.07 and 32.75 ± 4.96. Mean baseline serum sodium and creatinine were 118.6 ± 5.43(mEq/L) and 0.71 ± 0.32mg/dL. Pedal edema was noted in 55/61 (90.6%) patients and ≥ Grade II ascites in 53/61(86.8%) patients. Mean dosage and mean duration of therapy were 7.5(7.5-15)mg/day and 5.5±0.70 days.Median daily change in Na: 3(1,6) mEq/L. 48/61(78.6%) patients noted increase in Na>125 mEq/L. Median increase in the urine output from the baseline per 24 hours was 475ml/day(-100,700). Decrease in body weight was noted with median decline of -650 (-1200, 400) grams/day.Tolvaptan was well tolerated with only 8/61(13.11%) requiring discontinuation of drug.Increase thirst was noted 28/51(45.9%) of the patients, while new onset transaminitis in 8/61(13.11%) patients. 3/61 (4.9%) patients developed AKI(S.creatinine>1.5mg/dl);2(3.2%) developed HE(>grade II);2(3.2%) patients had worsening of INR(>1.8) requiring discontinuation of drug while 1/61(1.6%) patient witnessed post- EVL ulcer bleed.

Conclusions:Tolvaptan can be safely and effectively used in correcting hyponatremia in ACLF patients.

Abstract Submission No. 102048
O-1018

Clinical Outcomes among Cirrhotic Patients and their Compliance to Quality Indicators (QI) for Care

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Background: Cirrhosis constitutes a significant public health burden in the Philippines, responsible for 12696 deaths per year. Despite practice guidelines, significant gaps in care remain. Hence Quality Indicators (QI) have been developed as objective measures that may assist stakeholders in identifying potential areas for improvement.

Methods: A retrospective cohort study of adult cirrhosis patients admitted in a tertiary specialty hospital during a five year period was conducted. Detailed demographic, clinical, and outcome information was collected. Compliance with selected Quality Indicators across five domains was assessed based on chart review. The association between demographic and clinical data, compliance with Quality Indicators, and outcomes was analyzed using Pearson R and Chi-square statistics.

Results: 239 patients were included, and only 42.7% received High Quality of Care, defined as compliance with 75% of Quality Indicators for which a patient is eligible. Compliance with Quality Indicators was associated with decreased length of hospital stay (median 8 days, $p=0.0051$), increased time of survival (median 219 days, $p=0.0380$), and lower MELD-Na score compared to non-compliant patients.

Conclusion: Care rendered for Filipino cirrhosis patients in terms of compliance with Quality Indicators remains lacking. Since such compliance is associated with improved clinical outcomes, further studies are needed to formulate and adapt locally appropriate Quality Indicators to address identified gaps in clinical care.

Abstract Submission No. 200103
O-1019

Muscle Mass Dynamics is Associated with Long-term Liver-related Mortality in Cirrhotic Patients

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Objectives: Sarcopenia has a detrimental impact on the prognosis of individuals with liver cirrhosis, however, the clinical significance of alterations in muscle mass remains uncertain. This study aims to investigate the influence of loss of skeletal muscle mass (LSMM) on the prognostic outcomes among patients diagnosed with cirrhosis.

Methods: In this retrospective analysis, a total of 158 individuals with cirrhosis who visited our hospital during the period from January 2018 to August 2023 were included.

Results: Of the 158 cirrhotic patients, 95 (60.1%) patients were identified as LSMM. The median of $\Delta\text{SMA}/\text{y}\%$ was -0.9 (interquartile range [IQR], -3.8, 1.6) in all patients. Chronic kidney disease (CKD) was confirmed as a risk factor of LSMM. During a median follow-up period of 68.1 (IQR, 43.5, 105.0) months, 57 patients (36.1%) died due to the liver-related diseases. The competing risk model found that LSMM was significantly associated with liver-related mortality in cirrhotic patients (hazard ratio [HR], 1.86; 95% CI, 1.01-3.44, $p = 0.047$). Cumulative survival was significantly higher in patients without LSMM than in those with LSMM ($p = 0.004$). Survival rates at 1-, 3-, and 5-years were 96.8%, 81.0%, and 65.1%, respectively, in patients

without LSMM, and 97.9%, 80.0%, and 56.8%, respectively, in patients with LSMM.

Conclusion: The utilization of LSMM can be valuable in the prediction of liver-related mortality among individuals diagnosed with liver cirrhosis. Paying attention to the management of skeletal muscle might play a role in enhancing the prognosis of patients with cirrhosis.

Abstract Submission No. 200132
O-1020

Efficacy and safety of long-term rifaximin treatment for hepatic encephalopathy

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Aim: Rifaximin (RFX), a therapeutic agent for hyperammonemia in decompensated liver cirrhosis, was approved in Japan after a 12-week clinical trial. This study examined the efficacy and safety of long-term administration of RFX in real-world clinical practice.

Methods: Of 162 cirrhotic patients who started RFX in our department between May 2017 and April 2023, 97 patients who were treated with RFX for at least 12 weeks and had follow-up were included in this study. Serum ammonia (NH₃) levels and adverse events were examined in 80 patients who had never received kanamycin (KM) (new group) and 17 patients who switched from KM to RFX (switched group).

Results: Patient background (median, IQR) was 74 (63-79) years old, male/female = 55/42, CP score 8 (7-9), 29 patients with HCC, 37 patients with major PV shunt, 45 patients with ascites, 56 patients with diuretics, 57 patients with synthetic disaccharides agents, 84 patients with oral branched chain amino acids, coma grade (Inuyama Classification) of hepatic encephalopathy (HE) at start of treatment; I/II/III/IV/V=8/15/12/2/0, RFX treatment period 23(7-35) months. Serum NH₃ levels (μg/dL) were 77 (62-134) after 1 month (M), 81 (51-98) after 3 M, 88 (72-99) after 6 M, 84 (55-110) after 12 M, 85 (57-122) after 24 M, and 71 (54-111) after 48 M, significantly lower than 133 (84-181) at the beginning of treatment, respectively (all $P<0.05$). Similarly, NH₃ levels in the new group were significantly lower than those at the start of treatment from 1M to 48M (all $P<0.01$). NH₃ levels in the switched group did not change significantly from those before the switched administration until after 48M. In a sub-analysis, there was no significant difference in NH₃ levels between patients with and without HCC, and NH₃ was significantly higher in the group with ascites than in the group without ascites ($P=0.003$). 15 patients (15.5%) had HE recurrence during RFX administration. In a multiple logistic regression analysis, HE grade III or higher at the initiation of RFX was selected as a factor associated with HE recurrence ($P=0.038$, OR 17.32, 95%CI 1.332-183.7). There were no discontinuations due to adverse events, and no significant changes in Plt, PT, Alb, T-Bil, AST, ALT, eGFR until 48M.

Conclusion: Treatment efficacy was maintained up to 4 years after initiation of RFX, and there was no NH₃ elevation in patients who switched from KM. Long-term treatment with RFX was effective and safe, with no discontinuation due to adverse events, even in patients with poor hepatic function, and the risk of HE recurrence was high in patients with HE grade III or higher at the initiation of RFX.

Abstract Submission No. 200152

O-1021

Incidence and associated risk factors for recurrence of HRS-AKI in Patients with CirrhosisRajat Kalra¹, Praveen Sharma¹, Akshay Kale¹¹Sir Gangaram Hospital New Delhi India

Introduction: HRS accounts for approximately 25% of cases of pre-renal AKI in cirrhosis. Recurrence of HRS-AKI after treatment is variable, ranging from 25-50% in different studies. There is limited literature on the factors that predict recurrence of HRS-AKI.

Objectives: To assess the incidence and factors predicting recurrence of HRS-AKI in patients with liver cirrhosis. Patients diagnosed with HRS-AKI were recruited after applying inclusion and exclusion criteria and treated at physician's discretion. Patients with complete response to the treatment for HRS-AKI were followed. The primary outcome was recurrence of HRS-AKI at 3-month follow-up. The secondary outcome was identification of risk factors for recurrence of HRS-AKI.

Results: Ninety three patients were enrolled in the study. Sixty-four (68.81%) patients had a complete response to HRS-AKI treatment. During follow-up, HRS-AKI recurred in 11 (21.57%) patients. The mean of MAP at admission was significantly higher in patients without HRS-AKI recurrence (79.5 ± 7.34 mmHg) than in patients with HRS-AKI recurrence (74.86 ± 4.5 mmHg) (p-value= 0.003). The difference between MAP at last visit and MAP at admission was significantly higher in patients without HRS-AKI recurrence (1.6 ± 3.96 mmHg) than in patients with HRS-AKI recurrence (-2.82 ± 2 mmHg) (p-value= 0.0008). Patients who received midodrine had significantly higher MAP at last follow-up visit than patients who did not receive midodrine (2.44 ± 3.42 mmHg vs -1.06 ± 3.44 mmHg) (p-value= 0.0002).

Conclusions: A higher MAP on admission and a higher MAP on follow-up protect against recurrence of HRS-AKI. Administration of midodrine significantly increases MAP and may play a role in secondary prevention of HRS-AKI.

Abstract Submission No. 100136

O-1023

Simultaneous development of NASH and atherosclerosis in New Zealand and Japanese white rabbitsQIANQIAN ZHENG¹, Momoko Hayashi¹, Yoshibumi Kuwabara², Kuniji Ito², Yoshiaki Hojo², Fumiaki Arai², Kazuki Kamijima², Masakazu Takeiri², Xiaojing Wang⁰, Pan Diao¹, Jun Nakayama⁴, Naoki Tanaka⁰

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Non-alcoholic fatty liver disease (NAFLD), particularly non-alcoholic steatohepatitis (NASH), is sometimes accompanied by arteriosclerosis and ensuing cardiocerebrovascular diseases, such as acute coronary syndrome and cerebral infarction. Conversely, individuals with atherosclerotic cardiovascular diseases often have underlying NAFLD/NASH. Therefore, the simultaneous treatment of both

diseases is required. Animal models simulating human clinical conditions are indispensable for establishing therapeutic interventions in humans. However, there is a lack of rodent models for simultaneous investigation of NAFLD/NASH and atherosclerosis, because wild-type rodents basically exhibit higher high-density lipoprotein levels with lower low-density-lipoprotein levels compared to humans. Since rabbits exhibit similar lipoprotein profiles to humans, we hypothesized that rabbits may be the promising models for simultaneously evaluating NAFLD and atherosclerosis. We treated a newly developed high-fat high-cholesterol diet (HFHCD) containing palm oil 7.5%, cholesterol 0.5%, and ferrous citrate 0.5% with male New Zealand White rabbits and Japanese White rabbits, respectively, for 14 weeks and assessed the phenotypes of liver and aorta. Both rabbit strains exhibited NASH and atherosclerosis 8 weeks after commencing the HFHCD feeding, progressing to advanced fibrosis and complete arterial atherosclerosis at 14 weeks of the treatment. Additionally, inductions of genes related to inflammation and fibrosis, particularly at 4 weeks, were similar between the two strains. In conclusion, these white rabbit models are likely suitable preclinical models for simultaneous investigation for human NAFLD/NASH and atherosclerosis.

Abstract Submission No. 100158

O-1024

Interleukin-19 gene-deficient mice deteriorated liver fibrosis through TGF-beta and CCL2 signalingNaoshige Ono¹, Kazuhiro Nishiyama¹, Yasu-Taka Azuma¹¹Osaka Metropolitan University Graduate School of Veterinary Science Izumisano, Osaka Japan

IL-19 is a cytokine which is related to various inflammatory disease and mainly produced by immune cells, such as macrophages. Liver fibrosis is a chronic disease caused by the repetitive hepatocyte injury and characterized by the accumulation of extracellular matrix (ECM) including collagen. However, the effects of IL-19 in liver fibrosis remains to be unknown. Here, our group investigated the immunological function of IL-19 in a mouse model of carbon tetrachloride (CCl₄)-induced liver fibrosis. A liver fibrosis mouse model was established by CCl₄ administration (two times per week) for 8 weeks in IL-19 gene-deficient (KO) mice and wild-type (WT) mice. In CCl₄-induced liver fibrosis, serum ALT levels were higher compared to WT mice. The measurement of fibrotic area stained with Azan and masson trichrome revealed that IL-19 KO mice had worse liver fibrosis. Furthermore, the both expression levels of mRNA and protein alpha-SMA were increased in liver tissues of IL-19 KO mice compared to WT mice. In IL-19 KO mice, the increased mRNA expression levels of TGF-beta and TIMP-1, decreased levels of MMP-2 and MMP-9 mRNA were found compared to WT mice. Mechanistically, IL-19-high expressing RAW264.7 cells inhibited the migration of NIH3T3 cells through the inhibition of CCL2 pathway in the presence of CCl₄ and IL-4. These results indicate that IL-19 suppresses liver fibrosis by TGF-beta signaling activation, the migration of hepatic stellate cells and ECM reduction during liver injury. It is suggested that IL-19 is a potential target for liver fibrosis.

Abstract Submission No. 100284

O-1025

Risk of liver fibrosis in psoriatic patients with methotrexate used: utility of noninvasive approach

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Background: Methotrexate associated liver fibrosis is well established concern. Increasing evidence suggested that methotrexate was not the main culprit but concomitant diseases such as diabetes and obesity were. Transient elastography (TE) is widely used since it is non-invasive. When TE is not available, AST to Platelet Ratio Index (APRI) and Fibrosis-4 index (FIB-4) may be used. This study aimed to determine the association between liver fibrosis and cumulative dose of methotrexate, and evaluate accuracy of APRI, FIB-4 in comparison to TE.

Methods: A single-center retrospective study was conducted between March 2018 and February 2023 at Sawanpracharak Hospital. The patient's characteristics and risk factors were analyzed. All patients were assessed by TE, APRI and FIB-4. Significant liver fibrosis is defined by TE > 7.9 kPa. The cut off of APRI and FIB-4 are 0.5 and 1.45.

Results: 59 of 272 psoriatic patients using methotrexate had significant liver fibrosis. Having BMI (Body Mass Index) > 30, hypertension, hyperlipidemia and diabetes mellitus were significantly associated with liver fibrosis (table). The accuracy of APRI and FIB-4 were 88.6% and 80.8%. Performance of FIB-4 is similar to APRI, with area under the curve of 0.797 vs. 0.795. ($p = 0.529$) (figure)

Conclusion: Cumulative dose of methotrexate was not significantly associated with significant liver fibrosis, but other risk factors such as hypertension, hyperlipidemia, diabetes mellitus, and morbid obesity were. Both APRI and FIB-4 had high accuracy in diagnosing liver fibrosis comparing with TE and could be used as an alternative in areas with limited resources.

Abstract Submission No. 100366

O-1026

MSCs alleviate mouse liver fibrosis by inhibiting pathogenic function of intrahepatic B cells

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The immunomodulatory characteristics of mesenchymal stem cells (MSCs) position them as a promising therapeutic approach for Liver fibrosis (LF). In this study, MSCs significantly ameliorated LF as indicated by reducing myofibroblast activation, collagen deposition, and inflammation. Treatment efficacy of MSCs could be attributed to decreased infiltration, activation, proinflammatory cytokine production of intrahepatic B cells. Single-cell RNA sequencing unveiled a distinct intrahepatic B cells atlas and a subtype of naive B cells was identified, which was markedly abundant in fibrotic liver, displaying mature feature with elevated expression of several proliferative and inflammatory genes. Fibrosis was attenuated in mice ablated of B cells (μ MT) or in vivo treatment with anti-CD20. In addition, fibrosis was recapitulated in μ MT after adoptive transfer of B cells, which in turn could be rescued by MSC injection, validating pathogenic function of B cells and the efficacy of MSCs on B cell-promoted LF progression. Mechanistically, MSCs could inhibit the proliferation and cytokine production of intrahepatic B cells in vitro through exosomes, regulating MAPK

and NF-kappa B signaling pathways. Thus, intrahepatic B-cell, serving as a target of MSCs, plays an important role in the process of MSC-induced amelioration of LF, revealing novel mechanisms of MSC action.

Abstract Submission No. 100452

O-1027

Allogeneic vs Autologous Fecal Microbiota Transplantation against Liver Fibrosis: A Meta-Analysis

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Background: Non-alcoholic fatty liver disease (NAFLD), an obesity-related disorder, is the most common chronic liver disease with a 25% prevalence rate. Gut microbial dysbiosis is a validated pathogenic mechanism connected to the pathophysiology of NAFLD and its stages. Fecal microbiota transplantation (FMT) is used to alter the microbiome of an obese individual to that of a healthy one by increasing insulin sensitivity and small intestinal permeability. Current research supports the idea that autologous FMT is effective, but little is known about the effect of allogeneic/donor FMT. This study aims to determine the effect of allogeneic versus autologous FMT against liver fibrosis.

Methods: A comprehensive search of literature was done through multiple electronic databases until October 2023. This study included two randomized clinical trials, and RevMan 5.4 was utilized to compute.

Results: The fibrosis scores from the studies done by Craven and Witjes were compared. Resulting I2 of 68% with p-value of 0.08 denotes that heterogeneity does not exist. Also, the resulting standard mean difference is -0.07 (95% CI - 0.76 to 0.62) with $Z=20$ ($p=.85$). Likewise, in the forest plot, the diamond marker intersects axis of 0 implying that the difference between autologous and allogeneic FMT in the progression of fibrosis is not significant.

Conclusion: Fecal microbiota transplantation resulted in significant improvement in lipid metabolism among NAFLD patients. The result of no significance between allogeneic and autologous FMT impacts public health, since allogeneic is easier and more accessible to the general population.

Abstract Submission No. 100553

O-1028

Clinical verification of letrozole-mediated suppressive effect on liver fibrosis

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Letrozole (LET), an aromatase inhibitor, has been reported to have a suppressive effect on liver fibrosis in a mouse model (Sakai N, et al. J Gastroenterol 2023). Here we attempted to verify the suppressive effect of LET on liver fibrosis in the clinical situation. There were 317

and 855 breast cancer patients in whom LET and anastrozole (ANA) were prescribed at an interval of ≥ 24 months from 2006 to 2020. Among them, patients in whom LET/ANA had been continuously administered for ≥ 24 months and had the FIB-4 index ≥ 2.30 at baseline were selected. Finally, 23 LET-treated and 43 ANA-treated patients were included. All patients were female. There were no significant differences in age, disease stage, background liver disease and prior/concomitant drug therapy between groups. Changes in the FIB-4 index in the LET group were 2.92 (mean), 2.78, 2.79, 2.59 and 2.53 at baseline, 6, 12, 18 and 24 months; a significant decrease was observed at 18 and 24 months ($p=0.044$ and $p=0.013$) compared with baseline. On the other hand, changes in the FIB-4 index in the ANA group were 2.94, 2.95, 2.94, 2.87 and 2.86 at baseline, 6, 12, 18 and 24 months. Regarding APRI, a significant decrease was observed in the LET group at 18 and 24 months ($p=0.024$ and $p=0.026$) compared with baseline, whereas no significant decrease was observed in the ANA group. Our results showed that LET, but not ANA, improved FIB-4 and APRI, supporting the possible suppressive effect of LET on liver fibrosis.

Abstract Submission No. 100579
O-1029

Distribution of Chitosanase 3-like Protein (CHI3L1) in HBeAg-negative CHB Patients with Normal ALT

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Objective: To investigate the distribution of chitosanase 3-like protein (CHI3L1) in HBeAg negative chronic HBV infected individuals with normal ALT

Method: The data of this study was obtained from a single center prospective randomized controlled study, which involved HBeAg-negative but HBV DNA positive patients with sustained normal ALT. All patients had not received antiviral treatment. The serum CHI3L1 level was quantitatively detected using chemiluminescence enzyme-linked immunosorbent assay method, which was completed by Guangzhou Kingmed Diagnostics Group Co., Ltd.

Result: A total of 145 patients were included, including 79 males and 66 females, with an average age of 39.8 years. All patients had LSM ≤ 8.0 kpa. In this group of patients, the average level of CHI3L1 was 48.43 ng/ml, with 68.3% (99/145) of patients having serum CHI3L1 < 53.5 ng/mL, 22.1% (32/145) of patients having serum CHI3L1 between 53.5 ng/mL and 79 ng/mL, and 9.7% (14/145) of patients having serum CHI3L1 ≥ 79 ng/mL. Among these 145 patients, 132 had FIB-4 score < 1.45 , with an average serum CHI3L1 level of 54.62 ng/ml, and 7.5% (10/132) of these patients had serum CHI3L1 ≥ 79 ng/mL. There were 126 patients had APRI score < 0.5 , with an average serum CHI3L1 level of 53.96 ng/mL, and 6.3% (8/126) of these patients had serum CHI3L1 ≥ 79 ng/mL.

Conclusion: The distribution of serum CHI3L1 levels in some ALT normal HBeAg-negative CHB patients who have not received antiviral treatment is relatively high, and it is necessary to be cautious about the possibility of significant liver fibrosis in these patients.

Abstract Submission No. 100590
O-1030

Translational potential role of Zeb2 in liver fibrosis and NAFLD

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Background and Aims: Myofibroblasts, characterized by the expression of the matricellular protein periostin (*Postn*), mediate the pro-fibrogenic response during NAFLD. Previous studies have demonstrated that endothelial deficiency in zinc-finger E-box-binding homeobox 2 (*Zeb2*) attenuates liver fibrosis in mice. In the present study, we investigated the myofibroblast-specific role of *Zeb2* in liver fibrosis during the development of NAFLD and the underlying mechanism.

Methods: We generated myofibroblasts *Zeb2* knockdown mice, by injecting AAV6-*Postn*-sh*Zeb2* virus, and then established BDL and HFD-diet model to investigate the role of *Zeb2* in pro-fibrogenic response during liver fibrosis and NAFLD. RNA-seq was performed to detect the underlying mechanism of myofibroblast *Zeb2* in liver fibroblasts. The genemania predicted upstream gene of *Zeb2* was also verified.

Results: *Zeb2* knockdown retarded the fibroblast-myofibroblast transition (FMyT) in vitro and dampened liver fibrosis in mice. We also report that myofibroblast conditional deletion of *Zeb2*, achieved through injecting AAV6-*Postn*-sh*Zeb2* virus, led to amelioration of liver fibrosis. RNA-seq detect the underlying mechanism of myofibroblast *Zeb2* in liver fibroblasts. Moreover, genemania predicted PTPRD is the upstream gene of *Zeb2*. Slicing PTPRD expression significantly upregulate the level of *Zeb2* and then promote the development of NAFLD.

Conclusions: Accordingly, our data unveil a novel PTPRD-*Zeb2* axis that can potentially contribute to fibroblast-myofibroblast transition and NAFLD. Screening for small-molecule compounds that target this axis may yield therapeutic options for the mollification of NAFLD.

Abstract Submission No. 100665
O-1031

NogoB promotes liver fibrosis by USP14 mediated RIPK3-derived M 標 inflammation and necroptosis

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Background: Liver fibrosis is the result of chronic liver injury, current studies show early hepatic fibrosis can be reversed, regulating the immune response mediated by macrophages is the key to reverse liver fibrosis. Nogo-B is an endoplasmic reticulum-residential protein with distinctive functions. However, the role of Nogo-B in macrophages in liver fibrosis has not been clearly defined.

Methods: Expression analysis was conducted with human liver samples obtained from 30 patients with liver fibrosis and 19 individuals without fibrosis as controls. Myeloid-specific Nogo-B knockout (Nogo-B^{mko}) mice were constructed to explore function and mechanism of macrophage Nogo-B in 3 murine models of liver fibrosis induced by carbon tetrachloride injection (CCl₄), bile duct ligation (BDL) or methionine-deficient and choline-deficient diet (MCD) in vivo. Nogo-B^{mko} bone marrow-derived macrophages were used in vitro.

Results: Nogo-B expression in macrophages is increased and positively correlated with histological stages of liver fibrosis in humans and mice. Nogo-B deficiency significantly alleviated BDL, CCl₄ and MCD induced liver injury, inflammatory responses, and hepatic fibrosis. Nogo-B deficient macrophages relieved LPS-induced inflammatory responses and NLRP3 inflammasome activation. Notably,

expression of RIPK3 was effectively inhibited in Nogo-B deficient macrophages. Further research showed Nogo-B recruited USP14 to suppress RIPK3 ubiquitination and facilitated RIPK3 phosphorylation, increased macrophages' death in vivo and in vitro.

Conclusion: Nogo-B promotes macrophage's inflammation and necroptosis, enhances progression of liver fibrosis by recruiting USP14 to reduce RIPK3 ubiquitination and facilitate RIPK3 phosphorylation. It reveals key role of macrophage Nogo-B in liver fibrosis, and provides a key therapeutic target for liver fibrosis.

Abstract Submission No. 100703

O-1032

Systemic immune-inflammation index level negatively linked with liver inflammation and fibrosis

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Background and Aims: Systemic immune-inflammation index (SII) was calculated as platelet count $\times$ neutrophil count/lymphocyte count which was first raised by Hu et al at 2014. We aimed to investigate the association between SII and pathological severity of CHB.

Methods: This is a cross-sectional study of the subset of consecutive patients with CHB who underwent liver biopsy between November 7, 1997, and October 31, 2021. The demographic characteristics, clinical data were collected.

Results: A total of 838 eligible CHB patients were included in this study. Correlation analysis showed a significant negative correlation between SII and liver inflammation grades ($P < 0.001$). In univariate analysis, after progressive adjustment for various risk factors for liver injury, SII was still associated with significant liver inflammation ($P = 0.02$) and fibrosis events ($P = 0.005$) in the final multivariable model. The ORs for significant hepatic inflammation and fibrosis progressively decreased across tertiles of SII (all $P < 0.05$). There was no significant dependence of age, sex, ALT level, HBV DNA, HBeAg status, and antiviral therapy on this negative association (all $P > 0.05$). The AUCs of SII combined with ALT on liver inflammation $\geq G3$ (0.77 vs. 0.67, $P < 0.001$) and $G4$ (0.81 vs. 0.70, $P < 0.001$) were significantly higher than ALT alone.

Conclusion: SII was negatively associated with liver inflammation and fibrosis events in patients with CHB. Elevation in SII index and ALT can independently predict liver inflammation.

Abstract Submission No. 100825

O-1033

Characterize subpopulations in liver fibrosis derived from single-cell RNA sequencing analysis

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Background: Liver fibrosis progression and regression have been described in both human and animal models of liver diseases. However, the mechanism and driving factors are still widely unknown. Single-

cell RNA sequencing is transforming our understanding of novel subpopulations, cell-cell interaction, and potential factors that contribute to liver fibrosis regression, resulting in the discovery of therapeutic targets.

Methods: ScRNA-seq was performed on primary liver non-parenchymal cells (NPCs) isolated from the age-matched control, CCl₄-induced liver fibrosis, and recovery group 2 weeks after CCl₄ injection using the 10X Genomics Chromium platform. Computational analysis was performed in R.

Results: The recovery phase significantly reduced the fibrosis condition, liver inflammation, and regeneration compared to CCl₄ group. Integration and annotation of NPCs from control, fibrosis, and recovery revealed nine cell types. Five cell types contributing to liver fibrosis progression have been characterized including capillarized LSECs, M2 macrophages, activated B cells, profibrogenic and pro-inflammatory BECs, and activated HSCs. Furthermore, M2 macrophages consisted of three subpopulations: scar-associated macrophages, monocyte-derived macrophages, and proliferated macrophages. Notably, we found four cell types that contribute to liver fibrosis regression: periportal angiogenic LSECs, pro-resolution macrophages, NKT cell activation, and inactivated HSCs. Cell-cell interaction analysis revealed that autocrine was the hallmark signal that promoted the activation of HSCs involved in fibrosis formation. Significant ligand-receptor pairs contributing to liver fibrosis progression were Col4a1-Cd44, Lamb1-Itga1+Itgb1, Gas6-Axl, Efna5-Epha7, and Thbs1-Sdc4.

Conclusion: Both liver fibrosis progression and regression exposed cellular heterogeneity. The target of HSCs autocrine signals could be promising antifibrosis therapies.

Abstract Submission No. 100834

O-1034

FIBROSIS DISTRIBUTION IN LEAN vs. OBESE NASH-CIRRHOSIS BY SHG/TPE MICROSCOPY

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Background: Inclusion criteria for drug trials focusing on Non-Alcoholic Steatohepatitis (NASH) cirrhosis require patients classified fibrosis stage as F4 by pathologists. However, F4 classification lacks comprehensive recording of zonal fibrosis parameters based on NASH Clinical Research Network (CRN). Second Harmonic Generation/Two Photon Excitation (SHG/TPE) microscopy-based qFibrosis (qF) offers fully quantitative evaluations. This study compares zonal fibrosis distribution between lean [Body Mass Index (BMI) < 25] and overweight/obese (BMI ≥ 25) patients using qF.

Methods: 133 patients from Phase 2b Belapectin drug trials (NCT04365868) were included. Paired liver biopsies were evaluated using qF based on NASH-CRN parameters. Patients were categorized into two groups: lean (n=9) and overweight/obese (n=124) in Baseline (BL) group, and lean (n=7) and overweight/obese (n=126) in End-of-Treatment (EOT) group. Statistical analysis by Wilcoxon-rank-sum-test, heat maps employed for visualization.

Results: BL group had statistically significant difference in periportal fibrosis parameters between lean and overweight/obese patient (Figure 1). Despite smaller number of patients in lean group compared to overweight/obese group, consistent observation of this significant difference of fibrosis parameters such as fiber length, thickness, etc. in periportal region in BL and EOT groups indicates a possible difference in fibrosis morphology patterns based on BMI.

Conclusions: Consistent differences in periportal fibrosis parameters between lean and overweight/obese patients using qF indicates

SHG/TPE imaging provides additional information compared to conventional pathologist staging. These findings suggest there could be variations in zonal fibrosis distribution among NASH cirrhosis patients, based on BMI status. Further research with larger patient cohorts would be recommended to expand upon these preliminary observations.

Abstract Submission No. 100838
O-1035

Androgen receptor affects the proliferation and metabolism of hepatic stellate cells through EGFR

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Aim & Background: There are significant gender differences in the occurrence and progression of liver fibrosis, in which activation of hepatic stellate cells (HSCs) is an important step. Our study aimed to reveal the mechanism of androgen in the activation of HSCs.

Methods & Results: In the carbon tetrachloride (CCl₄)-induced liver fibrosis mouse model, the degree of fibrosis in male mice was more severe than that in female mice. In male mice, castration led to a reduction in the degree of liver fibrosis, and immunofluorescence showed that the androgen receptor was localized in perivascular non-parenchymal cells. In the activation of mouse primary hepatic stellate cells *in vitro*, androgen receptor (AR), α -SMA and Mmp2 were simultaneously increased. Treatment with 10nM DHT increased EGFR and CCND1 at 24h, α -SMA and GLUT1 increased at 72h. In LX2 cells, DHT treatment increased EGFR, and EdU staining showed a slight increase in cell proliferation ($p=0.055$). The Erk signaling pathway was also activated by DHT treatment. After AR knockdown in LX2 cells, the expression of EGFR and CCND1 was significantly decreased, and EdU staining showed that the cell proliferation ability was decreased ($p<0.05$). The key glycolytic enzyme PKM2 was significantly decreased and recovered after DHT supplementation.

Conclusion: In hepatic stellate cells, androgen binds to AR and promote EGFR expression, activate cell cycle progression and glycolysis, promote the activation of HSCs and the progression of liver fibrosis.

Abstract Submission No. 100964
O-1036

Does Timing of Gaining Weight Matter Risk of Non-alcoholic Fatty Liver Disease or Liver Fibrosis?

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Background: It is unknown whether the weight change patterns across adulthood are associated with NAFLD and its impact on liver fibrosis. **Method:** Based on the Friendship Community Cohort, we recruited 2824 participants, who were non-obese at the age of 25. According to their obesity status at 10 years prior and baseline, they were grouped as 4 weight change patterns: "persistent non-obese (PN)", "persistent obese (PO)", "recent obese (RO)" and "revert to non-obese (RN)". Liver fibrosis was defined as liver stiffness measurement > 7.3 kPa. Adjusted odds ratio (aOR) and 95% confidential interval (CI) were calculated by logistic regression.

Results: The analysis included 1037 participants, including 799 (77.0%) participants in PN group, 45 (4.3%) in PO group, 99 (9.5%) in RO group, and 82 (9.1%) in RN group. Compared with PN, PO (88.9% vs 29.5%, aOR= 6.90, 95%CI: 2.55-18.70) and RO (83.8% vs 29.5%, aOR= 6.25, 95%CI: 3.37-11.57) were significantly associated with NAFLD, while RN were not (35.1% vs 29.5%, aOR= 1.33, 95%CI: 0.79-2.25). Additionally, among patients with NAFLD, PO group (12.9% vs 3.4%, aOR= 4.17, 95%CI: 1.15-15.19) and RO group (9.3% vs 3.4%, aOR= 2.90, 95%CI: 0.98-8.56) had a significantly higher risk of liver fibrosis than PN group. In contrast, RN group (3.3% vs 3.4%, aOR= 0.97, 95%CI: 0.12-8.18) had no extra risk.

Conclusion: Weight gains in adulthood may increase the risk of NAFLD and a higher degree of liver fibrosis, but the excess risk can be significantly reduced if losing weight to non-obesity right now.

Abstract Submission No. 101246
O-1037

Fgl2-C3aR mediated NETs promote intravascular coagulation and liver fibrosis in NASH progression

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Background: Procoagulant imbalance was observed in non-alcoholic steatosis (NASH) patients with liver fibrosis, but the role of coagulation in NASH fibrosis remains largely unclear. Neutrophil extracellular traps (NETs) served as an essential factor in immuno-thrombosis. Here, we aim to study the role of NETs-mediated complement and coagulation activation in NASH fibrosis and the underlying mechanism. **Methods:** NETs were depleted by intraperitoneal injection of DNase 1. Wild type (WT) and *fgl2*^{-/-} C57BL/6 mice were treated either with 60% high fat diet (HFD) or methionine/choline-deficient (MCD) diet to induce NASH fibrosis. RNA-Seq of hepatic tissues or liver leukocytes were conducted in WT and *fgl2*^{-/-} mice. Bone marrow neutrophils from WT and *fgl2*^{-/-} mice were subjected to palmitic acid (PA) and LPS *in vitro*.

Results: Abundant neutrophil accumulation and NETs formation were observed in NASH progression. NETs depletion improved liver fibrosis, inflammatory response and lipid accumulation both in HFD and MCD models. Meanwhile, decreased coagulation activation, including lower level of plasma thrombin-anti-thrombin complex (TAT) and hepatic fibrin deposition was observed following DNase 1 treatment. Highly expressed on hepatic neutrophils, fibrinogen-like protein 2 (FGL2) colocalized tightly with NETs area. Fgl2 knockout inhibits NETs formation and coagulation activation in NASH progression. Combined with RNA-Seq analysis, *in vivo* and *in vitro* experiment identified that NETs formation was regulated by FGL2-C3aR axis. Treatment with C3aR antagonist alleviated NETs formation, coagulation activation and liver fibrosis *in vivo*.

Conclusions: NETs mediated coagulation dysregulation promotes NASH fibrosis progression. In depth, NETs formation was regulated by FGL2-C3aR axis.

Abstract Submission No. 101380
O-1038

Optimal cut-offs for diagnosis of liver fibrosis in chronic hepatitis B during antiviral treatment

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Background: Liver stiffness measurement (LSM) has been regarded as the most extensively accepted non-invasive method to evaluate liver fibrosis. However, cut-off values for diagnosis of liver fibrosis in chronic hepatitis B (CHB) during antiviral treatment are unknown.

Methods: Adult CHB patients from three clinical studies who had liver biopsy and LSM simultaneously at least 6 months after initiation of antiviral treatment were enrolled. Fibrosis stage was assessed according to the METAVIR scoring system. LSM were performed with FibroScan or Fibrotouch. The performance of LSM to identify liver cirrhosis in on-treatment CHB patients was analyzed by using area under receiver operating characteristic curve (AUROC).

Results: A total of 816 patients were enrolled and randomly divided into training set and validation set at a ratio of 2:1. About 74.3% (404/544) were male with a median age was 42.0 (34.3, 49.7) and the duration from initiation of antiviral treatment to liver biopsy was 1.5 (1.0, 3.1) years. The cut-offs of LSM for diagnosis of significant fibrosis, advanced fibrosis, and cirrhosis during antiviral treatment were 6.8, 7.6, and 7.9 kPa respectively. The sensitivity were 65.7%, 82.0%, and 78.6%, the specificity were 78.7%, 72.9%, and 90.4% respectively. The AUROC for diagnosis of F2, F3, and F4 were 0.796 (95% confidence interval 0.755-0.834), 0.828 (0.794 to 0.859), and 0.835(0.803 to 0.867).

Conclusion: Optimal cut-offs for diagnosis of F2, F3, and F4 in on-treatment patients with CHB were 6.8, 7.6, and 7.9 kPa respectively, which were much lower than the previous ones derived from untreated patients.

Abstract Submission No. 101997
O-1039

LIVERFASt identifies advanced (AF) especially well with Fibroscan in MASLD patients

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Background: L-FAST is an AI-based blood test that offers an overall assessment of the severity of presumed fibrosis, steatosis and activity in MASLD. L-FAST Fibrosis test (L-FAST-F) demonstrated prognostic value mortality (*AlimPharmacolTher2022*) and outperformed ELF (*JHepatolSuppl2022*)

Aims: To compare retrospectively in MASLD pts the performance for AF and CSF of one-step combination of noninvasive tests (NITs): L-FAST-F&LSM versus FIB-4&LSM.

Methods: Data was collected in a tertiary hepatology center (NCT01241227). Cutoffs used for AF and CSF were 0.49 and 0.59 for L-FAST-F and 12kPa and 8 kPa for LSM, respectively and for FIB-4 were 1.3/2.68, to rule-out/rule-in AF.

Results: 583 MASLD pts have been included with L-FAST-F, LSM, FIB-4 and LB [males 56.4%, median age 56.4yrs, 51.6%T2DM, median BMI 31.5Kg/m2 and LSM 9.6KPa, LB: 71.3% CSF, 45.2% AF and 17% F4]. N=399 pts had LB sample size ≥20mm and <6 month between LB and NITs. Among them, L-FAST-F and LSM in n=74 and LB confirmed AF in 70/74 (94.6%). FIB-4 and LSM, agreed only in n=51 pts and LB confirmed AF in 47/51 (92%). Among 172 pts with FIB-4 scores in the grey zone, LB identified 93/172 (54%) pts with AF and 46/93 (49.5%) had L-FAST-F AF. Among 61 pts with FIB-4 <1.3, LB identified 21/61(34%) pts with AF and 6/21 (29%) had AF with L-FAST-F. L-FAST-F and LSM agree for CSF in n=146 pts and LB confirmed AF in 138/146 (94.5%).

Conclusion: Concordant L-FAST-F&LSM, identified AF and CSF in more than 94% of pts and outperformed FIB-4&LSM for AF identification.

Abstract Submission No. 102052
O-1040

Deep attenuation transducer for liver stiffness measurement in obese patients with liver disease

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Background: Deep attenuation transducers (DAX), capable of imaging at depths of up to 40 cm, have not been clinically evaluated for liver stiffness measurement (LSM). The aim of this study was to evaluate the feasibility and reliability of DAX for LSM in patients with chronic liver disease.

Methods: 219 patients were enrolled. The performance of DAX was compared with conventional convex (c-convex) probes and M and XL probes of vibration-controlled transient elastography. Success rate (obtained after ≥ 10 valid measurements) and inadequate measurements (interquartile range/median ≥ 0.3) were evaluated. The effect of skin-to-liver capsule distance (SCD) on measurement success was analyzed.

Results: DAX successfully performed LSM in all patients with varying SCD. Notably, in patients with SCD ≥ 30 mm, DAX demonstrated a 100% success rate in obtaining 10 valid measurements, outperforming M probe (24.2%), XL probe (78.8%) and c-convex probe (76.7%). Inadequate measurement rates in patients with SCD ≥ 30 mm were lower for DAX (2.3%) compared to M probe (12.5%), XL probe (30.8%) and c-convex probe (18.2%). Areas under the curve for F4 diagnosis with shear wave speed were comparable between c-convex and DAX (0.916 and 0.918, respectively). An excellent intraclass

correlation (0.937, 95% CI 0.918-0.952) and no statistically significant bias was observed when comparing DAX and c-convex probes.

Conclusions: DAX demonstrates feasibility and reliability in LSM in different patient populations, while the XL probe has limitations, especially in obese patients.

Abstract Submission No. 200008

O-1041

Comparison of 2D-SWE Measurements in Evaluating Liver Fibrosis Using Different Instruments

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Background: Two-dimensional shear wave elastography (2D-SWE) is a noninvasive method to assess liver fibrosis, which is crucial for hepatocellular carcinoma (HCC) patients. It is of interest to understand whether 2D-SWE measurement values are different in the same population and to explore the potential clinical factors contributing to the variation of different instruments.

Purpose: This study aimed to investigate and compare 2D-SWE measurement and its influencing factors in two different devices, and to evaluate the ability and potential influence factors of them to assess liver fibrosis.

Methods: From October 2022 to September 2023, 290 HCC patients and 30 healthy volunteers were prospectively included. The 2D-SWE measurements were performed using Aixplorer V (SEmean) and APLIO i900 (CEmean). The study compared instruments' 2D-SWE measurement in evaluating the liver fibrosis stage and analyzed the potential influence factors.

Results: In patients included, most (89.8%) were males and the median age was 58.00 [IQR: 49.75, 67.00] years. Both the two instruments had excellent reproducibility (both ICC >0.90, $p < 0.001$). 2D-SWE measurement values of the two instruments were significantly different ($p < 0.001$), but the differences were only significant in liver fibrosis stage S4 patients ($p < 0.001$), rather than in volunteers or S0 to S3 patients (all $p > 0.050$). Multivariate linear regression analysis showed that the independent influence factors of Emean were alanine aminotransferase (ALT) ($p = 0.034$) and liver fibrosis stage ($p < 0.001$) of SEmean, while fibrosis stage ($p = 0.028$) was the only factor of CEmean.

Conclusion: Although 2D-SWE from different instruments were capable of evaluating liver fibrosis, they yielded varying measurement values in HCC patients. These discrepancies were predominantly observed in patients with S4 liver fibrosis, while not significant in healthy adults or patients with liver fibrosis stage of S0 to S3. One potential contributing factor to the differences between instruments could be the levels of ALT.

Abstract Submission No. 200145

O-1042

Crosstalk of LOX and LOXL1 affect liver fibrosis progression via notch passway

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Background: lysyl oxidase (LOX) family members (LOX and LOXL1 to 4) are crucial copper-dependent enzymes responsible for cross-linking collagens and elastin. Previous studies have revealed that LOX and LOXL1 are the most dramatically dysregulated LOX isoforms during liver fibrosis. However, the crosstalk between them and the underlying mechanisms involved in the pro-fibrotic behaviors of hepatic stellate cells (HSCs), as well as the progression of liver fibrosis, remain unclear.

Methods: pCol9GFP-HS4,5^{Tg} mice, *Loxl1*^{fl/fl}*Gfap*^{Cre} mice, human HSC line, and primary HSCs were enrolled to study the dysregulation pattern, profibrotic roles and the potential mechanisms of LOX and LOXL1 interaction involved in the myofibroblast-like transition of HSCs and liver fibrogenesis.

Results: LOX and LOXL1 were synergistically upregulated during liver fibrogenesis, irrespective of etiology, together orchestrating the profibrotic behaviors of HSCs. LOX and LOXL1 co-regulated in HSCs, whereas LOXL1 dominated in the co-regulation loop. Interestingly, the interaction between LOXL1 and LOX prolonged their half-lives, specifically enhancing the Notch signal-mediated myofibroblast-like transition of HSCs. Selective disruption of *Loxl1* in *Gfap*⁺ HSCs deactivated the Notch signal, inhibited HSC activation, and relieved carbon tetrachloride (CCl₄)-induced liver fibrosis.

Conclusions: our current study confirmed the synergistic roles and the underlying mechanisms of LOXL1 and LOX crosstalk in the profibrotic behaviors of HSCs and liver fibrosis progression, providing experimental evidence for further clear mechanism-based anti-LOXL1 strategy development in the therapy of liver fibrosis.

KEY WORDS: extracellular matrix; cycloheximide; fibrogenesis; collagen; myofibroblast

Abstract Submission No. 200161

O-1043

AHR improved cholestatic liver injury by reducing neutrophil infiltration and modulating BAs pools

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Background & aims: Cholestatic liver disease is defined as the bile acids (BAs) accumulation in the liver, which, if left untreated, can result in hepatic fibrosis, cholestatic cholangitis, cholestatic cirrhosis, and eventually, end-stage liver disease. Aryl hydrocarbon receptor (AHR) is a ligand-activated transcription factor with far-reaching effects on chronic liver disease. However, its role and mechanism in cholestatic liver damage is still unknown.

Methods: The roles and mechanisms of AHR in Cholestatic liver disease were investigated by using AHR overexpression mediated by using adeno-associated viral (AAV) vectors, or ITE (an AHR Ligand) received a 0.1% 3,5-diethoxycarbonyl-1,4-dihydrocollidine (DDC) diet.

Results: We found that AHR was differentially expressed in different stages of cholestatic liver disease, showing either down-regulation or an increase in protective effects. Overexpression of AHR increased body weight, decreased serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBil) and alkaline phosphatase (ALP); reduced porphyrin accumulation in liver tissue, and regulated the bile acid pool in the cholestatic mouse model induced by

DDC diet. Mechanistically, the DDC diet led to neutrophil infiltration, whereas overexpression of AHR reduced neutrophil recruitment by decreasing chemokine expression, which in turn improves cholestatic liver disease.

Conclusion: Our data indicate that AHR attenuated cholestatic liver injury. AHR function indicates that it may have an action in the clinical management of cholestasis.

Abstract Submission No. 200236

O-1044

Total Astragalus Saponins Attenuate Primary Sclerosing Cholangitis in Mice by Upregulation of TGR5

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Total astragalus saponins (TAS) are the main active components of *astragali radix*, and have potent anti-hepatic fibrosis activity. However, the therapeutic efficacy of TAS and their potential mechanisms in the treatment of primary sclerosing cholangitis (PSC) remain unclear. The results indicated that treatment with TAS, particularly with a dose of 56 mg/kg, significantly ameliorated the PSC-related liver injury, cholestasis, collagen deposition, ductular reaction (DR) and fibrosis in the DDC-induced and *Mdr2*^{-/-} spontaneous PSC mice. Furthermore, treatment with TAS significantly mitigated the PSC-related inflammatory responses in the liver of mice and HIBEpiC cells by inhibiting the expression of TNF- α , IL-6, and IL-1 β . Mechanistically, treatment with TAS rescued the PSC-decreased hepatic TGR5 and SIRT1 expression to attenuate the NF- κ B p65 phosphorylation. Notably, the therapeutic efficacy of TAS on PSC in DDC-induced mice was abrogated in TGR5^{-/-} mice, suggesting the anti-PSC effect of TAS may depend on enhancing TGR5 expression. In conclusion, treatment with TAS ameliorated DR, inflammation and liver fibrosis in both models of PSC mice by rescuing TGR5 expression. Our findings may aid in the design of new therapeutic strategies for the treatment of PSC.

Abstract Submission No. 200237

O-1045

Schisantherin A protects hepatocyte via upregulating DDAH1 to ameliorate liver fibrosis in mice

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Background: Hepatic fibrosis is the pivotal determinant in the progression of chronic liver diseases towards cirrhosis or advanced stages. Studies have shown that Schisantherin A (Sin A), the primary active compound from *Schizandra chinensis* (Turcz.) Baill., exhibits anti-hepatic fibrosis effects. However, the mechanism of Sin A in liver fibrosis remain unclear.

Purpose: To examine the effects and underlying mechanism of Sin A on hepatic fibrosis.

Study Design and Methods: The effects and mechanism of Sin A were investigated using liver fibrosis mouse models induced by carbon tetrachloride (CCl₄) or dimethylnitrosamine (DMN), as well as H₂O₂-induced hepatocyte injury *in vitro*.

Results: Sin A treatment ameliorated hepatocyte injury, inflammation, hepatic sinusoidal capillarization, and hepatic fibrosis in both CCl₄-induced and DMN-induced mice. Sin A effectively reversed the reduction of DDAH1 expression, the p-eNOS/eNOS ratio and NO generation and attenuated the elevation of hepatic ADMA level induced by CCl₄ and DMN. Knockdown of DDAH1 in hepatocytes not only triggered hepatocyte damage, but it also counteracted the effect of Sin A on protecting hepatocytes *in vitro*.

Conclusion: Our findings indicate that Sin A ameliorates liver fibrosis by upregulating DDAH1 to protect against hepatocyte injury. These results provide compelling evidence for Sin A treatment in liver fibrosis.

Abstract Submission No. 200242

O-1046

Salvianolic acid B attenuates liver fibrosis by targeting Ecm1 and inhibiting hepatocyte ferroptosis

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Background & Aims: Hepatocyte ferroptosis promotes the pathogenesis and progression of liver fibrosis. Salvianolic acid B (Sal B), a natural and potent antioxidant, exerts antifibrotic effects. However, the pharmacological mechanism and target remain unclear. The aim is to investigate the role of Sal B in attenuating hepatocyte ferroptosis and liver fibrosis.

Methods: Liver fibrosis was induced by CCl₄ in wild-type mice and hepatocyte-specific extracellular matrix protein 1 (*Ecm1*)-deficient mice, which were separately treated with Sal B, ferrostatin-1, sorafenib or cilengitide. Erastin- or CCl₄-induced hepatocyte ferroptosis models with or without *Ecm1* gene knockdown were evaluated *in vitro*. Subsequently, the interaction between Ecm1 and xCT and the binding kinetics of Sal B and Ecm1 were determined.

Results: Sal B significantly attenuated hepatic inflammation, collagen deposition, iron deposition, and lipid peroxidation in CCl₄-induced mice. *Ecm1* deletion in hepatocytes abolished the antifibrotic effect of Sal B. Mechanistically, Sal B protected against hepatocyte ferroptosis and liver fibrosis by upregulating Ecm1. The binding kinetics of Sal B and Ecm1 identified Ecm1 as a direct target for treating liver fibrosis with Sal B. Interestingly, Ecm1 interacted with xCT to regulate hepatocyte ferroptosis. Erastin- and CCl₄-induced hepatocyte ferroptosis *in vitro* was significantly attenuated by Sal B treatment, which was abrogated after knockdown of *Ecm1* in LO2 cells.

Conclusions: Sal B alleviates liver fibrosis in mice by targeting Ecm1 and inhibiting hepatocyte ferroptosis. The interaction between Ecm1 and xCT regulates hepatocyte ferroptosis and is a previously unknown mechanism of the therapeutic effect of Sal B on liver fibrosis.

Abstract Submission No. 100205

O-1047

The role of Vitamin E in the treatment of nonalcoholic steatohepatitis(NASH)

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AIMS: Oxidative stress plays a vital role in the transition from simple steatosis to nonalcoholic steatohepatitis (NASH). Vitamins with antioxidant properties have the ability to decrease the levels of reactive oxygen species and prevent oxidative damage in the cell that can lead to cellular senescence and apoptosis. Thus, the aim of this study is to explore the functions of vitamin E in the treatment and recovery of patients suffering from NASH.

Methods: 60 patients who were non-diabetic with NASH based on cytology were recruited into the studies. Their Alanine Transaminase (ALT) level was recorded prior to segregation. The subjects were divided into two main arms in which one arm received 500IU of Vitamin E while the second arm received a placebo. The tablets were taken once a day and were recorded. After three months, their ALT levels were measured and compared. A scatter plot was plotted to demonstrate the direct correlation between the level of ALT and the duration of the patients who were on vitamin E.

Results: Subjects that received 500IU of vitamin E daily recorded a significant reduction of ALT levels compared to the placebo arm. There was a direct correlation between the duration of patients on vitamin E and the reduction of the ALT in the scatter plot.

Conclusion: Vitamin E at the dose of 500 IU/day is beneficial in non-diabetic adults with active NASH. Longer follow-up RCTs are needed to assess the long-term safety and therapeutic value of vitamin E on clinical outcomes in NASH patients.

Abstract Submission No. 100253

O-1048

Correlation of HbA1c with the Degree of Liver Fibrosis and Steatosis by FibroScan® in Bacolod City

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Background: The liver plays a crucial role in glucose homeostasis and is an organ associated with diabetes mellitus (DM). This research aims to identify if there is a correlation between HbA1c level with the degree of liver fibrosis and steatosis as measured by FibroScan®. The FibroScan® is a new non-invasive modality and is the first and only one in Western Visayas.

Method: This is a retrospective study conducted in Bacolod City from April 2022-October 2022. Diabetic patients who underwent FibroScan® at Metro Bacolod Hospital and Medical Center (MBHMC) were included in the study. The FibroScan® results were retrieved from the FibroScan® unit of MBHMC and the HbA1c results were retrieved from the patients' respective physicians' office.

Results: A total of 56 patients were included in the study. This study shows a positive significant relationship between HbA1c and liver stiffness (r_s -value=0.306; p -value=0.022) indicating that the level of HbA1c is directly proportional to the level of liver stiffness and that the higher the HbA1c, the higher the degree of liver fibrosis. However, there is no significant relationship between the level of HbA1c and Controlled Attenuation Parameter (CAP) (r_s -value=0.306; p -value=0.726).

Conclusion: This study showed that HbA1c level in diabetic patients correlates proportionately with the degree of liver fibrosis as measured by FibroScan®, thus an elevated HbA1c predicts an increased risk for

developing liver fibrosis. However, HbA1c level and NAFLD did not have any significant correlation indicating that both may coexist and are independent of each other.

Abstract Submission No. 100881

O-1049

MAGP1 knockout inhibits hepatic fibrosis regression by remodeling ECM microenvironment

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Background & aims: Microfiber-associated glycoprotein 1 (MAGP1) is a glycoprotein involved in extracellular matrix (ECM) remodeling. By now, the relationship between MAGP1 and liver fibrosis has rarely been reported.

Methods: The roles and mechanisms of MAGP1 in liver fibrosis were investigated by using *Mfap2* knockout (*Mfap2*^{-/-}) mice and *Mfap2* overexpression mice by tail injection of adeno-associated virus vectors (serotype 6, AAV6) containing short hairpin RNAs (shRNAs) targeting *Mfap2*, undergoing carbon tetrachloride (CCl₄) administration, cessation or bile duct ligation (BDL) operation.

Results: MAGP1 was predominantly expressed in activated HSCs and dynamically increased with liver fibrosis progression and decreased in regression. *Mfap2* knockout had no significant effect on liver fibrosis progression, but aggravated intrahepatic inflammatory infiltration in CCl₄ mouse models and evidently retarded liver fibrosis regression after CCl₄ cessation. Whereas, in BDL mouse models, *Mfap2* ablation significantly exacerbated liver fibrosis progression but hardly affected intrahepatic inflammatory infiltration. Overexpression of *Mfap2* via AAV6 vectors by tail intravenous injection relieved inflammation in CCl₄ mouse models and fibrosis in BDL mouse models. Mechanically, HSCs-derived MAGP1 deficiency significantly promoted the ECM production and secretion including collagens, fibrillin-1, and lysyl oxidase-like protein 1 (LOXL1), resulting in ECM remodeling and subsequent alteration of ECM immune microenvironment. At the molecular level, the ECM-cell interaction pathway in liver, focal adhesion, was notably affected after *Mfap2* intervention *in vivo* and *in vitro*.

Conclusion: Our current study highlighted MAGP1 participated in liver fibrosis progression and regression via orchestrating liver ECM microenvironment, providing a potential therapeutic target for liver fibrosis.

Abstract Submission No. 101250

O-1050

Liver fibrosis deciphering clinical outcomes in CKD- brothers in arms in prognostic landscape?

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Introduction: It has been observed in various studies that liver fibrosis positively correlates with increased morbidity and mortality from diseases affecting various organ systems. There is significant similarity in the pathogenesis of chronic kidney disease (CKD) and liver fibrosis. The role of liver fibrosis scores (LFS) predicting the short-term clinical outcomes in hospitalized patients with CKD is unknown. This study aimed at studying the association of liver fibrosis scores with short term mortality and morbidity in CKD.

Methods: LFS namely NFS, GPRI and FIB-4 scores were calculated in adult CKD. Patients were followed up for a period of 28 days for good and poor composite outcome namely requirement of dialysis, NIV, hospital stay, neurological and cardiovascular outcome including death.

Results: Among 163 patients, 70.5% were below 60 years of age and 82.2% were male. 35% were diabetic and 52.1% had poor composite outcome at 28 day follow up. The AUROC for GPRI and FIB4 predicting poor outcome was 0.783 (95% CI: 0.71 - 0.855) ($p < 0.001$) and 0.62 (95% CI: 0.534 - 0.706) ($p = 0.008$) respectively. The AUROC for GPRI and NFS predicting all-cause mortality was 0.735 (95% CI: 0.627 - 0.843) ($p = 0.001$) and 0.876 (95% CI: 0.8 - 0.952), ($p < 0.001$) respectively.

Conclusion: LF scores reproducibly conveyed a higher risk of liver fibrosis in CKD. The scores (GPRI, NFS and FIB-4) significantly predicted poor outcome in patients with CKD. High GPRI score was better associated with poor outcome and increased mortality in both diabetics and non-diabetics.

Abstract Submission No. 101370
O-1051

Noninvasive proteomic biomarkers for liver fibrosis regression in patients with chronic hepatitis B

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Background & Aims: Liver fibrosis is reversible upon successful elimination or suppression of hepatitis B virus (HBV). However, to date, the assessment of liver fibrosis regression still largely depends on invasive biopsy-based histological evidence. The alternative noninvasive serum biomarkers for accurately diagnosing liver fibrosis regression remain unknown.

Methods: Chronic hepatitis B (CHB) patients biopsied in pairs at baseline ($n=141$) and at 78 (short-term, $n=103$) or 260 (long-term, $n=38$) weeks of antiviral treatment were included. Liver fibrosis regression was defined based on histological changes. Serum proteomic profiles were acquired using four-dimensional (4D) data-independent acquisition (DIA)-based proteomics. Multiple machine-learning algorithms were employed to screen noninvasive proteomic biomarkers for liver fibrosis regression.

Results: By pairwise comparison, serum proteins whose levels were significantly altered after antiviral treatment were input into multiple machine-learning models. In the short-term regression model, a signature comprising 8 serum proteins achieved the highest diagnostic performance with an AUROC of 0.74, superior to the changes of liver stiffness measurement (LSM), APRI, and FIB-4 (AUROCs were 0.61, 0.60, and 0.58, respectively). While the long-term regression model identified a signature with only 4 serum proteins whose AUROC was

0.91, better over LSM, APRI, and FIB-4 (AUROCs were 0.72, 0.70, and 0.69, respectively). More importantly, both models performed well when excluding patients with mild fibrosis (AUROCs were 0.82 and 0.96, respectively).

Conclusion: Our study pioneeringly identified the promising noninvasive proteomic biomarkers for liver fibrosis regression with CHB infection after a short- or long-term antiviral therapy.

Abstract Submission No. 101557
O-1052

Predicting Symptomatic PHLF in HCC Patients: Development and Validation of a Preoperative Nomogram

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Objective: To explore the feasibility of Liver stiffness (LS) and a nomogram based on LS for predicting symptomatic post-hepatectomy (PHLF) in patients with hepatocellular carcinoma (HCC).

Methods: A total of 266 patients diagnosed as HCC were enrolled prospectively from three tertiary referral hospitals from August 2018 to April 2021. Patients from one hospital were classified as the derivation cohort and internal validation cohort consecutively, and those from the other two hospitals were classified as the external validation cohort. All patients underwent preoperative laboratory examination to obtain parameters pertaining to liver function, two-dimensional shear wave elastography (2D-SWE) examination to obtain LS, and three-dimensional virtual resection of liver to obtain volume-related parameters. A nomogram was developed by using logistic regression and determined by receiver operating characteristic (ROC) curve analysis and calibration curve analysis.

Results: A nomogram was constructed with the following variables: liver remnant volume (LRV) ratio, LS greater than 9.5kPa, Child-Pugh grade and the presence of clinically significant portal hypertension (CSPH). This nomogram enabled differentiation of symptomatic PHLF in the derivation cohort (Area under curve [AUC], 0.915), internal 5-fold cross-validation (mean AUC, 0.918), internal validation cohort (AUC, 0.876) and external validation cohort (AUC, 0.845). The nomogram also showed good calibration in the derivation, internal validation and external validation cohorts (Hosmer-Lemeshow goodness-of-fit test, $p=0.641$, $p=0.06$ and $p=0.127$, respectively). Accordingly, the safe limit of LRV ratio was stratified using the nomogram.

Conclusion: A preoperative nomogram integrated LS, clinical and Volumetric features was useful in predicting postoperative outcome in patients with HCC.

Abstract Submission No. 101837
O-1053

The effect of persistent decline of pathological inflammation on the regression of liver fibrosis

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Aims: To analyze the persistent decrease of liver pathological inflammation on liver fibrosis regression in chronic hepatitis B (CHB) patients during antiviral therapy.

Methods: Treatment-Naïve patients with CHB who had three pathological liver perforations at baseline, 1.5 years and 5.0 years were enrolled in nationwide hospitals (NCT04939441). According to the dynamic changes of inflammation in the three liver biopsy pathology, patients were divided into persistent decrease group, stable group and increase group. The clinical indicators, inflammation and liver fibrosis were observed. Wilcoxon signed-rank test, Fisher's exact test and Pearson correlation coefficient were used for continuous variables, categorical variables and correlation analysis, respectively.

Results: A total of 119 subjects were enrolled, with an average age of 38.5±10.5 years and 75% males. The percentages of patients with Ishak score 12/3/4/5/6 were 27%, 33%, 30% and 29%, respectively. In the persistent decrease group, stable group and increase group, there were no significant differences in gender, age, ALT, PLT, HBV DNA and LSM before treatment. The means of inflammation were 7.3±2.5, 6.1±3.0 and 4.4±1.9. The regression rates of liver fibrosis were 63%, 43% and 27%, respectively and the progress rates were 9%, 18% and 27% in the three groups, respectively. The inflammation of all patients was associated with liver fibrosis at baseline and 1.5 years ($p<0.05$, $r=0.345$ and 0.268), but no difference was found at 5.0 years.

Conclusion: During antiviral therapy, the persistent decrease in liver pathological inflammation can improve the reversal of liver fibrosis.

Abstract Submission No. 101912

O-1054

AST/ALT Ratio to Predict Hepatic Fibrosis and Steatosis Compared to Fibroscan in Diabetes Patients

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Background: To compare the AST/ALT ratio with fibroscan for predicting hepatic fibrosis and steatosis in diabetes mellitus (DM) patients.

Methods: A cross-sectional study was conducted on DM patients, aged over 30 years. Patients using alcohol, hepatitis B or C, autoimmune hepatitis, and users of steatogenic drugs were excluded. The demographic description of the research subjects includes age and gender. Meanwhile, the variables explained include the AST/ALT ratio, CAP Score, and fibrosis score. Analysis was conducted using Spearman correlation, Mann-Whitney test, and ROC curve analysis.

Results: Of the 106 diabetes DM only 96 fulfilled the criteria. Mean age of 56.38 ± 8.46 years, 53 (55.2) were women. Liver fibrosis was found that 55 (57.3%) had F0, 20 (20.8%) F1, 15 (15.6%) F2, 3 (3.1%) F3, and 3 (3.1%) F4. A significant correlation was found between the AST/ALT ratio and age ($r = 0.225$). Sensitivity, specificity, PPV, NPV, and accuracy of AST/ALT ratio at the 0.44 cut-off for the differentiation of F2, F3, and F4 from F0 and F1 were 4.76, 98.67, 50.0, 78.7%,

Moreover, the Auroc of the AST/ALT ratio for the differentiation of F2, F3, and F4 from F0 and F1 was 0.530. The AST/ALT ratio at the 1.63 cut-off for the differentiation of S1, S2, S3 from S0 were 93.85, 16.13, 70.1, and 55.6% with Auroc of AST/ALT ratio for the differentiation S1, S2, S3 from S0 were 0.514.

Conclusions: The AST/ALT ratio in this study is unusable to predict hepatic steatosis and fibrotic significantly in diabetes mellitus patients.

Abstract Submission No. 101917

O-1055

PHR Ratio in Predicting Hepatic Steatosis and Fibrosis Compared to Fibroscan in Diabetes Patients

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Background: To identify The Role of the platelet/high-density lipoprotein cholesterol (PHR) ratio in predicting hepatic steatosis and fibrosis compared to Fibroscan in Diabetes Mellitus Patients.

Metode: A cross-sectional study was conducted on DM patients at Dr. Soetomo, Surabaya, Indonesia. Subjects aged over 30 years underwent laboratory examination and fibroscan examination. Patients using alcohol, hepatitis B or C, autoimmune hepatitis, and users of steatogenic drugs were excluded from this study. Meanwhile, the variables explained include the PHR ratio, CAP Score, and fibrosis score. Analysis was carried out with Spearman correlation and binary logistic regression.

Results: Of the 106 diabetes mellitus patients only 96 fulfilled the criteria. In this study with a mean age of 56.38 ± 8.46 years, 53 (55.2) were women. Liver fibrosis based on TE results, it was found that 55 (57.3%) had F0, 20 (20.8%) F1, 15 (15.6%) F2, 3 (3.1%) F3, and 3 (3.1%) F4. Compared with patients in the first PHR quartile, the corresponding odds ratio (OR) for fibrosis in the fourth quartile was 2.565 (95% CI, 1.418 to 5.864) ($p<0.05$), for steatosis in the fourth quartile was 3.125 (95% CI, 1.902 to 11.460) ($p<0.05$).

Conclusions: The effectiveness of PHR can be used as a marker of liver fibrosis and steatosis.

Abstract Submission No. 200202

O-1056

EVALUATION OF LIVER FIBROSIS BY FIBROSCAN IN METHOTREXATE TREATED PATIENT

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Background: Methotrexate (MTX) is a cornerstone in the treatment of rheumatic diseases. Although it is generally well tolerated, liver fibrosis may develop with long-term use. Non-invasive methods such as transient elastography (TE; Fibroscan) are used safely in the detection of hepatic fibrosis.

Methods: Fifty patients (43 with rheumatoid arthritis (RA), 7 with psoriatic arthritis (PsA)) receiving MTX and 50 healthy adults were included. Viral hepatitis, ethanol use, non-alcoholic steatohepatitis and other hepatic pathologies were excluded. Liver fibrosis was assessed by TE method, and the cutoff value of 7.1 kPa (kilopascal) was considered abnormal.

Results: Liver stiffness and steatosis value in TE were found to be significantly higher in the group receiving MTX compared to the healthy group ($p:0.001$). When the group receiving MTX was divided into two groups as $kPa \geq 7.1$ and below, it was determined that the cumulative dose of MTX and duration of drug use were significantly higher in the group with high fibrosis ($p:0.009$). When the patients were divided into three groups according to the cumulative MTX dose: 0-1499 mg, 1500-4999 mg, 5000 mg and above, the kPa value measured by TE was found to be significantly higher in patients receiving 5000 mg and above MTX compared to other doses. ($p:0.036$).

Conclusion: TE can be used as an effective method to detect liver fibrosis due to MTX use. It would be very accurate to evaluate patients with a cumulative MTX dose of 5000 mg and above with TE in terms of hepatic fibrosis.

Abstract Submission No. 101401

O-1057

Efficacy of Rebamipide in the Prevention of Aspirin or NSAID-induced Gastrointestinal Mucosal Injury

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Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most used medications worldwide. A major limitation of these drugs is gastrointestinal mucosal injury and bleeding. Several gastroprotective agents have been recommended but are limited by their long-term effects. Rebamipide is a promising mucoprotective agent, but its efficacy is not established. We performed a meta-analysis to assess rebamipide's effect on gastrointestinal injuries due to NSAID and aspirin use.

Methods: Four electronic databases were searched from inception to October 2023 for studies that compared rebamipide with placebo or standard gastroprotective agents. Data were pooled to obtain odds ratio (OR) with 95% confidence interval. Heterogeneity and publication bias were assessed with I^2 statistic and funnel plot, respectively.

Results: A total of 472 studies were screened, with 30 studies included. Pooled analyses showed that for NSAID use, rebamipide significantly reduced the outcome of gastrointestinal ulcers [OR:0.37 (0.19-0.70); $I^2=13\%$, $p=0.002$], bleeding [OR:0.16 (0.10-0.27); $I^2=87\%$, $p<0.00001$], and symptoms [OR:0.45 (0.23-0.88); $I^2=48\%$, $p=0.02$] as compared to placebo. Rebamipide is also comparable to standard proton pump inhibitors (PPIs) in preventing NSAID-induced mucosal breaks and bleeding. Addition of rebamipide to PPIs is superior to PPIs alone in preventing mucosal breaks [OR:0.38 (0.20-0.74), $I^2=41\%$, $p=0.005$]. For aspirin use specifically, rebamipide significantly reduced the incidence of mucosal breaks [OR:0.36 (0.17-0.78); $I^2=0\%$, $p=0.009$] as compared to placebo.

Conclusion: Rebamipide is effective in preventing gastrointestinal injuries, bleeding, and symptoms due to NSAID use. This study is the first meta-analysis that demonstrated the efficacy of rebamipide in aspirin-induced gastrointestinal injury.

Abstract Submission No. 101940

O-1058

Injury to hepatic sympathetic innervation promotes liver injury and metabolic dysregulation

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Hepatic sympathetic nerves (HSN) play a vital role in liver function. Injury to HSN affects hepatic functions, yet their precise contribution to liver disease progression and related molecular alterations remains unclear. Our aim is to the effect of hepatic sympathetic denervation on liver injury. We divided study into; GR-1 (Veh; $n=9$), rats with intact HSN; GR-2 (Sx; $n=12$), sympathectomized rats; GR-3 (Veh/Sx; $n=9$), rats with intact HSN plus bile duct ligation (BDL); and GR-4 (Sx/BDL; $n=9$), sympathectomized rats with BDL. Sympathectomy was observed by change in urine coloration, ptosis, and absence of sympathetic nerves marker (tyrosine hydroxylase; TH) in the liver samples. GR-2 exhibited mild steatosis and inflammation with no significant difference in AST and ALT levels. Liver histology indicated significantly increased fibrosis in GR-4 versus GR-3 ($p<0.05$). GR-3 exhibited progressive disorganization of sympathetic nerves correlating with fibrosis severity and inflammation. GR-4 displayed a gradual decrease in the gene expression of adrenergic receptors and gap junction proteins ($p<0.05$). Liver proteome revealed significant differences between GR-4 and GR-3, with 462 differentially expressed proteins (227 upregulated and 235 downregulated), showing significant activation of both fibrogenic (TNFR2, Wnt, FGF) and inflammatory (NLRP3, MAPK, PDGF) pathways ($p<0.05$). Interestingly, we also observed a significant metabolic dysregulation with the upregulation of the TCA cycle ($p<0.05$) and downregulation of the urea cycle ($p<0.05$) not only in GR-4 but also in GR-2. Overall, sympathetic denervation is associated with an increased progression of liver fibrosis and metabolic dysregulation due to impaired neuronal communication within the liver.

Abstract Submission No. 101999

O-1059

Autologous Haemopoietic Stem Cell Transplantation in Decompensated Cirrhotics via Portal Venous Route

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Introduction: Decompensated cirrhosis of liver is associated with decreased amounts of functional hepatocytes leading to compromised quality of life and increased mortality. It is possible that autologous haemopoietic stem cells administered to liver aid in hepatocyte mobilization and reversal of decompensated cirrhosis. Study assessed safety and primary efficacy, if any, of autologous haemopoietic stem cell transplantation in patients with decompensated cirrhosis of liver for its future standardization.

Methods: 33 patients included with decompensated cirrhosis of liver. All received injection with G-CSF (60 IU)/s/c daily for 3-4 days along with standard medical therapy. CD34-positive cells were isolated from peripheral blood using cell sorter. Subsequently transfused trans-hepatic route into portal vein. Patients were then followed up initially for 90 days.

Results: 23 males, 10 females. Age was 50.6yrs. 22 hepatitis B, 4 NASH, 2 hepatitis C, 5 cryptogenic cirrhosis of liver. Mean serum

bilirubin improved from 4.09mg/dl at baseline to 1.87mg/dl, 1.64mg/dl at 30 and 90 days respectively. Mean serum albumin rose from 3.08gm/L to 3.4gm/L at 90 days. Mean prothombin time improved from 17.57-16.65sec and 15.55sec at 30 and 90 days. Moderate to marked ascites was present in 9 at baseline, 4 and 1 had similar ascites at 30 and 90 days respectively. 1/33 died within 90 days of follow up. Cause of death was hepatic encephalopathy. No significant rise in AFP and no hepatic SOL was detected.

Conclusion: Autologus haemopoietic stem cell transplantation appears to be safe in patients with decompensated cirrhosis. Patients appear to be moderately benefitted with this approach.

Abstract Submission No. 102051

O-1060

Effect of Vonoprazan on Rebleeding among Patients with Upper GI Bleeding: A Meta-Analysis

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Background: Potassium-competitive acid blocker (PCAB) is a recent alternative to proton pump inhibitor (PPI) for potent acid suppression. This meta-analysis aimed to compare the efficacy and safety of PCAB versus PPI in preventing rebleeding in patients with upper gastrointestinal bleeding (UGIB).

Methods: Databases PubMed, Medline, and Cochrane were reviewed from 2010 to 2023. Abstracted from the eligible studies were population demographics, dosing of intervention (PCAB) and control (PPI). The primary outcome was the incidence of upper GI bleeding, while secondary outcomes included rate of ulcer healing and incidence of treatment-emergent adverse events. Cochrane Review Manager 5 was used for analysis and synthesis.

Results: Of 549 screen studies, 31 were underwent full-text eligibility assessment, and five were included in the final analysis. Risk of bias was high due to randomization concerns for the retrospective cohort studies. Both low dose vonoprazan (RR 0.76, CI 0.66-0.87, $p=0.000001$) and high dose vonoprazan (RR 0.76, 95% CI 0.71 to 0.80, $p=0.000001$) showed a trend towards benefit over PPI. No significant difference was found between rates of ulcer healing (RR 0.53, 95% CI 0.27 to 1.01, $p=0.05$), and rates of adverse events were similar between PCAB and PPI (RR 0.99, 95% CI 0.91 to 1.07, $p=0.77$).

Conclusion: Vonoprazan shows benefit over PPI on rebleeding prevention and ulcer healing, with comparable safety profile. Further studies are needed to determine the population most likely to benefit from it given economic limitations to its use.

Abstract Submission No. 100301

O-1061

An in-hospital HBV screening project improving the rates of diagnosis and treatment of hepatitis B

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Background: The rates of diagnosis and antiviral treatment for hepatitis B infection in China are 24% and 15% respectively in 2022, significantly lower than the WHO's 2030 target of "90% for diagnosis and 80% for antiviral treatment". Furthermore, the awareness of hepatitis B management in non-hepatology specialists is insufficient.

Methods: In March 2022, Guangdong Preventive Medicine Association and the Third Affiliated Hospital of Sun Yat-sen University jointly launched the "In-Hospital Hepatitis B Screening Management Project", which implemented the hepatitis B management of "hepatitis B screening - referral - diagnosis - treatment - follow-up" in the Third Affiliated Hospital. The program involved multi-departments of infectious disease, other clinical specialties, laboratory, information, medical administration, and clinical data center. Figure 1 shows the roadmap for in-hospital hepatitis B screening management.

Results: Through nine months of the project implement, compared to 2021, the rates of HBsAg screening (defined as number of individuals who underwent HBsAg testing divided by the total number of hospital visits during the same period, including inpatients and outpatients), patients' referral to the department of infectious disease, antiviral treatment, and regular follow-up in 2022 were increased from 7.95% to 8.36%, 11.23% to 19.32%, 57.18% to 62.48%, and 60.34% to 65.17%, respectively (Figure 2).

Conclusion: The in-hospital hepatitis B screening management project has facilitated patients' discovery and referral from non-hepatology departments, indeed improving the rates of screening, referral, antiviral treatment, and follow-up for hepatitis B patients. However, further promotion of this management mode is needed.

Abstract Submission No. 100395

O-1062

Task-shifting from doctors to paramedics for liver treatment at Yokkaich Digestive Disease Center

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Purpose: Our hospital is a small, specialised hospital located in a regional city in Japan. There are few liver specialists, and until recently, doctors have been responsible for multitasking, including picking up cases, providing guidance, performing surgeries, and presenting at academic conferences.

The COVID-19 pandemic necessitated support from other professionals to fill the absences of doctors and reduce their burden.

Method: This work was conducted through regular meetings considering possible task shifts among nurses, public health nurses, physical therapists, pharmacists, registered dietitians, clinical laboratory technicians, clinical radiology technicians, and hepatitis coordinators.

We verified whether results could be obtained by RFA (radiofrequency ablation), TACE (transcatheter arterial chemo-embolization), and MAFLD (metabolic dysfunction-associated fatty liver disease) treatments.

Results: RFA and TACE tasks were successfully shared between doctors and other staff members, including new nurses. Even MAFLD treatments conducted mainly by public health nurses and registered dietitians resulted in significant decreases in ALT, reducing the burden on doctors.

Conclusion: By shifting tasks to paramedics, we reduced the burden on doctors without compromising treatment results.

Abstract Submission No. 101269

O-1063

EUS-guided liver biopsy and portal pressure gradient measurement in cACLD and cirrhosis

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Background: EUS-guided liver biopsy (EUSLB) and portal pressure gradient measurement (EUS-PPG) are emerging areas in the field of endohepatology. However, data in cACLD and cirrhosis is limited. Hence, we explored the performance of EUSLB and EUS-PPG in such patients.

Methods: EUSLB and EUS-PPG performed in suspected cACLD (LSM >10kPa) or cirrhosis (on imaging) from June-2022 till september-2023 were reviewed. Indications for EUSLB included elevated transaminases or etiologic uncertainty where histology was expected to influence management. EUS-PPG measurement was performed in ESRD patients with suspected cACLD (post dialysis LSM>10 kPa) to assess CSPH and need for SLKT.

Results: 79 biopsies in 77 patients [age: 32 (22-47) years, males: 46.7%] with suspected cACLD or cirrhosis were reviewed. Seventy-seven (97.5%) samples were deemed adequate by the pathologist. Median core length was 25 (16-37) mm. The median number of CPT was 6 (3-7). Autoimmune liver disease (36.33%) and NAFLD/NASH (20.7%) were the commonest etiology. Most patients had fibrosis stages F3 (42.8%) and F4 (37.7%). Adverse events were noted in 4 patients (5.1%) [Perihepatic bleed (1.6%), transient needle-track bleed (2.5%) and mild self-limiting pain (1.2%)].

EUS-PPG was concomitantly measured in 7 patients with ESRD. CSPH was present in 1 patient (PPG =13 mm Hg; listed for SLKT). Among the remaining 6 patients without CSPH, 2 have undergone uncomplicated renal transplant.

Conclusion: EUSLB is safe with high diagnostic yield in cACLD and cirrhosis. EUS-PPG measurement is technically feasible and adds to the one-stop-shop endoscopic assessment of portal-hypertension.

Abstract Submission No. 101511

O-1064

RWE Study to Evaluate Effectiveness of PPIs Omeprazole and Pantoprazole for Relief of GERD/APD

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Objective: Gastro-Esophageal Reflux Disease manifests due to mucosal damage induced by reflux of gastric contents into esophagus. Proton Pump Inhibitors are considered to have comparable efficacies and safety profiles. Due to dearth of documented data on clinical practices and outcomes, this study aims to evaluate real-world evidence on effectiveness, safety of omeprazole and pantoprazole in patients not treated for GERD within 2 weeks preceding treatment initiation with PPIs.

Methodology: Study involves data extraction from 600 anonymized Electronic Medical Records (EMRs) procured from 15 physicians in India. Patients treated for at least 4 weeks with the PPIs are included. The primary objective is to determine the proportion of responders (symptomatic relief of heartburn, regurgitation, epigastric pain, nausea, vomiting, bloating).

Results: Omeprazole 20mg or Pantoprazole 40mg group is compared at each follow-up (2 weeks and 4 weeks). At 2 weeks, significantly more subjects showed resolution of Heartburn (87.98% vs 71.76%, p<0.001) in Omeprazole compared to Pantoprazole. Omeprazole showed significantly better resolution of Regurgitation (79.75% vs 69.7%, p= 0.029), Epigastric pain (84.21% vs 68.61%, p=<0.001), Vomiting (93.91% vs 81.58%, p=0.003) Bloating (87.73% vs 78.89%, p=0.026). At 4 weeks, significantly more subjects showed resolution in Omeprazole compared to Pantoprazole (95.63% vs 86.57%, p=0.002). Regurgitation (98.10% vs 90.51%, p=0.003) and Epigastric pain (95.26% vs 89.6%, p=0.034) showed statistically significant result favoring Omeprazole as compared with Pantoprazole.

Discussion & Conclusion: Omeprazole is more effective in faster relief of GERD/APD symptoms (2 weeks) and comparable to/more effective than pantoprazole (4 weeks) depending on specific symptoms.

Abstract Submission No. 101879

O-1065

Spur cell anemia successfully treated with liver transplantation

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Background: Spur cell anemia (SCA) is a rare hemolytic anemia characterized by the presence of erythrocytes with spiny projections, which arises in alcoholic cirrhosis. Repeated blood transfusions lead to liver failure but no effective treatment has been established.

Case presentation: A 38-year-old woman with a history of heavy alcohol use presented to our clinic. She developed ascites due to alcoholic cirrhosis 8 months before. She abstained from alcohol but her jaundice persisted, with bilirubin ranging from 4-8 mg/dL. She presented with macrocytic anemia with increased reticulocytes and decreased haptoglobin, suggesting hemolytic anemia. After 5 months, she developed gross hematuria with aggravated anemia, and was admitted to our hospital. Her laboratory findings were as follows: RBC 165,000/ μ L, Hb 6.4 g/dL, MCV 112 fL, PLT 49,000/ μ L, reticulocytes 9.6%, TB 9.6 mg/dL, DB 5.6 mg/dL, AST 50 U/L, ALT 30 U/L, LDH 302 U/L, ALP 118 U/L, γ -GTP 15 U/L, albumin 2.6 g/dL. A workup by hematologists excluded autoimmune hemolytic anemia or others. We noticed abnormal erythrocytes with spiny projections in her smear. Based on this acanthocytes and her background, alcohol cirrhosis, we diagnosed her with SCA. After multiple blood transfusions, her liver failure became critical. A liver transplantation was performed using her husband as donor. Following transplantation, the acanthocytes disappeared and her jaundice resolved.

DISCUSSION: This case report demonstrates the successful treatment of SCA with liver transplantation. Liver transplantation should be considered as a potential treatment option for patients with SCA although the availability of donors is limited especially for alcoholic cirrhosis.

Abstract Submission No. 100289

O-1066

Gut Microbiome Signatures in Obese Children with MAFLD through Full-Length 16S rRNA Sequencing

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Background: The gut microbiota plays a crucial role in metabolic-associated fatty liver disease (MAFLD). Next-generation sequencing explores the gut microbiome, but traditional short read 16S rRNA sequencing lacks species-level detail. The newly developed full-length 16S rRNA sequencing (FL16S) may offer the potential for higher resolution. However, its impact on MAFLD signatures remains uncertain. **Methods:** We employed FL16S sequencing to identify gut microbiome signatures in 80 age-, sex-, and BMI-matched case-control pairs of obese children with and without MAFLD. Fecal DNA was sequenced with PacBio Sequel IIe system, and Amplicon Sequence Variants (ASVs) were taxonomically assigned against NCBI reference database. We compared the microbiome signatures between MAFLD and non-MAFLD pairs.

Results: MAFLD subjects exhibited higher serum alanine aminotransferase, triglycerides, and insulin resistance. Top 10 abundant taxa showed significant species-level differences, particularly with *Bacteroides ovatus* and *Bacteroides dorei*. Welch's test indicated lower abundance of *Bacteroides ovatus*, *Bacteroides dorei*, and *Blautia wexlerae* in the MAFLD group, and higher *Eubacterium rectale* and *Megamonas funiformis*. At the genus level, *Prevotella*, *Bacteroides*, *Shigella*, and *Collinsella* scored higher in linear discriminant analysis effect size (LEfSe), and at the species level, *Bacteroides ovatus*, *Bacteroides vulgatus*, *Bacteroides dorei*, and *Collinsella aerofaciens* exhibited high scores. The gut microbial communities between the MAFLD and non-MAFLD groups were effectively differentiated using partial least squares-discriminant analysis (PLS-DA).

Conclusions: FL16S enables detailed genus and species-level identification in gut microbiomes. Obese children with or without MAFLD exhibit distinct microbiome signatures. This insight aids in comparing studies before and after FL16S, potentially enhancing its clinical utility.

Abstract Submission No. 100666

O-1067

RCT of Methylprednisolone in cholestasis infants: is an opportunity to prevent biliary atresia?

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Background: A progressive immunological mechanisms underlie biliary atresia. Biliary atresia outcome is still not optimal even though the Kasai operation has been carried out. This study aims to analyze the effectiveness of methylprednisolone in liver function test and inflammatory biomarkers in cholestasis.

Methods: The RCT was conducted in Dr. Soetomo General Academic Hospital, Surabaya. The inclusion criteria, included being > 14 days to 3 months old and cholestasis. Subjects were randomly assigned to methylprednisolone or to placebo for 2-week randomized treatment period. Laboratory measurements (direct and total bilirubin, AST, ALT, GGT) and inflammatory biomarker were performed. Analysis was performed using SPSS with p significant < 0,05.

Results: A total of 40 subjects were methylprednisolone (n=20; mean age 8,39 ± 3,11 week) and placebo (n=18; 2 drop out; mean age 8,98 ± 2,80 week) groups. The methylprednisolone group had direct bilirubin 8,36 ± 4,84mg/dL; AST 187,05(42,00-911,00) U/L; ALT 170,43 ± 134,43 U/L; IL2 171,29 (73,70-378,57) ng/L; IL2 119,57 ± 59,69 ng/L; IL6 119,57 ± 59,69 ng/L; IL10 138,15 ± 70,62 ng/mL; IFN-γ 42,54 ± 12,17 ng/L; TGF-β 316,58 (163,68-606,16) ng/L; ANCA 1,70 (0,66-3,25) ng/L. There was no difference in laboratory results on both groups (p>0.05). After 2-week treatment, direct bilirubin, total bilirubin, AST, IL10, and IFN-γ were significantly reduced in the methylprednisolone group (p<0,05) compared to placebo.

Conclusion: Methylprednisolone was efficacious in reducing bilirubin and inflammatory biomarkers compared to placebo. The present study supports immunological process involved in cholestasis and may an opportunity of new therapies to prevent biliary atresia process.

Abstract Submission No. 101149

O-1068

HEPATIC LCH AS HARBINGER OF MULTI-SYSTEM LCH - PROTOCOL FOR DIAGNOSIS AND EARLY PREDICTION

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Background: Hepatic involvement is usually seen as part of multisystem Langerhans Cell Histiocytosis(LCH), but primary presentation of LCH as cholestatic liver disease is rare. Available guidelines has no mention on diagnostic criteria or algorithm for diagnosis of primary manifestation of LCH as isolated Hepatic LCH.

Methods: Review of prospectively collected database from Jan2023to August2023. LFT of other children were also analyzed.

Results: Four cases were included and median age at initial presentation was 16months. All(n=4)100% presented with short duration fever, cholestatic jaundice, pale-stools, abdominal distension, hard-hepatomegaly with predominant left-lobe enlargement. GGT(Gamma-glutamyl-transferase) elevation(>10times) and serum-alkaline-phosphatase(SAP>4times) was seen in all cases(n=4)(sensitivity-100%). MRCP showed Sclerosing cholangitis pattern in 25%(n=1). Immunohistochemistry(IHC) from all liver biopsies were negative(sensitivity=0%). Average interval between initial presentation to decompensation was 3months and for confirmation of diagnosis was 4.75months, diagnosed only after decompensation. Diagnosis was confirmed by IHCs from biopsies of nail-matrix, skin, liver-explant and lymph-node. During initial presentation, if SAP,GGT is elevated >4times and >10times respectively, without obstruction, sensitivity and specificity is 100%(95%CI- 0.98-1), NPV and PPV=1 (95%CI- 0.395-1)in predicting early hepatic LCH. Once decompensated, the combined high SAP-GGT values are not maintained.

Conclusion: As the window period from initial presentation to decompensation is only 3months, if SAP and GGT is elevated >4times and >10times respectively during initial presentation, if obstructive causes are ruled out, PET scan can be done initially to identify the metabolically active areas to be biopsied to maximize the yield for histopathological diagnosis early, as earlier initiation of chemotherapy has better prognosis.

Abstract Submission No. 101435

O-1069

Does intestinal permeability impact the morbidity in cirrhosis? A novel prognostic model of outcome

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Introduction: Increased intestinal permeability (IP) is the gateway to a cascade of events in cirrhosis. Polyethylene glycol (PEG) is an upcoming tool to assess IP. Zonulin and intestinal fatty acid binding protein (IFABP) are biomarkers of tight-junctions and epithelial damage. We aimed to evaluate and interrelate the biomarkers of gut integrity and PEG in cirrhosis.

Methodology: Cirrhotic children and controls (extrahepatic portal-venous obstruction) were prospectively enrolled. Five hours after ingestion of 1 gm/kg of PEG3350, urine was collected and processed by proton-nuclear magnetic resonance (¹H-NMR) spectroscopy to derive the integrated-PEG (I-PEG) value (area under the peak-curve). Serum intestinal fatty acid binding protein (IFABP) and zonulin were assessed on the same day. With the risk factors, a model was created to predict outcome in cirrhotics.

Results: Cirrhotic children (n=56) versus controls (n=35), aged (13.7±3.5 vs. 10.6±2.9 years, p=0.6) had I-PEG (12.9±5.1 vs 3.8±4.2, p=0.02), zonulin (96.6±24 vs 16.3±5.1 ng/mL, p<0.01) and IFABP (4.9±3.3 vs. 1.8±1.2 ng/mL, p<0.01). Among cirrhotics, I-PEG was significantly higher in decompensated (n=20) vs. recompensated (n=36) patients (11.8±7.1 vs 4.9±3.9, p=0.03) and large vs. small esophageal varices (12.4±4.8 vs 6.3±2.2, p=0.03). I-PEG correlated with IFABP (r=0.77, p<0.01), zonulin (r=0.88, p<0.01) and pediatric end-stage liver disease (PELD) score (r=0.67, p=0.03). Zonulin >25ng/mL (OR:3.08, CI:1.05-4.12, p<0.01) and I-PEG>5 (OR:3.19, CI:2.2-7.73, p=0.01) were independent predictors of hospital readmissions over next 6 months. The risk factor model (AUROC:0.87, p<0.001, 92% sensitivity; 60% specificity) predicted morbidity better than isolated PELD or Child-Turcotte-Pugh scores (Fig1).

Conclusions: I-PEG and zonulin risk factor model predicts short-term morbidity in cirrhotic patients.

Abstract Submission No. 101455
O-1070

Bacterial translocation in cirrhosis: Correlation of jejunal cultures and endotoxin assay

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Introduction: There is limited data on bacterial translocation (BT) and small intestinal bacterial overgrowth (SIBO) in pediatric cirrhosis. We aimed to evaluate and interrelate the endotoxin assay, breath test and jejunal cultures in cirrhosis.

Methodology: A prospective study enrolled cirrhotic children for jejunoscopy, glucose hydrogen-breath test (GHBT, normal <12ppm above baseline), serum and ascitic lipopolysaccharide-binding protein (LBP, normal <5mcg/mL). Jejunal culture (aerobic and anaerobic media) antibiotic sensitivity (Kirby-Bauer disc diffusion method) and resistance genes (conventional polymerase chain reaction) were assessed. The median, minimum, and maximum areas under curve of GHBT

were estimated using Ghoshal BreathCalc (Patent appl.No. 202111029055). Extrahepatic portal-venous obstruction patients were controls.

Results: Of the 56 cirrhotic children (pediatric end-stage liver disease score, PELD 15.4±4.3, 18 (32%) had evidence of ascitic fluid infection (AFI) with AF-LBP 7.6±3.3 mcg/mL (fig1). Twelve of 21 (57%) cirrhotics with positive jejunal culture had one or more morbidity outcomes (hospital readmission, systemic infection, renal dysfunction, recurrent AFI, persistent hyponatremia and relative adrenal insufficiency) over next 6 months. Of these twelve, six had high AF-LBP (18±2.7), serum LBP (33±8.7) and jejunal culture multidrug antibiotic resistance (mecA, NDM-1, mcr-1, SHV-1, NDM-1 genes). All six patients died in next 8 (3-12) months. Serum LBP correlated with absolute neutrophil count (r=0.77, p<0.01) and pediatric end-stage liver disease (PELD) score (r=0.87, p=0.03). Serum LBP cut-off >7.8 mcg/mL (AUROC 89%, sensitivity 88%, specificity 64%, p=0.02) predicted short term morbidity events. All ten patients with AF-LBP >10 mcg/mL had renal dysfunction.

Abstract Submission No. 200199
O-1071

Unravelling the mystery of cholestatic liver disease using WES: Unusual presentation of PFIC 8

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Introduction: Progressive familial intrahepatic cholestasis (PFIC) is inherited disorder of defective bile acid secretion with more than 10 types described and have heterogenous clinical presentation. The literature on new variants of PFIC is scarce. This report identifies a unusual presentation of PFIC 8 in adolescence.

Case: 14-year-old healthy adolescent girl born of third degree consanguineous marriage couple was incidentally diagnosed to have portal hypertension secondary to liver cirrhosis when admitted for dengue fever. Her liver function tests were suggestive of cholestatic hepatitis with elevated GGTP with preserved synthetic functions. There was no history of jaundice, abdominal pain, clay stools or itching in the past or in other family members. Autoimmune workup revealed positive ANA (1:100), negative ASMA and hypergammaglobulinemia. MRCP did not reveal obstructive biliary pathology. Her liver biopsy showed features of bile duct destruction with mild cholestasis and interface hepatitis. She was treated with steroids with presumed diagnosis of autoimmune hepatitis (IAIHG score 6). However, her liver functions did not show any improvement. Whole exome sequencing was sent which revealed homozygous mutation of gene KIF12(-) at intron 9 suggestive of PFIC -8. She has being treated with ursodeoxycholic acid.

DISCUSSION: Kinesin like protein - KIF 12 mutation results in cholestasis by disrupting hepatocyte polarity. In the reported literature majority have presented in infancy with few during adolescence with high GGTP cholestasis with scarce literature on their longterm outcomes.

Conclusion: PFIC must be considered as diagnostic possibility while evaluating cholestatic liver disease and confirmed with genetic testing.

Abstract Submission No. 200224
O-1072

IFITM1 forecast HBsAg seroconversion in children with CHB

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Objectives: To explore the role of interferon-induced transmembrane protein 1(IFITM1)predict HBsAg seroconversion in children with chronic hepatitis B(CHB).

Methods: A total of 106 children with HBeAg-positive CHB aged 1 to 18 years, treated with interferon α (IFN α) 48 weeks follow up 24 weeks. Based on the results of HBsAg seroconversion, the patients were divided into HBsAg seroconversion group and non HBsAg seroconversion group. Univariate and multivariate COX regression were used to identify the impact factors associated with HBsAg seroconversion. The area under the receiver operating characteristic curve (AUROC) was used to assess the prediction for HBsAg seroconversion.

Results: HBsAg seroconversion rate at week 48 were 45.28%. Patients with HBsAg seroconversion showed a significantly high baseline IFITM1 levels in comparison to those patients without HBsAg seroconversion($p < 0.05$). Univariate and COX multivariate regression analysis showed that age(HR=0.709, 95%CI: 0.618-0.815, $p < 0.001$) and IFITM1 levels (HR=1.11, 95%CI: 1.01-1.219, $p=0.03$) were independent predict factors for HBsAg seroconversion. ROC curve showed that the prediction efficiency of IFITM1 was good, the area under the receiver operating characteristic curve (AUROC) 0.689, 95%CI: 0.581-0.798, $p=0.001$). Using IFITM1 levels $>1.58\text{ng/ml}$ as the cutoff value, the positive predictive value(PPV) and negative predictive value(NPV) for HBsAg seroconversion were 72.73% and 75%, respectively, with a sensitivity of 82.75%, and specificity of 62.50%, respectively.

Conclusions: baseline IFITM1 could be used as an early predictor of HBsAg seroconversion treated with interferon in children with CHB.

Abstract Submission No. 100197
O-1073

Referral trends and real-world application of transient elastography in pediatric NAFLD in Singapore

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Aim: Pediatric non-alcoholic fatty liver disease (NAFLD) is a progressive disorder that is increasing in incidence globally. The study aims to describe the clinical profile and longitudinal outcome, including the utility of vibration-controlled transient elastography (VCTE) in children with NAFLD at a single tertiary liver unit in Singapore.

Methods: Retrospective review of patients aged 0-18 years referred for NAFLD from 2003 to 2020 was conducted. Diagnosis was based on persistent elevation of alanine transaminase $\geq 2\times$ upper-limit of normal in at-risk patients, and/or radiologic detection of hepatic steatosis, with the exclusion of other aetiologies. VCTE-derived liver stiffness measurement (LSM) of $\leq 7.0\text{kPa}$, $7.1-9.0\text{kPa}$ and $\geq 9.1\text{kPa}$ were used to differentiate normal (F0-F1), significant fibrosis (F2) and advanced fibrosis (F3-F4) respectively.

Results: The study included 210 patients (72.4% male, mean age 11.6 years). New cases increased from 1.7/1000 referrals in the 2003-2008 era, to 12.7 and 24.5/1000 referrals in the 2009-2014 and 2015-2020 eras respectively. Significant proportion had dyslipidemia (41.4%), impaired glucose tolerance/diabetes (IGT/DM, 26.7%) and hypertension (17.1%). Only 6.2% had resolution of NAFLD after mean follow-up of 3.7 years. Based on VCTE ($n=65$), 41.5% had normal LSM, while 26.2% and 32.3% had increased likelihood of significant and advanced fibrosis respectively. Age ≥ 16 years (odds ratio (OR) 8.9),

IGT/DM (OR 6.5) and aspartate transaminase $>70\text{U/L}$ (OR 11.0) were independent risk factors associated with increased likelihood of advanced fibrosis.

Conclusion: Incidence of pediatric NAFLD has increased dramatically in Singapore. Based on LSM estimation, pediatric NAFLD may be associated with increased risk of developing advanced fibrosis by late adolescence.

Abstract Submission No. 100396
O-1074

Endoscopic Cystogastrostomy in Children with Pancreatic Pseudocyst

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OBJECTIVE: Endoscopic cystogastrostomy is routinely used in adults with symptomatic pancreatic pseudocysts, but literature in children is scarce.

METHODS: Records from January 2017 to April 2023 were analysed for children with symptomatic pseudocysts.

Results: Fourteen children included. Age was 15 (5-18) years, 11 (78.6%) males. Pain in 13 (92.9%), weight loss in 11 (78.6%), constipation in 11 (78.6%) and recurrent vomiting in 9 (64.3%). Fever in 5 (35.7%). The cyst volume was 550 (IQR 500-700) ml with 10% (IQR 10%-30%) necrosis. Endoscopic cystogastrostomy was completed in all except one. Resolution of symptoms in 12 (85.7%) with no mortality. Complications in 4 (28.6%), post procedure infection in 3 (21.4%) and pneumoperitoneum in 2 (14.3%). Stent migration was in 1 (7.1%). Followup of 21 (6-39) months. Follow up size 3 (0-5) cms. Recurrence occurred in 4 (28.6%) at 3 (2.25-3) months post procedure. Stent removal was done in all at 3 (1.75-4.25) months. On risk predictive analysis, presence of any complication (75% vs 10%, OR 27.000, 95% CI 1.260-578.354, $p=0.015$) and early stent removal (1.5 months vs 4 months months, mean difference 2.567, 95% CI 0.051 to 4.943, $p=0.023$) were found to be associated with recurrence. On logistic regression, presence of complications was associated with symptom recurrence and improved the correctness of classification from 71.4% to 85.7%.

Conclusion: Endoscopic cystogastrostomy is effective in resolving symptoms and reducing cyst size in children. Complications occur in 28% of patients and are associated with large cyst size of > 12 cms. Presence of any complication increases the risk of symptom recurrence 27 folds

Abstract Submission No. 100635
O-1075

Predictors for hypervascular hepatic nodules in patients with Fontan-associated liver disease

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Background: Hepatic hypervascular tumors may develop and become serious problems in patients after the Fontan operation. However, the risk factor has yet to be identified. Therefore, this study aims to evaluate the predictors associated with hepatic hypervascular tumors in post-Fontan patients.

Methods: In this prospective, single-center study, 75 post-Fontan patients were included (38 female/37 male). The mean age was 23.6 years old, and the mean post-Fontan years was 15.3 years. Between August 2015 and March 2023, MRI was performed to detect hepatic nodules and possible abdominal abnormality. The laboratory data, serum biomarkers for liver fibrosis, transient elastography, and intravoxel incoherent motion (IVIM) MRI were collected for liver stiffness evaluation.

Results: Among 75 post-Fontan patients, hypervascular hepatic tumors were detected in 18 (24%) patients. Only 1 (2.3%) of the lesion was proven to be hepatocellular carcinoma. Asplenia was a significant factor in predicting hepatic hypervascular tumor (AUC 0.659, $p=0.002$). The severity of liver fibrosis evaluated with IVIM MRI, transient elastography and medical scores was not associated with the presence of hypervascular hepatic tumors. A combination of serum hemoglobin (Hb), platelet, alkaline phosphatase (ALP), and gamma-glutamyl transpeptidase (GGT) help predict the occurrence of hepatic hypervascular tumors (AUC 0.727, $p=0.029$). The composite model of asplenia, serum platelet, ALP and GGT will increase diagnostic performance even more (AUC 0.762, $p=0.012$).

Conclusion: Asplenia significantly predicted the development of hepatic hypervascular tumors in post-Fontan patients, while liver fibrosis levels did not. Blood tests, including Hb, platelet, ALP and GGT can enhance the prediction model.

Abstract Submission No. 101316

O-1076

Galactosemia in children: predictors and risk factors of outcome

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Background: Galactosemia constitutes 2% of all neonatal cholestasis. Despite early diagnosis and dietary exclusion, there may be adverse liver and neuro-ophthalmic outcomes. We analysed the risk factors of outcome in galactosemia patients.

Methods: Diagnosis was based on galactose-1-phosphatase uridyl transferase (GAL-1-PUT) enzyme <10 U/gHb or mutation of GALT gene. Risk factors of death or neuro-ophthalmic morbidity (poor neurocognition, learning disability persistent cataract or amblyopia despite cataract surgery) were analysed from a prospectively maintained database.

Results: Fifty-one galactosemia patients presented as infantile cholestasis. Their median age of symptom onset and diagnosis were 10(1-90) and 45(7-450) days respectively. Figure 1 shows the natural history on lactose-free diet. Among the 43 survivors, 28 had follow-up with >6 months were analysed for long term outcome. All had normalisation in liver functions. Ten(36%) had adverse neuro-ophthalmic outcome. Eighteen patients are currently asymptomatic in follow up till now. Multivariate analysis of non-survivors($n=8$) versus survivors($n=28$) identified risk factors: refractory ascites (88% vs.18%, $p=0.012$), persistent coagulopathy at 4 weeks (88% vs.25%; $p=0.02$), and culture-positive sepsis (63% vs 43%; $p=0.04$). In addition, pediatric end-stage liver disease (PELD) score <21 (sensitivity 78%; specificity 50%, $p=0.02$) and Child score <7.5 (sensitivity 89%; specificity 61%, $p=0.01$) predicted survival. PELD score correlated with culture-positive sepsis ($p=0.05$). In the 10 patients with poor neuro-ophthalmic morbidity, no risk factors could be identified.

Conclusion: Refractory ascites, uncorrectable coagulopathy at 4 weeks of diagnosis and sepsis were associated with poor liver outcome.

PELD and Child score predict survival. Long term neuro-ophthalmic morbidity is not associated with disease severity at onset.

Abstract Submission No. 101332

O-1077

Is ascites a risk factor of mortality in pediatric acute liver failure?

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Introduction: Hepatitis A virus (HAV) in developing nations is one of the leading causes of acute liver failure (ALF) in children. Survival with native liver (SNL) is guarded. We aimed to study the factors that are associated with outcome in this condition.

Methods: A prospectively maintained database registered all ALF admitted between 2017-2022. Poor outcome (PO) was defined as death or requirement of liver transplantation. Underlying chronic liver disease was excluded.

Results: Comparison of HAV-ALF ($n=55$) vs non-HAV-ALF ($n=44$) [hepatitis B ($n=12$), hepatitis E ($n=2$), Epstein-Barr ($n=7$), parvovirus ($n=6$) and indeterminate ($n=19$)] showed age ($7\pm4.0y$ vs $9.9\pm4.6y$, $p=0.002$), duration of illness (33.9 ± 23.8 vs 21 ± 6.8 days, $p=0.04$), PELD score (31.4 ± 14.1 vs 27.4 ± 20.1 , $p=0.07$) and SNL (51% vs 38%, $p=0.1$). Among HAV-ALF, 61% had ascites (35% at presentation, 26% during admission; jaundice to ascites duration 17 ± 22 days) and 65% had encephalopathy (55% at presentation, 10% during admission; jaundice to encephalopathy duration 15.5 ± 19 days). PO was seen in 90% of those who developed ascites prior to encephalopathy(41%) and required large volume paracentesis(33%). Violin plots (Figure 1) shows comparison of liver function with final outcome. On multiple step-wise logistic regression, ascites preceding encephalopathy [OR 2.1(1.6-3.3), $p=0.002$], spontaneous bacterial peritonitis [OR 1.8(1.2-2.3), $p=0.02$] and PELD score [OR 4.3(2.3-4.8), $p=0.001$] were independent predictors of PO. At presentation, PELD score cutoff <23.5 (AUROC 0.86) and serum albumin >3.1 g/dL (AUROC 0.77) were associated with SNL.

Conclusions: Ascites preceding encephalopathy and spontaneous bacterial peritonitis are associated with poor outcomes in acute liver failure. Universal vaccination policies need to be reinforced.

Abstract Submission No. 101448

O-1078

Characteristics and Outcomes of Biliary Atresia in a Limited Facility of Liver Transplantation

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Background: Biliary atresia is an obstructive cholangiopathy leading to liver fibrosis. Biliary atresia is the most common cause of liver transplantation in the pediatric population. Although management strategies have been implemented worldwide, the rate of delayed treatment is still high. This study aims to describe the characteristics and outcomes of biliary atresia in a limited facility of liver transplantation.

Methods: This study is a prospective study performed in infants with biliary atresia at Dr. Soetomo General Academic Hospital, Surabaya in 2021 - 2023. Demographics, laboratory and biopsy parameters, and

outcomes were analyzed. Analysis was performed using SPSS version 25.

Results: There were 94 infants, consisting of 41 boys and 53 girls with a mean age of 16±17 weeks. 55 (58.5%) were from rural areas, 52 (55.3%) were born by cesarean section (38±1.78 weeks). The onset of jaundice occurred 4 ± 3 weeks after birth. A total of 80 (85.2%) infants survived and 39 (41.4%) presented with portal hypertension. A total of 77 (81.8%) had liver fibrosis. Kasai were performed in 11 (11.7%) of the cases. The IgG-CMV, rubella, and toxoplasma reactivity occurred in 80 (84.7%), 37 (39.3%), and 8 (8.5%) cases, respectively. Meanwhile, reactive IgM CMV, Rubella and Toxoplasma were found in 34 (36.1%), 7 (7.4%) and 8 (8.5%) cases, respectively.

Conclusion: Delayed referral rate for biliary atresia has remained high. The high rate of CMV infection in biliary atresia may provide a basis for exploring alternative medical therapies to prevent fibrosis and reduce the need for liver transplantation.

Abstract Submission No. 101497
O-1079

Hyperinsulinemia Inducing Late Onset Transient Cholestasis in Neonates: a Case Report

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A term low birth weight baby boy (Caucasian-African-American descent) was born from a mother with gestational diabetes, urinary tract infection, brownish vaginal discharge, fetal distress, and PROM with C-section. The mother had a history of one stillbirth and two miscarriages. The baby was admitted to NICU at 10 hours of age because of early-onset neonatal sepsis and critically low blood glucose. Antibiotic therapy and high glucose infusion rate (GIR 13 mg/kg/min) were given. Because of the lack of response, the critical sampling was done and revealed hyperinsulinemia (>6.3 µU/mL). The ocreotide therapy for hyperinsulinemia was started while waiting for diazoxide therapy. At four weeks of age, he had yellowish skin and sclera, yellow-pale stool but without bloody stool or hepatomegaly. There were no infections or parenteral nutrition used. Laboratory examination showed an increase of direct bilirubin (7.09 mg/dL), AST, ALT, and alkali phosphatase with normal gamma-glutamyl transferase (GGT) levels. Neonates with hyperinsulinemia tended to have cholestasis (median of conjugated bilirubin level: 5 mg/dL) after four days of hypoglycemia onset. The risk factors are fetal distress, hyperglycemia during pregnancy, prematurity, chorioamnionitis, and parenteral nutrition. The proposed mechanism is related to the effect of diabetes during pregnancy, which causes fetal hyperinsulinemia that leads to chronic hypoxemia and oxidative stress. In vivo study showed that a hypoxic state will induce a change in histological structure (predominantly cholangiocytes) and alteration of hepatobiliary transporter genes, such as decreases mRNA level of Ntcp, Bsep, and Mrp2 (hepatocyte transporters) and decrease mRNA level of Cfr (cholangiocyte transporter).

Abstract Submission No. 101533
O-1080

ZFYVE19 disease: a facultative ciliopathy initiated by failure of cell division and cell death

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Background & Aims: ZFYVE19 disease is a recently discovered disorder characterized by progressive portal fibrosis, portal hypertension and eventually liver decompensation. To elucidate the underlying mechanism, *Zfyve19*^{-/-} mice and ZFYVE19 knockdown / knockout cells were generated.

Methods: *Zfyve19*^{-/-} mice were generated by targeted knockout using CRISPR/Cas9 technology and challenged with alpha-naphthyl isothiocyanate (ANIT) to induce biliary fibrosis. Their livers were characterized at the tissue, cellular, and molecular levels. Findings were compared with those in wild-type (WT) mice and in ZFYVE19-disease patients.

Results: The *Zfyve19*^{-/-} mice were normal with respect to general and hepatobiliary features. However, when challenged with alpha-naphthyl isothiocyanate, *Zfyve19*^{-/-} mice developed changes resembling those in ZFYVE19-disease patients, including elevated serum liver injury markers, increased number of bile-duct profiles with abnormal cholangiocyte polarity, and biliary fibrosis. Failure of cell division, centriole and cilia abnormalities, and increased cell death were observed in knockdown / knockout cells. Increased cell death and altered mRNA expression of cell death - related signaling pathways was demonstrated in livers from *Zfyve19*^{-/-} mice and patients. TGF-β and JAK-and STAT3 signaling pathways were upregulated *in vivo*, as were chemokines such as C-X-C motif ligands 1, 10, and 12.

Conclusions: Our findings demonstrated that ZFYVE19 disease is a facultative ciliopathy with novel histological features. Failure of cell division with ciliary abnormalities and cell death activates macrophages and leads to biliary fibrosis via TGF-β pathway in the disease.

Abstract Submission No. 101985
O-1081

NATURAL HISTORY AND RENAL INVOLVEMENT OF CONGENITAL HEPATIC FIBROSIS AND CAROLI DISEASE

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Background and Objective: Congenital hepatic fibrosis(CHF) and Caroli syndrome has varied clinical presentations with or without renal involvement. Our study aimed to describe clinical manifestations and natural history of children with CHF and Caroli.

Methods: Retrospective review of case records of CHF and Caroli children(n=21) diagnosed on basis of clinical features, radiological and compatible histopathological findings in a single centre. Children

were followed up and endoscopic, radiological and biochemical surveillance was recorded and analyzed.

Results: Twenty-one children (Caroli=6, CHF=16) were enrolled and male predominance(76%) was noted. Consanguinity was noted in 76% and 23% had affected siblings. Median age at initial presentation was 2yrs and abdominal distension was the most common presentation (47.6%) followed by variceal bleeding (23.8%), cholangitis (14.2%), incidental diagnosis (9.5%) and pancytopenia (4.76%). Median age at presentation and diagnosis was later with variceal bleeding compared with abdominal distension being 5.6yrs and 18months respectively($p=0.0001$). Renal involvement was present in 76%, most common was ARPKD, 18% had developed CKD. Caroli had 100% renal involvement. There was no statistical difference in the age of presentation of CHF with or without renal involvement($p=0.5998$). Growth faltering was noted in 52% not related to the degree of either renal involvement or portal hypertension. Portal hypertension was seen in 76%. Only one child had variceal bleeding on follow up.

Conclusion: Abdominal distension, organomegaly, variceal bleeding and cholangitis are the common clinical manifestations of CHF and Caroli disease. Renal involvement did not correlate with severity of hepatic manifestations or involvement.

Abstract Submission No. 102011

O-1082

Pediatric acute liver failure: Experience from a tertiary care center in India

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Background: Pediatric ALF encompasses a spectrum with varied etiologies and timely intervention and appropriate choice of therapies may halt rapid progression and prevent unfavorable outcome. We aimed to study the outcomes and identifying prognostic variables in predicting 30-day transplant free survival in PALF.

Methods: In this retrospective analysis done at tertiary care center at Hyderabad, India. 24 patients with PALF within last 1 year were analyzed. Aim of the study was to analyze 28-day transplant free survival outcomes of PALF, incidence of infections and various prognostic variables.

Results: The mean age of presentation is 8.12 ± 3.2 years with viral being the most common etiology in 15/24 (62.5%) followed by Wilson flare 4/24 (16.6%) and others 5/24 (20.8%). Mean time from onset of jaundice to encephalopathy was 6.34 ± 2.2 days. Sepsis was noted in 5/24(20.8%) and AKI in 5/20 (20.8%) patients. 28-day transplant free survival was noted in 70.8% (17/24) patients. Spontaneous recovery was noted in 41.1% (7/17). Plasma exchange (PLEX) was performed in 47 % (8/17); CRRT in 11.7% (2/17);Liver transplantation in 2 patients. Median time to transplant free recovery was $10\{4.2-21.2\}$ days. Mean number of PLEX sessions were 2.12 ± 0.42 . On Multivariate analysis, baseline NH3 {HR (95% CI) 1.42,(0.920-4.18), $P=0.01$ } ;Grade of encephalopathy(baseline){HR(95%CI),3.57(1.45-8.41), $P=0.01$ };PELD score {HR(95%CI), 1.865 (0.854-5.354), $P=0.04$ } were found to be significant in predicting 30 day transplant free survival.

Conclusion: Timely management of PALF and early intervention will guide in prognosis and management.

Abstract Submission No. 200140

O-1083

LIVER TRANSPLANTATION FOR PROGRESSIVE PEDIATRIC BUDD CHIARI SYNDROME

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Background: Budd Chiari syndrome (BCS) in children is uncommon and there is limited published literature on liver transplantation (LT).

Methods: Ten children who underwent LT for BCS from 2017- 2023 were analysed for radiological intervention(RI), indication of transplant, intraoperative challenges, early and late complications and graft survival after transplantation.

Results: A total 60 paediatric LT were performed over 4.5 years of which 10 patients (8 males and 2 females) had BCS. 8/10 children had prior RI (Five had TIPSS and 4 had Hepatic vein venoplasty). Hepatopulmonary syndrome (HPS) was the most common indication for LT and developed post RI in 6 children . The median age and weight of children at transplant was 61 months (IQR 26 - 109) and 12.85kg (IQR 10.4 - 23) respectively. The median duration from onset of symptoms to LT was 42 months (IQR 14 - 80). HPS resolved after a median period of 25 days (IQR 15.5 - 60). The median duration of post-transplant follow up is 4yrs 5 months (IQR 1 year 10 months - 4 years 10 months).Vascular complications (including 1 recurrence) and biliary complications were seen in 30% patients respectively which were amenable to RI. The 1 year & 3-year survival rates both were 75%.

Conclusion: LT has shown good long-term outcomes in children with BCS. HPS seems to occur despite RI in paediatric BCS. Recurrent BCS post LT can be salvaged using RI. Higher biliary and vascular complications are likely related to HPS & previous RI.

Abstract Submission No. 200193

O-1084

Anti-HBc levels predict HBsAg seroclearance in children with CHB

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Objectives: To explore the role of anti-HBc predict the HBsAg clearance in children with chronic hepatitis B(CHB).

Materials and Methods: 56 children with HBsAg-positive CHB aged 1 to 10 years, treated with interferon α (IFN α) 48 weeks follow up 24 weeks. Based on the results of HBsAg clearance, the patients were divided into HBsAg clearance group and non HBsAg clearance group. Univariate and multivariate regression was used to identify the impact factors associated with HBsAg clearance. The area under the receiver operating characteristic curve (AUROC) was used to assess the prediction for HBsAg loss.

Results: HBsAg loss rate at week 48 were 50.0%. Patients with HBsAg loss showed a significantly high baseline anti-HBc levels in HBsAg loss group($p < 0.05$). Univariate and multivariate analysis showed that age, baseline anti-HBc and HBsAg levels at week 12 were independent predict factors for HBsAg loss. Although the baseline anti-HBc levels(AUROC 0.704(95%CI 0.567-0.841, $p=0.0001$) was lower than that of HBsAg at week 12(AUROC 0.866, 95%CI 0.765-

0.967, $p=0.0001$), the ROC curve showed that the prediction efficiency of baseline anti-HBc combined with HBsAg levels at week 12 was higher than that of HBsAg alone (0.931 vs 0.866, $p=0.000$), the positive predictive value (PPV) and negative predictive value (NPV) for HBsAg loss were 84.4% and 95.8%, respectively, with a sensitivity of 96.4% and specificity of 82.1%.

Conclusions: Baseline anti-HBc combined with HBsAg levels at week 12 could be used as an early predictor of HBsAg loss treated with interferon in children with CHB.

Abstract Submission No. 200218

O-1085

Early decreased HBV RNA and HBsAg levels predicts treatment effect in children with CHB

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Objective: To explore the role of serum HBV RNA in children with CHB during antiviral treatment.

Methods: 222 children with CHB aged 1-17 years old received 48 weeks IFN α alone or combination with nucleoside analogues (NAs) was studied. Ability of HBV RNA predicting HBsAg loss was evaluated by the area under the receiver operating characteristic (AUROC).

Results: HBsAg loss rate in HBeAg positive children was 32.0% at week 48. In predicting HBsAg loss, the combination of reduced levels of HBV RNA and HBsAg at 24 th weeks was pronounced superior to other combinations of HBV biomarker reduced levels. HBV RNA from baseline to week 24 reduced levels $>2.7 \log_{10}$ copies/ml combined with HBsAg reduced levels $>2.02 \log_{10}$ IU/ml had a strong ability predicting HBsAg loss at week 48, the positive predictive value, negative predictive value, sensitivity and specificity was 78.9%, 86.8%, 100.0% and 72.9%, respectively.

Conclusions: The decline degree of HBV RNA combined with HBsAg from baseline to week 24 of treatment can be used an early marker of predicting HBsAg loss in HBeAg positive children.

Abstract Submission No. 100065

O-1086

Assessment of the APASL Guidance for Albumin Infusion in Therapeutic Paracentesis: RD Design

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Background: The 2023 APASL Guidelines recommend albumin infusion to prevent post-paracentesis circulatory dysfunction when removing ≥ 5 liters of ascites. However, the optimal cutoff for initiating albumin infusion after the large-volume paracentesis (LVP) remains understudied.

Methods: We conducted a retrospective cohort study at a U.S. academic healthcare center on outpatients who underwent LVP between 2019 and 2022. Patients with spontaneous bacterial peritonitis, post-LVP diuretic adjustments, and/or hospitalization were excluded. The

institution strictly followed the guidelines, making the cohort suitable for a Quasi-experimental, sharp regression discontinuity (RD) design. This allowed us to estimate the local average treatment effect of albumin infusion on serum creatinine and sodium trajectory.

Results: Over the study period, 1457 LVPs were performed on 236 unique patients. Administering albumin infusion at the threshold of 5 L of ascites removal significantly reduced serum creatinine levels by 0.05 (95%CI: 0.01-0.097) and 0.048 (0.01-0.086) mg/dl/day and increased serum sodium levels by 0.34 (95%CI: 0.12-0.6) and 0.39 (0.16-0.61) mEq/L/day, respectively, compared to those without albumin infusion. Results across sensitivity analyses were consistent, underscoring the robustness of the effect size estimation. The RD plots also indicated worsened serum creatinine/sodium levels after draining 3-4 liters of fluid, approaching levels similar to or worse than with albumin infusion at 5 liters or more.

Conclusions: RD models supported the 2023 APASL Guidelines. Additionally, the findings suggest conducting clinical trials to evaluate the efficacy of albumin infusion in patients who undergo LVP and have 3-5 or 4-5 liters of ascites removed.

Abstract Submission No. 100474

O-1087

Hepatic Encephalopathy after TIPS in cirrhosis and sarcopenia: A Systematic Review and Meta-analysis

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Backgrounds: The association between the presence of sarcopenia in patients with cirrhosis and the onset of hepatic encephalopathy (HE) after transjugular intrahepatic portosystemic shunt (TIPS) is yet to be established. We conducted a systematic review and meta-analysis to provide a thorough summary of the available evidence on this association.

Methods: A thorough search of the literature was performed in the PubMed, EMBASE, and Web of Science databases. The protocol was duly registered on PROSPERO (CRD42023398856). The hazard ratio (HR) and corresponding 95% confidence intervals (CIs) for the occurrence of HE after TIPS were extracted from studies comparing cirrhotic patients with and without sarcopenia. These data were then combined using a random-effect model.

Results: A total of 1135 patients from seven cohort studies that met our eligibility criteria were included in the meta-analysis. Our findings indicate a significantly higher risk of post-TIPS HE among cirrhotic patients with sarcopenia compared to those without sarcopenia (HR, 2.35; 95% CIs, 1.32-4.19; $p=0.004$; $I^2=75\%$). The findings remained consistent through sensitivity analysis and across subgroups stratified by liver disease etiology, study location, and severity of hepatic dysfunction.

Conclusion: The study demonstrated that sarcopenia was strongly linked to an increased likelihood post-TIPS HE among cirrhotic patients.

Abstract Submission No. 100510

O-1088

Safety & Efficacy of Endoscopic Glue vs EUS guided Coil+glue in the Treatment of Gastric Varices:RCT

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Background: Gastric varices are typically treated by Endoscopic injection of glue. Various complications have been described related to this treatment. EUS offer a unique opportunity to directly visualize and access GV

Aim: To compare the safety and efficacy of Endoscopic glue injection technique to EUS guided coil with glue

Methods: RCT was done from Feb 2020 to Aug 2021. Patients were randomized into 2 groups. Group A patients received endoscopic glue injection and Group B patients received EUS-guided coils and glue injection. CT Chest was performed in all patients to detect pulmonary embolism. Patients were followed at 1, 3 and 6 months. Primary outcome was to compare the occurrence of PTE between 2 groups. Secondary outcome was to evaluate the efficacy of 2 techniques in the complete obliteration of varices, rebleed rates and reinterventions required in both groups

Results: 34 patients were enrolled and 17 patients were included in each group. PTE was documented in 3 (17.6%) patients in group A and in only 1 (5.8%) patient in group B. Of 16 patients in group A, 10 (62.5%) had complete obliteration at 1 month, whereas 15 (93.75%) had complete obliteration of the gastric varices in group B ($p=0.03$). In group A, 7 (43.75%) required reintervention on follow up due to incomplete obliteration, whereas in group B, only 1 out of 16 (6.25%) required reintervention ($p=0.03$). In group A, 2 (12.5%) had rebleed at 3 months follow up whereas in group B, none of the patient had rebleed ($p=0.144$)

Conclusion: EUS-guided coil+glue was highly effective in obliteration of GV and reducing need for reinterventions when compared to endoscopic glue. Also, the risk of embolism with EUS guided treatment was low when compared to Endoscopic treatment.

Abstract Submission No. 100796

O-1089

Point-of-care cardiac ultrasound (POCUS) monitoring & Fluid resuscitation in Cirrhosis with sepsis

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Background: Point-of-care ultrasound (POCUS) is used to determine volume status, presence of cirrhotic cardiomyopathy (CCM), inferior vena cava (IVC) dynamics and fluid responsiveness in cirrhosis with severe sepsis. We compared the response of 3 resuscitation strategies in the first 6 hours: (1) early 20% albumin (2) balanced salt solution (BSS) or (3) combined BSS and late 20% albumin.

Methods: POCUS was done within 3h of admission to the liver intensive care unit and at 24h, 48h & 72h in patients with cirrhosis with mean arterial pressure (MAP) < 65 mmHg. Resuscitation target was maintenance of MAP ≥ 65 mmHg. We evaluated predictors of circulatory failure and mortality using POCUS & serum biomarkers. CCM was defined per CCM Consortium (2020) criteria.

Results: We enrolled 180 patients (67% men, mean 49 ± 12.7 years, 47% alcohol associated). SOFA score 8.2 ± 2.7 and MELDNa 27.9 ± 4.7. Overall, 90-day mortality was 36.1%. Patients receiving 20% albumin within 1st hour, (Early albumin, N=78), only BSS in 1st 6 hours (N=65) and BSS followed by late 20% albumin > 3 hours of ICU admission (Late albumin, N=37) were compared. CCM was diagnosed in 78 (43.3%) and was independently predictive of mortality. On multivariable analysis, the CCM variables: e' velocity (aHR-0.98, $P=0.040$), LAVI (aHR-1.1, $P=0.019$), biomarkers-endotoxin level

(aHR-1.2, $P=0.001$), NTproBNP (aHR-1.004, $P=0.001$), Galectin-3 (aHR-1.1, $P<0.001$) and SOFA score (aHR-1.3, $P<0.001$), and not the type of fluid predicted fluid nonresponse. Predictors of mortality were SOFA score (aHR-1.4, $P=0.043$), MELDNa (aHR-1.9, $P=0.038$), e' velocity (aHR-0.82, $P=0.034$), cardiac index at 72h (aHR-0.31, $P=0.006$) and not the type of fluid. The 28-day mortality outcomes did not differ in the three resuscitation fluid arms (37.2%, 36.9% & 18.9%, respectively; $P=0.053$).

Conclusion: Successful resuscitation of patients with cirrhosis and sepsis is dependent on their cardiac function and SOFA score rather than the choice of resuscitation fluid.

Abstract Submission No. 100904

O-1090

Reating diagnostic models for liver cirrhosis patients with portal hypertension using HVPg

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Background: Portal hypertension in liver cirrhosis leads to complications like ascites, esophageal varices, and hepatic encephalopathy. Accurate assessment of portal hypertension relies on invasive hepatic venous pressure gradient (HVPG) measurement, which is not widely available. Non-invasive models for stratifying portal hypertension in liver cirrhosis are lacking.

Methods: This study included liver cirrhosis patients from multiple centers in Shandong Province, China for HVPG measurement. Patients were divided into three subgroups based on disease stage: compensated portal hypertension (HVPG=5-10mmHg), clinically significant portal hypertension (HVPG≥10mmHg), and decompensated portal hypertension. Pearson correlation coefficients were used to explore the relationships between 19 clinical features and portal venous pressure. Non-invasive models were developed for each subgroup to guide clinical practice.

Results: In compensated portal hypertension (HVPG=5-10mmHg), the model equation was $Y=850.543-17.725*ALB+14.299*LSM-38.478*WBC-4.102*TBIL-4.186*HA$. The area under the curve (AUC) for diagnosing progression to clinically significant portal hypertension (HVPG≥10mmHg) was 0.75 (0.641-0.859). For clinically significant portal hypertension, the model equation was $Y=216.767+1.203*PT+2.135*gender$ (1 for male, 0 for female). The AUC for diagnosing progression to decompensated portal hypertension was 0.821 (0.726-0.916). For decompensated portal hypertension with HVPG≥10mmHg, the model equation was $Y=0.65+0.003*WBC-0.31*HA$. The AUC for predicting the risk of severe decompensation events was 0.778 (0.58-0.975).

Conclusion: Portal hypertension occurs at different stages of liver cirrhosis, and as portal venous pressure increases, the diagnosis and treatment of liver cirrhosis become more challenging. Non-invasive models for stratifying portal hypertension can assist in diagnosing and monitoring portal hypertension throughout the disease course, enhancing the sensitivity of clinical diagnosis.

Abstract Submission No. 101351

O-1091

Hypersplenism in non-cirrhotic portal hypertension- debunking the spleen's guilt

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Background: Hypersplenism is a common occurrence in non-cirrhotic portal hypertension (NCPH), manifesting as bicytopenia or pancytopenia in majority of these patients. Splenic stiffness measurement (SSM) is increasingly being validated for assessment of portal hypertension.

Therefore, we evaluated the correlation between splenic stiffness and hypersplenism.

Methods: Consecutive patients (n=89) with non-cirrhotic portal hypertension were enrolled in the study. SSM/LSM (liver stiffness measurement) values were obtained using FibroScan® Expert 630 machine. Pearson correlation coefficient was calculated to analyse correlation between hematologic parameters and splenic stiffness. Simple linear regression analysis was done with SSM as explanatory variable.

Results: Median age was 35 (17-70) years. Female preponderance was observed (51/89, 57.3%). 48 of 89 (53.9%) patients had non-cirrhotic portal fibrosis/idiopathic portal hypertension (NCPF/IPH) and 41 patients (46.1%) had extra-hepatic portal vein obstruction (EHPVO). Median values of hematologic parameters were: hemoglobin 9.8 (3.5-14.2) g/dL, leukocyte count- 3.4 (0.8-13.6) $\times 10^9$ /L and platelet count- 80 (20-636) $\times 10^9$ /L. Mean spleen size was 19 (± 4) cm. Mean SSM and LSM values were 60.5 (± 24.4) kPa and 8.3 (± 3.2) kPa respectively. Spleen size positively correlated with SSM values (Pr<0.0001). The hematologic parameters (Hb, leukocyte and platelet count) correlated with each other but not with splenic size or stiffness (Pr<0.05).

Conclusion: The severity of cytopenias due to hypersplenism is independent of the splenic size or stiffness.

Abstract Submission No. 101378

O-1092

Clinical profile of adolescents presenting with Portal Hypertension at a tertiary care center

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AIMS AND BACKGROUND: Portal Hypertension (PHT) is a major cause of morbidity and mortality in pediatric liver diseases. We aimed to study patients' characteristics and outcome in adolescent population presenting with PHT.

Methods: Prospectively collected liver clinic database from January 2014 to December 2022 was analyzed to identify the profile of newly diagnosed adolescent patients presenting with features of PHT.

RESULTS: Total 125 (79[63.2%] boys) patients reviewed. The etiology of PHT were Extrahepatic portal vein obstruction (EHPVO, n=45[36%]), Non-cirrhotic portal fibrosis (NCPF, n=25[20%]), Budd-chiari syndrome (BCS, n=18[14.4%]) and liver cirrhosis (n=37,29.6%). The causes of cirrhosis were AIH (n=4[10.8%]), Wilson's disease (n=12[32.4%]), Hepatitis B (n=8[21.6%]), Caroli's disease (n=1[2.7%]) and cryptogenic (n=12[32.4%]). The presentation was variceal bleed (n=44[35.2%]), ascites (n=39[31.2%]), jaundice (n=26[20.8%]) and hepatic encephalopathy (n=6[4.8%]). EHPVO and NCPF, presented with variceal bleed(50%) ,while BCS and cirrhosis presented with ascites (63%). Esophageal and Gastric varices at index endoscopy were present in 77 (61.6%) and 27 (21.6%) cases. During 65 months median follow up, recurrent variceal bleed was seen in 6 and 5 cases of EHPVO and NCPF respectively despite on surveillance endoscopy. Over a median follow-up of 5 years 6(4.8%) patients died, all due to progressive liver failure.

Conclusion: Vascular diseases of the liver are the most common causes of PHT in adolescents and have a good prognosis.

Abstract Submission No. 101941

O-1093

Propofol sedation in Gastroscopy in Cirrhotics and utility of Psychometric , ICT CFF from recovery

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Background- Minimal hepatic encephalopathy (MHE) impairs health related quality of life and predicts overt hepatic encephalopathy (HE) in cirrhotic patients. Cirrhotics are at increased risk of development of complications related to sedation. Aim- To study effect of propofol sedation during upper gastrointestinal (UGI) endoscopy in cirrhotics and utility of psychometric tests, inhibitory control test (ICT) and critical flicker frequency (CFF) in assesment of recovery from sedati

Methods: 204 cirrhotic patients were taken to assess the effect of propofol sedation during UGI endoscopy. Out of 100 cirrhotic patients 49 % (49 patients) were diagnosed as MHE on the basis of psychometric tests.. All patients underwent CFF test , ICT and combination of psychometry (NCT A,B); digit symbol test(DST), line tracing test(LTT) and serial dotting test(SDT) at baseline..CFF and ICT done at 30 min and repeated every 30 mins for 2 hours. Psychometry repeated at 2 hour

Results: 125/204 cirrhotics (61 %) had MHE before the endoscopy .In propofol group there was no significant deterioration in psychometry..Significant deterioration from baseline was seen in CFF at 30 min(38.8

Conclusion: Propofol sedation for UGI endoscopy is safe and associated with improved recovery in cirrhotics. CFF is less time consuming, easy to perform, more sensitive and more specific than ICT to diagnose MHE

Abstract Submission No. 101991

O-1094

High-shear induced activation of piezo1 develops portal-hypertension via cytoskeleton remodelling

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Background and Aim: Liver Sinusoidal Endothelial Cells sense & respond to portal blood flow induced shear stress & hydrostatic pressure via mechanocrine signalling, regulates the endothelial homeostasis & vascular tone. Disturbed shear promotes endothelial dysfunction and portal hypertension. Role of mechanosensors and its contribution in portal dynamics is unexplored. We investigated the involvement of high shear induced mechanosensors in the development of portal hypertension.

Methods: Experimental high shear rat model was developed by resection of 70% liver (Phx). Hepatic hemodynamic was monitored at 24 and 48hrs post Phx. Shear flow was evaluated by transonic flow system and intra-vital imaging with Rhodamine-6G-fluorophore-stained platelet. Further proteomics analysis was performed. Molecular, cellular and histological analysis was performed in liver tissue.

Result: Hemodynamic studies revealed that portal blood flow index was markedly increased +222% and +122% at 24hrs and 48hrs respectively post 70% Phx and PP was raised (17.19 ± 3.28 +83.33% and 17.66 ± 2.51 +150%) at 24h and 48h respectively in comparison to controls. Two-fold raise in Shear stress was observed in portal vein. Proteomic analysis revealed activation of PIEZO1 in high shear stress which leads to increased Ca^{2+} influx to calcium signalling. Upregulated Calmodulin, calpain and SERCA complex activates myosin-light-chain-kinase (MLCK) leading to cytoskeleton hypercontractility and rearrangement further cause vasoconstriction, and involved in the development of portal hypertension. Mechanosensors VEGFR2, PIEZO1, CD-31, α -SMA, vWF, ET-1 genes were upregulated.

Conclusion: High shear activates PIEZO1 dependent Ca^{2+} mechanosensitive ion channel promotes cytoskeleton rearrangement, causing vasoconstriction which further increases hepatic resistance, ultimately leading to portal hypertension.

Abstract Submission No. 102005
O-1095

Steroid response in Alcoholic hepatitis(AH) induced ACLF is based on severity of portal hypertension

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Introduction: Alcoholic hepatitis (AH) induced ACLF is a distinct clinical syndrome characterized by high short term mortality. Treatment with prednisolone in patients with AH-induced ACLF has shown promising results. We investigated the role of portal hypertension in patients with AH-induced ACLF.

Methods: Patients presenting with AH-Acute on chronic liver failure (ACLF) using APASL criteria were prospectively enrolled between April 2020 -August 2023 at ILBS New Delhi. All patients who underwent hepatic venous pressure gradient (HVPG) along with transjugular liver Biopsy were included. The objective of the study was to study the role of portal hypertension in determining response/outcomes to treatment in AH-ACLF.

Results: Altogether 74 patients were analysed of which 42 patients were steroid responders (Group 1) while 32 patients (Group 2) were non responders with predominant males (95.9%) with 28 day mortality seen in 20 (27%) patients. Predictors of response at baseline included alcoholic hepatitis histological score (AHHS) score >6, MELD score >25, AARC score >8, Platelet count <110 cu/mm, INR >2.2, HVPG, LSM and mDf Score ($p < 0.01$). HVPG >20.5 mmHg predicted steroid non-response with an AUROC-81.1 (95%CI-70.2-90.6) ($P < 0.01$) with sensitivity 79% and specificity 70%. Predictors of mortality included AHHS score, presence of SBP, pneumonia, hepatic encephalopathy, HVPG >18 mmHg, high risk esophageal varices, platelet count <110 cu/mm and acute kidney injury (AKI) ($P < 0.01$). HVPG >22.5 mmHg independently and significantly predicted mortality ($p < 0.01$). HVPG on comparison with MELD/AARC/AHHS score significantly predicted steroid response with an AUROC-81 (95%CI-70.1-90.4) ($P < 0.01$).

Conclusion: Presence of HVPG >20 mmHg is an important determinant of sub-optimal outcome in patients with AH-ACLF patients. Such patients should be considered for alternative therapy at presentation.

Abstract Submission No. 102013
O-1096

Inhibition of HMGB1 ameliorate sepsis induced LSECs dysfunction and portal hypertension in cirrhosis

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Background and Aim: In liver cirrhosis, Septic shock is shattering disease progress to multiple organ failure. Sepsis cause disturbed endothelial homeostasis, hepatic microvascular complications, portal hypertension. Persistent systemic inflammation regulates HMGB1 that triggers hepatic injury. Its role in hepatic vascular pathogenesis is not explored. We investigated role of HMGB1 in sepsis induced LSEC dysfunction and portal hypertension in cirrhosis.

Methods: Experimentally, sepsis was induced by intraperitoneal administration of LPS in both CCl₄-cirrhotic and non-cirrhotic animals. CCl₄ cirrhotic rats (Gr1), CCl₄+LPS (Gr2), CCl₄+LPS+Glycyrrhizin (Gr3) were compared with controls (Ct1). Non cirrhotic Ct+LPS (Ct2), Ct+LPS+Glycyrrhizin (Ct3). Hepatic hemodynamic was monitored followed by ex-vivo Hepatic microvascular-functionality analysis. Cellular, Molecular and histological analysis was performed in hepatic tissues.

Results: Studies shows a noticeable increase in PP (9.5 ± 1 ; +31.9% (Ct2), vs 7.2 ± 1 ; in Ct1) a marked reduction in Ct3 (8.2 ± 0.4 ; -13.6%) vs Ct2 ($p = 0.01$) was observed. However, we observed significantly raised PP (12.6 ± 1 ; +26% (Gr2), vs 10 ± 1 ; in Gr1) a marked reduction in Gr3 (10.8 ± 0.2 ; -14%) vs Gr2 ($p = 0.01$) was observed. Gr2 animals also had increased flow index ($p = 0.001$) and PBF ($p < 0.05$) in comparison to Gr1 and Gr3. Endothelial function was also corrected in Gr3 vs Gr2 & Gr1. Inflammatory cells infiltration was evidently reduced in both Ct3 and Gr3 rats vs Ct2 vs Gr2 respectively. Gene expression of TNF-alpha, IL-6 were significantly upregulated in Gr2 and Ct2 ($p < 0.05$) vs Gr3 and Ct3. Moreover, Endothelial dysfunction gene CD31 ICAM1, VCAM1, fold was downregulated ($p < 0.05$) in Gr3 vs Ct3 vs Gr2 & Ct2.

Conclusion: This study demonstrated that pharmacological inhibition of HMGB1 ameliorates PP and protects vascular function during sepsis in liver cirrhosis.

Abstract Submission No. 200248
O-1097

Comparison of EUS PV with intra-operative direct PV pressure in pretransplant cirrhotics-pilot study

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Introduction: Direct portal pressure measurement under EUS-guidance (EUS-PPM) is a promising alternative to conventional indirect Hepatic Venous Pressure Gradient (HVPG). In patients undergoing liver transplantation for cirrhosis, high pre-operative portal vein (PV) pressure requires intra-operative portal vein inflow modulation (PIM). This pilot study aims to assess correlation between EUS-PPM with direct intra-operative portal pressure measurement (IO-PPM).

Methods: Liver cirrhosis patients scheduled for liver transplant within next 48 hours were included. EUS-PPM was performed using a 25G or 22G EUS-FNA needle to puncture PV. Both, compact manometer (CM) and arterial transducer (AT) were used to measure the intra-vascular pressure, pre- and intra-operatively. EUS PV was punctured trans-duodenally under conscious sedation. A mean value of 3

consecutive readings were taken for both methods. IO-PPM was done just soon after laparotomy using AT.

Results: All 25 patients (23 males) underwent pre-operative EUS-PPM & IO-PPM (100 % technical success). Pre-operative EUS-PPM ranged from 18–44 mm Hg using CM & 22–56 mm Hg using AT. IO-PPM ranged from 14–38 mm Hg. No adverse events were observed. EUS-PPM using 22G FNA needle was more consistent than with 25G needle ($\Delta 2$ vs $\Delta 10$). Pre-transplant PP were similar using 22G needle with CM and AT. IO-PPM was consistently lower than pre-operative EUS-PPM by $\Delta 8$ mm Hg.

Conclusion: In this pilot study, EUS guided direct PV puncture & PPM using compact manometer is a safe and correlates well with AT, both preoperatively & intra-operatively. 22G FNA needle yields consistent results compared to 25G FNA needle.

Abstract Submission No. 100227

O-1098

Evaluation of useful factors for reclassifying “unclassified group” under Baveno VII criteria

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Background: The Baveno VII criteria proposed an algorithm using platelets count and liver stiffness to identify clinically significant portal hypertension (CSPH). While it could identify CSPH, there were many unclassified patients who did not belong to either definite CSPH or improbable CSPH. Therefore, it was necessary to improve the algorithm by adding new factor.

Methods: This retrospective study included 73 chronic liver disease patients from 2018 to 2023 in single center. CSPH was defined as hepatic venous pressure gradient ≥ 10 mmHg. We evaluated splenic stiffness, splenic volume, ALBI score, and FIB-4 index as reclassifying factor. The cutoff value for CSPH was calculated by ROC analysis. It was set where the positive predictive value was $> 90\%$ or the negative predictive value was $> 90\%$. We compared the proportion of the unclassified group between the modified Baveno VII criteria.

Results: The cutoff value for including or excluding CSPH was 39.2 kPa/26.3 kPa for splenic stiffness, 707.01 ml/ 187 ml for splenic volume, -1.54/ -3.09 for ALBI score, and 8.12/ 3.71 for FIB-4 index. 38.4 % of the patients belonged to the unclassified group according to the conventional Baveno VII criteria. However, proportion of the unclassified group was reduced in the modified Baveno VII criteria. The proportion was 9.6 % for splenic stiffness, 24.7 % for splenic volume, 31.5 % for ALBI score, and 20.5 % for FIB-4 index.

Conclusions: We could appropriately reclassify the unclassified group by modified Baveno VII criteria with splenic stiffness.

Abstract Submission No. 100401

O-1099

Clinical features of extrahepatic portal vein obstruction: retrospective single-center study

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Background and aim: Extrahepatic portal vein obstruction (EHPVO) is a rare disease. The rarity of EHPVO makes controlled studies impractical, diagnosis difficult, and therapeutic strategies diverse. The purpose of this study was to elucidate the clinical characteristics of EHPVO.

Methods: We conducted a retrospective analysis of the hospital database between January 2000 and July 2023, evaluating the medical records of 14 patients (7 male, 7 female, mean age 41.6 years, range 12–74 years).

Results: Twelve of 14 EHPVO patients (85.7%) had intestinal varices. These included 9 esophageal (64.3%), 11 gastric (78.6%), and 6 ectopic varices (42.9%). Ten of 14 (71.4%) had a history of intestinal bleeding. Regarding comorbidities, 5 of 14 (35.7%) suffered from vascular diseases, including 2 mesenteric vein thrombosis, 1 acute myocardial infarction, 1 Budd-Chiari syndrome, and 1 pulmonary embolism. Three patients (21.4%) with JAK2V617 mutation were diagnosed as myeloproliferative neoplasm (MPN). The elevation of white blood cell and platelet counts, and decrease of protein S were shown in EHPVO with MPN, compared with EHPVO without MPN. EHPVO with MPN revealed no thrombocytopenia despite hypersplenism. Under treatment for portal hypertensive and/or thrombotic complications, all the 14 EHPVO patients were alive during follow-up for a median of 5 years (range 1–33 years).

Conclusion:

EHPVO in adults is frequently associated with underlying risk factors for hypercoagulation, and patients should be screened for comorbidities such as vascular and hematological disease. Proper treatment for portal hypertension-associated complications and hypercoagulable state might lead to good prognosis of EHPVO patients.

Abstract Submission No. 100439

O-1100

Outcomes of Cirrhotic Patients with Acute Variceal Bleeding and Concurrent Hepatocellular Carcinoma

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Background/Aims: The treatment outcomes and risk factors for prognosis of acute variceal bleeding (AVB) in hepatocellular carcinoma (HCC) patients remain unclear. Hence, we assessed the clinical outcomes and prognostic factors of these patients.

To evaluate the treatment outcomes and risk factors of cirrhotic patients with hepatocellular carcinoma (HCC) and acute variceal bleeding (AVB).

Methods: This is a retrospective case-control study. Consecutive patients with HCC and AVB admitted between 2016 and 2019 were included. For each patient with HCC, a patient without HCC was matched by age, sex, and Child-Pugh class. Follow-up was continued until death and transplantation.

Results: A total of 286 patients were included. The five-day treatment failure, 6-week mortality, and 1-year mortality rates of the whole cohort were 26.6%, 19.6%, and 36.1%, respectively. Patients with HCC had higher 6-week and 1-year mortality respectively (26.6% vs. 12.6, $P=0.003$; 53.3% vs. 18.9%, $P<0.001$). Among AVB patients with HCC, alpha-fetoprotein (AFP) levels (HR, 1.001; 95% CI, 1.000–1.002; $P=0.001$), BCLC stage (C-D vs. 0-B) (HR, 8.753; 95% CI, 1.934–39.612; $P=0.005$), and Child-Pugh score (HR, 1.503, 95% CI, 1.235–1.830; $P<0.001$) were independent risk factors of 6-week mortality in multivariate analysis. Furthermore, the risk of 6-week mortality was 71.4% among patients with a Child-Pugh score ≥ 9 and BCLC stage C-D, much higher than patients with low Child-Pugh score (<9) and earlier BCLC stage (0-B) ($P<0.0001$).

Conclusion: Among patients with cirrhosis and AVB, patients with HCC had a worse outcome than patients without HCC. The Child-Pugh score, AFP levels, and stage of HCC are strong predictors of 6-week mortality in patients with HCC.

Abstract Submission No. 100487

O-1101

Effect of Time to TIPS on Outcomes in Patients with Variceal Bleeding

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Background: The pre-emptive transjugular intrahepatic portosystemic shunt (TIPS) within 72 hours is recommended. Nevertheless, recent research emphasizes the challenges associated with the timely provision of TIPS within this limited timeframe. The objective of this study was to assess the impact of time for performing TIPS on patient outcomes and identify a more appropriate timeframe.

Method: This study enrolled patients referred to our hospital for TIPS procedure between January 2012 and December 2021. The duration between the recent variceal bleeding episode and the TIPS procedure was documented. Predetermined outcomes were assessed concerning various groups at four distinct time intervals: 72 hours, 5 days, 14 days, and 28 days. The primary outcome was the long-term survival rate.

Results: A total of 1180 patients were included in the study. There were no significant differences in patient outcomes between the early and late TIPS groups when patients were grouped by 72 hours, 14 days, and 28 days. However, when comparing the late TIPS (>5 days) group to the early TIPS (≤5 days) group, a significantly lower 5-year survival rate was observed in the late TIPS group (71.0% vs 80.4%; HR, 1.88; 95% CIs, 1.14-3.12; P = 0.014). The variceal rebleeding rate did not show a significant difference between the two groups (P = 0.91).

Conclusion: Early TIPS within a 5-day window may confer a survival benefit in contrast to TIPS procedures performed beyond this timeframe. It may be advisable to expand the timeframe for pre-emptive TIPS to align with current clinical practices.

Abstract Submission No. 100524

O-1102

Shear Wave Dispersion predicted the high-risk EGV in patients with compensated cirrhosis

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Objectives: To explore the clinical value of two-dimensional ultrasonic shear wave elastography (SWE) and shear wave dispersion (SWD) in the diagnosis of high-risk esophageal gastric varices in patients with cirrhosis.

Methods: A total of 123 cirrhosis patients were included, which were divided into high-risk esophageal gastric varices (high-risk EGV) group (n =60) and low-risk esophageal gastric varices (low-risk EGV) group (n =63). Both SWE and SWD were adopted to examine each patient's liver synchronously.

Results: In total patients, the results of SWD and SWE of high-risk EGV group were significantly higher than low-risk EGV group respectively. The area under the curve (AUC) of SWD predicted high-risk EGV was 0.709(95%CI:0.616-0.802). In compensated patients, the AUC of SWD diagnosed high-risk EGV was elevated to 0.786(95%CI:0.656-0.916), the optimal cutoff value was 15.35 m/s/kHz, the sensitivity, specificity, PPV and NPV was also elevated to 81.8%, 80.6%, 80.8% and 81.6% respectively, while in decompensated patients the AUC was 0.637(95%CI: 0.494-0.780). Stratified analysis by etiology in compensated cirrhosis patients showed that the AUC diagnosed by SWD in patients with viral hepatitis for high-risk EGV was higher than in non-viral hepatitis patients (0.777 VS 0.722). According to SWE, the AUC of high-risk EGV in total, compensated and decompensated cirrhosis was 0.606(95%CI: 0.506-0.706), 0.596(95%CI: 0.449-0.743), and 0.579(95%CI: 0.434-0.725), respectively, indicating limited diagnostic value.

Conclusion: SWD predicted the existence of high-risk EGV in patients with compensated cirrhosis non-invasively and provided a complementary method to determine whether high-risk EGV exists or not in patients, while SWE had limited diagnostic value.

Abstract Submission No. 100788

O-1103

Procoagulant risk & Clinical Outcomes following Dabigatran anticoagulation in Portal Vein Thrombosis

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Background: Portal vein thrombosis (PVT) refers to partial or complete occlusion of the portal vein lumen by a thrombus or presence of *portal cavernoma*. In this study, we prospectively assessed the risk of PVT based on clinical, procoagulant, HCC related factors and resolution in patients on anticoagulation using direct oral anticoagulants (DOACs).

Methods: All patients attending the liver clinic services between September 2021- October 2023 were screened and patients, aged between 18-65 years, either gender, with a new diagnosis of PVT were included. Eligible non-Cirrhotic or Child A/B cirrhotic patients were started on anticoagulation with *Dabigatran*.

Results: Of 6808 patients screened, 207(3%) patients new onset PVT[aged 52.4±15.3y, 61.8% men];115 (55.8%) with compensated cirrhosis, 27(13.1%) decompensated cirrhosis and 65(31.6%) without cirrhosis. 6 (2.9%) following COVID-19 infection, 48(23.3%) were HCC related. Clinical presentation was asymptomatic (65,31.6%), abdominal pain (117,56.5%), gastrointestinal bleeding (21,10.2%), ascites (70,33.8%)& mesenteric ischemia (2, 1%). Procoagulant mutations were JAK2V617F (21, 10.2%), CALR (2, 1%) & factor V Leiden(2,1%), respectively. Protein-C and Protein-S deficiency was seen in 77(37.2%)and 85(41%). 110/206(53.1%) were started on anticoagulation(dabigatran-104,nicoumalone-6). Complete resolution of PVT was seen in 37/207(17.9%), 31/110(28.2%) on anticoagulation and only 6/97(6.2%) with spontaneous resolution. On Dabigatran, 29/104(27.9%) had complete resolution and 50/104(48.%) had partial resolution or stable thrombus. Progression of PVT was seen in 25/207(12.1%) and death was seen in 54(27 in HCC-PVT) over 2years. Cox Regression based predictors of PVT progression were MELDNa(aHR 2.1;95%CI:1.8-4.3, P<0.001)

Conclusion: PVT has significant impact on clinical outcomes and mortality.Appropriate use of Dabigatran may improve resolution rates.

Abstract Submission No. 100919

O-1104

Pay attention to the practical application value of HVPG in patients with liver cirrhosis

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Currently, early liver cirrhosis is asymptomatic but histological changes are present, suggesting an initial silent phase with speculation about cirrhosis reversal. However, our study found that over 57% of patients with early liver cirrhosis had HVPG >5 mmHg, and 18% had clinically significant portal hypertension (CSPH).

The Baveno VII consensus in 2021 suggested a low 3-year risk of cirrhosis-related events in patients with chronic liver disease and liver stiffness (LSM) <10 kPa. However, our study revealed that among patients with liver cirrhosis and LSM <10 kPa, 29% had HVPG <5 mmHg, 49% had HVPG 5-10 mmHg, and 22% still had HVPG >10 mmHg. This indicates that cACLD cannot be ruled out in patients with LSM <10 kPa.

Our study found that as HVPG increased in cirrhosis with portal hypertension, decompensated events also increased, up to 76.67%. Child-Pugh scoring, which evaluates liver function, primarily indicated grades A and B in decompensated liver cirrhosis. However, there was no significant correlation between liver function and HVPG in decompensated cirrhosis. Most decompensated cirrhosis with portal hypertension exhibited mild to moderate liver dysfunction. This implies that even when treating patients with decompensated liver cirrhosis and liver function classified as grades A or B, high HVPG should not be overlooked. In our follow-up, carvedilol was used for medical intervention. After 3-6 months, retesting showed a decreasing trend in HVPG measurements in patients with decompensated liver cirrhosis following carvedilol treatment, with an overall average decrease rate of 23.86%. In two cases, the decrease exceeded 50%.

Abstract Submission No. 101268

O-1105

Baveno VII algorithm to rule out decompensation in patients with HBV-related cirrhosis and varices

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Background: Combination of Baveno VII and spleen stiffness is a tool to safely rule out clinically significant portal hypertension (CSPH) in patients with compensated advanced chronic liver disease (cACLD), but their comparative performance for hepatic decompensation remains unclear.

Methods: Using a prospective cohort of patients with cirrhosis between 2019 and 2021, who admitted to upper endoscopy and were also submitted to liver and spleen stiffness measurement (LSM, SSM) by transient elastography (TE) within 1 week, we compared 4 non-

invasive models in ruling out CSPH (SSM <21 kPa model, Baveno VII model, combined Baveno VII-SSM <21 kPa model, combined Baveno VII-SSM ≤40 kPa model). Liver decompensation and hepatocellular carcinoma (HCC) were compared between 2 groups of patients within each model and outside each model. We calculated the rate of decompensation-free incidence in rule-out groups according to different models.

Results: 741 patients with HBV-related cirrhosis and esophageal varices were analysed. None of the patients in the rule-out groups defined by the above models developed decompensation during a median follow-up of 37 months. The proportions for decompensation-free were the highest for the combined Baveno VII-SSM ≤40 kPa model (35.6%). Decompensation-free rates for the other models ranged from 4.7% for SSM <21 kPa model to 24.3% for combined Baveno VII-SSM <21 kPa model. Of the combined Baveno VII-SSM ≤40 kPa model with HCC surveillance, the patients among both groups developed HCC.

Conclusion: The algorithm combining Baveno VII criteria with SSM ≤40 kPa could exclude clinical decompensation in patients with HBV-related cirrhosis and varices.

Abstract Submission No. 101271

O-1106

The predictive value of hemodynamic indicators predict poor prognosis after TIPS.

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Background: The purpose of this study is investigating the predictive value of hemodynamic alterations in post-TIPS overt hepatic encephalopathy (OHE) within 3 months and liver reserve function deterioration within 6 months.

Method: A total of 176 patients with de novo TIPS implantation recruited retrospectively from 2019 to 2022 in two centers. The patients were followed-up every 3 months for 1 year to assess and re-evaluate intrahepatic vasculature and intra-stent diameter, velocity and blood flow changes, as well as clinical symptoms and liver reserve function. The diagnosis of OHE was based on the West-Heaven criteria (WHC). Liver reserve function deterioration was defined as elevated Child-Pugh (CTP) score.

Results: 149 patients were included, and 30.87% had episodes of OHE within 3 months after TIPS, of which 95.65% were WHC II and 4.35% were WHC III. Patients with portal pressure gradient difference (ΔPPG) >18.5 mmHg measured in the operation had a higher risk of post-TIPS OHE[w1]. At 6 months postoperatively, 42.36% had liver reserve function deterioration, of which 61.11% CTP score degrading A to B, 38.89% B to C. Patients with portal vein blood flow <1897.00 ml/min measured at 3 months after TIPS was an independent predictor of liver reserve function deterioration at 12 months postoperatively. **Conclusions:** The more obvious decrease in PPG, the higher the possibility of OHE occurrence were observed. And the patients with lower portal vein blood flow were more likely to have liver reserve function deterioration.

Abstract Submission No. 101273

O-1107

Spleen stiffness measurement using MR elastography for the noninvasive assessment of HVPG

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Aims: To assess the diagnostic value and influencing factors of MR elastography (MRE) in sinusoidal / postsinusoidal portal hypertension (PH) with HVPG as the gold standard.

Methods: In this prospective study, patients with sinusoidal / postsinusoidal PH underwent MRE, and ultrasound-based elastography (SWE/ARFI) of the liver and spleen, as well as HVPG measurement. The correlation between liver stiffness and spleen stiffness with HVPG was assessed. ROC analysis was used to determine the utility of MRE, SWE, and ARFI for diagnosing PH. The influencing factors for MRE measurements were explored using multivariate analysis.

Results: A total of 93 patients with MRE, 56 with SWE and 35 with ARFI were included. MRE-SS correlated positively with HVPG ($r = 0.214$, $p = 0.040$), while MRE-LS had no correlation with HVPG ($r = -0.133$, $p = 0.210$) (showed in Figure). AUROC for MRE-SS, SWE-SS, and ARFI-SS were 0.76, 0.82, and 0.74 for diagnoses of HVPG ≥ 12 mmHg; and 0.58, 0.65, and 0.62 for HVPG ≥ 20 mmHg, respectively (showed in Table). SWE-SS displayed the best performance in the diagnoses of HVPG grade. Only PLT affected MRE-SS results in univariate and multivariate analysis.

Conclusion: MRE-SS correlated positively with HVPG, and demonstrated a better discrimination of HVPG ≥ 12 mmHg with unsatisfactory performance of HVPG ≥ 20 mmHg.

Abstract Submission No. 101290

O-1108

Porto-sinusoidal vascular disease with risk factors had worse liver disease and poorer outcomes

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Background: Porto-sinusoidal vascular disease (PSVD) is a rare entity and often associated with various risk factors (RF). We aimed to compare the manifestation and outcomes of PSVD in patients with and without known RF in a Chinese cohort.

Methods: This retrospective study enrolled liver-biopsy confirmed patients with PSVD, with demographics, comorbidities, laboratory tests and outcomes collected. Cox regression analysis was used to assess associations between baseline characteristics and the prognosis.

Results: Totally 143 patients with PSVD (median age: 47 years, 64% female) were included, with 90 having RFs (RF-PSVD=62.9%) and 53 having no known RFs (noRF-PSVD=37.1%). RFs included immunological disorders (35.0%), prothrombotic conditions (32.9%), history of omphalitis (2.8%), congenital defects (2.8%), hematological disorders (2.1%) and exposure to oxaliplatin (0.7%). The RF-PSVD group exhibited significantly higher rates of gastroesophageal varices (88% vs. 55%, $p < 0.001$), portosystemic collaterals (94% vs. 58%, $p < 0.001$), and splenomegaly (96% vs. 80%, $p = 0.004$). Additionally, the RF-PSVD group showed significantly lower level of serum albumin (36.7 vs. 40.0, $p = 0.001$), higher INR (1.21 vs. 1.13, $p < 0.001$), and a higher prevalence of portal vein thrombosis (PVT) (31% vs. 13%,

$p = 0.017$). During a median follow-up of 29.6 months, the RF-PSVD group had a significantly higher incidence of first/further hepatic decompensation ($p = 0.015$) and higher mortality/liver transplantation (7.6% vs. 4.9%, $p = 0.570$). Multivariate regression identified RF (HR=5.93, $p = 0.018$), age (HR=1.04, $p = 0.028$), and ascites (HR=4.34, $p = 0.009$) as independent factors associated with hepatic decompensation.

Conclusions: PSVD with identifiable RFs had more severe portal hypertension, poorer liver function reserve, higher PVT prevalence, and worse clinical outcomes.

Abstract Submission No. 101307

O-1109

Gallbladder Wall Thickness And Other Non-Invasive Tests For The Screening Of Esophageal Varices

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A complication of liver cirrhosis is portal hypertension, the formation of esophageal varices (EV) with risk for hemorrhage. The gold-standard for diagnosis of EV is endoscopy but due to associated costs and risks, non-invasive tests for screening for EV have been studied. The authors aim to evaluate the diagnostic accuracy of gallbladder wall thickness (GBWT), spleen length and other laboratory parameters for screening for EV.

This retrospective cross-sectional analysis included cirrhotic patients in a tertiary hospital in the Philippines wherein abdominal ultrasound, liver stiffness measurement, upper endoscopy and blood tests were analyzed.

Sixty three patients were analyzed, 25 (39.68%) had EV on endoscopy. Among the EV group, 56% had GBWT ≥ 4 mm, compared to 15.8% in the non-EV group ($P < 0.001$). Patients with EV were predominantly male, had more severe liver disease (CTP B and C, higher MELD-Na and FIB-4), and evidence of portal hypertension (ascites, portal hypertensive gastropathy) ($p < 0.05$). Multivariate regression analysis showed that GBWT ≥ 4 mm (aOR 6.47, 95% CI 1.24-33.67) and Spleen Length > 13 mm (aOR 12.74, 95% CI 1.59-101.82) had higher odds for predicting EV. GBWT (cut-off > 3 mm) had a sensitivity and specificity of 80% and 68.42% with an AUC of 0.845 (CI 0.753-0.938) while spleen length (cut-off > 120 mm) had a sensitivity and specificity of 60% and 81.58% with AUC of 0.732 (CI 0.596-0.869).

GBWT and Spleen length are independently associated with the presence of EV in cirrhotic patients and may be a good predictor for the presence of EV.

Abstract Submission No. 101521

O-1110

Combined Baveno VII-SSM model performed good to identify CSPH in individuals with HBV-related cACLD

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Background and Aims: The Baveno VII consensus mentions several non-invasive tools (NITs) for diagnosing of clinically significant portal hypertension (CSPH) in patients with compensated advanced chronic liver disease (cACLD). We aimed to evaluate and compare the diagnostic performance of the Baveno VII-mentioned algorithms and other recently proposed NITs in individuals with HBV-related cACLD.

Methods: Consecutive individuals with HBV-related cACLD who underwent hepatic venous pressure gradient (HVPG) measurement, liver stiffness measurement (LSM) and spleen stiffness measurement (SSM, using a 100 Hz shear wave frequency) were prospectively enrolled from December 2021.

Results: From December 2021 to October 2023, 292 patients were screened and 121 were enrolled for analysis. For ruling in CSPH, the SSM>50 kPa [positive predictive value (PPV) 96.3%, specificity 98.5%] and Baveno VII-SSM dual cutoff (50 kPa) (PPV 91.2%, specificity 95.5%) algorithms both performed great. For ruling out CSPH, the Baveno VII and Baveno VII-SSM dual cutoff (21 kPa) (NPV 100%, sensitivity 100%) algorithms both had negative predictive value (NPV) and sensitivity at 100%. For ruling in CSPH, the sequential Baveno VII-SSM model showed specificity at 94.0% and PPV at 90.0%, for ruling out, the sensitivity was 96.4% and NPV was 94.3%. The Baveno VII-SSM dual cut-off (21-50 kPa) model had 45.5% of patients in the grey zone. With the sequential Baveno VII-SSM model, 47 (38.8%) patients were in the indeterminate zone.

Conclusions: We validated that the addition of SSM using 100 Hz shear wave frequency with Baveno VII proposed cutoff values significantly improves the clinical applicability of the algorithm based on LSM and platelet count for CSPH diagnosis.

Abstract Submission No. 101565

O-1111

Outcome of interventional radiology for hepatic encephalopathy with port-systemic shunt

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Background/aim: Hepatic encephalopathy (HE) is caused by ammonia and other neurotoxic substances, which increased in patients with cirrhosis, acute liver failure, and port-systemic shunt (PS). Drug treatment is the first choice, but there are some cases poorly controlled. In this study, we investigated the efficacy of interventional radiology (IVR) in cases of refractory HE with PS.

Methods: Among patients admitted to our department with HE between January 2012 and November 2022, we investigated the changes in symptoms and data before and after IVR in 10 patients who were poorly controlled with drug treatments.

Results: Patients were 6 males and 4 females with median age 67.5 years. Background liver was alcoholic/NASH/PBC/AIH in 5/3/1/1 cases, respectively. Median serum ammonia level was 174.5 µg/dL, and Child-Pugh score was 7/8/9/10 in 2/4/2/2 patients, respectively. All patients had grade II-III HE. Extrahepatic shunts were found at spleno-renal, gastro-renal, paraumbilical, inferior mesenteric, superior mesenteric, or heart diaphragm veins. As IVR, vascular plug placement and coil embolization were performed in 9 cases and retrograde transvenous embolization under balloon occlusion (B-RTO) was done in 4 cases. HE improved to grade 0-I in all patients within 1 week after treatments and persisted even after 3 months of follow-up. In addition, serum ammonia, albumin, and ALBI scores were also improved. No severe complications occurred but only two patients had fever.

Conclusion: IVR was effective for refractory HE patients with PS. Not only improvement of HE and serum ammonia level, but also improvement of hepatic functional reserve was observed.

Abstract Submission No. 101868

O-1112

Correlation of Splenic and Liver stiffness measurement with variceal bleeding in NCPH and Cirrhotics

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Background and Aims: The cut-offs of non-invasive tests (NITs) including liver and spleen stiffness measurement (LSM and SSM) have been shown to correlate well with hepatic venous pressure gradient (HVPG) to predict presence of varices and bleeding in cirrhosis. However, there is paucity of data on LSM and SSM for assessing varices and bleeding in non-cirrhotic portal hypertension (NCPH) patients. We evaluated 300 patients, with NCPH and cirrhosis, bleeders, and non-bleeders to compare whether NITs can clearly segregate them.

Methods: Patients with NCPH (n=150, 129 EHPVO and 21 NCPF; 75 bleeders) and cirrhosis (n=150; 75 bleeders) were recruited. Patients with non-bleed complications were excluded in both groups. We correlated LSM and SSM in relation with variceal bleeding in both groups of patients.

Results: In cirrhosis patients, the mean LSM in bleeders was higher (43.5 ± 19.7 than non-bleeders 33.7 ± 18.5 kPa, $P=0.002$). Similarly mean SSM (79.5 ± 11.8 kPa, 55.7 ± 12.6 kPa ($P<0.0001$), and mean HVPG were higher (17.4 ± 2.4 12.8 ± 2.3 mmHg, $P<0.0001$) in bleeders than non-bleeders. In NCPH, the mean LSM (5.6 ± 1.08), in bleeders and (5.3 ± 1.02) non-bleeders which were significantly lower than that observed in cirrhosis patients. The mean SSM on the other hand in the NCPH bleeders was higher than in non-bleeders (90 ± 7.5 v/s 70 ± 7.8 kPa, $p<0.0001$), both being higher than that observed in cirrhosis patients. The SSM cut-off of 70 kPa had a sensitivity of 90 % and specificity of 76% for predicting variceal bleed in cirrhotics, AUROC (0.913). Similarly, SSM cut off 75 kPa, sensitivity of 92% and specificity of 80 % for predicting variceal bleed in NCPH, AUROC (0.975). SSM was significantly higher in cases of NCPH bleeders (90.11 ± 7.50 kPa v/s cirrhotic bleeders (79.53 ± 11.8 kPa with p value- <0.0001). SSM/LSM ratio was 16.01 in NCPH bleeders as compared to 1.89 in cirrhotic bleeders. On univariate analysis LSM, SSM, HVPG and on multivariate analysis splenic stiffness HR {1.216(1.158-1.275)} and HVPG {HR 1.357(1.147-1.75)} were significant in predicting bleed in cirrhotics. On uni-variate analysis and multivariate analysis for predicting bleed in NCPH, SSM, {HR 1.085(1.029-1.144)} and hypersplenism, HR {0.379(0.157-0.91)} were significant.

Conclusion: Higher SSM correlate with variceal bleeding in patients with liver cirrhosis and NCPH compared to non-bleeders

Abstract Submission No. 101998

O-1113

BETA-RESPONSE: Non-invasive tests vs HVPG in assessing NSBB response in acute variceal bleed

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Introduction: HVPG determines success of EVL and vasopressor combination therapy in controlling AVB and preventing rebleed. NITs are valuable as HVPG is invasive.

Methods: Cirrhotics > 18yrs who underwent EVL for AVB were prospectively enrolled. After enrolment maximal dosage of NSBB was achieved within 5 days. HVPG was done baseline and at 6weeks. NITs

- LSM, SSM by TE performed at baseline, 3, and 6 weeks, followed for 3months.

Results: 210 patients [mean age 49.14±10.6 years, males 92.3%, predominant etiology ethanol 41% and MAFLD 33%]. HVPg at 6weeks showed 67 (39.6%) patients responded to carvedilol with a reduction in mean HVPg from 18.72±2.43 to 15.89±2.97mmHg. LSM and SSM showed mean reduction of 6.6kPa and 10kPa in responders, with cut-off reduction of >3kPa (AUC 0.762, Sn 75%, Sp 32%, PPV 43.3, NPV 63) and >5.5kPa (AUC 0.738, Sn 84%, Sp 26%, PPV 45.2, NPV 73%) for predictability of response. Of 98 HVPg non-responders, 22(10%) rebled within 3months (8 after enrolment but <6wks), 6(2.8%) out of 67 HVPg responders rebled within 6 weeks. These HVPg responders had reduction in LSM and SSM, however there was no improvement in platelet count which may predict rebleed in HVPg responder. None of the HVPg responders with HVPg reduction to [SS1] [AD2] <12mm of Hg rebled. Other liver related events: Ascites [4(2.4%) vs 10(6%)], HE [1(0.6%) vs 3(1.8%)].

Conclusion: Reduction in LSM and SSM predicts NSBB response. HVPg response to <12mm of Hg is free of development of bleeding or decompensation. NIT non-responder at 3weeks are HVPg non-responders at 6 weeks.

Abstract Submission No. 102084

O-1114

Targeted and response-guided albumin therapy improves outcomes of ascites in cirrhosis patients

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Background: Targeting serum albumin (SA) above 4 gm/dl with long-term albumin administration improves outcomes in patients with uncomplicated ascites. However, the cost and scarcity of albumin is a limitation. We aimed to compare a targeted (above 3 gm/dl) and response-guided albumin strategy (Alb-Tr) in improving 6-month mortality compared to standard medical treatment (SMT).

Methods: Open-label, randomized controlled trial. Patients in (Alb-Tr) arm received 20% albumin targeting SA>3 gm/dl at 60grams for 2 weeks followed by 40 grams/week target SA>3 gm/dl or ascites control, or for a maximum of 12 months.

Results: The baseline characteristics were comparable in both groups, [Alb-Tr; n=60 versus SMT; n=60]. A trend towards reduced mortality was noted in (Alb-Tr) [2(3.8%) vs. 8(15.4%); Log rank p=0.06, HR 4.21, (0.89-19.8)]. The control of ascites was superior in (Alb-Tr) (56% vs. 30%; p<0.001). A lower incidence of acute kidney disease (AKD) (15% vs. 53%; p<0.001), chronic kidney disease (CKD) (13% vs. 28%; p=0.043), infections (43% vs. 75%; p<0.001), hepatic encephalopathy (3% vs. 15%; p=0.027) was seen in Alb-Tr. A higher proportion of patients achieved the target SA>3 gm/dl in Alb-Tr (97.9% vs. 32%; p<0.001). Patients with target SA>3gm/dl had lower AKD (50% vs 22%; p=0.003), sepsis (75% vs. 54%; p=0.04) and better ascites control (33% vs. 55%; p=0.034). A significant decrease in the renal biomarkers (Cystatin C, IL-18, KIM-1 and decrease in C-reactive protein) were observed in Alb-Tr group while levels increased in SMT.

Conclusion: A lower target of 3gm/dl and response-guided albumin strategy reduces mortality, adverse renal outcomes and achieves better ascites control in patients with RA. (NCT04679571)

Abstract Submission No. 102091

O-1115

Carvedilol versus Band Ligation for Prophylaxis of Variceal Bleeding in Arterial Hypertension Cases

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Background and study aims: Up to our knowledge, no study was performed on primary prophylaxis of variceal bleeding in cirrhosis with systemic arterial hypertension. So, we will evaluate the safety and efficacy of carvedilol versus endoscopic band ligation (EBL) for the primary prophylaxis of variceal bleeding in hypertensive cirrhotic patients.

Patients and Methods: In this randomized controlled trial, 306 cirrhotic hypertensive patients with large and/or risky esophageal varices were randomized into EBL and carvedilol groups. Carvedilol was given orally at an initial dose of 6.25 mg twice daily, and titrated up to achieve a normotensive response. When maximum of 25mg twice daily was given without satisfactory control of blood pressure, diuretic and enalapril was added.

Results: Variceal bleeding within a follow up period of one year was found to be 1.3% in EBL group versus 2.6% in carvedilol group without statistically significant difference (P=0.680). In carvedilol group, systolic blood pressure, diastolic blood pressure and mean arterial pressure were significantly decreased at 3 months of follow up till the end of the study, while heart rate was significantly decreased at 9 months of follow up till the end of the study when compared with the baseline (P<0.001). Adverse events were significantly higher in the EBL group (25.49%) than carvedilol group (10.46%) (P<0.05).

Conclusion: Carvedilol was safe and effective in the primary prophylaxis of esophageal variceal bleeding in cirrhotic patients with systemic arterial hypertension.

Abstract Submission No. 200147

O-1116

ENDOVASCULAR TREATMENT FOR ACUTE- SUBACUTE EXTENSIVE SPLANCHNIC VENOUS THROMBOSIS - A CASE SERIES

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Introduction: Extensive Splanchnic venous thrombosis (ESVT) includes thrombosis of porto-mesenteric venous system and hepatic veins (HV) which may co-exist. There are scarce reports in world literature on management of ESVT with Endovascular treatment (EVT). We report our experience of management of ESVT with EVTs for revascularisation which is first such case series from India.

Methods: Seven patients with acute-subacute ESVT were evaluated for clinical presentation, EVT and outcome. Heparin was started at diagnosis and for persistent symptoms mechanical thrombo-aspiration (MT), angioplasty (AG), catheter directed thrombolysis (CDT) for SMV thrombosis were done. TIPSS was created if HVPg was >10mmHg and SMV stenting done for long segment SMV thrombosis.

Results: All patients with ESVT (5 males, 2 females) had abdominal pain and 2 had ascites. Median symptom duration was 12 days (4-30 days). Thrombophilia was seen in 5. Other two had cirrhosis and Mycosis fungoides. Four had PVT and SMVT while 3 patients had thrombosis of all 3 HV with PVT and SMVT. EVT was performed after a median of 14 days (MT in 5, AG in 4, CDT in 6, TIPSS in 7 and SMV

stenting in 2). Technical success was 100%, clinical success 85.7% with 2 patients requiring surgery (for perforation and bowel ischemia). Primary patency rate at 1, 6, 12 months was 85.7%, 83.3%, 66.7% respectively. 3 patients required re-intervention after a median of 8months (1-17months).

Conclusion: Endovascular treatment for acute -subacute Extensive Splanchnic venous thrombosis is an effective treatment modality in selected patients with fair long-term outcomes.

Abstract Submission No. 100150

O-1117

SSBs consumption increases the risk of metabolic syndrome and its components in adults.

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Aims: This review aims to synthesize the evidence linking habitual SSBs intake with MetS in adults, emphasizing the need for policy and regulatory actions.

Methods: Four databases were comprehensively searched for relevant meta-analyses of prospective studies up to July 2023. The outcome of interest was MetS in adults, encompassing its component conditions. The present review was registered with PROSPERO (CRD42023402549).

Results: Of the 16 eligible meta-analyses identified, 30 summary estimates were obtained for the impact of SSBs consumption on obesity, type 2 diabetes, hypertension, and MetS. Seven were rated as 'High' methodological quality, with the rest classified as 'Moderate' and 'Low' quality, consisting of three and six references, respectively. A comparison of the highest and lowest levels of SSBs consumption revealed an increased risk of 18% (95% CI: 13%e24%), 12% (95% CI: 11%e14%), 29% (95% CI: 25%e32%), and 29% (95% CI: 7%e52%) for obesity, hypertension, type 2 diabetes, and MetS, respectively. Consistently, the findings from dose-response analyses are in agreement with and corroborate the existing evidence that SSBs are a significant risk factor for the development of MetS and its related conditions. Noticeably, the evidence quality was predominantly deemed highly suggestive and convincing. Moreover, consensus on specific criteria to identify studies related to SSBs in literature searching was lacking, and most primary studies were conducted in developed countries and Europe.

Conclusions: Our findings suggest that more rigorous and targeted policy interventions are warranted to curtail SSBs consumption in order to alleviate the global burden of MetS.

Abstract Submission No. 100241

O-1118

Association between PM2.5 exposure and mortality in patients with HCC in Tianjin,China

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Several studies have shown the effects of PM_{2.5} exposure on respiratory and cardiovascular systems. However, there is few evidence of adverse effects of PM_{2.5} exposure on survival in patients with hepatocellular carcinoma (HCC) in China. This study investigated the association between long-term exposure to PM_{2.5} and HCC mortality in Tianjin, China. It also explored the impact of sociodemographic factors on this association.

Methods: A retrospective cohort study of 1520 HCC patients was conducted, divided into two groups based on PM_{2.5} exposure levels. Individual exposure was assessed using historical monitoring data and inverse distance weighting. Survival analysis, Cox models, and sensitivity analyses were performed.

Results: Higher PM_{2.5} levels were linked to lower survival rates. Every 10 µg/m³ increase in PM_{2.5} raised the hazard ratio for HCC mortality by 1.36. Age > 60 and early-stage HCC patients showed increased susceptibility to PM_{2.5}-induced mortality. Independent risk factors for HCC death included albumin, aminotransferases, first treatment, tumor status, BCLC stage, and high PM_{2.5} levels. The predictive value of these factors was assessed using ROC curves. The area under the ROC curve predicting the risk of death in the first, third, and fifth years after HCC diagnosis was 0.889, 0.853, and 0.837, respectively.

Conclusion: Severe air pollution in Tianjin, with PM_{2.5} concentrations exceeding regulatory limits, was associated with increased HCC mortality. Older individuals and early-stage patients were more susceptible to PM_{2.5}-related effects. Combining several risk factors improved prognostic assessment for HCC patients.

Abstract Submission No. 100381

O-1119

Global burdens of cirrhosis in children and adolescents from 1990 to 2019

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Background: Cirrhosis data on the burden and trends were sparse in children and adolescents. We aimed to assess the trends in 204 countries and territories over the past 30 years in children and adolescents aged under 19 years.

Methods: Data on cirrhosis was collected by the Global Burden of Disease (GBD) 2019 database from 1990 to 2019. We reported on numbers, rates, and average annual percentage changes (AAPCs) of incidence and disability-adjusted life-years (DALYs) of cirrhosis at global, regional, and national level.

Results: Globally, incident numbers of cirrhosis in children and adolescents increased from 204767 in 1990 to 241364 in 2019, an increase of 17.9%, with an AAPC 0.13 (0.10 to 0.16). Substantial change in incidence of cirrhosis in 1996, 2006, 2009, and 2017. Prevalence (AAPC=-2.27 [-2.39 to -2.15]), mortality (AAPC=-1.68 [-1.86 to -1.5]), and DALYs rate (AAPC=-1.72 [-1.88 to -1.56]) of cirrhosis have decreased significantly. Cirrhosis incident rates varied between sex and age groups. Rates of cirrhosis caused by alcohol use (AAPC=1 [0.8 to 1.1]; incidence cases increased most obvious 48%), hepatitis C (AAPC=0.4 [0.4 to 0.5]), NAFLD (AAPC=0.5 [0.3 to 0.6]) have been increasing, while only hepatitis B (-0.3 [-0.4 to -0.2]) decreasing. Incidence cases of cirrhosis were increased in low (101.6%) and low-

middle sociodemographic index(SDI 21.1%) areas, while decreasing in middle and above SDI areas. At the regional level, the largest increases count was observed in Sub-Saharan Africa.

Conclusions: Global incidence rate of cirrhosis has been increasing, while the DALYs rate has been decreasing in children and adolescents. Morbidity of cirrhosis caused by hepatitis B declined, while hepatitis C, NAFLD, and alcohol use increased.

Abstract Submission No. 100714
O-1120

Health-Related Quality of Life in Patients with HBV Infection: A Systematic Review and Meta-Analysis

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Background: Despite nearly 300 million persons estimated to be living with hepatitis B virus (HBV) infection globally, health-related quality of life (HRQOL) in HBV-related disease has not been well characterised. We aimed to summarise existing data on HBV-related HRQOL and quantify health utility by stage of disease.

Methods: Embase, Global Health, PubMed, and Web of Science were searched for articles investigating HBV HRQOL. Meta-analyses for utility scores were pooled by stage of disease and utility instrument; meta-regression was further adjusted for the effect of current health expenditure as a percentage of gross domestic product (CHE/GDP).

Results: Twenty-one articles from eighteen studies, comprising 9114 patients, were included. 70% of studies were performed in the Western Pacific Region, and 50% using the EuroQoL-5D-3L instrument. HRQOL was found to decrease with advancing stages of HBV-related disease. Meta-regression showed the following predicted mean utilities for the different stages of HBV infection: non-cirrhotic 0.839, compensated cirrhosis 0.819 ($p=537$), decompensated cirrhosis 0.723 ($p=0.001$) and hepatocellular carcinoma 0.746 ($p=0.012$). The type of tool used affected HRQOL, and a higher CHE/GDP was associated with improved HRQOL.

Conclusions: HBV infection, particularly in the advanced stages of decompensated cirrhosis and hepatocellular carcinoma, significantly impairs patients' HRQOL. These results have important implications for global hepatitis elimination efforts and are useful for economic analyses. However, further research is needed, particularly in high-burden, low-income settings where data is lacking.

Abstract Submission No. 100792
O-1121

Sugar and Artificially Sweetened Beverages and Liver Health: A Prospective Cohort Study

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Background: Evidence links sweetened beverages to risks of obesity, diabetes, and specific cancers but not liver outcomes. We aimed to evaluate the associations of sweetened beverages and associated plasma proteomic signatures with risk of a spectrum of liver outcomes. **Methods:** We analyzed data from 168,975 individuals (ages 40-69) in the UK Biobank with available dietary data on sugar and artificially sweetened beverage intake. Liver outcomes were ascertained using data from the in-hospital, cancer or death registry including NAFLD, cirrhosis (compensated and decompensated), liver cancer, and severe liver disease (SLD: hepatocellular carcinoma and others). We used elastic net regression to calculate the proteomic signature (Olink platform profiling) related to sweetened beverages and Cox proportional hazards regression models to estimate hazard ratios (HR) and 95% confidence intervals (CIs) for sweetened beverages or proteomic signatures and liver outcomes.

Results: After a median follow-up of 8.9 years, we documented 1080 NAFLD, 931 liver cirrhosis, 464 liver cancer, and 536 severe liver diseases. Each daily serving of sugar-sweetened beverages linked with 11% higher risk of NAFLD (HR [95% CI]: 1.11[1.03-1.19]), 19% (1.19[1.10-1.29]) of cirrhosis, and 16% (1.16[1.05-1.28]) of SLD but insignificant with liver cancer (1.11[0.92-1.33]). Higher artificially sweetened beverage intake also was associated with increased risk of NAFLD (1.13[1.05-1.20]), cirrhosis (1.20[1.11-1.29]), and SLD (1.19[1.08-1.31]). The proteomic signatures of sugar-sweetened beverages (116 proteins) and artificially sweetened beverages (105 proteins) showed stronger positive associations with risk of NAFLD, cirrhosis, and SLD ($P_{\text{trend}} < 0.001$) with HRs ranging from 1.73 to 2.33 for one-unit standard deviation increase.

Conclusions: In this prospective cohort, sugar- and artificially sweetened beverages and their proteomic signatures are associated with a spectrum of liver diseases.

Abstract Submission No. 100819
O-1122

Level of Knowledge and Awareness on Non-Alcoholic Fatty Liver Disease among Filipinos

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Background: The global burden of non-alcoholic fatty liver disease (NAFLD) is rising parallel with metabolic syndrome and other non-communicable diseases. This post hoc analysis of data from the non-communicable disease study in the National Capital Region (NCR) aims to examine the different factors that affect knowledge and awareness of NAFLD.

Methods: Data from a population-based cohort study were collected. Awareness of NAFLD and willingness to undergo testing for NAFLD was correlated with demographic and socio-economic factors. A multiple regression analysis was then utilized to check for correlation.

Results: 1561 subjects were included in the analysis. In the awareness section, majority of participants (67.8%) were unaware of or had never heard of NAFLD although 40.59% of respondents believed that they were at risk for NAFLD. 61% of participants likewise considered getting tested for NAFLD. Most respondents believed that the top condition that affects fatty liver is high cholesterol/ dyslipidemia (65.77%). On multivariable analyses, those aged 60 and above (OR 6.29, $p < 0.05$), with professional/ technical/ managerial occupation (OR 5.34, $p < 0.01$) and those with dyslipidemia (OR 2.92, $p < 0.01$) were

predictive of NAFLD awareness. Factors that affected willingness to be screened for NAFLD included college/post graduate degree, obese or overweight and those with dyslipidemia ($p < 0.05$).

Conclusions: Our study demonstrated that there remains a significant knowledge gap in terms of awareness in NAFLD. This highlights the need for public education campaigns especially in at-risk groups such as among diabetics and obese with the goal of implementing early detection, diagnosis and treatment.

Abstract Submission No. 100991

O-1123

Hepatocellular Carcinoma Surveillance is Cost-Effective in Steatotic Liver Disease

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Background: Without hepatocellular carcinoma (HCC) surveillance, HCC from non-alcoholic fatty liver disease (NAFLD) tends to be diagnosed at a later stage and has worse outcome than HCC from other etiologies. We aimed to investigate the cost-effectiveness of using non-invasive tests (NITs) to identify high-risk non-cirrhotic NAFLD patients and initiate HCC surveillance.

Methods: Cost-utility analysis was performed using Markov model in Thailand and the United States (US) settings. NIT protocols including 1) Fibrosis-4 Index (FIB-4) of ≥ 1.3 , 2) transient elastography (TE) of ≥ 8 kPa, and 3) FIB-4 with TE were used to initiate HCC surveillance by biannual ultrasonography with alpha-fetoprotein (AFP) (**Figure**). Incremental cost-effectiveness ratio (ICER) was calculated using total costs and quality-adjusted life-years (QALYs) gained for each protocol. NIT protocols were considered cost-effectiveness based on a willingness-to-pay of \$4,665/QALY (160,000 THB) and \$50,000/QALY in Thailand and the US, respectively.

Results: In Thailand setting, FIB-4 with TE was cost-effective with ICER of \$4,041/QALY. FIB-4 alone and TE alone were not cost-effective with ICERs of \$6,583 and \$7,391/QALY, respectively (**Table**). Similarly in the US, combining FIB-4 with TE was the only cost-effective strategy with ICER of \$28,025/QALY. By one-way sensitivity analysis, adjusting the HCC incidence in non-cirrhotic NAFLD patients from 0.1-0.6% did not affect the cost-effectiveness results. By probabilistic sensitivity analysis, FIB-4 with TE had the highest probability of being cost-effective at the WTP threshold in each setting.

Conclusions: Using FIB-4 together with TE to initiate HCC surveillance was cost-effective and may help improve the outcome of NAFLD-related HCC.

Abstract Submission No. 101043

O-1124

Developing a national database and online reporting dashboard for hepatitis B and C in Indonesia

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Background: To support monitoring and evaluation of the national hepatitis program in Indonesia and enable evidence-based decision-making, Indonesia developed SIHEPI, an electronic patient management information system that includes multi-level dashboards.

Methods: SIHEPI enables healthcare workers to enter data and manage hepatitis patients, and national program stakeholders to track case volumes and service delivery gaps. The methodology to develop this system included: 1) Mapping user requirements; 2) System design & development, including data validation rules; 3) System testing; 4) Deployment across >1,000 health facilities; 5) Maintenance. Data collected includes HCV treatment, sustained virologic response testing at 12 weeks (SVR12), disaggregated by sex, age, cirrhosis, year, facility, and geography, HBsAg screening in pregnant women, and hepatitis commodity management.

Result: As of September 2023, SIHEPI captured: 36,427 patients testing positive for HCV, 10,108 initiating HCV treatment, and 95.8% of those with SVR12 results cured; >1.8 million pregnant women tested for HBsAg with 1.53% positive. A dashboard visualizes the data (see figure). Despite effective rollout of SIHEPI, challenges have included underreporting at health facilities due to workload, poor internet connection in remote areas, and segregation and limited reporting on patients with private insurance.

Conclusion: This data digitization initiative demonstrated that viral hepatitis data can be collected in Indonesia despite geographical constraints (38 provinces, >17,000 islands). The system generates and visualizes high-quality national program data to drive evidence-based decisions for program improvement. Upcoming plans include developing an HBV dashboard, integration with health facility information system, and expansion to capture HBV treatment volumes for pregnant women.

Abstract Submission No. 101148

O-1125

Does Universal Health Coverage (UHC) Program Lead to Better Public Health? A Systematic Review.

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The Government of Indonesia enacted an amendment (National Act Number 24 Year 2011), in response to the establishment of the health insurance program or known as *Jaminan Kesehatan Nasional (JKN)*. This mandate stated that the program of JKN is managed by the Social Security Public Agency for Health, named *Badan Penyelenggara Jaminan Kesehatan (BPJS-K)*. Despite an ambitious goal to enrol all Indonesians in JKN by 2019 to meet the standards of Universal Health Coverage (UHC) set by WHO, geographical barriers delayed progress. To address this, the government enacted BPJS-K Act Number 3 of 2019, compelling citizens to comply with the JKN program. Consequently, the system increased essential service consumption, reducing the proportion of Out-of-Pocket (OOP) payments to total health expenditure (THE) from 48.5% (2014) to 32.1% (2019). By June 2022, approximately 238 million Indonesians (87.16% of the population) were JKN members. This achievement made the JKN the biggest single-payer health insurance system in the world. However, the

geographical challenges in Indonesia is a big deal for the government. Thus, the UHC might be promising agenda from the government to provide better public health. But, it needs more effort to enact it. Therefore, a more progressive and right on target program are obligatory to make UHC as a successful program to provide better public health in Indonesia.

Abstract Submission No. 101213

O-1126

Seroprevalence of Hepatitis E Infection in Healthy Blood Donors in an Endemic Country

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Background: HEV can be transmitted via contaminated blood products. This mode of transmission is of importance in immunocompromised and pregnant patients. Screening of blood products for HEV is not routinely done in Pakistan. There is dearth of literature regarding viremia and seroprevalence of HEV among asymptomatic, healthy blood donors.

Materials & Methods: A prospective, cross-sectional study was conducted at Liaquat National Hospital's blood bank facility. Besides routine testing, blood samples were collected for Anti HEV antibodies (IgG and IgM) and ALT. Those who tested positive for anti-HEV IgM were tested for HEV-RNA by real-time reverse transcription polymerase chain reaction assay.

Results: Among 515 individuals with age range of 18-57 years were enrolled, mean ALT values recorded were 42.8447±32. Anti HEV IgG was positive in 365 individuals (71%). Anti HEV IgM was found positive in 31 (6%) individuals, but HEV RNA PCR were negative in all patients. Correlation analysis showed positive relationship with high level of BMI and ALT values.

Conclusion: High seroprevalence of Anti HEV IgM among healthy blood donors emphasizes the need for robust measures of routine screening for HEV of all blood products in endemic countries to prevent transfusion dependent transmission with special consideration when the recipients are either immunocompromised or pregnant.

Clinical Significance: Epidemiological statistics of HEV emphasize on the impact of counter measures for prevention related to enhancement of public health.

Abstract Submission No. 101738

O-1127

Estimation of Global, Regional, and National Burden of Adult NAFLD and NASH Using A Novel Strategy

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At present, there is a dearth of comprehensive data at the global, national, and regional levels regarding the adult non-alcoholic fatty liver disease (NAFLD) prevalence. The objective of this study is to ascertain the prevalence of NAFLD and its related condition, non-alcoholic steatohepatitis (NASH), among adolescents worldwide and in specific regions, utilizing BMI as a determining factor.

Using the data extracted from the NHANES database, sigmoidal fitting curves were generated to establish the relationship between BMI and the risk of NAFLD/NASH. Utilizing BMI data from the NCD-RisC database at both global and regional levels, the prevalence of NAFLD/NASH among adults was estimated from 1975 to 2016, encompassing global, regional perspectives. Additionally, projections were made to forecast the prevalence of adult NAFLD/NASH from 2017 to 2030.

In 2016, the global prevalence of NAFLD was 41.12% for males and 37.32% for females, while the prevalence of NASH was 15.79% for males and 16.48% for females. The prevalence of NAFLD/NASH increased with higher BMI in both genders. Over the period from 1975 to 2016, there has been a gradual increase in the global prevalence of NAFLD/NASH in adults, and this trend is expected to continue between 2017 and 2030. In males, the prevalence of adult NAFLD/NASH was found to be highest in High-income Western countries, while it was highest in Central Asia, Middle East, and North African countries after 1995.

The prevalence of adult NAFLD/NASH has been observed to increase annually. The BMI has been identified as a reliable predictor of NAFLD/NASH prevalence.

Abstract Submission No. 101789

O-1128

Updated Definition of Healthy ALT Levels in a Metabolically and Histologically Normal Population

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Background & Aims: This study reevaluates the upper limit of normal (ULN) for alanine aminotransferase (ALT), traditionally set at 40 U/L, using histological and metabolic parameters in Asian living liver donors.

Methods: We conducted a retrospective analysis of 5,455 potential living liver donors from 2005 to 2019. Patients were screened for hepatitis B, C, HIV, and alcohol use. Histologically and metabolically healthy participants was assessed using the modified Prati criteria (body mass index <23 kg/m², triglyceride ≤200 mg/dL, fasting glucose ≤105 mg/dL, total cholesterol ≤220 mg/dL). The new healthy ULN of ALT was determined at the 95th percentile among participants without hepatic steatosis or metabolic dysfunction.

Results: The median age of the cohort was 30 years, with a predominance of males (66.2%). While 3,162 (58.0%) did not have hepatic steatosis, 1,553 (49.1%) met the modified Prati criteria, being metabolically healthy. The new healthy ULN of these participants was 34 U/L for males and 22 U/L for females, significantly lower than the conventional 40 U/L. A 'borderline' ALT category (34-40 U/L for males, 22-40 U/L for females) was also introduced to participants at risk of hepatic steatosis or metabolic dysfunction.

Conclusion: Our study suggests that the traditional ALT ULN is higher than healthy levels for a metabolically and histologically verified Asian population. The proposed ULN values are 34 U/L for males and 22 U/L for females. The introduction of a 'borderline' category

aids in better disease risk stratification, highlighting the need for updated ULN of ALT.

Abstract Submission No. 101905
O-1129

Prevalence and risk factors for non-hepatic cancers in cirrhosis: a c

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Background and Aims: Non-hepatic cancers (NHC) are under-recognized in patients with liver cirrhosis, but cause poor outcomes. The present study aims to explore the prevalence of NHC in such patients and identify its associated risk factors.

Methods: Patients with a diagnosis of liver cirrhosis who were consecutively admitted to our hospital between January 1, 2010 and June 30, 2014 were retrospectively screened. They were divided into NHC, primary liver cancer (PLC), and non-cancer groups. After adjusting for age and sex, logistic regression analyses were performed to explore the risk factors of NHC in cirrhotic patients. Adjusted odds ratios (aORs) with their 95% confidence intervals (CIs) were calculated.

Results: Overall, 2509 patients were included. Prevalence of NHC and PLC was 6.22% (156/2509) and 22.20% (557/2509), respectively. NHC mainly included gastric cancer (n=22), pancreatic cancer (n=17), lung cancer (n=14), lymphoma (n=12), and breast cancer (n=11). After adjusting for age and sex, the NHC group had a significantly higher proportion of history of smoking (aOR=1.994; 95% CI=1.231-3.231, p=0.005), but lower proportions of history of encephalopathy (aOR=0.344; 95% CI=0.147-0.804, p=0.014) and history of heart disease (aOR=0.300; 95% CI=0.173-0.519, p<0.001) as compared to the non-cancer group. HBV (aOR=0.863; 95%CI=0.581-1.281, p=0.465), HCV (aOR=0.908; 95%CI=0.503-1.642, p=0.750), and alcohol abuse alone (aOR=1.254; 95%CI=0.779-2.017, p=0.351) as the etiology of liver cirrhosis were not significantly associated with the risk of NHC.

Conclusions: Smoking may be associated with a higher probability of NHC in patients with cirrhosis, but the probability of NHC may be compromised by encephalopathy or heart disease.

Abstract Submission No. 200001
O-1130

Determining the public health implications of hepatitis B curative treatments.

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Background: Hepatitis elimination as a global public health threat will only occur with sustainable and tolerable curative treatments. While significant activity is being conducted to identify the constituent elements of curative treatments, their implementation will require significant reorientation of current clinical and public health approaches to hepatitis B.

Methods: An interdisciplinary advisory committee oversaw exploratory semi-structured qualitative interviews with 31 stakeholders experienced in global, regional or local public health policy, scientific and/or clinical investigation, or translational research. Interview

analysis identified social, political, economic and ethical issues related to developing and implementing hepatitis B curative treatments.

Results: Key themes included that descriptions and priorities for cure science reflected individual and professional frameworks, and recognised the need to prepare and reorientate clinical and public health infrastructure to effectively implement any cure. Other implications included a need for global or regional resourcing given the economic realities of many countries with greater burden of the infection, with social and cultural implications identified including the social impact and marginalisation resulting from hepatitis B infection.

Conclusions: While work progresses on curative hepatitis B treatments, it will be for naught without decentralising and simplifying current clinical and public health approaches to hepatitis B. The social impact of hepatitis B is often as significant as its clinical implications, with curative treatments having more impact than removing a virus from the body. Curative treatments will not only benefit individuals, but fundamentally affect families where hepatitis B occurs across generations and often across multiple countries.

Abstract Submission No. 200027
O-1131

Hepatitis screening in People Living in Poverty in Pakistan: Step towards finding missing millions.

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Background: Viral hepatitis caused 1.1 million deaths in 2020. World Health Organization has developed a strategy to eliminate hepatitis by 2030. Globally, millions of people living with HBV or HCV are undiagnosed. World Hepatitis Alliance has started an initiative named "Find the Missing Millions" to trace the millions of undiagnosed Hepatitis cases.

Objectives: To Find the Missing Millions in Pakistan by screening Hepatitis B and C in high risk populations living in poverty in Pakistan.

Methodology: We are doing Hepatitis awareness and screening in high risk populations groups in Pakistan including People who inject drugs, Transgender population, Refugees, Thalassaemia patients and street children.

Results: The prevalence of HCV was found 55.73% in thalassemia positive patients. All the patients above 20 years of age were found positive for HCV. While the prevalence of HBV was found 3.08%. We screened 11 Refugees camps in Muzaffarabad region for the presence of HBV & HCV. The prevalence of HBV and HCV was found 4.36% and 6.54% respectively. In Transgender population the prevalence of HBV, HCV and HIV was found 10.04%, 13.87% & 9.33% respectively. The prevalence of HCV was found 72% in people who inject drugs while HCV/HIV co-infection was found in 12% of PWIDs.

Conclusion: The prevalence of hepatitis was found very high in high risk groups. There is dire need to speed up hepatitis screening and find the missing millions living with hepatitis in Pakistan.

Abstract Submission No. 200208
O-1132

Risk of Cigarette Smoking and Liver Disease Based on Demographic Characteristics

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Smoking has been found to be a strong contributor for many diseases. Despite the fact that cigarette smoking is directly associated with respiratory diseases, its relationship with liver disease is rarely analyzed from the perspective of demographic variety. This study aims to analyze the risk of cigarette smoking to liver diseases based on demographic level. Information of 34,250 respondents from Indonesian Family Life Survey (IFLS) is analyzed to answer the research question. IFLS is a national representative data of Indonesia. Analyses are conducted using logit regression model. Additionally, the comparison of effects is done using the calculation of marginal effects. In general, there is a positive trend between smoking status and liver disease diagnoses. After conducting regression analyses, results show that statistically there is a positive significant relationship between these two variables. Furthermore, findings also reveal that the risk of cigarette smoking is twice bigger for the elderly (60 years old and above) than non-elderlies. When the cut off age is changed, it shows that smokers aged under 40 are fewer than a half less likely to be diagnosed liver disease than those who were above 40 years old. It implies that the risk of liver disease from cigarette smoking is acceleratively increase with age. In conclusion, this study found that there is not only a positive but also accelerative effect of cigarette smoking and liver disease.

Abstract Submission No. 100731
O-1133

Universal Screening for Hepatitis B Infection Before Initiating Chemotherapy is Cost-Effective

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Background: Cancer patients undergoing chemotherapy have an increased risk of hepatitis B virus (HBV) reactivation. However, HBV screening rate prior to initiating chemotherapy treatment remains low. The study aims to assess the cost-effectiveness of HBV screening and prophylaxis before receiving chemotherapy.

Methods: Cost-utility analysis was performed using Markov model. Yearly universal HBV screening using hepatitis B surface antigen (HBsAg), anti-hepatitis B surface antibody (anti-HBs) and anti-hepatitis B core antibody (anti-HBc) was compared with no screening strategy. Patients with positive HBsAg received tenofovir as prophylactic medication. Incremental cost-effectiveness ratio (ICER) was calculated using total costs and quality-adjusted life-years (QALYs) gained for each strategy. Cost-effectiveness was determined using a willingness-to-pay (WTP) threshold of 4,665 USD/QALY (160,000 THB/QALY).

Results: Universal HBV screening was cost-effective with ICER of 1,719 USD/THB. By subgroup analysis, HBV screening was cost-effective in both solid organ tumors and hematologic malignancies with ICERs of 3,396 and 2,116 USD/QALY, respectively (**Table**).

By one-way sensitivity analysis, universal HBV screening remained cost-effective after adjusting the incidence of chronic HBV infection from 1-10% or varying the reactivation rate in patients without prophylaxis from 10-20%. However, when the reactivation rate in patients with antiviral prophylaxis was higher than 8%, screening and initiating prophylactic medication was not cost-effective. By probabilistic

sensitivity analysis, universal HBV screening had a probability of 99.9% for being cost-effective.

Conclusions: Due to better access and lower cost of antiviral medication, universal HBV screening to initiate HBV prophylaxis prior to receiving chemotherapy is cost-effective.

Abstract Submission No. 100836
O-1134

Effectiveness of community and primary care models in promoting HBV testing for global elimination

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Background: Globally, <10% of HBV-infected persons are tested; thus, <2% are receiving recommended anti-viral therapies. The WHO recommends community- and primary care-based testing for HBV to address the inequities in access to screening and treatment. This study determined the effectiveness of different intervention models to promote HBV testing uptake in community and primary care settings toward global elimination goals.

Methods: A systematic review (PROSPERO-CRD42023455781), encompassing PubMed, Embase, Scopus, and CINAHL databases, was conducted, covering individual/cluster-randomized controlled trials up to 8/23/2023 and in English. Random-effect meta-analysis models were applied for sufficiently comparable subgroups of intervention models. Quality of evidence was assessed using ROB2.

Results: Of the unduplicated 6,617 studies identified, 19 trials were included, with 17 studies from high-income countries. 16 studies were included in the meta-analysis (**Figure 1**). Community-based intervention strategies included education programs by lay health workers (Pooled RR = 5.1 [95%CI = 2.6; 10.1], I² = 95%) or healthcare workers (17.2 [4.5; 66.2], 95%), or through digital platforms (1.6 [0.5; 4.5], 95%). Primary care-based intervention strategies consisted of the deployment of the electronic alert system (4.9 [0.7; 32.6], 96%), financial incentives to healthcare providers (one study; 11.4 [10.4; 12.4]), and the use of point-of-care rapid testing (one study; 1.4 [1.3; 1.5]).

Conclusion: This study highlights the pivotal role of healthcare worker-based educational programs in increasing HBV testing uptake in community or primary care settings. Thus, future interventions to increase healthcare workers' HBV education can enhance HBV diagnosis uptake and elimination goals globally.

Abstract Submission No. 100967
O-1135

Cost-Effectiveness of Hepatocellular Carcinoma Surveillance in Viral-Suppressed Chronic Hepatitis B

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Background: Despite persistent viral suppression through antiviral medication, chronic hepatitis B virus (HBV)-infected patients are still at risk for hepatocellular carcinoma (HCC) development. The incidence of HCC in non-cirrhotic viral-suppressed patients is significantly lower than cirrhotic patients. Therefore, to individualize HCC surveillance based on individual patient's risk, we aim to assess the cost-effectiveness of alternative HCC surveillance strategies.

Methods: Cost-utility analysis was performed using Markov model in Thailand and the United States (US) settings. Compared with biannual ultrasonography with alpha-fetoprotein, the cost-effectiveness of alternative HCC surveillance strategies were assessed, including 1) Annual ultrasonography with AFP and 2) Annual ultrasonography alone. Incremental cost-effectiveness ratio (ICER) was calculated using total costs and quality-adjusted life-years (QALYs) gained for each strategy. Strategies with ICERs above the willingness-to-accept (WTA) threshold of \$9,330/QALY (320,000 THB) in Thailand and \$100,000/QALY in the US were considered cost-effective.

Results: Annual ultrasonography with and without AFP were cost-effective in Thailand and the US settings. Compared to biannual ultrasonography with AFP, annual ultrasonography with and without AFP resulted in ICERs of 128,924 and 83,105 USD/QALY in Thailand, 371,700 and 227,400 USD/QALY in the US, which were above the WTA in the respective settings (Table). Additionally, the proportion of HCC-related mortality remained similar in all surveillance strategies. By probabilistic sensitivity analysis, annual ultrasonography had the highest probability of being cost-effective in Thailand and the US settings.

Conclusions: Alternative HCC surveillance strategies, including annual ultrasonography with and without AFP are cost-effective options for HCC surveillance in non-cirrhotic viral-suppressed HBV-infected patients.

Abstract Submission No. 101013

O-1136

How the Caregiver Could Increase the QoL of Elderly with Post-Liver Transplantation and Dementia?

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Potential curative treatment for liver disease is Transplantation (LT), although long-term survival is less than satisfactory. Indonesian elderly with independence barriers reached 3.7% and very dependent on the caregivers' existence. However, certified informal caregivers are not available in Indonesia, yet.

This study uses the 5th wave of the 2014 Indonesia Family Life Survey (IFLS) to explore how the availability of caregivers in maintaining the Elderly QoL post-LT with Dementia comorbidity.

Indonesian elderly reach 10.8% and 48% of them have chronic diseases. 18.6% of Liver cancer patients recorded in Indonesia are at Elderly age. 23.7% of them were identified as having symptoms of dementia with moderate to severe (assessed using the mini-cognitive test

scoring). The elderly needing long-term care due to these health conditions reaches 9.7% and 88% of them do not have caregivers. Only less than 1% of the elderly are cared for by paid caregivers and are concentrated in urban areas. The majority of the elderly are cared for by their families or tend to "age in community". 36% of Elderly post-LT benefit from health insurance and government social assistance. Using the Geriatric Depression Scale (GDS) it is known that the percentage of Elderly post-LT with dementia who has caregivers with mental health problems is lower than respondents who do not have caregivers.

Indonesia is urgent to meet the availability of certified informal caregivers with standardization modules and training. Expanding the coverage of health insurance for the provision of caregivers is a top priority because it mitigates mental health problems.

Abstract Submission No. 101304

O-1137

The cascade of care for hepatitis C virus infection among adults in Sindh province, Pakistan

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Background/Aims: Approximately 9.8 million people are living with hepatitis C virus (HCV) infection in Pakistan. To achieve HCV elimination, high levels of treatment are needed. Assessing the HCV cascade-of-care (CoC) is essential for guiding elimination initiatives.

Material and methods: A household serosurvey was conducted in Sindh province in 2019, utilising a two-stage stratified sampling design. The survey collected self-reported data on previous HCV testing and treatment history, and blood samples were taken for HCV-antibody (HCV-Ab) and HCV-RNA testing. We assessed the CoC and used multilevel binary logistic regression to identify factors associated with ever being tested for HCV. Adjusted Odds Ratios (aOR) with 95% Confidence Intervals (95%CI) were estimated.

Results: The study identified 397 HCV-Ab-positive individuals. Of these, 115 individuals (115/397=28.9%) had ever been tested for HCV and 100 (100/115=86.7%) reported testing positive for their last HCV test. Of these individuals, 61 (61/100=61%) reported having been treated, with 28 (28/61=45.9%) having an undetectable HCV-RNA test result in the survey. Regression analysis suggested that individuals with a family history of hepatitis (aOR=18.8, 95%CI: 6.5-54.3), ever-invasive dental procedure history (aOR=3.2, 95%CI: 1.2-8.4), ever blood transfusion history (aOR=2.7, 95%CI: 1.0-7.1), and secondary or higher education level (aOR=4.2, 95%CI: 1.4-12.8) compared to illiterates were more likely to have ever been tested for HCV.

Conclusions: Levels of HCV testing and the subsequent cascade-of-care in Sindh province, Pakistan, need to be dramatically improved to achieve HCV elimination in this setting. People with lower education levels need to be targeted in future testing initiatives.

Abstract Submission No. 101398

O-1138

Impact and cost-effectiveness of scaling up HCV treatment among people who inject drugs in Vietnam

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Background: In Vietnam, many hepatitis C virus (HCV) infections occur among people who inject drugs (PWID). Over 2016-2019, the DRIVE intervention combined four respondent-driven sampling (RDS) surveys to increase HIV-testing and treatment among PWID in Haiphong, Vietnam, which has ~5000 PWID. Referral to opioid agonist therapy (OAT) was also improved. An additional intervention, DRIVE-C, undertook an RDS survey to scale-up HCV testing and treatment.

Methods: A model of HCV transmission among PWID was calibrated in a Bayesian framework using data from Haiphong (mainly DRIVE/DRIVE-C). We evaluated the decrease in HCV incidence resulting from the DRIVE+DRIVE-C interventions, with no future interventions (denoted status quo/SQ), and the additional impact of providing HCV-testing and treatment in OAT and HIV treatment centres plus annual RDS interventions (HCV testing+treatment) over 2024-2029 (denoted DRIVE-plus). Over a 26-year time horizon (2024-2050), we estimated the incremental cost-effectiveness ratio (ICER) per disability adjusted life-year (DALY) averted for DRIVE-plus compared to SQ.

Results: For SQ, HCV incidence decreases from 14.8 (95% credibility interval 11.7-18.6) per 100 person-years (/100pyrs) in 2016 to 9.3/100pyrs (7.2-12.7) in 2020, remaining stable until 2030 because of scale-up of OAT (12 to 49% over 2016-2019). For DRIVE-plus, HCV incidence decreases to 2.1/100pyrs (1.2-4.1) by 2030, or 6.1/100pyrs (3.8-9.8) with just the additional RDS surveys. The mean ICER for DRIVE-plus is €682/DALY averted; cost-effective at a willingness-to-pay threshold of €2,048/DALY averted (0.5*GDP).

Conclusion: Using RDS surveys and other care settings to scale-up HCV-testing and treatment is a cost-effective strategy to reduce HCV incidence among PWID.

Abstract Submission No. 101503

O-1139

Climate change&Liver diseases&impact of adaptation strategies to deal with this challenge(Pakistan)

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Climate change(CC)is aglobal distressing problem that contributes to global burden of diseases,mortality&changes in pattern of health problems.Purpose of study is to review serious consequences ofCC on liver diseases&impact of adaptation strategies&mechanisms of remapping to reduce liver diseases

Methods: This study was conducted in3tertiary care hospitals of city over aperiod of3years to evaluate number of vectorborne,water/food-borne,parasitic diseases affecting liver.Meanwhile,Adaptation

strategies were developed&implemented for vulnerable groups that is patients coming to hospitals,free camps being conducted every3monthly at new location in city supporting physicians,&nurses at different levels,&making small videos over local channel to educate mass.Observing trend of then&now liver infections in same tertiary care hospitals

Results: Total of1600patients presented to hospitals with liver infections

Vectors transmitting parasitic/viral diseases are extremely sensitive to CC,630patients presented with Dengue,Malaria,&Congo hemorrhagic fever related liver complications(39.3%).

Ambient temperature,floods,&humidity may have significant role in distribution of intermediate hosts&pathogens that cause liver diseases.Due to recent flood events in Pakistan an increase in incidence of hepatitisA(HAV)&E viral infection(HEV)was observed.Based on data between2020&2022&flood event scenarios,incidence of HAV&HEV infections were562(35.1%)&408(25.5%)patients respectively.

After implementation of adaptation strategies at different levels,incidence of liver diseases related to CC showed a decreasing trend.Incidence of HAV(39.1%vs60.9%p=0.03),&HEV infections(28.7%vs81.3%p=0.012)decreased.

A decrease in malaria&Dengue infection was also seen after educating the masses regarding protective measures like use of the net,repellents,&a clean environment(36.8%vs73.2%;p=0.001)&(27%vs73%)but incidence of Liver disease related to Congo fever didn't change statistically significantly.

Conclusion: In conclusion,impact of CC on liver health is definite.Thus,there is an urgent need for properly sustained eco-health services provided by hepatologists.By adaptating&mitigating proper strategies we can improve the expectations&predicted scenarios of hepatic health impacts due to CC

Abstract Submission No. 101747

O-1140

Early detection of liver disease: How Puskesmas take important role among 17k islands in Indonesia?

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More than 28 million Indonesians are liver patients. Liver disease is the fifth most prominent cause of death for the elderly and is 3.3 times more likely to cause death. Government social insurance financing burden for liver disease in 2018 was one of the highest (\$235 million). The MoH carries out a preventive program that reaches remote areas through various screenings by Utilizing Community-Based Health Centers (*Puskesmas*) which are expected to be liver disease early detection.

We utilize a longitudinal survey dataset from the 2014 Indonesia Family Life Survey (IFLS) to evaluate the effectiveness of the *Puskesmas* in improving the function of liver disease early detection.

Liver disease prevalence among observations is 1.9% and increases in senior citizens by two times or 3.8% (60%: men). 40% of elderly with liver disease access treatment at the *Puskesmas*. *Posyandu Lansia*, as an extension of *Puskesmas*, is also utilized by older people for routine health checks, obtaining food/supplements, and various meetings from 80,353 *Posyandu Lansia* spread across 81,616 villages. *Posyandu Lansia* is also a space for the elderly to access financial services, religious, and political activities. *Puskesmas* is highly effective in

improving the senior QoL in various aspects of life. However, 56% of older people who do not have insurance prefer traditional practitioners. *Posyandu Lansia* can be a forum that carries out early detection of liver disease and is very accessible to improve the elderly QoL. It also needs to address the covered social insurance for treatment and caregivers.

Abstract Submission No. 101769

O-1141

Medical - social assessment of the prevalence of primary liver cancer in Kazakhstan.

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Relevance of the study: According to official statistical data for 2020 in Kazakhstan, primary liver cancer - hepatocellular carcinoma (HCC) occupies 9th place in the total cancer morbidity and 7th place in the structure of mortality from malignant neoplasms.

Aim of the study: To study the prevalence of liver cancer in Kazakhstan.

Results and discussions: Standardized incidence rates per 100 thousand population of liver cancer were 4.9 in 2019, and 4.1 in 2020, Rate of increase = -16.3. In 2019 mortality from liver cancer was 3.4 per 100 thousand people, 3.1: men - 4.4/4.1, and women 2.6/2.1, respectively in 2020. Rank in the mortality structure - 10th place in 2019; 8th place in 2020. By regions - the top three high mortality rates from liver cancer in 2020: East Kazakhstan - 4.8. West-Kazakhstan - 4.8, Pavlodar - 4.4; the three lowest indicators: Almaty city - 1.8; Atyrau - 2.1; Aktobe and Nur-Sultan - 2.2. The number of deaths from malignant neoplasms, not registered with oncological organizations - in the first place liver cancer in 2019 and 2020, in the second place blood cancer, in the third place - pancreatic cancer.

Conclusion: Liver cancer is in the first place among those who died without being on dispensary registration during 2019 and 2020 in Kazakhstan. As well as mentioned earlier, liver cancer is among the top three malignant neoplasms with one-year mortality and low five-year survival rate.

Abstract Submission No. 101831

O-1142

Cost-effectiveness of CHB therapy - implication of new therapy vs expanding the existing therapy

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Background: Chronic Hepatitis B (CHB) remains a significant global health challenge, necessitating effective and cost-effective therapeutic strategies. This study evaluated the impact and cost-effectiveness of different therapeutic strategies on HBV functional cure.

Methods: A Markov state-transition model was used to evaluate cost-effectiveness of three strategies of antiviral treatment, i.e. infinite nucleos(t)ide analogues (NA, entecavir) treatment, add-on PegIFN to stop NA (PegIFN+NA), and add-on new therapy to stop NA (New+NA). The model simulated chronic HBV infection status of 10,000 patients (aged 50+ years, NA-suppressed, HBeAg-) with virological and clinical relapse and retreat, in Asia-Pacific (AP) region where the majority of CHB patients reside.

Results: PegIFN+NA is estimated to reduce HCC and HBV-related deaths by 50.1% and 41.3%, respectively, by 2050, compared to infinite NA treatment. The reduction with New+NA is 42.6% and 36.4%, respectively. Incremental cost-effectiveness ratio (ICER) for PegIFN+NA is 2,725 USD/QALY in AP, ranging from 12,410 USD/QALY in high-income countries/areas to 2,569 USD/QALY in low-income countries. For a comparable ICER, the cost for a new therapy must not exceed a one-time treatment cost of USD11,431 in AP. New+NA (discounted QALYs = 21.3) is less effective than infinite NA (21.7) in high-income countries, regardless of the new therapy's cost. For a higher cost of new therapy, e.g., USD20,000, NEW+NA would never be cost-effective with an ICER equal to GDP per capita.

Conclusions: High cost and efficacy requirements of new therapy for CHB may limit its widespread application. Utilizing combination therapy could present a cost-effective strategy to attain a functional cure.

Abstract Submission No. 101872

O-1143

High exposure to hepatitis C virus in Saravan, Laos: Identification of several risk practices

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Background: HCV prevalence in Laos varies, with estimates ranging from 1.1% to 3.9%. A study by our group in Salavan province (in the South of Laos) found an unexpectedly high prevalence of 24.4%. We conducted a follow-up study to investigate the epidemiology of the infection in more detail and to determine associated risk-practices.

Methods: For the follow-up study, 402 participants were recruited (160 HCV infected cases and 242 controls; age-matched ± 5 years). After informed consent, blood samples were taken and tested for anti-HCV antibodies by ELISA. Positive samples were subjected to reverse transcription PCR to obtain sequences for phylogenetic analyses.

Results: Among the cases, 58.8% had detectable viral load. These participants were referred to the district hospital for treatment. More than half (58.0%) of the participants stated to have received parenteral medicine, and among those, 72% reported re-use of syringes. Tattooing was frequent (33.1%) and associated with having higher odds for being positive (adjusted odds ratio (aOR)=1.8(95% CI 1.2-2.8); p=0.01). In addition, accidental blood exposure for example when assisting people during accidents was also associated with HCV seropositivity (aOR=1.9(1.2-2.9); p<0.01). HCV sequence analyses are on-going and

phylogenetic inference investigations are planned to further elucidate virus origin, spread and evolution in this population.

Implications: We found high HCV prevalence in Southern Laos and associated risk factors. Our findings highlight the need for more research and extensive HCV testing and treatment in Laos. Advanced sequence analysis could help understand HCV transmission patterns.

Abstract Submission No. 200015

O-1144

Efficacy of COVID-19 Vaccine in Patients with HCC: Analysis of Data from a Prospective Cohort Study

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Aims: To investigate the efficacy of COVID-19 vaccines for SARS-CoV-2 infection in patients with hepatocellular carcinoma (HCC).

Methods: From January 2022 to October 2022, all consecutive patients diagnosed with HCC in a prospective, multicenter, observational cohort were analyzed in this study. Infection-free survival and overall survival were compared between the two groups by univariate and multivariate COX regression analyses.

Results: One hundred and forty-one patients with (n = 107) or without COVID-19 vaccination (n = 34) were included. Two hundred and fifty-nine doses of COVID-19 vaccines were injected in the vaccinated group. Vaccine-related adverse events occurred after 37 doses (14.3%), and the majority of the adverse events were classified as mild or moderate (94.6%). Median infection-free survival in the vaccinated group (14.0 vs. 8.3 months, p = 0.010) was significantly longer than it in the unvaccinated group. COVID-19 vaccination (HR = 0.57, 95%CI: 0.36-0.89, p = 0.015) and ECOG performance score ≥ 1 (HR = 1.92, 95%CI: 1.04-3.54, p = 0.036) were found to be the two independent protective factors for infection-free survival. Median overall survival was not reached in the two groups. Overall survival at 12 months was 90.5% in the vaccinated group and 75.5% in the unvaccinated group (p = 0.070). Maximum tumor diameter (HR = 0.31, 95%CI: 0.12-0.80, p = 0.015) and SARS-CoV-2 infection (HR = 2.70, 95%CI: 1.13-6.48, p = 0.026) were the two independent risk factors for overall survival.

Conclusions: COVID-19 vaccines could effectively reduce the SARS-Cov-2 infection in patients with HCC.

Abstract Submission No. 200028

O-1145

Evaluation of the performances of three rapid ICT test being used for detection of HCV antibodies.

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Background: Large number of HCV rapid screening tests are available in the market and many of them have substandard results.

Objectives: To evaluate the performance of 3 best HCV rapid test available in market.

Methods: We enrolled 300 subjects including 50 pregnant women, 50 blood donors and 200 HCV positive individuals. Blood samples from all the 300 participants were screened by using three rapid screening

test for anti-HCV including Intec Products Advanced Quality Rapid Anti-HCV Test, SD Bioline One Step anti-HCV test, and CTK Biotech's OnSite HCV Ab Rapid Test. The performance of these three rapid tests was also compared with the Roche Anti-HCV II test performed on the cobas 601 platform based on the electrochemiluminescence immunoassay principle.

Results: In total, 300 samples were analyzed in this study, out of which 92 were negative for anti-HCV and 208 were found positive for anti-HCV. The sensitivity of Intec test, SD Bioline test and CTK Biotech test were 98.56%, 97.59%, and 95.67%, respectively. The specificity of CTK Biotech test and SD Bioline test were found 100% whereas the specificity of Intec test was found 98.91%. The positive predictive value (PPV) of CTK Biotech and SD Bioline was 100%, but Intec products showed 99.51% PPV. The negative predictive values of the Intec product, SD Bioline, and CTK Biotech were 96.80%, 94.84%, and 91.09%, respectively.

Conclusion: The rapid test evaluated in this study showed very good results and they can be used for Hepatitis screening on large scale.

Abstracts

Poster Free Papers

Abstract Submission No. 100064

P-0001

Hospitalizations for Alcohol-Associated Hepatitis in the Era of Early Liver Transplantation

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Background: Liver transplant (LT) is a recent option available in the United States (US) to treat those with severe, refractory alcohol-associated hepatitis (AH). We examined changes in clinical characteristics of patients admitted with AH and tracked hospital outcomes as practice changes involving LT have shifted.

Methods: Using the National Inpatient Sample, we performed a cross-sectional analysis of patients admitted with AH during the years 2016-2020 in the US. Differences in clinical characteristics over time were assessed. To compare outcomes between 2016-2017 (when LT was less common) and 2018-2020 (when LT was more common), we conducted linear and logistic regression. Propensity-score matching was used compare outcomes between patients with and without LT.

Results: From 2016-2017 to 2018-2020, patients admitted with AH tended to have a higher frequency of infection (p=0.006), hepatorenal syndrome (<0.001), and ascites (<0.001). Hospital costs and length of stay (LOS) were highest in transplant hospitals, and costs rose over time in both NT teaching and non-teaching hospitals (p<0.001). Mortality decreased in NT teaching hospitals [aOR 0.7 (95% CI: 0.6-0.8)] and slightly decreased in NT non-teaching hospitals [aOR 0.7 (95% CI: 0.5-1.0)]. In the propensity-matched cohort involving LT versus non-LT patients, there was a 13% absolute reduction in in-hospital mortality, but this came at a higher cost (p<0.001) and length of stay (p<0.001).

Conclusion: The severity of AH has been increasing over time, yet mortality has declined, after adjusting for severity of disease. All patients who underwent LT survived; however, the healthcare burden of LT is substantial.

Abstract Submission No. 100181

P-0002

Global Burden of Disease Study 2019: Epidemiology of Alcohol-Related Complications in Young Women

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Alcohol consumption has witnessed a significant increase over the last two decades. Alcohol-associated liver disease (ALD) and alcohol use disorder (AUD) represent substantial public health risks, with women being more vulnerable to these complications. This study aimed to explore the epidemiology of ALD and AUD in women aged 15-49 using data from the Global Burden of Disease Study (GBD) 2019.

Data from GBD 2019 were utilized to extract annual frequencies and age-standardized prevalence rates (ASPR), mortality, and disability-adjusted life years (DALYs) for alcohol-associated cirrhosis (AC), alcohol-associated hepatocellular carcinoma (AL-HCC), and AUD in young women from 2010 to 2019. Data were stratified by age, region, country, and sociodemographic index (SDI). Statistical analyses, including misclassification correction and Jointpoint regression, were conducted to assess temporal trends.

In 2019, there were an estimated 17.43 million cases of AUD, 1.27 million cases of AC, and 2,532 cases of AL-HCC in young women globally. AC accounted for the highest number of deaths (14,521), followed by AUD (9,336), and AL-HCC (1,251). AUD resulted in 2.19 million DALYs, while AC and AL-HCC contributed 698,328 and 58,239 DALYs respectively. The highest burden of AUD was in Europe (ASPR: 2,047.76), with declining ASPR in most regions. Europe similarly had the highest AC burden (ASPR: 185.73), with increasing prevalence in most regions. Western Pacific had the highest AL-HCC burden (ASPR: 0.21), with increasing prevalence in most regions.

This study highlights the significant burden of alcohol-related complications in young women, especially with the increasing prevalence of AC and AL-HCC. Understanding these epidemiological trends is essential to develop effective targeted public health interventions.

Abstract Submission No. 100191

P-0003

The Global Burden of Alcohol-Associated Cirrhosis and Cancer in the Young

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Introduction: Alcohol consumption is a known contributor to liver cirrhosis and cancer genesis. Now alcohol-related health issues in young adults are increasing. This study, based on data from the Global Burden of Disease (GBD) 2019 study, aims to estimate the global burden of alcohol-associated cirrhosis (AAC) and cancer in young adults, considering region, gender, and sociodemographic index (SDI) factors. **Methods:** Data from GBD 2019, were used to gather information on cancer-related mortality and disability-adjusted life years (DALYs) associated with alcohol from 2000 to 2019. Estimation methods included Bayesian geospatial regression analysis and population-attributable fraction calculations. SDI gauged the impact of development on alcohol-associated health issues.

Results: Between 2000 and 2019, the burden of AAC in young adults increased, with higher rates in males. Southeast Asia had the highest prevalence, deaths, and DALYs of AAC. Furthermore, young adult cancer burden attributable to alcohol increased by 5.05% in terms of deaths and 6.06% in terms of DALYs. Lip and oral cavity cancer had the highest burden among cancer types. High SDI countries' cancer ASDRs and ASDALYS related to alcohol showed the most substantial declines, but increased in low and high-middle SDI countries.

Conclusion: Alcohol consumption has a significant impact on the health of young adults, leading to increased cirrhosis and cancer-related deaths and DALYs. These effects vary by region, gender, and development level. Effective public health interventions and policies are essential to reduce the burden of alcohol-related diseases, particularly among young adults.

Abstract Submission No. 100262

P-0004

Clinical Significance of Systemic Inflammation in Cirrhotic Patients with Acute Decompensation

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BACKGROUND: Some evidence suggests that the systemic inflammatory response syndrome (SIRS) contributes to the poor outcome of Acute decompensation (AD) of cirrhosis. The aim of this study is to assess prevalence of SIRS and its relationship with in-hospital outcome and acute-on-chronic liver failure (ACLF).

METHODS: A total of 1,162 alcoholic LC (liver cirrhosis) patients with AD were enrolled. ACLF was defined in the CANONIC study as an AD resulting in liver failure. Presence of SIRS was assessed on admission and during hospital stay. Main clinical outcomes were death and secondary clinical outcome is to evaluate association with SIRS and ACLF.

RESULTS: SIRS was present on admission in 308 of 1162 patients (26.5%). Presence of SIRS and ACLF at admission was not associated with 28-day mortality ($p=0.925$). On univariate analysis, presence of SIRS and ACLF during hospital day ($p<0.001$), model for end-stage liver disease (MELD) score ($p<0.001$), lactate ($p<0.001$) was associated with 28-day mortality ($p=0.001$). On multivariate analysis, presence of SIRS and ACLF during hospital day were associated with 28-day mortality ($p < 0.001$). ACLF was not associated with SIRS ($p=0.858$) and was associated with MELD score ($p < 0.001$).

CONCLUSIONS: SIRS frequently occurs in patients with cirrhosis. The presence of SIRS with ACLF during the hospital is a major independent prognostic factor in patients with cirrhosis. SIRS and ACLF affect independently 28-day mortality in LC

Abstract Submission No. 100428

P-0005

Narirutin reduced alcohol-induced hepatic injury by modulating MAPK14 in the zebrafish model

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Background: Alcohol-associated liver disease (ALD) ranges from alcoholic steatosis to cirrhosis. Narirutin (NRT), prominent in citrus peels, holds anti-inflammatory, antioxidant, and lipid-lowering properties. This research focused on the protective effects of NRT on liver damage caused by alcohol and the mechanisms involved.

Methods: Zebrafish larvae served as the model for studying the impact of NRT on liver injury due to ethanol (EtOH). Evaluations of liver phenotype, morphology, and biochemistry were conducted to ascertain the hepatoprotective effects of NRT. Network pharmacology and molecular docking helped in exploring potential targets of NRT in combating EtOH-induced hepatic damage. A DARTS assay was used for assessing the binding affinity of NRT to MAPK14, with subsequent validation through RT-qPCR and Western blot.

Results: Assessments indicated that NRT exhibits therapeutic potential in countering EtOH-induced liver injury, as evidenced by improvements in various hepatic parameters. NRT also mitigated changes in gene expressions related to oxidative stress, lipogenesis, and the ER/unfolded protein response. Insights from network pharmacology and molecular docking revealed that the protective action of NRT likely involves modulation of the p38 MAPK pathway, particularly through interaction with MAPK14.

Conclusions: NRT contributes to the alleviation of liver damage induced by alcohol. This effect is achieved through the inhibition of lipid synthesis, augmentation of antioxidant mechanisms, and reduction of ER stress-induced apoptosis, mediated through modulation of MAPK14.

Abstract Submission No. 100646
P-0006

Intestine FXR agonist ID119031166 modulates ethanol and bile acid metabolism in ethanol-fed hamsters

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Background: Chronic alcohol intake impacts enterohepatic bile acid circulation, and intestinal FXR deficiency may play a crucial role in the severity of alcoholic liver disease. Here, we assessed the potential effects of intestinal FXR agonist ID119031166 in hamsters with free access to 15% ethanol and fed either a chow diet or free choice (FC) diet (choice between control chow or high fat/cholesterol diet, and normal water or 10% fructose water).

Methods: After 28 weeks of FC diet, ID119031166 30 mg/kg or vehicle were given orally QD to FC diet-fed hamsters with 10% fructose water containing 15% ethanol for 5 weeks. 4-week-old hamsters were fed a chow diet with 15% ethanol in drinking water for 16 weeks, then ID119031166 30 mg/kg or vehicle were given orally QD for 5 weeks. Liver histology and liver parameters were assessed. mRNA expression levels were measured by qRT-PCR.

Results: Ethanol feeding in FC diet-fed hamsters raised hepatic TG levels compared to normal hamsters. In the liver, ID119031166 markedly reduced liver TG levels and down-regulated CYP7A1, CYP2E1, ADH1, ALDH1, IL6, and TGFβ1 genes. Long-term ethanol intake in chow diet-fed hamsters induced a higher inflammation score, reduced hepatic TC levels, and up-regulated CYP7A1 and ADH1 genes. Compared to vehicle, ID119031166 reduced ethanol-supplemented water intake and inflammation score, restored liver TC levels, and down-regulated Cyp7A1 and ADH1 genes.

Conclusion: Our findings suggest that ID119031166 modulates ethanol and bile acid metabolism by regulating key metabolic genes in chronic ethanol exposure.

Abstract Submission No. 100777
P-0007

Decadal Temporal Burden of Alcohol-associated Liver Disease in the Asia-Pacific Region

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Background: Alcohol-associated liver disease (ALD) represents a high and rising health problem worldwide. Despite multiple studies conducted for this study in the West, there is a lack of studies that examined the burden in this region.

Methods: We utilized data from the Global Burden of Disease 2019 study to conduct a comprehensive analysis of the prevalence, death, and disability-adjusted life years (DALYs) along with age-standardized rate (ASR) associated with ALD, specifically cirrhosis and liver cancer, in the Asia-Pacific region, including Southeast Asia (SEA) and Western Pacific (WP) regions, from 2010 to 2019.

Results: The burden of alcohol-associated cirrhosis cases and alcohol-related liver cancer in the Asia-Pacific region witnessed a significant increase over the decade from 2010 to 2019, surpassing 7 million cases and 6.79 million cases, respectively, with a notable male predominance. ASRs for death and DALYs due to alcohol-associated cirrhosis in the WP region showed a declining trend, with annual percentage changes (APC) of -1.18% and -1.17%, respectively. Conversely, liver cancer cases related to alcohol displayed an increasing pattern, with ASRs for death and DALYs showing APC of +0.54% and +0.65%, respectively. Meanwhile, ASRs for death and DALYs for both conditions remained stable in the SEA region.

Conclusion: The burden of ALD in the Asia-Pacific has increased, underscoring the timely intervention to tackle this high and rising burden.

Abstract Submission No. 101487
P-0008

Room for improvement in managing alcohol abuse: Results from a questionnaire in Thailand.

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Background: Alcohol abstinence improves outcomes in patients with alcohol-related liver disease. However previous reports showed that alcohol abuse is commonly treated poorly by hepatologists in other countries. We report the results of a questionnaire distributed to doctors across Thailand.

Methods: A questionnaire related to clinical practice, referral problems, and desire for further training related to alcohol abuse was made on googleform and sent to Hepatologist/gastroenterologist (Hep/GI), general internal medicine (IMed), general practitioners (GP), and psychiatrists (Psy) via common social media platforms for professional groups. The answers were collected between January - March 2023.

Results: 64 Hep/GI doctors, 40 GPs, 17 IMed, and 20 Psys returned answers from 47 out of 77 counties in Thailand. Results showed that only 15%, 6%, 22% and 32% of Hep/GI, IMed, GP and Psy used formal screening tools to screen for alcohol abuse. For non-psychiatric specialties 18-22.5% of respondents did not have psychiatric services in their hospital. 47-57.5% of this group never or infrequently prescribed anything to reduce alcohol consumption in heavy alcohol drinkers, and very few (0-15%) had confidence in managing alcohol abuse overall. Many wanted to learn more about alcohol addiction and 64.7-89.7% thought Clinical Practice Guidelines would be useful.

Discussion: Alcohol abuse was rarely formally screened for by Hep/GI, IMed and GPs. Prescriptions to reduce alcohol consumption was never or infrequently given to heavy alcohol users by 47-65% of respondents from this group, and few ($\leq 15\%$) were confident in managing alcohol abuse.

Abstract Submission No. 101586

P-0009

Global Burden of Alcohol-Related Complications in Young Women

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Introduction: The surge in alcohol consumption, notably among young women, has led to a substantial rise in alcohol-related complications, necessitating a comprehensive understanding of the epidemiological landscape. This study focuses on addressing the existing gaps in research by examining the prevalence, mortality, and disability-adjusted life years (DALYs) of alcohol-associated cirrhosis (AC), alcohol-associated hepatocellular carcinoma (AL-HCC), and alcohol use disorder (AUD) in young women globally.

Methods: Data from the Global Burden of Disease study 2019 were analyzed to extract information on the burden of AC, AL-HCC, and AUD in women aged 15-49. The study utilized statistical methods, including Joinpoint regression, to assess trends over the period 2010-2019. The analysis categorized results by region, nation, and socio-demographic index (SDI).

Results: In 2019, global prevalence figures for AUD, AC, and AL-HCC in young women were 17.43 million, 1.27 million, and 2,532 cases, respectively. Europe exhibited the highest burden of AC and AUD, while the Western Pacific region had the highest burden of AL-HCC. While AUD prevalence showed a decline, AC demonstrated an upward trend. Notably, despite the high burden in Europe, AL-HCC was concentrated in the Western Pacific. Trends in mortality and DALYs varied across regions and SDI levels.

Conclusion: The last decade has witnessed a concerning escalation in the global burden of alcohol-related complications among young women. Urgent public health strategies are needed, particularly in Europe and the Western Pacific region, considering the varying disease dynamics across regions and SDI levels.

Abstract Submission No. 101719

P-0010

Dose-Dependent Relationship between Alcohol Consumption and the risk of Hepatocellular Carcinoma

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Objectives: This study aimed to establish the dose dependent model between alcohol consumption on the risk of cirrhosis and hepatocellular carcinoma (HCC) in patients with hepatitis B virus (HBV) infection.

Methods: Studies on HBV patients published from inception to August 6th, 2023, were identified through PubMed, Embase, the Cochrane library, Web of Science, and four Chinese databases. A random effects model was performed to obtain the pool data on the risk of alcohol for the incidence of cirrhosis and HCC. Furthermore, we established a dose dependent model of alcohol consumption on the risk of cirrhosis and HCC.

Results: A total of 33,222 HBV patients from 45 studies were identified. Compared with non-drinkers, the overall pooled ORs of drinkers were 2.61 (1.46-4.66; $I^2=94\%$, $p<0.001$) for cirrhosis and 2.27 (95%CI: 1.50-3.43; $I^2=90\%$, $p<0.001$) for HCC. Compared with low-level drinkers, the estimated pooled ORs of high-level drinkers were 2.34 (95%CI: 1.59-3.44; $I^2=87\%$, $p<0.001$) for cirrhosis and 2.42 (95%CI: 1.90-3.09; $I^2=80\%$, $p<0.001$) for HCC. Furthermore, a liner dose dependent analysis showed that each daily consumption of alcohol of 12 g increased the risk for cirrhosis by 6.2% and the risk for HCC by 11.5%.

Conclusions: Alcohol dose dependently increases the risk of cirrhosis and HCC and patients with alcohol drinkers $>12g$ per day should be strictly monitored in the management of HBV infection.

Abstract Submission No. 101898

P-0011

The significance of extracellular vesicle number in patients with alcoholic liver injury

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Background and aim: Extracellular vesicles (EVs) are released from various cell types and its number reflects cell condition. In addition, EVs contain the components of cells, including proteins and nuclear acids. Thus, EVs are bioactive and contribute to activation of other cells. Currently, the number of EVs has been reported to increase in mice and patients with alcoholic liver injury. However, little information is available on the association between the number of EVs and

liver function. In this study, we aimed to investigate the number of EVs and liver function in patients with alcoholic liver injury.

Methods: A total of 48 patients with alcoholic liver injury who visited Jichi Medical University hospital were enrolled in the present study. All patients were agreed to participate in the study. The number of labeled EVs in the serum were counted using flowcytometry.

Results: Among 48 patients, 44 were male. The median of age was 65 years old. The median of EV number was 2.62 million/ml. In agreement to our previous data, the number of EVs increased in parallel with an increase of triglyceride (TG). Thus, we investigated the correlation between liver function tests and the EV/TG ratio. There were positive correlations between EV/TG and AST, EV/TG and ALT, EV/TG and ALP, and EV/TG and M2BPGi. In addition, there were negative correlations between EV/TG and serum albumin. Indeed, there was a significant difference in EV/TG between high and low albumin group (<4.0 g/dl).

Conclusion: There is a negative correlation between EV/TG and serum albumin.

Abstract Submission No. 101968

P-0012

Network pharmacology analysis and in vivo experiments reveal mechanisms of JPHX formula in acute ALD

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Background: Currently, there is still a lack of significant pharmacological treatments for alcoholic liver disease (ALD). JianPiHuoXue formula (JPHX), as a traditional Chinese medicine, has shown a therapeutic effect to ALD in clinical practice. Therefore, this research aims to preliminarily the pharmacological mechanism of JPHX in acute ALD.

Method: A thermo QE plus liquid chromatography tandem high-resolution mass spectrometer was used for the determination of the chemical constituents of JPHX. TCMSP database, GeneCards database, uniprot database, omim database, the STRING platform, and Cytoscape3.7.2 were used to construct the network of JPHX in the treatment of ALD. The acute ALD mice model was established by a persistent alcohol diet, and JPHX was given by intragastric administration. Meanwhile, transcriptomics of liver tissues was performed to investigate the mechanism of JPHX in acute ALD.

Result: JPHX has 49 main active compounds, of which Luteolin, Tanshinone IIA, and Wogonin may be its main compounds alleviating ALD. Network pharmacology analysis predicted that AKT1, TNF, and IL-6 may be the key targets. GO and KEGG analysis shows that the pathways involved in regulating immunity, mediating inflammatory response and so on. In vivo experiments, JPHX did play a role in anti-inflammatory and alleviating liver damage. Transcriptome and enrichment analysis showed that it may be related to the regulation of lipid metabolism, bile acid metabolism, and anti-inflammatory pathways.

Conclusion: JPHX can alleviate acute ALD. It may be related to the intervention of inflammatory response, immune regulation, bile acid metabolism, and lipid metabolism, which needs further verification by molecular biology.

Abstract Submission No. 200179

P-0013

Rare Case of Alcoholic Fatty Liver in Indonesian Adolescent Female: A Case Report

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Introduction: Ethanol is mainly metabolized within the liver causing damage upon intoxication. An early sign of ethanol-related damage is steatosis which is indicated by fat deposits within the hepatocytes. This case report help to remind clinicians that alcohol intoxication may still be a possible etiology in cases of acute liver failure.

Case: A sixteen-year-old teenage girl presented with fever, abdominal discomfort, and labored breathing. A history of unlabeled alcoholic cocktail consumption for the last two months was discovered. Further physical examination found a blood pressure of 95/65 mmHg, icteric sclera, palpable liver border 6 cm below the costae arch, and swelling of both lower extremities. Laboratory investigation resulted in signs of anemia (Hb 9.4 g/dL), bilirubinemia (total 3.7 mg/dL, direct 3.4 mg/dL), non-reactive HBs-Ag, increased ALT/AST (105/191 U/L), extended PPT (21.2 seconds), increased triglycerid and gamma-glutamyl transferase (1172 mg/dL and 357 U/L), hypoalbuminemia. Abdominal ultrasound was indicative of ascites and fatty liver. The patient was diagnosed with alcoholic fatty liver.

Conclusion: High alcohol intake remains dangerous because its association with increased plasma triglycerides, as well as with cardiovascular disease, alcoholic fatty liver and the development of pancreatitis. The female patient, aged 16 years, was diagnosed with alcoholic fatty liver disease or steatohepatitis, which is the initial stage of alcohol-related fatty liver disease.

Abstract Submission No. 100055

P-0014

Autoimmune Hepatitis Triggered by Covid-19 Vaccination: Safety of Repeat Dosing

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Background: Autoimmune hepatitis (AIH) is an uncommon chronic inflammatory liver disease. Recently, there were reports of AIH triggered by mRNA Covid-19 vaccinations but none on safety of repeat vaccination dosing.

Methods: We report 2 cases of AIH diagnosed with liver biopsy and revised original AIH pre-treatment score >15 , post treatment score >17 , occurring after mRNA Covid-19 vaccination and subsequent response to repeat dosing.

Results: Patient A is a 35-year-old Chinese female who presented with jaundice 8 weeks after mRNA Covid Vaccination in May 2021. She was diagnosed with AIH (pre-treatment score 17), initial results Bil95 ALP138 ALT691 AST550 IgG26.58. She was started on prednisolone and azathioprine with normalization of liver panel and IgG. She subsequently had repeat mRNA Covid-19 vaccination in February 2022

while on azathioprine monotherapy without any hepatic event or worsening of laboratory results.

Patient B is a 55-year-old Chinese female with epilepsy and protein C deficiency. She was diagnosed with AIH (pretreatment score 23) 4 weeks after mRNA Covid-19 vaccination in July 2021. Initial results Bil31 ALP102 ALT134 AST269 IgG40.06. She was started on prednisolone and azathioprine with normalization of liver panel and IgG. She subsequently had repeat mRNA Covid-19 vaccination in January 2022 while on azathioprine and low dose prednisolone without any hepatic event or worsening of laboratory results.

Both patients remain well on current follow up.

Conclusion: We report 2 cases where repeat mRNA Covid-19 vaccination was safely administered in patients who had AIH likely triggered by mRNA Covid-19 vaccination.

Abstract Submission No. 100243

P-0015

Association between serum myostatin levels and prognosis in primary biliary cholangitis

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Background: Primary biliary cholangitis (PBC) is an autoimmune-mediated cholestatic liver disease which can progress to liver-related death. Prognostic biomarker is needed in PBC patients. The association between myostatin level and prognosis in PBC patients is unclear.

Methods: In this retrospective study, we enrolled 119 PBC patients. Myostatin levels before ursodeoxycholic acid treatment were measured using ELISA. We analyzed their associations with the clinical characteristics in PBC patients.

Results: Serum myostatin levels in PBC patients was significantly lower than that of healthy controls (PBC; 2343 pg/mL, healthy controls; 4059 pg/mL, $P < 0.001$). The prevalence of patients with low myostatin levels was high in patients with severe histological fibrosis. Leucine-rich $\alpha 2$ glycoprotein levels were high in patients with low myostatin compared with those of patients with high myostatin. High myostatin in PBC patients was associated with longer survival without liver-related complications (hazard ratio: 0.25, 95% CI: 0.07–0.84, $P = 0.025$) independent of aspartate aminotransferase-to-platelet ratio index and histological stage.

Conclusions: Low myostatin levels were associated with severe fibrosis, high inflammatory conditions, and poor prognosis in PBC patients. Measurement of circulating myostatin can be used as a prognostic biomarker in PBC patients.

Abstract Submission No. 100248

P-0016

NAFLD increases risk of hepatocellular carcinoma in patients with autoimmune hepatitis

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Background: There have been few large-scale studies exploring the factors associated with the occurrence of hepatocellular carcinoma (HCC) in patients with autoimmune hepatitis (AIH). This study aimed to ascertain the risk of HCC in AIH patients and identify associated risk factors, with special focus on non-alcoholic fatty liver disease (NAFLD).

Methods: We examined claims data from the Korean National Health Insurance Service from 2007 to 2020. The study incorporated 7,382 AIH patients and an age-sex-matched control group of 58,538 individuals, in 1:8 ratio. We compared the incidence rates of HCC between these groups, and investigated the risk factors linked to HCC in AIH patients.

Results: During a median follow-up of 5.9 years, 160 AIH patients were diagnosed with HCC, yielding an incidence rate of 3.60 per 1,000 person-years. In contrast, the matched control group had an incidence rate of 0.48 per 1,000 person-years. After adjustments, AIH patients had a 4.51-fold heightened risk of HCC relative to the control group. Within the AIH cohort, coexisting NAFLD significantly increased the risk of HCC, as did other factors such as older age, decompensated cirrhosis, and current smoking. The presence of concurrent extrahepatic autoimmune diseases did not influence the prognosis. Additionally, glucocorticoid treatment seemed to be associated with a reduced risk of HCC in a 2-year landmark analysis.

Conclusions: AIH patients face a heightened risk of HCC compared to matched controls. Together with appropriate medical treatment, proactive interventions and lifestyle modifications for concurrent NAFLD are recommended in these patients.

Abstract Submission No. 100493

P-0017

Epidemiology and Clinical Outcomes of PBC In Canterbury, New Zealand: A Population-Based Study

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Introduction: Primary Biliary Cholangitis (PBC) is an autoimmune cholangiopathy that can profoundly impact quality of life and may progress to cirrhosis. Population studies demonstrate a rise in incidence and prevalence in the developed world. Treatment options to slow progression remain limited with ursodeoxycholic acid (UCDA). Our population-based study aims to determine PBC incidence, prevalence and outcomes in Canterbury, New Zealand.

Method: Patients who fulfilled the diagnostic criteria of PBC were identified from public and private practices in Canterbury between 2015 and 2021. Cases were also identified upon review of liver biopsies and positive Anti-mitochondrial antibodies in the Canterbury region in the last 10 years. Incidence and prevalence rates were calculated using Census data from Statistic NZ.

Results: The Prevalence of PBC in Canterbury between 2015 and 2021 has increased from 14.7 per 100,000 to 16.9 per 100,000. The incidence over this time is 0.90 per 100,000 per year. Over the studied period, the prevalence and incidence in Europeans is 17.5 per 100,000 and 0.91 per 100,000 respectively; in Non-Europeans, it is 16 per 100,000 and 1.2 per 100,000 respectively. Only 53-77% of patients met response criteria defined by PARIS-I, Paris-II, and Barcelona Criteria at 12 months.

Conclusion: Our study demonstrates a rising prevalence with stable incidence of PBC and suggests improved survival of this enlarging

cohort. Unlike other autoimmune diseases, ethnicity does not influence PBC incidence. More than a quarter of PBC patients had an inadequate response to UDCA, highlighting the urgent need for effective second-line treatment.

Abstract Submission No. 100559
P-0018

A case of hepatitis-type PBC with AIH showing anti-smooth muscle antibody positivity alone

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Some primary biliary cholangitis (PBC) patients are estimated to have features that overlap with autoimmune hepatitis (AIH). We present a case of atypical PBC with AIH accidentally discovered.

Case report: The patient was a 39-year-old female who was unexpectedly diagnosed with liver dysfunction during a routine check-up. Laboratory examination revealed no hepatitis virus markers, ANA < ×40, AMA (M2)Ab < 1.5, anti-LKM-1Ab (-). Two months after the initial examination, liver function worsened with increased AST of 189 IU/L, ALT of 233 IU/L, ALP of 908 IU/L, and IgG of 2372 mg/dl. Serologically, anti-smooth muscle antibody (ASMA) was elevated to 320 times. Histopathologically, liver biopsy revealed the expansion of inflammatory cell infiltration, interface hepatitis, and granuloma in the portal area. Interlobular bile ducts showed features of chronic cholangitis. The liver parenchyma showed inflammatory cell infiltration and emperipolesis, accompanied by centrilobular zonal necrosis (CZN) in parts. Based on the above-mentioned findings, this patient was diagnosed with hepatitis-type PBC with AIH and initially treated with PSL 25 mg/day and UDCA 600 mg/day. The PSL dose was gradually decreased over 1 year. After pregnancy, she is currently taking PSL 5 mg/day and UDCA 600 mg/day. No signs of recurrence have been observed.

Conclusion: Since atypical autoimmune liver diseases might be hidden in liver dysfunction of unknown cause, it is necessary to make a comprehensive diagnosis considering the clinical course and histopathological findings. Especially, ASMA might be crucial for diagnosis. This case of hepatitis-type PBC with CZN, which is often found in AIH, is instructive.

Abstract Submission No. 100938
P-0019

The Role of Metabolic associated Diseases and Liver Steatosis in autoimmune hepatitis

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Background/Aims: This study aimed to investigate the impact of metabolic associated diseases (MADs) on patients with autoimmune hepatitis (AIH).

Methods: This cross-sectional study analysed the clinical characteristics of 283 AIH patients who underwent liver biopsy from January 2016 to February 2022. The study collected extensive clinical and histological data.

Results: Among the enrolled AIH patients, 87.3%, 38.9% or 43.1% had MADs, NAFLD, or severe fibrosis, respectively. AIH patients with NAFLD were older and predominantly overweight/obese. Fibrosis was more severe in patients with NAFLD than in those without (50.9% vs. 38.2%, $p < 0.05$). Severe liver fibrosis (stages 3 to 4) was independently associated with male gender (odds ratio, 4.388; $p = 0.030$), age ≥ 60 (odds ratio, 6.053; $p = 0.007$), higher TC level (odds ratio, 2.913; $p = 0.028$), and combination with MADs (odds ratio, 28.969; $p = 0.020$).

Conclusions: The study findings suggest that metabolic factors aggravate hepatic fibrosis in AIH patients, highlighting the importance of screening for MADs and NAFLD among these patients. Proactive interventions should be provided to manage the progression of AIH.

Abstract Submission No. 100946
P-0020

A Diagnostic Challenge: A Case of Antinuclear Antibody-Negative Autoimmune Hepatitis

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Significance: Autoimmune hepatitis (AIH) may present with atypical features that may be challenging to diagnose. Majority (89%) of adult patients with AIH will detect antinuclear antibody (ANA). However, a subset of patients (10-15%) may not present with this attribute and fail to meet AIH diagnostic criteria leading to underdiagnosis of the disease. This paper will discuss the diagnosis and management of ANA-negative Autoimmune Hepatitis.

Clinical Presentation: A case of a 27-year-old female with 1-month history of fatigue, abdominal pain, and intermittent low-grade fever. Patient is nonalcoholic, with no history of recent travel nor drug intake.

Management: Blood works revealed anemia, leukopenia with neutrophilic predominance, hypoalbuminemia, prolonged INR, elevated liver enzymes (AST, 10x ULN, ALT 3.2x ULN) and alkaline phosphatase (3x ULN). Acute viral hepatitis markers were unremarkable. Abdominal CT scan showed normal sized liver with diffuse steatosis. Patient developed jaundice with increasing serum transaminases and bilirubin trends. Serum IgG was normal. ANA and SMA were negative. ANA-negative autoimmune hepatitis was highly considered. Thus, Prednisone (1mg/kg) was initiated. Liver biopsy showed macrovesicular steatosis, interface hepatitis with lymphoplasmacytic cell infiltration. Revised Diagnostic Criteria score was 16, with probable diagnosis for AIH. Patient had improved symptoms, decreased serum transaminases and normal coagulation parameters upon discharge.

Recommendation: Autoimmune Hepatitis may present with diversified features which may not fit the typical pattern of the disease. Autoantibody-negative AIH may occur and high index of suspicion is warranted. Application of AIH scoring systems must be used cautiously as cases may be missed if utilized inappropriately.

Abstract Submission No. 101230
P-0021

Severe type 1 autoimmune hepatitis and idiopathic hypereosinophilic syndrome: a rare case report

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BACKGROUND: Idiopathic hypereosinophilic syndrome (HES) is an uncommon condition. Concurrent severe type 1 autoimmune hepatitis (AIH) is extremely rare while on pre-existing immunosuppression. **CLINICAL CASE:** A 65 year old Chinese lady on follow-up with well controlled idiopathic HES presented with acute transaminitis secondary to severe AIH. She had been diagnosed 8 years prior with hypereosinophilia, biopsy proven urticarial vasculitis and multisystem involvement (bone marrow, respiratory and gut). Treatment at the time included pulse methylprednisolone, cyclophosphamide and subsequently maintenance azathioprine. Azathioprine was increased due to a flare of HES in February 2023. Due to transaminitis, azathioprine was withheld and prednisolone started. Transaminitis worsened requiring admission. Viral hepatitis markers were negative and there had been no new drug use. Mild elevation of serum immunoglobulin-G levels were noted but antinuclear antibodies were negative. Liver biopsy demonstrated marked lymphoplasmacytic infiltrate with interface hepatitis consistent with AIH. Anti-smooth muscle antibodies subsequently returned positive. Despite use of high dose oral steroids, liver function continued to worsen requiring intravenous methylprednisolone 250mg for 3 days. Throughout, she had no hepatic encephalopathy suggestive of acute liver failure. With high dose steroids, her transaminases started to downtrend and she was discharged on high dose oral prednisolone with normalization of transaminases at Day 60. **CONCLUSION:** This case of severe de-novo AIH occurred whilst on immunosuppression for idiopathic HES. While there are no guidelines on the use of high dose steroids in severe AIH, the use of IV methylprednisolone was successful in averting a liver transplant for this patient.

Abstract Submission No. 101395

P-0022

Patients with PBC-specific antibodies and cholestasis may not be primary biliary cholangitis

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Background & Aims: Patients with positive primary biliary cholangitis (PBC)-specific antibodies and evidence of cholestasis fulfill the diagnostic criteria of PBC. However, PBC-specific antibodies can appear in various diseases, and abnormal liver biochemistry might have non-PBC origins. Do these patients have PBC? Our study focused on patients with PBC-specific antibodies and cholestatic index elevation attributable to non-PBC etiologies.

Methods: We enrolled patients with positive PBC-specific antibodies at Beijing Friendship Hospital, Capital Medical University, between February 2017 and May 2023. Changes in liver biochemistry after non-ursodeoxycholic acid (UDCA) etiological treatments were monitored via electronic medical records and/or telephone interviews.

Results: One hundred and fifty-five patients with positive PBC-specific antibodies and elevated ALP and/or GGT levels due to non-PBC diseases were enrolled. One hundred patients had non-PBC liver diseases including non-alcoholic fatty liver diseases (n=36), drug-induced liver injury (n=35), autoimmune hepatitis (n=9), and others (n=20). Fifty-five patients had non-liver diseases, predominately consisting of connective tissue diseases (n=28). The median follow-up was 15.9 (4.7-25.6) months, and patients taking UDCA were excluded. After

treatment targeting primary diseases, 73 patients exhibited decreases in both ALP and GGT levels, eventually normalizing within normal ranges. Among patients with persistently elevated liver enzymes, 12 patients underwent liver biopsy, and no specific manifestations of PBC were observed. Additionally, 55 patients had elevated GGT levels but normal ALP levels.

Conclusion: Patients with PBC-specific antibodies and cholestasis may not be PBC. For patients with non-PBC liver diseases and connective tissue diseases, treatments of primary diseases can normalize cholestatic index instead of UDCA.

Abstract Submission No. 101421

P-0023

Fenofibrate add-on therapy improves transplant-free survival in primary biliary cholangitis patients

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Abstract

Aim: Fenofibrate has shown biochemical benefit in primary biliary cholangitis (PBC) patients with a suboptimal response to ursodeoxycholic acid (UDCA), but its long-term efficacy on survival remains unknown.

Methods: In this retrospective-prospective cohort study, we enrolled 160 PBC patients with a suboptimal response to UDCA and followed up on these patients to obtain laboratory results and adverse events. Finally, we evaluated long-term survivals analyzed with Kaplan-Meier plotting and log-rank test.

Results: The fenofibrate add-on therapy group showed more significant improvements in alkaline phosphatase (ALP) and gamma-glutamyl transferase levels compared to UDCA monotherapy group after one year of treatment, resulting in a normalization rate of 60.9% for ALP and 45.3% for both ALP and total bilirubin. Importantly, compared with UDCA monotherapy group, the fenofibrate add-on therapy group had a better transplant-free survivals of 5-year (89.7% vs 75.3%) and 10-year (87.0% vs 47.6%), with a hazard ratio of 0.3282 (95% CI: 0.1334-0.8073, P<0.05). Twenty-one cases (25.6%) developed adverse events, with liver injury being the most frequent one (17.1%).

Conclusions: Fenofibrate add-on therapy improved not only biochemical responses but also long-term transplant-free survival in PBC patients with suboptimal response to UDCA. However, liver injury needs to be closely monitored and properly managed.

Keywords: Fenofibrate, ursodeoxycholic acid, primary biliary cholangitis, survival

Abstract Submission No. 101744

P-0024

Usefulness of 3-year administration of pemafibrate for patients with PBC with dyslipidemia

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Background: The usefulness of bezafibrate for primary biliary cholangitis (PBC) has been previously reported. However, the long-term efficacy of pemafibrate, a sPPAR α , in PBC has not been fully analyzed. In this study, we investigated the efficacy and safety of pemafibrate for 3 years during additional treatment of patients with ursodeoxycholic acid (UDCA)-refractory PBC.

Methods: Patients with PBC with dyslipidemia attending our hospital whose biliary enzymes did not normalize with adequate doses of UDCA alone or UDCA plus bezafibrate were included. Patients were added pemafibrate or switched from bezafibrate. Patients who were followed for 3 years were evaluated.

Results: The group of UDCA alone plus pemafibrate (n=13) showed significant reductions in ALP (median 122 to 92 IU/L), γ -GTP (median 62 to 35 IU/L), TG (median 120 to 72 mg/dL) and IgM (median 156 to 129 mg/dL) after 3 months of treatment. 3 years later, ALP was significantly lower than that before treatment. ALP levels at 3 years were significantly lower than before treatment. In the group that switched from UDCA and bezafibrate to pemafibrate (n=14), there was no significant improvement in biliary enzymes or other parameters, but Cr levels at 1 year were significantly improved compared to pre-treatment levels (0.58 to 0.53 mg/dL). No side effects of rhabdomyolysis were observed during the course of the study.

Conclusion: Long-term combination therapy with pemafibrate for 3 years was considered effective and safe for PBC patients with dyslipidemia whose biliary enzymes were not normalized by UDCA alone.

Abstract Submission No. 101773

P-0025

Gut Microbiota Characteristics of Patients in the Decompensated Phase of Primary Biliary Cholangitis

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Background: The role of gut microbiota in the progression of primary biliary cholangitis (PBC) is crucial. In this study, we compared the gut microbiota of patients in the decompensated phase of cirrhosis due to PBC, Hepatitis B Virus-related cirrhosis (HBV-RC), and healthy controls (HCs) from Beijing Ditan Hospital.

Methods: We utilized 16S rRNA gene sequencing to profile the gut microbiota of PBC patients (n=40), HBV-RC patients (n=40), and matched HCs (n=30). Differential abundance analysis was performed to identify key gut microbiota associated with each group. Correlations between these differentially gut microbiota and clinical indicators were examined. Finally, a diagnostic model for the decompensated stage of PBC cirrhosis was constructed based on the identified gut microbiota differences.

Results: In contrast to the gut microbiota of HCs, the patients with HBV-RC and PBC exhibited reduced diversity, as evidenced by alpha-diversity (ACE, Chao1, PD and Shannon index), beta-diversity (PCA, PCoA and NMDS) and a distinct microbial composition. Significantly, the observed differences in microbial composition among patients with PBC were found to be closely associated with clinical indicators (ALP, TBIL, IgG and IgM). Furthermore, utilizing these identified differences, we constructed a random forest model for diagnosis, with an area under the receiver operating characteristic curve of 0.78.

Conclusion: Patients with PBC exhibited notable changes in gut microbiota, marked by reduced *patescibacteria* at the phylum level and elevated levels of *streptococcus* and *veillonella* at the genus level. These findings suggest the potential utility of gut microbiota as a non-invasive diagnostic tool for PBC.

Abstract Submission No. 101775

P-0026

Shugan Lidan Formula regulates gut microbiota, Th17/Treg balance and bile acid metabolism in PBC.

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Background: Primary biliary cholangitis (PBC) is an autoimmune liver disease characterized by inflammatory destruction of the intrahepatic bile ducts. The current pharmaceutical treatments for PBC have limited efficacy for partial patients. A previous study showed that Shugan Lidan formula (SLF) combined with ursodeoxycholic acid can improve the biological response rate in PBC patients, but the mechanisms were unclear.

Methods: Poly I:C induced PBC mice were measured by liver function, hematoxylin and eosin (H&E) staining and immunohistochemistry (IHC) staining. Alteration in gut microbiota and bile acid metabolism were examined through 16S rRNA sequencing and non-targeted metabolomics. Inflammatory cytokine production was measured in serum and liver tissue using enzyme-linked immunosorbent assays (ELISAs) and real-time PCR. Frequencies of Th17 and Treg cells in the spleen were determined by flow cytometry.

Results: Treatment with SLF ameliorated Poly I:C induced PBC mice in liver function, histology score and CK19 expression. 16S rRNA sequencing revealed that SLF treatment significantly altered the gut microbiota diversity and composition in PBC mice. Fecal microbial transplantation (FMT) mitigated Poly I:C-induced PBC mice, demonstrating its role in pathogenesis and therapy. SLF treatment also reduced proinflammatory cytokines levels including IL-1 β , TNF- α , IL-6, and IL-17A in serum and liver tissue. Non-targeted metabolomics analysis manifested the increased of bile acid. Additionally, SLF can downregulate the Th17/Treg balance to maintain intestinal homeostasis.

Conclusion: SLF showed therapeutic benefit against in mice in a way relying on effects on gut microbes. The underlying protective mechanism was associated with the improved Treg/Th17 balance and bile acid metabolism.

Abstract Submission No. 101889

P-0027

Treatment Course and Prognosis of Steroid-Resistant Autoimmune Hepatitis in Our Hospital

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Steroid therapy stands as the global frontline approach for autoimmune hepatitis (AIH) due to its remarkable efficacy; nevertheless, cases of relapse after steroid tapering or inadequate responses requiring non-steroidal immunosuppressive therapy have emerged, often influenced by fibrosis development and steroid discontinuation. This study evaluates the prognosis of patients normalized with non-steroid therapy. The cohort comprises 58 patients treated between January 1st, 2010, and March 31st, 2021. Eight patients received immunosuppressive drugs (AZA, cyclosporine, tacrolimus, tacrolimus plus abatacept, and MMF), with three fatalities observed. Initial laboratory values showed differences in ALT and AST between steroid and immunosuppressant groups, with lower albumin levels in the latter. Steroid discontinuation

history was prevalent in immunosuppressant users, and deaths were attributed to advanced cirrhosis and liver failure. Kaplan-Meier survival analysis revealed 87.5% and 48.3% 5- and 10-year survival rates for patients with advanced fibrosis at diagnosis. A 66.7% 10-year survival rate was noted for non-steroid-treated patients. However, prognosis did not significantly differ between steroid and non-steroid responders. These results indicate the importance of initiating treatment before fibrosis develops.

Abstract Submission No. 200093
P-0028

Rapid response associated with lower cirrhosis risk in Taiwanese patients with autoimmune hepatitis

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Background: Autoimmune hepatitis (AIH) is a rare disease and may advance to cirrhosis. Rapid treatment response has been shown to be associated with favorable outcomes, while delayed response may indicate patients who need an alternative therapy. This study aimed to evaluate the relationship of treatment response and long-term outcomes in Taiwanese patients with AIH.

Methods: This retrospective cohort study included 37 histologically confirmed AIH patients undergoing prednisolone treatment at National Taiwan University Hospital. Patients were categorized into complete biochemical response (CBR), insufficient response (IR), and non-response (NR) groups based on the International Autoimmune Hepatitis Group (IAIHG) response endpoints proposed in 2022. The primary endpoint was cirrhosis development.

Results: Of the diagnosed AIH patients, 9 patients had cirrhosis and 28 patients did not. Nearly half of cirrhotic patients were noted in the NR group (NR vs non-NR: 57.1% vs 16.7%, $p < 0.05$). Over a median follow-up period of 53 months, 5 non-cirrhotic patients progressed to cirrhosis, and 2 patients developed HCC. The cirrhosis progression rate was lower in the CBR group compared with the IR and NR groups (5.6% vs. 28.6% vs. 66.7%, $p < 0.05$). None of the CBR patients developed HCC.

Conclusions: Cirrhotic patients at the time of AIH diagnosis tended to have poor treatment response. A rapid treatment response was associated with a lower risk of cirrhosis.

Abstract Submission No. 200174
P-0029

Mesenchymal stem cells suppress inflammation in AIH via HIF-1 α /AHR/AHRT/CD39

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Background: Autoimmune hepatitis (AIH) is a chronic parenchymal hepatitis mediated by autoimmune reaction. It is routinely treated with immunosuppressants like azathioprine, but often with serious side effects. Mesenchymal stem cells (MSCs) have been found to exert therapeutic effects in related liver disease. However, the specific mechanism remains to be further explored.

Methods: Embryonic stem cell derived MSCs were injected into mice with ConA induced AIH to assess changes in serology and liver pathology. Transcriptomics was used to explore the differences in gene expression, and the role of HIF-1 α /AHR/AHRT/CD39 signaling in AIH was verified by qPCR.

Results: MSCs-treated mice with AIH had more significant reductions in liver injury and inflammatory cytokine, and higher anti-inflammatory cytokine than mice treated with PBS. The liver function related indicators of ALT (21422.0 ± 7275.73 vs. 4512.0 ± 2877.83 , $P < 0.01$), AST (12276.0 ± 7186.72 vs. 2080.0 ± 1516.58 , $P < 0.05$) and TNF- α , IFN- γ , IL-6, IL-17A were decreased, anti-inflammatory cytokine IL-10 was elevated in plasma. The Ishak Score of liver pathological sections (10.0 ± 1.58 vs. 1.60 ± 0.89 , $P < 0.001$) was reduced. Compared with AIH mice, the expressions of AHR, AHRT and CD39 were increased and HIF- α expression was reversed after MSCs treatment.

Conclusions: By activating the HIF- α /AHR/AHRT/CD39 signaling pathway, embryonic stem cell derived MSCs significantly alleviated the liver inflammatory response of mice with AIH, which can be regarded as an alternative therapeutic effect of AIH.

Abstract Submission No. 200200
P-0030

GRAVES' DISEASE WITH AUTOIMMUNE HEPATITIS AND PRIMARY SCLEROSING CHOLANGITIS- AN OVERLAP SYNDROME

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Autoimmune hepatitis (AIH) is a chronic inflammatory disease that results from autoantibody mediated hepatocyte injury. Given its immune mediated mechanism, concurrent autoimmune disorders including AIH with Graves' disease are reported. Our case study illustrates the diagnostic challenge to determine the cause of liver dysfunction in patients presenting with Graves' disease.

Case report: 11-year-old adolescent girl, a case of untreated hyperthyroidism presented with acute liver failure with obstructive jaundice, hepatosplenomegaly, ascites and coagulopathy. Viral hepatitis and sepsis were ruled out. Ceruloplasmin was 32mg/dl. Autoimmune hepatitis was diagnosed based on positive ANA, elevated IgG levels and interface hepatitis on liver histology. MRCP done showed slit like CBD with proximal and mid CBD narrowing suggesting sclerosing cholangitis and overlap syndrome.

Thyroid gland was enlarged with TSH level < 0.005 uIU/ml. TSH receptor and thyroid peroxidase antibody was positive. Radioiodine uptake scan showed increased uptake in thyroid gland.

Child underwent radio frequency ablation (RAI) of thyroid gland and was started on propranolol for tachycardia, steroids 60mg/day and azathioprine. At 12 weeks follow up patient is anicteric with improving liver function and is hypothyroid. She is on steroids of 5mg/day, azathioprine 2.5mg/kg and thyroid replacement therapy.

Discussion: 15-79% of untreated hyperthyroid patients suffer from liver dysfunction. It can be caused by hyperthyroidism per se or side effects of anti- thyroid drugs or as associations with AIH. Limited studies have been reported in pediatric population about the clinical course and treatment strategies in concomitant AIH and graves' disease. Our study concludes that high index of suspicion is required to diagnose concomitant AIH and graves disease. A brief review of literature on clinical course and treatment is discussed.

Abstract Submission No. 100303
P-0031

On Drug-Induced Liver Injury

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Background: Drug-induced liver injury (DILI) encompasses a range of pathophysiologies. In Japan, the 2004 Japanese Gastroenterological Association score (Japan score) is widely utilized for diagnosis. However, this score does not account for recent Immune Checkpoint Inhibitors (ICIs). Cases of DILI are classified into hepatocellular, cholestatic, or mixed types based on ALT and ALP values. Our study aimed to review the characteristics of our DILI patients.

Patients & Methods: We retrospectively analyzed 34 DILI patients admitted from 2013 to 2022, which included three cases of ICI-related injuries.

Results: Out of the 34 patients, 13 were males and 21 were females. The average $\pm$ standard deviation for age was 69.1 ± 17.3 years. ALT and ALP levels were 546.9 ± 554.6 and 1306.2 ± 1643.2 , respectively. By type, 16 were hepatocellular, 15 were cholestatic, and 2 were mixed. Among 24 cases subjected to the Drug Lymphocyte Stimulation Test (DLST), 18 tested positive. Scores were notably higher in DLST-positive cases but were lower in ICI-related cases. Distinct groups emerged based on ALT levels for hepatocellular and ALP levels for cholestatic cases.

Discussion: Despite potential false negatives, the DLST remains a valuable diagnostic tool. While the Japan score proves effective for traditional DILI cases, it falls short for ICI-related cases. Both hepatocellular and cholestatic types can be distinctly differentiated through ALT and ALP values, suggesting distinct pathophysiologies for each type.

Conclusion: The Japan score is not optimal for diagnosing ICI-induced DILI. The differentiation between hepatocellular and cholestatic types points to distinct underlying pathophysiologies.

Abstract Submission No. 100567
P-0032

ONE TAKE WONDER: A CASE OF CELECOXIB INDUCED ACUTE LIVER INJURY

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INTRODUCTION: Celecoxib, is a widely prescribed drug for symptomatic pain control. Data regarding its potential to cause deleterious hepatotoxicity is limited.

CASE PRESENTATION: This case report presents a 42 years old man who developed jaundice less than 24 hours after intake of 1 tablet of Celecoxib (200mg) for a tooth extraction. He did not have signs of hepatic encephalopathy, fever nor rash. There was no previous drug allergy nor alcohol intake. Laboratory workup showed elevated serum transaminases, alkaline phosphatase and hyperbilirubinemia with R factor of 9. His Prothrombin time later on progressively dropped. Serologic tests for Hepatitis A, B & C were non-reactive. ANA, anti-SMA, Serum Immunoglobulin G, AMA, and p-ANCA were all negative. Imaging tests of the liver including Triphasic CT scan & MRCP showed no evidence of biliary obstruction. His cholestasis and course of liver disease were prolonged, and ultimately he underwent liver biopsy which showed portal and lobular inflammation and hepatocanicular cholestasis favoring drug-induced liver injury. Celecoxib was

withdrawn, Ursodeoxycholic acid and antihistamines were started to address his persistent pruritus. His liver biochemical and function tests gradually improved with symptom resolution after 4 months.

CONCLUSION: Conventional non-steroidal anti-inflammatory drugs like celecoxib may still be associated with significant hepatotoxicity. Prompt discontinuation of the drug is necessary.

Abstract Submission No. 100762
P-0033

Drug-induced liver injury secondary to Rivaroxaban masquerading in Acute Cholangitis & Pancreatitis

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Introduction: Rivaroxaban, a newer anticoagulant, is increasingly being used, with a paucity of data on systemic side-effects. In this case, we present a rare case of rivaroxaban induced DILI which initially masqueraded as acute cholangitis and pancreatitis

Clinical Case: A 76-year-old lady with a history of ischemic heart disease and atrial fibrillation presented with abdominal pain, bloating and jaundice. Liver panel on admission showed total bilirubin 138.9, direct bilirubin 113.9, ALT 343 AST 589 ALP 402 GGT 389, pancreatic amylase 192 and lipase 168. She was screened for viral hepatitis (A/B/C/E/CMV/EBV-all negative) and underwent a cross-sectional imaging with CT Abdomen-Pelvis, which showed dilated common bile duct (CBD) with intra-ductal densities. She later underwent ERCP with extraction of CBD stones. (Table 1)

However, on follow up liver panel remained deranged with worsening of transaminases whereas bilirubin showed improvement (Table 1). Differentials include autoimmune hepatitis or DILI. Liver autoimmune workup were negative, thus patient underwent liver biopsy. Three potential drugs were considered: Amlodipine, atorvastatin and Rivaroxaban (Table 2) Review of drug history revealed that rivaroxaban was recently started and held off for ERCP. Liver biopsy (Figure 1) showed hepatocellular injury lobular inflammation, hepatocyte drop-out and apoptotic hepatocytes involving Zones 3 and 2 lobular parenchyma, in keeping with clinical impression of DILI with rivaroxaban having both highest RUCAM and likelihood score (Table 2) This is further confirmed by improvement of transaminases upon cessation of rivaroxaban

Clinical Significance: Rivaroxaban is a potential cause for DILI that physicians should be aware of.

Abstract Submission No. 101252
P-0034

Secondary Sclerosing Cholangitis Following Pola-r-CHP Therapy

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Background: Polatuzumab is an anti-CD79b antibody currently used in the treatment of diffuse large B-cell lymphoma (DLBCL) in conjunction with rituximab, cyclophosphamide, doxorubicin, and prednisolone (P-r-CHP).

Case: A 48-year-old female patient was referred due to liver dysfunction (ALP 1386 U/L, AST 375 U/L, ALT 376 U/L, GGT 806 U/L, LD 241 U/L). The patient had been diagnosed with DLBCL four months earlier and had undergone five courses of P-r-CHP therapy. During the initial stages of chemotherapy, liver enzymes became elevated.

Magnetic resonance cholangiopancreatography (MRCP) conducted after two courses of chemotherapy indicated mild narrowing and dilatation of the intrahepatic bile duct (IHBD). Fortunately, these abnormalities improved following chemotherapy.

Liver biopsy at the time of referral revealed moderate periportal inflammation and fibrosis. After administering Ursodeoxycholic acid, liver function tests improved for three months but worsened thereafter (T-Bil 3.69 mg/dL, ALT 915 U/L, AST 155 U/L, ALT 213 U/L, GGT 2038 U/L). A subsequent liver biopsy showed fibrotic expansion and ductular reaction in the portal area. A follow-up MRCP revealed irregular intrahepatic bile ducts with multiple strictures and dilatations, more pronounced than earlier findings. We diagnosed this case as secondary sclerosing cholangitis (SCC). Eventually, the liver function began to improve without additional therapy.

Discussion: This case marks the first instance of SCC following P-r-CHP therapy. Considering the absence of reported SCC induced by R-CHOP therapy, it was highly probable that Polatuzumab was the causative factor.

Conclusion: In cases of liver dysfunction after P-r-CHP therapy, it is necessary to consider the possibility of SSC.

Abstract Submission No. 101381
P-0035

AST/ALT elevation during systemic therapy for HCC and other cancers in the era of immunotherapy

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Objective: After the approval of immune checkpoint inhibitors (ICIs), the management and differentiation of immune-related adverse events (irAEs) and other causes of liver injury have become more important for systemic therapy of hepatocellular carcinoma (HCC). We investigated the characteristics of AST/ALT elevations observed during immunotherapy for HCC, and other cancers.

Methods: In the multicenter cohort with advanced HCC (cohort1), 165 patients received atezolizumab plus bevacizumab between October 2020 and September 2021, and in the single center cohort with other cancers, 646 patients (cohort2) received anti-PD-1/PD-L1 antibody, and 53 patients (cohort3) received anti-PD-1 plus anti-CTLA-4 antibody between October 2014 and September 2021 were included in the analysis. Data on AST/ALT elevation were collected retrospectively, and the causes and risks of AST/ALT elevation were analyzed.

Results: The incidence of grade 2 or higher AST/ALT elevation was 13.3% (22/165) in cohort 1, 8.5% (55/646) in cohort 2, and 20.8% (11/53) in cohort 3. Among patients with grade 2 or higher AST/ALT elevations, irAE was diagnosed in 13.5% (3/22) in cohort 1, 34.5% (19/55) in cohort 2 and 63.6% (7/11) in cohort 3. Although AST/ALT elevations were common in cohort 1, only 3 cases were diagnosed as irAE, and only 1 case required corticosteroids. Grade 2 or higher AST/ALT elevations were more common in patients with large intrahepatic tumor volume, suggesting that the cause may be tumor-related.

Conclusions: The differentiation of intrahepatic tumor-related AST/ALT elevations is important for the diagnosis of irAE hepatitis, especially in HCC patients.

Abstract Submission No. 101618
P-0036

Angiotensin Receptor Blockers and Drug-Induced Liver Injury: A Cohort Study Using Common Data Model

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Angiotensin receptor blockers (ARBs) are one of the most commonly used anti-hypertensives in South Korea. In 2021, a need for national compensation was acknowledged by the Korea Ministry of Food and Drug Safety for a drug-induced liver injury (DILI) after azilsartan use, the youngest drug among ARBs. Not much has been known about the association between ARBs and DILI. To further investigate ARB-induced liver injuries, we executed a retrospective new-user cohort study using electronic-healthcare data-based common data model database (2017–2021). In this study, patients were designated to treatment groups according to the ARB prescribed at cohort entry, i.e., azilsartan, eprosartan, telmisartan, fimasartan, valsartan, olmesartan, losartan, irbesartan, or candesartan. DILI was operationally defined by adapting the definition from the International DILI Expert Working Group. We conducted cox regression analyses to derive hazard ratios (HRs) and applied propensity score-based inverse probability of treatment weighting. As a result, a total of 229,881 ARB users from 20 university hospitals were included. The crude incidence of DILI ranged from 15.6 to 82.8 by treatment groups. In all treatment groups, the most common type of DILI was the cholestatic type and the majority were of mild severity. In overall, the risk was significantly lower in olmesartan users compared to valsartan users (HR: 0.73 [95% confidence interval (CI): 0.55-0.96]). In patients receiving monotherapy, the risk was significantly higher in azilsartan users compared to valsartan users (HR: 6.55 [95% CI: 5.28-8.12]).

Abstract Submission No. 200231
P-0037

Dapsone Syndrome Relapse: Unraveling a Complex Case

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Background: Dapsone syndrome is a rare hypersensitivity reaction marked by symptoms like high fever, maculopapular rashes, hepatitis, lymphadenopathy, and lymphocytosis. Typically, these manifestations occur within the initial 6 weeks of treatment. A reported case involves an individual with borderline tuberculoid leprosy who experienced a relapse of this syndrome.

Clinical significance: A relapsing course of Dapsone syndrome is rare and must be identified early for proper management.

Case Report: A 45-year-old female diagnosed with Boderline Tuberculoid Leprosy was started on combination of antibiotics containing Dapsone who developed fever along with maculopapular rashes all over her body on her 25th day of treatment. Laboratory investigations revealed lymphocytosis with abnormal liver function.

She was diagnosed with Dapsone syndrome and her Anti-leprotic therapy were stopped and was started on steroids and other supportive measures. Her liver enzymes showed a declining trend and rashes subsided and steroids was stopped. However, after 2 weeks she experienced a recurrence of the same widespread rashes along with deranged liver function. The patient was again treated with intravenous steroids along with other supportive measures. Rashes and swelling subsided within 4 days of starting high-dose steroids along with gradual

improvement in biochemical parameters. She was free of hepatic, dermatological and other parameters in next 4 weeks.

Conclusion: Dapsone stands as the primary treatment choice for all types of leprosy, generally well tolerated by patients. Within the spectrum of rare hypersensitivity reactions, Dapsone syndrome emerges. In the mentioned case, the recurrence of dapsone syndrome was observed, and was treated accordingly.

Abstract Submission No. 100056
P-0038

The risk of hepatocellular carcinoma in chronic hepatitis B patients with low-level viremia

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Background: The past research results show that patients with chronic hepatitis B patients (CHB) who maintain serum HBV-DNA <2,000 IU/mL of low-level viremia (LLV) are not at low risk of developing hepatocellular carcinoma (HCC). The aim of this study was to investigate the risk and risk factors of HCC in CHB with LLV.

Methods: This retrospective cohort study includes patients with chronic hepatitis B who received antiviral therapy for more than 12 months at three medical institutions including Chi Mei Medical Center in southern Taiwan, from 2008 to 2020, and patients will be divided into LLV group, maintained virological response (MVR) group comparison. The cumulative incidence of progression to HCC has been assessed using the Kaplan-Meier method. Cox regression analysis is performed to determine the final risk and prognostic factors.

Results: During the follow-up period, the 3, 5, and 10-year cumulative HCC risks in the LLV group were 3.56%, 4.96%, and 9.51%, respectively; in the MVR group, they were 3.64%, 4.98%, and 10.54%, respectively (p-value: 0.970). Independent risk factors for HCC in LLV patients identified by multivariate Cox regression analysis were male (adjusted hazard ratio [aHR]: 1.78, 95% CI: 1.04-3.04; P=0.036), age (aHR: 1.05, 95% CI: 1.03-1.07; P<0.001), presence of cirrhosis (aHR: 2.01, 95% CI: 1.17-3.45; P=0.012) and platelets (aHR: 2.19, 95% CI: 1.26-3.79; P=0.005).

Conclusion: This study determined Important critical factors in the development of HCC in LLV patients. The risk of HCC in patients with LLV status during follow-up was comparable to that in the MVR group.

Abstract Submission No. 100068
P-0039

Macrophage-derived exosomal miRNA-30a-5p transmit interferon antiviral activity via PI3K-AKT axis

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Background: Previous reports revealed that IFN- α -induced macrophage-derived exosomes were rich in antiviral molecules. MicroRNA-30a-5p has been shown to act as a cancer suppressing gene in variety of cancers. However, the specific role of miRNA-30a-5p in hepatocellular carcinoma and the underlying mechanism remains unclear.

Method: Huh7 cell transiently transfected with HBV C2 subgenotype plasmid was co-cultured with IFN- α -induced macrophage-derived exosomes or miRNA-30a-5p mimics, respectively. Elisa assay was used to test the HBsAg level. qRT-PCR was used to detect the expression of miR-30a-5p. Scratch assay was performed to determine migration of HCC cells. Western blot was used to detect the PI3K/AKT signaling pathway-related proteins.

Results: Huh7-HBV/C2 cells co-cultured with IFN- α -induced macrophage-derived exosomes or miRNA-30a-5p mimics was significantly increased with miRNA-30a-5p expression and down-regulated with HBsAg level. The migration ability of Huh7-HBV/C2 cells was significantly increased and the PI3K-AKT pathway was activated comparing with Huh7 cell. However, the migration ability and activation of PI3K-AKT pathway can be inhibited by IFN- α -induced macrophage-derived exosomes and miRNA-30a-5p mimics.

Conclusion: Exosomes can transfer IFN- α -induced miRNA-30a-5p from macrophages to HBV-infected hepatocytes to against HBV replication and inhibit HBV-infected hepatocytes migration via PI3K-AKT signaling axis

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Abstract Submission No. 100195
P-0040

TREATMENT OF TENOFOVIR ALAFENAMIDE IN THE CHB

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Introduction: WHO estimates that 296 million people were living with chronic hepatitis B infection in 2019, with 1.5 million new infections each year. The latest data shows that 10.6-11.6 % of Mongolian population are infected with hepatitis B virus infection.

Goal: Evaluate the clinical and virological outcome of tenofovir alafenamide treatment in patients with hepatitis B infection.

Materials and Methods: The clinical trials have evaluated TAF in HBeAg positive and HBeAg negative HBV patients. The trials have similar design and randomized, Single-blind, the subjects are unaware of which group they have been assigned to studies. The primary efficacy endpoint was the proportion of patients with HBV-DNA <29 IU/ml at weeks 96. Other virological result endpoints were the proportion of patients with HBsAg seroconversion at weeks 96.

Results: The virologic endpoints, an HBV-DNA < 29 IU/ml at weeks 96, was achieved by 243(79.1%) receiving TAF, 111(75.4)% of patients which were non-inferior to the 106(78.5%) patients receiving TDF (95% confidence interval (CI) 9.7-2.5); p = 0.26. After of treatment at week 96, significant higher rates of ALT normalization was seen in the TAF group compared to the TDF group (209(68%) "vs" 83(56.4%) "vs" 82(60.8%), p = 0.001) **Result:** At 96 weeks of treatment, patients receiving TAF had significantly smaller reductions in

bone mineral density(BMD) compared with patients receiving TDF. At weeks 96, median changes in eGFR were significantly smaller in the TAF recipients compared with the TDF recipients.

Conclusion: TAF and switching from TDF to TAF are similar efficacy and safety in long-term treatment of TDF.

Key words: HBV-DNA, qHBsAg, HBeAg, tenofovir alafenamid fumarate, tenofovir disoproxil fumarate

Abstract Submission No. 100314

P-0041

Hepatitis B vaccination post serological testing and antibody levels of vaccinated HCWs in Mongolia

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Background: In 2012, Ministry of Health and Sports made a decision to vaccinate healthcare workers for 2 doses of hepatitis B vaccine and aimed to increase the immunization coverage. We aimed to assess immunity against HBV among vaccinated HCWs in Mongolia.

Methods: A cross-sectional study involving 1082 HCWs, Blood samples from the subjects were analyzed for HBsAg, anti-HBs, and anti-HBc for HBV serology using ELISA.

Results: There are 32.4% (351/1082) were post vaccination immunity, 56.4% (611/1082) had post infection immunity. 90.3 percent of people with post-infection immunity were born before Universal Hepatitis B immunization (since 1992) and it is statistically significant high. In terms of age of participants with post-infection immunity, 31.4% were in 40-49 years old, and 22.9% in over 50 years old, which is statistically higher than post-vaccination immunity in this age group. Of those surveyed full dose vaccinated and born after 1992, 32.2% had post-infection immunity and 51.9% had post-vaccine immunity. The mean anti-HBs titers was 295.50 IU/ml [81.58-949.34 IU/ml].

Conclusions: The study revealed that majority of the HCWs had post-infection immunity. HBV vaccines should be administered after testing HBsAg, anti-HBs, and anti-HBc parameters.

Abstract Submission No. 100324

P-0042

Assessment of KAP towards Hepatitis B infection and vaccination status among HCWs in Mongolia

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Background: Hepatitis B virus (HBV) infection can be prevented by vaccination. Exposure to blood or body fluids poses a high risk of transmission of HBV in health care workers (HCWs). We aimed to

determine knowledge, attitude, and practices regarding HBV prevention compared to vaccination coverage among HCWs.

Methods: It was cross-sectional, multi-stage sampling study, conducted 1135 HCWs from 36 healthcare facilities in two urban and four rural provinces of Mongolia. Participants who consented to the study completed a standardized self-administered questionnaire between July 2020 and Dec 2022.

Results: 47.4% of the participants had a full three doses of HBV vaccine. The rate of the correct answer and vaccination doses are related, where the correct answers (3 - 5) were higher in the group of participants who had a full dose of the vaccines. No correct response rate was higher, mainly among the participants who were not vaccinated, one dose, and already infected groups. 71.9% of those assessed as having a high risk were fully vaccinated against HBV. A significant difference was observed between age groups ($\chi^2=12.57$, $p<0.001$), perception of HBV infection ($\chi^2=8.14$, $p=0.004$), formal attendance to the official training ($\chi^2=28.28$, $p<0.0001$). 1.02 - 1.99 times higher tend to receive all three full doses HBV vaccine than the rest of the group.

Conclusion: The low level of vaccination coverage is relevant to the level of KAP among the HCWs of the country, therefore, intensive campaigns should be conducted with a focus on the particular issue.

Abstract Submission No. 100403

P-0043

PreS1BP Mediates Inhibition of Hepatitis B Virus Replication by Promoting HBx Protein Degradation

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Background: PreS1-binding protein (PreS1BP), recognized as a nuclear protein and tumor suppressor, influences the replication of various viruses, including vesicular stomatitis virus (VSV) and herpes simplex virus type 1 (HSV-1). Its role in HBV replication and the underlying mechanisms, however, remain elusive.

Methods: We investigated PreS1BP expression levels in an HBV-replicating cell and animal model and analyzed the impact of its overexpression on viral replication metrics. HBV DNA, cccDNA, HBsAg, HBcAg, and HBV RNA levels were assessed in HBV-expressing stable cell lines under varying PreS1BP conditions. Furthermore, co-immunoprecipitation and ubiquitination assays were used to detect PreS1BP-HBx interactions and HBx stability modulated by PreS1BP.

Results: Our study revealed a marked decrease in PreS1BP expression in the presence of active HBV replication. Functional assays showed that PreS1BP overexpression significantly inhibited HBV DNA, cccDNA, HBsAg, HBcAg, and HBV RNA levels. At the molecular level, PreS1BP facilitated HBx degradation in a dose-dependent fashion, whereas siRNA-mediated knockdown of PreS1BP led to an increase in HBx levels. Subsequent investigations uncovered that PreS1BP accelerated HBx degradation via K63-linked ubiquitination in a ubiquitin-proteasome manner. Co-immunoprecipitation assays further established that PreS1BP enhances the recruitment of the proteasome 20S subunit alpha 3 (PSMA3) for interaction with HBx, thereby fostering its degradation.

Conclusions: These findings unveil a unidentified mechanism wherein PreS1BP mediates HBx protein degradation through the

ubiquitin-proteasome system, consequentially inhibiting HBV replication. This insight positions PreS1BP as a promising therapeutic target for future HBV interventions. Further studies are warranted to explore the clinical applicability of modulating PreS1BP in HBV therapy.

Abstract Submission No. 100431

P-0044

Alteration of gene expression after anti-viral therapy in HBV infected chimeric mouse liver

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Background: Analyzing the impact of hepatitis B virus (HBV) infection on intracellular gene expressions using human liver tissues is difficult to exclude the influence of host immune response. In this study, we analyzed changes in gene expression by using HBV-infected humanized mouse livers under severe immune-suppressive condition.

Methods: Eleven mice carrying human hepatocytes in their livers (PXB mice, PhoenixBio Co., Japan) were prepared. Five mice were sacrificed without HBV infection, as control. The remained 6 mice were inoculated HBV-contained serum. Three of 6 HBV-infected mice were sacrificed after HBV DNA levels reached a plateau. The remaining three HBV-infected mice were sacrificed after HBV DNA levels declined to undetectable levels following antiviral therapy with entecavir and PEG-interferon. Next-generation sequencing (NGS) was performed using human hepatocytes obtained from these 11 mice.

Results: The expression of genes involved in the gonadotropin-releasing hormone receptor pathway, CCKR signaling, integrin signaling, inflammatory pathway, and T cell activation was significantly altered in the liver after HBV infection. After antiviral therapy, the levels of 37 of 89 genes decreased by HBV infection were restored, and the levels of 54 of 157 genes increased by HBV infection were suppressed. Interestingly, among the 54 genes whose expression was increased by HBV infection and decreased by antiviral therapy were genes associated with hypoxia and KRAS signaling.

Conclusions: Several genes associated with cell proliferation and carcinogenesis via hypoxia and KRAS signaling were significantly down-regulated by antiviral therapy, suggesting their potential application in the suppression of liver carcinogenesis.

Abstract Submission No. 100740

P-0045

sCD146, A Novel Serum Biomarker for HBV-Related Liver Fibrosis Progression

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Background: sCD146 is believed to be associated with liver cirrhosis. However, the association between sCD146 and liver fibrosis progression in HBV-infected patients remains under-researched.

Methods: The study used Western Blot to assess sCD146 in serum of healthy individuals and HBV-infected patients from Beijing Ditan Hospital, comparing expression levels across healthy, CHB, CHB with fibrosis, and cirrhotic subjects, followed by validation through gel electrophoresis analysis.

Results: we detected 240 serum samples utilizing Western Blot, comprising healthy individuals (21.67%), and patients with CHB (40.00%), CHB with fibrosis (11.67%), CHB with cirrhosis (26.67%). In our analysis (figure 1), compared to the control, there was no variation in the CHB group. Differences were noted between the CHB and the CHB with fibrosis groups, but they lacked statistical significance ($P=0.082$). A marked difference was observed in the CHB with cirrhosis group compared to the other categories ($P<0.050$), indicating that sCD146 levels elevate in correlation with the increasing severity of fibrosis. To further confirm the molecule detected was sCD146 rather than the membrane receptor-type CD146, we conducted gel electrophoresis analysis, revealing only the extracellular region of CD146, excluding the transmembrane and intracellular segments. Moreover, the relative quantitative value in the CHB with cirrhosis group was higher than that in the control group, which validated our hypothesis regarding sCD146 and was consistent with Western Blot findings.

Conclusion: we discovered sCD146 levels in the serum exhibited an ascending trend with the progression of fibrosis in HBV-infected patients by Western Blot. Furthermore, it confirmed that the molecule detected by this method is sCD146.

Abstract Submission No. 101150

P-0046

A novel inducible uPA transgenic mouse for human liver chimeric model establishment

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Human hepatocyte chimeric liver mouse models are valuable in studies on hepatitis viruses, liver-targeted drug development as well as drug metabolism and toxicology. This kind of models, such as uPA-SCID, FRG and TK-NOG, are generally difficult to breed and manipulate and are expensive. We report a new mouse model, URG, which is engineered to overexpress uPA specifically in liver under Tet-On system regulation, and to be Rag2 and Il2rg gene knockout so that allows human hepatocyte engraftment. The URG mice are healthy and normal in breeding. When inducing with Dox, liver injury occurs in the mice, as indicated by the elevated ALT/AST and pale appearance of the livers. Transplanting 1 million primary human hepatocytes into Dox-induced URG mice achieved a high chimeric rate of liver, with up to 9mg/mL of human albumin in serum, and 80% human CK-18 antibody positive stain area in liver sections. With continuous Dox inducing, the human albumin concentration in the mouse serum peaked at around 6 weeks post transplantation and sustained for at least 6 months. Some functional proteins specifically secreted by human hepatocytes, such as ApoCIII, Apo(a), PCSK9, Angptl3, C1INH etc., which are hot targets for new drug development, were also detected in the serum of models. When being inoculated with live HBV isolates obtained from either clinic or supernatant of HBV expressing cell cultures, a high virus titer close to that of hepatitis B patients could be detected. Therefore, URG is an useful mouse strain to establish humanized liver models.

Abstract Submission No. 101215

P-0047

Characteristic Changes in the Oral Cavity in Particular the Periodontium with HBV

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Background: Interest in the study of combined pathology in recent years is due to the accumulation of new facts, the emergence of new information about the interorgan, intertissue and intercellular levels of interaction in the system of the whole organism. In this regard, the question of the relationship between diseases of internal organs, in particular liver damage of viral etiology (HBV) and oral cavity organs, is relevant.

The aim of the study was to study the condition of the periodontium during HBV.

Material and methods: To study the periodontium, 95 patients with HBV were examined: 24 (25.3%) women and 71 (74.7%) men. The average age of the patients was 40.17±13.48. The control group included 100 people without HBV, 38 (38%) women and 62 (62%) men, the average age of patients was 37.99±16.66. The dental status of patients with HBV was assessed and compared with the control group.

Results: The detection rate of periodontal diseases in the HBV patients we examined was 100%. An objective examination of the oral cavity revealed a number of pathological changes in the gums: hyperemia and swelling - in 66.3% (63) cases ($p < 0.001$) compared to the control, cyanosis - 31.6% (30) cases ($p > 0.308$), atrophy - 38.9% (37) and bleeding gums 74.7% (71) ($p < 0.001$) compared with control. Gingival desquamation in 4.2% (4) of HBV ($p > 0.0545$).

Conclusion: Thus, the analysis shows that with HBV, gum disease resembles the clinical picture of inflammatory periodontal diseases, in particular, catarrhal and hypertrophic gingivitis, as well as chronic generalized periodontitis.

Abstract Submission No. 101680

P-0048

Oral combination vaccine against Anthrax & Hepatitis B: development & characterization

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Infections are still leading cause of morbidity & mortality & most of which can be prevented by vaccination. However, there are too many vaccines to be administered, increasing cost of immunization. Combination vaccines can answer these problems by development of single vaccine containing all possible antigens.

The goal of present study was to see the effect of 2 antigens when given in combination. Bilosomes can provide needle free, painless approach for immunization. Recombinant hepatitis-B surface antigen(HBsAg) & recombinant protective antigen(rPA) were candidate antigens. Bilosomes containing rPA & HBsAg were prepared by lipid cast film method. Antigen loaded bilosomes were characterized *in-vitro* for shape, size, antigen entrapment & stability in various body fluids. Fluorescence microscopy was done to confirm the uptake of bilosomes. The *in-vivo* study comprised of immunization of Balb/c mice & estimation of IgG response in serum & sIgA in various body secretions using specific ELISA.

Bilosomes formed were multilamellar & stable in gastric & intestinal fluids. Fluorescence microscopy suggested that bilosomes were taken up by gut associated lymphoid tissues. *In-vivo* data demonstrates that combination produced both systemic as well as mucosal antibody responses upon oral administration at higher dose levels as compared to intramuscular immunization but fail to produce any synergistic effect. When rPA & HBsAg given in combination, HBsAg(high dose) potentiates the production of anti-rPA antibody. Also they elicited measurable sIgA in mucosal secretions, while alum adsorbed antigens failed to elicit such responses.

Abstract Submission No. 101681

P-0049

Antibody coated Liposomes for Transmucosal vaccination

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The critical role of vaccine delivery system in "rational vaccine design" has been widely recognized. Thus research work was envisaged involving development of antibody coated liposome for transmucosal immunization against hepatitis-B which may offer increased uptake of nanoliposome through transmucosal surface of nasal route & sustaining release of HBsAg to evoke relatively high IgA titre in mucosal surface.

Liposomes were prepared by lipid cast film method & then IgG antibody was cross linked on the surface. Coated liposomes were characterized *in-vitro* for their shape, size, % antigen entrapment & stability. Fluorescence microscopy was performed to confirm deposition pattern in respiratory tract. The *in-vivo* part of the study comprised of estimation of IgG response in serum & sIgA in various body secretions using specific ELISA.

Observation of fluorescence images of nasal mucosa, lungs & spleen, revealed that these antibody coated liposome, were significantly taken up by mice respiratory mucosal surface, which made them promising carriers for mucosal vaccination.

Considerable immune responses were produced by developed system that may be due to induction of MALT as well as contribution of peripheral airways. Higher immunity induced by ACL HBsAg may be attributed to its cationic nature, antibody coating & subsequent mucoadhesive property. Thus mucosal immunization with lipid vesicle through nasal administration may be effective in prophylaxis of diseases transmitted through mucosal routes as well as systemic infections. The strategy can be made more appropriate by determination of paracellular transport, nasal mucociliary clearance, mucosal toxicity assessment etc.

Abstract Submission No. 101682

P-0050

Bipolymer based Novel Nanoparticles in Microsphere System as Vaccine Adjuvant

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Novel strategies are required for achievement of safe & effective immunization beyond conventional strategies. Frequent booster dosing can be avoided by development of mucosal/adjuvant vaccine delivery system, which can produce both humoral & cell-mediated responses. Work envisaged uses combined hydrophilic(gelatin nanoparticles,GN)

with a hydrophobic polymeric system (PLGA microspheres) which creates a biodegradable system for HBsAg delivery. GN & PLGA microspheres were prepared by double emulsification method & composite system by phase separation method. Composites were optimized & characterized *in-vitro* for their shape, size by Scanning & Transmission Electron Microscopy, %antigen entrapment & stability. *In-vivo* study comprised of estimation of IgG response in serum & sIgA in various body secretions along with Fluorescence microscopy. *In-vitro* studies exhibited an initial burst release from GN, degradation of antigen from PLGA microspheres & a continuous release from composite system. This supports hypothesis to formulate single shot vaccine with such system (to mimic booster dosing). Fluorescence studies showed selective uptake of composites by NALT. Humoral response generated by single dose of composites was comparative to marketed formulation receiving booster dose. Composite system generated effective sIgA antibody which was not elicited by marketed formulation. Thus, it could be concluded from present study that bipolymer based composite system are capable to provide sufficient protein stability & can be promising candidate for development of single shot vaccine, not only against Hepatitis but against all those diseases that invade host by mucosal surfaces.

Abstract Submission No. 101683
P-0051

Solid Lipid based Nanoparticulate system for effective vaccine delivery

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Search for innovative ways of vaccination has intensified recently with declining vaccine coverage & growing public concern about new virulent disease outbreaks. Work envisaged here explores potential of Solid Lipid Nanoparticles (SLN) in efficient protein delivery through surface modifications using subcutaneous route (SC).

SLN were prepared by Solvent Injection Method. Characterization was done by Electron Microscopy, X-Ray Diffraction Analysis, *In-vitro* release, Kinetics of uptake by flow cytometer, Evaluation of cell apoptosis, T-cell proliferative assay, TH1/TH2 cytokine profile & Internalization studies by spectral bioimaging. *In-vivo* study comprised fluorescence studies & estimation of IgG in serum, sIgA in various body secretions using specific ELISA.

Particulate system is better carrier system for immunization because of less diffusivity & restricted movement. SLNs act as signal for phagocytic cells. Surface modified SLNs can entrap greater amount of antigen, are sustained release & rapidly internalized by antigen presenting cells. *In-vitro* T-cell proliferation & induction of TH1 type of immune response clearly marks, potential of this novel carrier system. Fluorescence studies showed better uptake of modified SLNs. Higher & more sustained antibody titer obtained with modified SLNs suggests their better immunological potential. Thus, SC immunization could be an efficient alternative approach for vaccination against hepatitis. Formulations developed can be further explored for incorporation & delivery of other proteins & peptides should subsequently be subjected to pilot plant scale-up & clinical trial to establish their potential for SC immunization against hepatitis-B.

Abstract Submission No. 101722
P-0052

HBV Vaccination Status and Associated Factors among Healthcare Workers in Kampot and Kep, Cambodia

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Background: Healthcare Workers (HCWs) are at risk of acquiring hepatitis B virus (HBV) infection and are highly recommended to be vaccinated. There is no information about vaccination coverage among HCWs in Cambodia. This study aimed to evaluate vaccination status among HCWs in Cambodia and to identify its associated factors.

Methods: A Cross-sectional study was conducted among HCWs in Kampot and Kep provinces from September to October 2023 using the questionnaire survey. Participants were recruited from 1,309 HCWs in 83 health facilities using systematic random sampling. Vaccination status was described in percentage, and multivariate logistic regression was performed to identify the factors associated with HBV vaccination status.

Results: A total of 259 participants were included in the study. Knowledge of HBV infection and HBV vaccine was 62.9% and 65.6%, respectively. About 60% received the HBV vaccine, of those, 128 (82.6%) received ≥ 3 doses. HCWs with higher education are more likely to be vaccinated than those with primary degrees [$p=0.0067$; OR=3.4; CI=1.4-8.3]. Having good knowledge of HBV infection and HBV vaccine is more likely to receive vaccine compared to those who have inadequate knowledge [$p<0.0001$; OR=8.1; CI=3.9-16.8; $p=0.0001$; OR=4.4; CI=2.1-9.2], respectively.

Conclusion: The vaccination coverage among HCWs is low (60%) compared to Vietnam (83%), Thailand (68%), and Japan (84%). This study found that knowledge of HBV infection and HBV vaccine are good factors associated with vaccination status. Providing education on HBV infection and HBV vaccine to HCWs is needed. Additionally, HBV vaccine could be mandatory for HCWs.

Abstract Submission No. 101823
P-0053

HBV genetic structure in some minority groups in Ha Giang province, Vietnam

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Introduction: The HBV genetic structure is considered one of the drivers to develop chronic infection. HBV genotypes are associated with the level of viral load, the severity of liver damage and the risk of developing hepatocellular carcinoma. The aim of this study was to investigate the genotypic heterogeneity of the HBV population circulating in Hmong living in three districts of Yen Minh, Bac Me, Dong Van of Ha Giang Province, Vietnam.

Materials and methods: Totally, the complete genome of 20 HBV isolates obtained from HBsAg-positive individuals belonging to the

Hmong ethnic group living in Ha Giang province, Vietnam, were amplified using overlapping PCR fragments followed by Sanger sequencing. Analysis of nucleotide sequences was carried out using the Mega program version 10.0. and SimPlot version 3.5.1. Phylogenetic analysis performed using the Maximum-Likelihood method.

Results: Based on phylogenetic analysis of the complete genome, seven HBV isolates belonged to rare C8 subgenotype, eight to the C2 subgenotype and five to the B2 subgenotype which are widespread in Vietnam. SimPlot analyses revealed that all five subgenotype B2 isolates had the recombination part belonged to C genotype in the pre-core/core region of the genome.

Conclusion: The genetic structure of the HBV circulating among the Hmong in the Ha Giang province differs from the HBV populations in megacities and agricultural provinces of Vietnam. Molecular genetic studies of regional HBV populations will contribute to effective surveillance of HBV infection and will be useful for predicting the development of the epidemic process in various regions of Vietnam.

Abstract Submission No. 200247

P-0054

Investigating Feasibility and Strategy for Controlling HBV Transmission in Indonesia by Math Model

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In Indonesia, Hepatitis B virus (HBV) infection remains a substantial public health challenge that demands immediate interventions to mitigate its impact. The World Health Organization (WHO) has set an ambitious goal of achieving a prevalence of only 0.1% of HBV surface antigen (HBsAg) among Indonesian children by 2030, with the aim of eradicating viral hepatitis as a significant public health threat. Despite commendable progress in hepatitis B control, uncertainties persist regarding the feasibility of attaining this target and the necessary strategies in Indonesia. This study endeavors to assess the feasibility of reaching the WHO's 0.1% HBsAg prevalence target among Indonesian children by 2030 and pinpoint critical developments required to meet this goal. Employing a dynamic compartmental model that considers both age and time variables, the study captures the intricate dynamics of Hepatitis B virus (HBV) infection, offering insight into the current state of hepatitis B control in Indonesia. The model relies on data and input parameters, likely encompassing historical HBV prevalence rates, vaccination coverage, treatment efficacy, and other pertinent epidemiological and healthcare-related factors specific to Indonesia. Encouragingly, positive trends emerge as HBsAg prevalence steadily decreases across age groups, indicating progress in reducing Hepatitis B infection. Indonesia is projected to be on track to achieve the WHO's 0.1% HBsAg prevalence target for children under 5 by 2037. The integration of peripartum antiviral prophylaxis (PAP) with existing strategies significantly reduces child HBsAg prevalence, expediting progress with elevated success rates.

Abstract Submission No. 100051

P-0055

Long-term hepatitis B surface antigen profile and seroclearance following antiviral treatment

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Aim: Hepatitis B surface antigen (HBsAg) seroclearance, an indicator of recovery from hepatitis B virus (HBV) infection, is uncommon in long-term nucleos(t)ide analog (NUC) therapy. We compared the incidence of HBsAg seroclearance in patients with and without NUC discontinuation to identify predictors of HBsAg seroclearance.

Methods: This retrospective study enrolled adult patients with chronic HBV infection followed for ≥ 12 months after NUC discontinuation (finite group) and those treated with NUCs for >3 years (non-finite group). Demographic, clinical, and laboratory data were analyzed.

Results: The study cohort included 978 patients, including 509 and 469 patients in the finite and non-finite groups, respectively. Cumulative HBsAg seroclearance incidence was significantly higher in the finite group than in the non-finite group ($p = .006$). The 5- and 10-year cumulative HBsAg seroclearance incidence were 6.6% and 18.9% in the finite group and 3% and 14.6%, in the non-finite group, respectively. The likelihood of HBsAg seroclearance was higher in those with end of treatment (EOT) HBsAg levels of <100 IU/mL and in those without clinical relapse (CR). The cumulative 3-year CR incidence was 16.8%. The incidence of liver decompensation and hepatocellular carcinoma were 4.1 and 0.4 per 1000 person-years, respectively. The hepatocellular carcinoma incidence did not significant differ between the finite and non-finite groups ($p = .941$).

Conclusions: The higher HBsAg seroclearance incidence in patients receiving finite therapy, and the increased likelihood of HBsAg seroclearance in those with EOT HBsAg levels of <100 IU/mL and in those without CR should be considered during decision-making of treatment options.

Abstract Submission No. 100067

P-0056

A comparative trial of metabolic parameters in chronic hepatitis B who were treated with TDF or TAF.

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Background: Tenofovir alafenamide (TAF) is more widespread use than Tenofovir disoproxil fumarate (TDF) due to lower nephrotoxicity and bone loss. However, TAF is still controversy in poor metabolic outcomes compared to TDF. Aim of the study is to evaluate the effect of TAF and TDF on metabolic parameters and Atherosclerotic cardiovascular disease (ASCVD) risk in chronic hepatitis B (CHB) patients.

Methods: A total of ninety CHB patients treated with TDF were enrolled in the study. We randomized to switching to TAF (TAF group, n=46) and continue TDF (TDF group, n=44). Metabolic profiles were assessed at 24-week and 48-week intervals through biochemical test and bioelectrical impedance analysis. The primary outcome was comparing metabolic profile changes from baseline between 2 groups at 48 weeks.

Results: The mean age of the patients was 59.4 ± 8.2 years, with a male predominance of 63% and mean BMI was 23.5 ± 4.1 kg/m². The baseline characteristics including body mass index (BMI), fasting blood sugar (FBS), total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), glycated hemoglobin (HbA_{1c}) were similar between both groups. At week 24, the TAF group were significantly higher

compared to the TDF group in TC, FBS, and HbA_{1c}. The percent changes in waist circumference and BMI in TAF group were also significantly greater than in TDF group. However, patients in TDF group showed significantly increase in creatinine and decline in GFR.

Conclusions: For preliminary result (week 24), CHB treated with TAF significantly increased in TC, HDL, FBS, HbA_{1c}, and BMI compared to those treated with TDF.

Abstract Submission No. 100072
P-0057

Effectiveness and safety of TAF in patients with first-time HBV-related decompensated cirrhosis

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AIM: To evaluate the effectiveness as well as renal and lipid profiles of tenofovir alafenamide (TAF) in patients with first-time hepatitis B virus-related decompensated cirrhosis (HBV-DC).

METHODS: In this retrospective analysis, treatment-naïve patients with first-time HBV-DC who were treated with TAF from January 1, 2020 to December 31, 2022 were screened. We evaluated the virological and serological responses, hepatic and renal function, serum phosphorus and blood lipid changes during 48 weeks of treatment.

RESULTS: The final analysis included 52 patients. Mean age was 46 years and 73.1% were male. Baseline median CTP score was 8.37. The proportions of patients achieving undetectable HBV DNA at week 12, 24 and 48 were 38.5%, 63.5% and 84.6%, respectively. The rate of alanine transaminase (ALT) normalization were 71.2%, 82.7% and 82.7%, respectively. Forty (76.9%) patients showed improvement in the CTP score of 2 points at week 48. There were no significant changes in estimated glomerular filtration rate (eGFR) from baseline to week 48. However, of the 10 patients with eGFR<90mL/min/1.73m² at baseline, the eGFR levels increased to over 90mL/min/1.73m² and maintained the level to week 48 in 3 patients. Serum phosphorus increased over time by a mean level of 0.08±0.16mmol/L at week 48 (t=3.392, p=0.001). For lipid profile, the levels of TG had no significant changes at each time point when compared to baseline. Low-density lipoprotein cholesterol (LDL-C) level increased by 0.51±0.87mmol/L after 48 weeks of treatment (t=3.383, p=0.002), whereas total cholesterol/high-density lipoprotein cholesterol (TC/HDL-C) levels decreased continuously from 4.73±3.01 to 3.56±1.12.

Conclusions: TAF was effective for viral suppression and hepatic function improvement, and had a good renal safety in patients with HBV-DC. However, blood lipid should be closely monitored.

Key words: Chronic hepatitis B; Decompensated cirrhosis; Tenofovir alafenamide; Effectiveness; Safety

Abstract Submission No. 100131
P-0058

Assessing effectiveness of antiviral therapy in untreated HBV cirrhotic patients with low/no viremia

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Objective: To evaluate the effectiveness of antiviral treatment in untreated patients with HBV related cirrhosis and low or no viremia.

Methods: One hundred and eighty-eight individuals with low or no viremia HBV related cirrhosis who had a minimum follow-up period of 6 months at First Affiliated Hospital of Xinjiang Medical University were enrolled and divided into two groups: a treatment group who received antiviral therapy (n=128) and a control group who did not (n=60). A comparative analysis of virological indicators, liver function parameters, and prevalence of complications between these two groups were conducted.

Results: The baseline characteristics of these two groups were similar, with no significant differences in sex or age (P > 0.05). After 6 months of antiviral treatment, the HBeAg conversion rate was 9.57%, the HBV DNA conversion rate was 20.67%, serum albumin (ALB) levels increased, the Child-Turcotte-Pugh (CTP) score decreased, and there was a 7.81% reduction in the prevalence of gastrointestinal bleeding, a 14.84% decrease in ascites prevalence, and a 17.19% decrease in spontaneous peritonitis prevalence (P < 0.05). In contrast, the control group showed a 6-month HBeAg conversion rate of 27.66% and a significant increase in the Model for End-Stage Liver Disease (MELD) score (P < 0.05).

Conclusion: Antiviral therapy led to notable reductions in HBeAg and HBV DNA positivity, substantial enhancements in liver function, and a significant decrease in the prevalence of complications associated with cirrhosis in patients with low or no viremia HBV related cirrhosis. Additionally, some of these patients were able to transition from a decompensated to a compensated phase of cirrhosis.

Abstract Submission No. 100138
P-0059

Effectiveness of Solanum Procumbens Combined with Tenofovir in Treatment of Chronic Hepatitis B

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Aims: Evaluating the effectiveness of Solanum procumbens (SP) combined with Tenofovir disoproxil fumarate (TDF) in the treatment of hepatitis B virus (HBV).

Methods: Study on a randomized controlled clinical trial in HBeAg (+) 150 HBV patients at Cam Khe Clinic from May 2020 to April 2023, who divided into 3 groups treated with: TDF 300mg, TDF 300mg combined with SP 300mg and SP 300mg.

Results: Percentages of ALT, AST ≤ 40 UI/L after 6, 12, 18 months of SP-TDF group were higher than the TDF group and SP group (p<0.01). Early response of HBV DNA in the SP-TDF group were higher than in the TDF group and SP group (p<0.01). The rates of response to reduce HBV DNA below the detection threshold in the SP-TDF group after 6, 12, 18 months were higher than TDF group and SP group (p<0.01). The rate of the seroconversion from HBeAg (+) to HBeAg (-) in the SP-TDF group after 6, 12, 18 months were higher than the TDF group and SP group (p<0.01). The rate of HBeAg (-) and anti HBe (+) in the SP-TDF group after 6, 12, 18 months were higher than the TDF group and SP group (p<0.01).

It quickly reduce AST, ALT values returned to normal in the SP group. Some patients had side effects of headache and epigastric pain in SP-TDF groups.

Conclusions: The combination of SP and TDF is more effective than TDF or SP alone in the treatment of HBV.

Abstract Submission No. 100229

P-0060

Entecavir versus tenofovir disoproxil fumarate in chronic Hepatitis B with severe acute exacerbation

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Background: The efficacy of different nucleos(t)ide analogs in the treatment of CHB with severe acute exacerbation (SAE) remained unclear. Thus, this study aimed to compare the short-term efficacy of TDF and ETV in patients having CHB with SAE.

Methods: We analyzed consecutive patients with treatment-naïve CHB receiving TDF (n = 36) or ETV (n = 65) for SAE. The primary endpoint was overall mortality or receipt of liver transplantation (LT) by 24 weeks. The secondary endpoints are the comparison of ETV versus TDF influences on renal function and virological and biochemical responses at 4, 12, 24, and 48 weeks.

Results: The baseline characteristics were comparable between the two groups. By 24 weeks, 8 (22%) patients in the TDF group and 10 (15%) patients in the ETV group had either died (n= 15) or received liver transplantation (LT) (n= 3) ($P= 0.367$). Cox-regression multivariate analysis revealed age ($p = 0.003$), baseline international normalized ratio of prothrombin time ($p = 0.024$), and early presence of hepatic encephalopathy ($p = 0.003$) as independent factors associated with mortality or LT. The two groups of patients achieved comparable biochemical and virological responses at 48 weeks. No significant difference was found in the estimated glomerular filtration rate (eGFR) between the TDF and the ETV groups. However, a significant reduction in the eGFR at 48 weeks, as compared with the baseline, was found in each group.

Conclusions: TDF and ETV achieved similar short-term clinical outcomes and treatment responses in CHB patients with SAE.

Abstract Submission No. 100278

P-0061

A Model Based on CHI3L1 for Expecting Liver Severity of Hepatitis B Virus Infections in the IT Phase

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Background: Whether to treat patients with CHB during the IT period is a matter of ongoing debate. We created and assessed a novel diagnostic model for identifying this question.

Methods: From Nov. 2018 to Dec. 2022, 253 CHB patients underwent liver biopsy at Ningbo No. 2 Hospital, including 44 patients in IT phase. IT patients randomly assigned into two cohorts. Logistic regression model was developed and validated to predict the severity of hepatic inflammatory fibrosis in CHB patients with IT.

Results: CHI3L1, ALB, ALT / AST were identified as independent predictors of liver lesion severity in CHB patients with IT. CHI3L1 and ALT/AST showed a positive correlation with severity, whereas ALB showed a negative correlation with severity. The three were combined to build the model (named as CAA index), which demonstrated good performance. The CAA index achieved an area under the receiver operating characteristic curve (ROC) of 0.916 (95% CI, 0.820 - 1.000), a critical value of 0.539, as well as a sensitivity of 0.800, a specificity of 0.867, a negative predictive value (NPV) of 0.786, and a positive predictive value (PPV) of 0.750. The ROC of the validation set was

0.875 (95% CI, 0.683 - 1.000) with a cut-off value of 0.549, a sensitivity of 0.800, and a specificity of 1.000.

Conclusions: This diagnostic model has some value in diagnosing significant liver tissue damage among CHB patients in the IT phase. It assesses the severity of the patient's liver lesion severity and helps determine whether treatment is necessary.

Abstract Submission No. 100281

P-0062

The epidemiological and clinical characteristics of SARS-CoV-2 infection in patients with HBV/HIV

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Findings regarding the association between coronavirus disease 2019 (COVID-19) and hepatitis B and human immunodeficiency virus (HBV/HIV) infection, and whether antiviral therapy can protect patients with HIV/HBV from severe COVID-19, have been inconsistent in traditional observational studies. This study aimed to investigate the potential links between the current use of antiviral therapy and the rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and symptoms of infection in patients with SARS-CoV-2 and HBV/HIV. Using a questionnaire-based survey, we recorded whether participants had been infected with SARS-CoV-2, and the symptoms and severity of COVID-19 after the illness. Among 756 participants, chi-square tests showed a higher incidence of COVID-19 in the HBV infection group (75.6%, $P=0.047$) and the HIV infection group (77.6%, $P=0.036$). These two groups exhibited fewer symptoms than the control group ($P<0.001$). The differences in the prevalence of most symptoms were also significant. Our findings suggest that patients with HBV or HIV infection have a higher risk of contracting SARS-CoV-2 than the general population; however, antiviral treatment relieves the symptoms of COVID-19.

Abstract Submission No. 100293

P-0063

Age and concomitant liver diseases are associated with patient's retention in HBV care continuum

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Background: Despite improvements in the treatment paradigm for chronic hepatitis B (CHB), inadequate linkage to care remains an obstacle and published data on patient's retention in care post-diagnosis is limited. We aimed to explore factors associated with patient's retention in the CHB care continuum after diagnosis.

Methods: CHB patients identified from a prior HBV screening programme in Hong Kong in 2015-2016 were recruited for clinical,

virological and transient elastography assessment, as well as questionnaire assessment regarding different socio-economic aspects.

Results: 430 CHB patients (34.7% male, median age 61 years) were recruited. 32 (7.4%) had advanced fibrosis (liver stiffness [LS] >9 kPa) while 8 (1.9%) patients were cirrhotic (LS >12 kPa). Concerning retention in care, 288 (67%) patients had attended regular follow-up since the diagnosis and 86 (20%) patients were on anti-viral treatment. Among those untreated (n=344), 50 (14.5%) had indications for treatment (elevated HBV DNA >2000 IU/mL plus abnormal ALT or detectable HBV DNA plus advanced fibrosis/cirrhosis). From multivariable analysis, older age (OR 1.05, 95%CI 1.03-1.07) and the presence of concomitant liver diseases e.g., fatty liver disease (OR 3.07, 95% CI 1.63-5.80) were the two independent factors associated with retention in the CHB care continuum. Socio-economic factors, including family income, occupation and educational level, showed no association.

Conclusion: Linkage to care for CHB patients in Hong Kong is suboptimal. Patients of older age and those with concomitant liver diseases are more likely to be retained in CHB care continuum. Enhancement of patient education, especially in the younger generation, is needed.

Abstract Submission No. 100338
P-0064

Suboptimal rate of management for the prevention of HBV reactivation in immunosuppressive therapy

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Background: Although HBV patients have a risk of reactivation after immunosuppressive therapy (IST), the status of their risk management is not clear in Japan. The aim of this study is to describe the proportion of the appropriate management for the prevention of HBV reactivation when undergoing IST in HBV patients

Methods: We conducted a retrospective cohort study using the JMDC Japanese claims database. Patients who had HBV-related diagnoses, underwent two or more HBV-DNA tests between 2011/4/1 - 2021/6/30 (suggestive of mainly HBV carriers or resolved infection as per the Japan Society of Hepatology (JSH) guideline), and who subsequently initiated IST were included. Patients who underwent appropriate HBV reactivation risk management were defined as either 1) receiving prophylactic nucleos(t)ide analogue therapy, or 2) receiving at least one HBV-DNA test every quarter within a 360-day period after initiation of IST.

Results: A total of 6,242 patients met the eligibility criteria, with a mean age of 53.01 (±10.8) years old and 55.8% male. The proportions of patients with appropriate management, stratified by the HBV reactivation risk level of IST was: 43.1% (276/641) for high-risk, 40.2% (223/555) for intermediate-risk, and 15.9% (741/4965) for low-risk. Patients who visited large hospitals (with 100+ beds) had higher odds of receiving appropriate management compared with those who visited small hospitals or clinics.

Conclusion: Despite the JSH guideline recommending prophylaxis of HBV-related hepatitis in patients going through IST, the appropriate management is not ideal. This is especially the case for ensuring smaller hospitals or clinics, highlighting the need for further educational activities.

Abstract Submission No. 100347
P-0065

A Real-World Study of Different Antiviral Regimens in Treatment-Naïve CHB with High Viral Load

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Background: Treatment-naïve CHB patients with HVL often exhibit suboptimal responses to antiviral therapies. This study investigates the real-world efficacy and safety of different antiviral regimens.

Methods: Between January 2021 and August 2022, CHB patients with HBV DNA >10⁷ IU/mL were collected from four hospitals in Shenzhen. The primary endpoint was the proportion of patients with HBV DNA <100 IU/mL at 48 weeks, and other endpoints included changes in HBsAg, HBeAg, ALT, and eGFR at 48 weeks.

Results: 391 patients were enrolled in the study, with 296 patients undergoing statistical analysis after baseline characteristics were adjusted using inverse probability weighting. The patients were distributed into four groups: ETV (n=62), TDF (n=89), TAF (n=36), TDF+LDT/ETV (n=109). The proportion of patients achieving HBV DNA <100 IU/mL at 48 weeks was significantly lower with ETV (50%) compared to the TDF (70.8%), TAF (72.2%), and TDF+LDT/ETV (75.2%) (P<0.05). There were no significant differences in HBsAg reduction among the four groups, but the HBeAg seroconversion rate was significantly higher in the TAF group. The ALT normalization rate was significantly higher in the TAF group (72.2%) compared to the others (P<0.05). Stratified analysis of ALT revealed no significant differences in virological response among the four groups when ALT was <1xULN or >4xULN (P>0.05). There were no significant differences in eGFR among the groups.

Conclusion: In treatment-naïve CHB patients with HVL, combination therapy did not demonstrate superiority over monotherapy in antiviral efficacy at 48 weeks, while ETV was significantly less effective than the others. TAF exhibited superiority in ALT normalization.

Abstract Submission No. 100349
P-0066

Antiviral therapy and hepatocellular carcinoma risk after hepatitis B surface antigen seroclearance

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Background: Antiviral therapy (AVT) reduces the risk of hepatitis B virus-related hepatocellular carcinoma (HCC). We explored the influence of AVT status at HBsAg seroclearance on the HCC risk after hepatitis B surface antigen (HBsAg) seroclearance.

Methods: Patients with chronic hepatitis B (CHB) who achieved HBsAg seroclearance between 2003 and 2022 were retrospectively reviewed. The primary outcome was HCC development after HBsAg seroclearance.

Results: Of the study population, 1,280 (84.2%) and 241 (15.8%) patients achieved HBsAg seroclearance without AVT (spontaneous clearance group) and with AVT (AVT-induced clearance group),

respectively. During the follow-up (median 4.3 years), 37 (2.4%) patients developed HCC after HBsAg seroclearance. The cumulative incidence of HCC was similar between the AVT-induced and spontaneous HBsAg seroclearance groups (HR=0.461; $P=0.150$), whereas it was significantly lower in the AVT-induced than spontaneous HBsAg seroclearance group (HR=0.442; $P=0.005$). In multivariate analysis, spontaneous HBsAg clearance, ALBI grade ≥ 2 , liver cirrhosis, and platelet count $<50 \times 10^9/L$ were independently associated with the increased risk of HCC development. The newly established risk prediction model based on these variables, ACAP (antiviral therapy, cirrhosis, ALBI, and platelet count) score had time-dependent area under curves of HCC prediction at 5 and 8 years of 0.814 and 0.803, and its Harell's C-index was 0.805, respectively. The ACAP score exhibited good discriminative performance in the internal validation and sensitivity analysis, and outperformed existing HCC risk prediction models.

Conclusions: HCC risk differed according to AVT status at HBsAg seroclearance. The newly established risk prediction model may help clinicians to make timely interventions and surveillance strategies.

Abstract Submission No. 100377
P-0067

HBV-DNA Levels, Steatosis and ALT in Hepatitis B: A Cross-Sectional Study

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Background: The relationship between serum HBV DNA level with steatosis and alanine aminotransferase (ALT) remains controversial. The aim is to find the relationship between HBV-DNA levels with steatosis and ALT in hepatitis B patients.

Methods: An analytic observational study with a cross-sectional design was conducted at Dr. Muhammad Hoesin Central General Hospital in Palembang, Indonesia from June to August 2023. The study included 54 hepatitis B patients who met the inclusion criteria. The data was analyzed using Spearman correlation and one-way ANOVA. A p -value <0.05 was considered significant.

Results: Most of the subjects were under 45 years old, with a median body mass index of 23.5 kg/m² and a median HBV-DNA level of 21.0 IU/mL. Differences in body mass index were observed based on steatosis grade and ALT levels ($p<0.05$), but there were no differences in age and gender when stratified by steatosis grade and ALT. A correlation was found between HBV DNA levels and ALT ($r = 0.269$, $p = 0.049$). In contrast, no statistically significant differences were detected in HBV DNA levels among patients with varying steatosis grades ($p > 0.05$).

Conclusion: In patients with hepatitis B, it's common to have hepatic steatosis. However, the grade of steatosis was not independently associated with HBV-DNA levels but was correlated to ALT levels.

Keywords: HBV-DNA levels, Steatosis, ALT, Hepatitis B

Abstract Submission No. 100384
P-0068

A case of hepatitis B virus reactivation in patient treated with nintedanib

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The Asian Pacific Association for the Study of the Liver, the Japan Society of Hepatology, the European Association for the Study of the Liver, and other societies have established clinical practice guideline for management of hepatitis B reactivation. Recent years, new tyrosine kinase inhibitors have appeared one after another, therefore it is inevitable that there is a time lag between the launch of new tyrosine kinase inhibitors and the recommendations for hepatitis B virus management in the guidelines. We experienced hepatitis B reactivation in patient treated with nintedanib which was introduced in 2015 for treatment of idiopathic pulmonary fibrosis. The main molecular targets of nintedanib are the fibroblasts growth factor receptor, the platelet-derived growth factor receptor and the vascular endothelial growth factor receptor. Recently, IL-15 has been reported to contribute to the elimination of hepatitis B virus, and platelet-derived growth factor and platelet-derived growth factor receptors have been implicated in the production and activation of IL-15. We thought that nintedanib may suppress the function of IL-15 by inhibiting platelet-derived growth factor receptors, thereby triggering hepatitis B reactivation. The drug information of nintedanib does not mention hepatitis B reactivation and, to our knowledge, this is the first report of reactivation with this medicine.

Abstract Submission No. 100414
P-0069

Effectiveness and safety of TAF for 48 weeks in ETV-experienced HBsAg-positive CHB Patients

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Background: Tenofovir alafenamide (TAF), as well as entecavir (ETV), is widely used as first-line treatment for chronic hepatitis B (CHB) patients. However, there are few studies concentrating on the effectiveness of sequential therapy from ETV to TAF in patients with maintained high level of HBsAg. We conducted a multicenter prospective cohort study to assess the effectiveness, safety, as well as HBsAg decline and cytokines profile of 48-week TAF treatment in CHB patients who were previously treated with ETV.

Methods: We enrolled 41 CHB patients with ETV-experienced (> 1 year), HBeAg positive, complete virological response (HBV DNA $\leq$ 20 IU/mL, alanine aminotransferase (ALT) < 1 upper limits of normal (ULN, Female: 40 U/L, Male: 50 U/L), HBsAg > 3000 IU/mL and willing to switch to TAF treatment. Blood samples were collected at 0, 12, 24, and 48 weeks to detect HBsAg level and cytokines (IFN- λ 3, IP-10).

Results: A total of 41 patients received sequential therapy with ETV and TAF. The median level of baseline HBsAg was 3.7 log₁₀ IU/mL. After 48 weeks of TAF treatment, HBsAg declined significantly by a mean level of 0.1 log₁₀ IU/mL. Among the patients, 34.1% experienced HBsAg decline of more than 0.1 log₁₀ IU/mL, while no patient achieved HBsAg clearance. Additionally, 5 patients (12.2%) achieved HBeAg clearance. Compared with baseline, there were almost no change in serum creatinine, blood phosphorus or calcium. During the 48-week treatment, IP-10 declined significantly compared with baseline (0W, 12W, 24w, 48w mean: 524.6 vs 369.7 vs 271.5 vs 319.0 pg/mL, all p value < 0.05). Similarly, IFN- λ 3 slightly decreased during 48-week treatment (0W, 12W, 24w, 48w mean: 6.8 vs 6.1 vs 5.68 vs 5.48 pg/mL, p < 0.05). Finally, we found that higher baseline IFN- λ 3 was related with the HBsAg decline (p = 0.02) after 48 weeks, and 5 HBeAg clearance patients after the treatment had a higher IFN- λ 3 at 48 weeks than those not cleared (p = 0.03).

Conclusion: TAF demonstrated a significant ability to decrease HBsAg and good renal safety after 48 weeks of sequential therapy. Moreover, baseline IFN- λ 3 level may be related with HBsAg decline.

Abstract Submission No. 100420

P-0070

Safety and Efficacy of Tenofovir Alafenamide in patients with CHB and hepatic decompensation

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Background/Aim: There are limited safety and efficacy data available to support tenofovir alafenamide (TAF) use in chronic hepatitis B (CHB) patients with hepatic decompensation. We conducted an interim analysis from an prospective, ongoing, multi-center study aimed to investigate the safety and efficacy of TAF in CHB patients with hepatic decompensation.

Patients and Methods: Nucleotide(s) analogues (NUCs) treatment naïve or experienced (except for TAF) CHB patients with hepatic decompensation (Child-Turcotte-Pugh [CTP] score $\geq$ 7), were eligible for enrollment. Enrolled patients initiated TAF 25mg once daily de novo

or switch from other NUCs for up to 144 weeks. The viral suppression (HBV DNA < 20 IU/mL), improvement in CTP score, Model for End-stage Liver Disease (MELD) score, and liver-related mortality at 48 weeks of TAF therapy were assessed.

Results: At the time of this interim analysis, 24 patients were enrolled and the majority of whom were male (20/24), with a median (range) age of 60 (24-84) years. Twelve patients had prior NUC experience. Thirteen (54%) patients had liver cirrhosis assessed by ultrasound at enrollment. The median (Q1, Q3) HBV DNA level was 591 (33, 596493) IU/mL and three were HBeAg positive. The proportion of patients with HBV DNA level < LLOQ progressively increased from 21% (5/24) at baseline to 58% (11/19) at W12, 77% (13/17) at W24, and 85% (11/13) at W48 of TAF therapy. The proportion of patients with normal alanine aminotransferase (ALT) level (< 40 U/L) also increased from 17% at baseline to 58% at W12, 77% at W24, and 69% at W48. Recovery from hepatic decompensation (CTP < 7) was observed in 12/19 (63%) patients at W12, 10/17 (59%) patients at W24, and 8/13 (62%) patients at W48. The median MELD score declined from 13.4 to 10.0 at W12, 7.7 at W24, and 10.7 at W48. None of the patients received liver transplant and 3 patients died (one each due to GI bleeding, meningitis, and traffic accident). No participants discontinued treatment due to an adverse event and no study drug related serious adverse events have been reported.

Conclusion: After 48 weeks of TAF treatment, hepatic function improved in the majority (62%) of CHB patients with hepatic decompensation at baseline. The safety profile was consistent with the known safety profile of TAF and no new safety concerns emerged. Further investigation of long-term outcomes will be assessed in this ongoing study.

Abstract Submission No. 100463

P-0071

Clinical Characteristics Of Low Vi

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Objective: The clinical management of ALT persistently normal HBV infection with indeterminate phase is a hot topic recent years. We aimed to analyse the clinical characteristics of untreated low viral load HBeAg-negative chronic HBV infection with indeterminate phase.

Methods: This historical cohort enrolled 139 ALT persistently normal HBV DNA < 2000 IU/ml untreated HBeAg negative chronic HBV infection. According to baseline HBsAg grouped indeterminate phase (IP, n=80) and immune control (IC, n=59). Compared the indexes different from baseline to end point. The cumulative rates of HBsAg decline, HBV DNA negative, persistence of normal ALT and persistence of normal LSM between groups.

Results: Of the enrolled patients, 42.45% were male with a mean age of 38.79 years, all patients median follow-up 34 (24-48) months. There were significant differences of HBsAg and HBeAb for between baseline and end point for IP patients, the levels of HBeAb, HBV DNA, ALT, AST, ALB and LSM were no significant differences. In IC group, HBsAg, HBeAb and ALT levels had significant differences, HBeAb, HBV DNA, AST, ALB and LSM levels had no significant differences. 66 patients underwent liver biopsy during follow-up, 32.61%, 15% had moderate liver injury in IP and IC, respectively. The cumulative rates of HBsAg decline and HBV DNA negative existed significant differences between groups, but the persistence of normal ALT and LSM had no significant differences.

Conclusion: Most patients of low viral load HBeAg negative chronic HBV infection with indeterminate phase were in hypoviremia long term, some patients had damage of liver, probably progressed to

cirrhosis or hepatocellular carcinoma, antiviral therapy should be actively initiated for HBV DNA positive.

Abstract Submission No. 100479
P-0072

Real-world 96-week data on NUCs for hepatitis B virus-associated acute-on-chronic liver failure

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Background: Comparative studies of the effectiveness and safety of three first-line drugs in acute-on-chronic liver failure are scarce, especially in terms of long-term survival, and we aimed to analyze data on three first-line drugs in a real-world setting.

Methods: A total of 132 HBV-ACLF patients hospitalized at Shandong Public Health Clinical Center were enrolled. All patients received treatment with TAF (n=46), ETV (n=45), or TDF (n=41) and comprehensive medical treatments. The maximum follow-up was up to 96 weeks.

Results: By week 12, 36 (78.2%) patients in the TAF group, 24 (58.5%) patients in the TDF group, and 26 (57.8%) patients in the ETV group had survived without liver transplantation. After 96 weeks, the survival rates are 35 (76.1%) in TAF, 20 (48.8%) in TDF, and 21 (46.7%) in ETV. There was a statistically difference in patient survival between TAF and TDF (P=0.0058) and TAF and ETV (P=0.0022), while no difference between TDF and ETV (P=0.8109). The median survival time was 155 days in the ETV group, 189 days in the TDF group, and too few deaths in the TAF group (11 deaths out of 46) to estimate the median survival time. After 96 weeks, the rate of undetectable DNA increased to 85.7% for TAF, 60% for TDF, and 61.9% for ETV.

Conclusion: This real-world data showed that TAF is more effective than ETV and TDF in improving short-term and long-term survival rates in HBV-ACLF patients and reducing viral load.

Abstract Submission No. 100480
P-0073

Alterations in Renal Tubular Function in Real-World CHB Patients on TDF and ETV Administration

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Background: With aging, CHB patients need more urgent attention to kidney function nowadays. Compared with glomerular function, tubular function plays an important role in early screening of renal function in CHB patients. Therefore, we aimed to understand the rate of abnormal renal tubular function in patients with CHB through a cross-sectional study.

Methods: 204 patients with CHB from Qingdao Sixth People's Hospital were included in this cross-sectional observation. Renal tubular function indicators (α 1-MG, β 2-MG, NAG, and RBP) were investigated.

Results: A total of 204 are included, and the average age was 46. Overall, 5.9% of patients obtained all four indicators as abnormal. The rate is RBP 21.5%, NAG 22.6%, 2-MG 82.4%, and α 1-MG 87%. Based on

the abnormal extent, we found that for the RBP, 3.4% were 1-2 times, 9.8% were 2-5 times, and 8.3% were more than 5 times. For the NAG, 16.2% of them were 1-2 times, 4.9% of them were 2-5 times, and 1.5% of them were over 5 times. For the β 2-MG, 47% were between 1 and 2 times, 31% were 2 and 5 times, and 4.4% had levels over 5 times. For the α 1-MG, 42% were 1-2 times, 35% were 2-5 times, and 10% were more than 5 times.

Conclusion: The aberrant proportion of the renal tubule indicators, especially β 2-MG and α 1-MG, was higher in CHB patients. During the long-term use of TDF and ETV, we should pay more attention to the renal tubule indicators to monitor renal safety.

Abstract Submission No. 100481
P-0074

Effectiveness and safety of TAF on patients with hepatitis B-related decompensated cirrhosis

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Background: Decompensated cirrhosis is one of the most dangerous stages of chronic hepatitis B patients. TAF is used as a first-line agent, and there are limited data on TAF in decompensated cirrhosis. We aimed to evaluate the safety and effectiveness of TAF in decompensated liver disease.

Methods: A total of 23 patients were enrolled in this study and were evaluated for changes in biochemistry, virology, and liver and kidney function before and after TAF treatment. The maximum follow-up was up to 120 weeks.

Results: The mean Child-Pugh score at baseline in the enrolled patients with decompensated cirrhosis was (7.88 $\pm$ 2.25), the mean MELD score was (9.08 $\pm$ 4.42), and the mean eGFR was (130.70 $\pm$ 41.64). Among them, the rate of abnormal ALT levels was 47.83% (11/23), and the rate of detectable DNA (>500 IU/ml) was 65.22% (15/23). 12 patients completed 72 weeks and the mean Child-Pugh score was (3.83 $\pm$ 1.60), the mean MELD score was (4.82 $\pm$ 2.76) and the mean eGFR level was (139.50 $\pm$ 41.82). There was a statistically significant difference in Child-Pugh scores and MELD scores from baseline to 72 weeks of treatment (t1=6.379, P=0.001; t2=2.746, P=0.025). There is no difference on the eGFR levels before and after TAF therapy (t=-0.852, P=0.413). All patients had normal ALT and only 1 patient had detectable HBV DNA. 7 patients completed 120 weeks treatment and no significant changes in ALT, DNA, eGFR, Child-Pugh scores, and MELD scores.

Conclusion: In patients with hepatitis B-associated decompensated cirrhosis, long-term TAF therapy significantly improves liver function with high viral suppression and renal safety.

Abstract Submission No. 100491
P-0075

Plasma Hepassocin levels in relation to Chronic Hepatitis B infection progression

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BACKGROUND: Chronic Hepatitis B infection remains an important health issue in Taiwan, with HCC still ranked top in cancer incidence and mortality. Finding biomarkers to identify HBV carriers at higher risk of disease progression remains an important issue. Since hepatokines are primarily synthesized and secreted by the liver and have profound effects on whole-body metabolism, it is plausible that hepatokines may have significant effects on liver biology and diseases as well.

METHODS: We evaluated the association between circulating hepassocin levels and risk of HBV progression including liver cirrhosis, HCC and liver related death among 2731 subjects in the REVEAL-HBV cohort in Taiwan.

RESULTS: We found that the risk of developing liver cirrhosis started to increase and reach statistically significant at the third quartile (HR=1.15, 95% CI=0.75 – 1.76; HR=3.04, 95% CI=2.13 – 4.34; HR=2.85, 95% CI=2.00 – 4.05 for the 2nd, 3rd and 4th quartiles compared to the first, respectively), with a significant dose-response trend ($p<0.001$). Higher plasma hepassocin levels were associated with a two-fold increased risk of HCC when compared to the lowest quartile, after the adjustment of all other important risk factors. The hazard ratios were 0.81 (95% CI=0.48 – 1.38), 2.35 (95% CI=1.53 – 3.61) and 2.54 (95% CI=1.65 – 3.90) for each incremental quartiles, with a significant dose-response trend ($p<0.001$). Consequently, those with higher hepassocin levels at baseline were at increased risk of dying from liver related causes in a dose-response fashion.

CONCLUSION: We found that higher plasma hepassocin levels was associated with higher chance of being HBeAg and high HBV viral load, thus leading to higher chance of developing liver cirrhosis, HCC and eventually died from liver related causes. Hepassocin could be a good biomarker in predicting the long term disease progression for chronic HBV carriers.

Abstract Submission No. 100520
P-0076

Ultrasensitive HBsAg Next Qualitative assay predicts HBsAg rebound after therapy discontinuation

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Few patients lose HBsAg (<0.05 IU/mL) on current therapies and HBsAg seroreversion after therapy withdrawal is frequent. Currently, no good predictors of which patients will maintain HBsAg loss and which will serorevert after therapy discontinuation exist. We used HBsAg Next (LOD=0.005 IU/mL) to assess whether residual HBsAg is present in individuals with HBsAg seroreversion compared to those without. Patients experiencing on-therapy HBsAg loss (<0.05 IU/mL) from INACTIVE (NCT02992704) and SWAP (NCT01928511) clinical trials were tested with HBsAg Next Qualitative (LOD=0.005 IU/mL, Abbott Laboratories) during their final treatment week and at 24-weeks after therapy discontinuation. Results were compared to HBsAg Quantitative (LOQ=0.05 IU/mL, Abbott Laboratories). Between INACTIVE and SWAP studies, 36 individuals had HBsAg <0.05 IU/mL during their final treatment week and 25/36 (69.4%) maintained HBsAg <0.05 IU/mL at 24-weeks after therapy

discontinuation while 11/36 (30.6%) had HBsAg seroreversion. HBsAg Next was reactive (S/CO≥1.0) during the final treatment week in 10/11 (90.9%) seroreverters and was non-reactive (S/CO<1.0) in 19/25 (76.0%) patients who maintained HBsAg <0.05 IU/mL. At follow-up, 19/20 (95.0%) individuals with on-therapy HBsAg Next non-reactive results maintained HBsAg <0.05 IU/mL. Relative risk (95% CI) of HBsAg Next reactivity and seroreversion was 12.5 (2.476-72.14, $p=0.0003$). Low levels of HBsAg detectable with HBsAg Next were present in nearly all individuals with seroreversion and absent in most without seroreversion. These results suggest that higher sensitivity HBsAg assays can predict patients at risk of HBsAg seroreversion after therapy discontinuation and could aid in identifying candidates for therapy removal.

Abstract Submission No. 100530
P-0077

Is it time to rethink our strategy in Hepatitis B virus (HBV) booster vaccination?

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Background: Current guidelines do NOT recommend routine Hepatitis B (HBV) boosters for immunocompetent individuals, due to persistence of HBsAg-specific memory B and CD4+ T cells despite decline of antibody titres.

Purpose: We describe a case of acute HBV in a healthy 57-year-old male 3 years after three-dose HBV vaccination with adequate post vaccine HBs antibody titre (anti-HBs).

Method: Case Report and Literature Review

Results: In December 2018, the patient received 3-dose Twinrix vaccination series after negative testing for HBsAg, Anti-HBs and anti-HBcAb. Post vaccination testing February 2020 confirmed a positive anti-HBs (34.34 mIU/mL), with subsequent anti-HBs of 2.40 mIU/mL in June 2021, and <2.0 mIU/mL in December 2021, with corresponding negative HBsAg. In March 2022, he presented with acute HBV hepatitis (Anti-HBc IgM positive, HBV DNA 2.01 E+6 IU/mL) with peak laboratory values of Bilirubin 331 umol/L, INR 1.3, ALT 3708 U/L, AST 1407 U/L, ALP 364 U/L and GGT 422. Lab and imaging was negative for autoimmune or obstructive causes. Liver biopsy was consistent with acute hepatitis. Laboratory values normalized after starting Tenofovir (TDF), with subsequent HBsAg loss and re-emergence of anti-HBs that persisted beyond 1 year.

Conclusion: This patient developed acute HBV despite being vaccinated 3 years prior with a positive anti-HBs titre. This raises the question of the need for serial anti-HBs testing post vaccination, and whether there is a role of booster vaccines for patients with early decline in anti-HBs titres. If adapted, this may lead to significant changes in public health strategies against HBV.

Abstract Submission No. 100546
P-0078

Chronic hepatitis B in pregnancy – screening needed, monitor for flare after cessation

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Introduction: Hepatitis B virus (HBV) infection remains a significant public health concern in Asia, necessitating a focus on reducing mother-to-child transmission. Antiviral therapy is recommended for pregnant women with HBV DNA load exceeding 200,000 IU/ml. We aim to determine high viral load prevalence in pregnant individuals with HBV and study the impact of discontinuing antiviral therapy on postpartum liver function tests.

Methods: In a single-center retrospective audit, data was gathered from pregnant women with chronic HBV referred to a specialist center between August 2015 and August 2023, with medical board approval.

Results: 112 subjects were identified with mean age 34.5 ± 4.4 years, 28 had high HBV DNA ($>200,000$ IU/ml). 2 were already on treatment, 31 received treatment during pregnancy, 1 declined, and 2 with lower HBV DNA initiated treatment after discussion. 30 received Tenofovir-disoproxil-fumarate, and 1 received Tenofovir-Alafenamide. Pregnant patients with HBV DNA $>200,000$ IU/ml had a mean ALT of 31.46 ± 21.31 U/L, while those with lower HBV DNA had a mean ALT of 19.54 ± 9.76 U/L. All patients were followed after treatment initiation, with no serious adverse events reported. Among 28 subjects with available follow-up data, 7 required restarting treatment due to elevated HBV DNA levels associated with high ALT, all within 6 months post cessation.

Conclusion: High HBV DNA remains prevalent in pregnant females requiring treatment during pregnancy. Post-treatment cessation demands vigilant monitoring, as a notable number of patients experience elevated ALT, necessitating treatment reinstatement.

Abstract Submission No. 100556
P-0079

Prospect and dynamics of novel serum biomarkers of fibrosis in Hepatitis B virus related CLD

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Background: Liver biopsy is the gold-standard method for staging liver fibrosis, but the procedure is invasive and expensive. Noninvasive novel serum biomarkers of fibrosis are the current research interest. Cytokeratin (CK)18 is a filament protein which is proteolytically cleaved during liver damage. Chitinase 3-like protein 1 (CHI3L1) is a member of the chitinase family without chitinase activity.

Objectives: To assess the role of serum CK-18 fragment M30 level and serum Chitinase 3-like 1 (CHI3L1) levels and histological severity in patients with Hepatitis B Virus (HBV)-related compensated chronic liver disease (CLD). Materials and methods: This cross-sectional study evaluated 50 treatment-naïve patients with chronic hepatitis B with compensated CLD. Liver biopsy was done, and fibrosis was categorized using the METAVIR scoring system; Serum CK-18 M30 were measured by ELISA and serum CHI3L1 was measured by immunoassay.

Results: Serum concentrations of CK18 were not significantly increased in a stepwise fashion from A0 to A3 but were significantly increased in a stepwise fashion from F1 to F3. There was highly significant positive correlation between the stages of fibrosis (F1 to F3) and Serum CK-18 fragment M30 level ($r = 0.839$; $p = 0.0157$). Importantly, serum M30 CK-18 levels were able to discriminate mild versus moderate-advanced fibrosis (AUC: 0.84). The difference in median CHI3L1 across the groups was statistically significant.

Conclusion: This study found a positive correlation among CK-18 fragment M30, serum CHI3L1 level and hepatic histological severity in patients with HBV-related compensated CLD. So they can be used as potential noninvasive biomarker of fibrosis.

Abstract Submission No. 100578
P-0080

Tenofovir alafenamide reduced renal tubular damage in patients of chronic hepatitis B with entecavir

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Background and aims: Urinary α_1 -microglobulin (α_1 -MG), β_2 -microglobulin (β_2 -MG), urinary N-acetyl- β -glucosaminidase (NAG) and retinol-binding protein (RBP) have predictive effects on renal tubular injury, the purpose of this study is to investigate whether the renal tubular abnormalities in chronic hepatitis B (CHB) patients during long-term entecavir (ETV) treatment could be improved after altering to tenofovir alafenamide (TAF).

Method: This study included 224 CHB patients of abnormal renal tubular markers from June 2022 to September 2023, of which 122 patients continuing ETV and 102 patients of altering to TAF for 6 months. Propensity score matching was used to analyze the differences of renal tubular indexes between the continuing ETV treatment and altering to TAF treatment.

Results: A 1:1 propensity score match yielded 62 patients in each treatment group. The baseline characteristics, the ratio of complete virology response, liver blood phosphorus, the estimated glomerular filtration rate (eGFR), α_1 -MG, β_2 -MG, NAG, RBP were comparable between the two groups. After 6 months, the level of eGFR (ETV $101.5 \text{ mL}/(\text{min} \times 1.73 \text{ m}^2)$ TAF $100.1 \text{ mL}/(\text{min} \times 1.73 \text{ m}^2)$, $p > 0.05$), RBP (Δ ETV -0.159 Δ TAF -0.213 , $p > 0.05$), the ratio of complete virology response (ETV 87.1% TAF 91.9%, $P > 0.05$) weren't statistically different. The difference ratio of α_1 -MG, β_2 -MG, NAG, blood phosphorus was statistically significant ($p < 0.05$). TAF decreased more than ETV in α_1 -MG, β_2 -MG, NAG (Δ ETV -4.016 , -0.373 , -0.852 , Δ TAF -12.050 , -1.272 , -5.583), TAF increased less than ETV in blood phosphorus (Δ ETV $+0.019$, Δ TAF -0.286).

Conclusion: Altering to TAF of CHB patients with renal tubular abnormalities after long-term use of ETV, the treatment efficacy remains comparable and can improve renal tubular damage, indicating that TAF has better renal safety than ETV.

Abstract Submission No. 100593
P-0081

Management of HBV infection in pregnant women in Armenia and case of high viral replication

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Background: The global strategy for elimination of HBV-infection includes a prevalence target of HBsAg in children of five years of age of $<0.1\%$ by 2030. Pregnant woman with a viral load $\geq 200,000$ IU/mL may transmit HBV to their infant even when the infant receives the

timely birth dose vaccine, Hepatitis B immune globulin (HBIG) and completes the hepatitis vaccine series.

Methods: Guidelines on Management of patients with chronic hepatitis B rely on EASL guidelines from 2017, include approach on preventive treatment with tenofovir disoproxil fumarate (TDF) for PMTCT in HBV DNA $\geq 200,000$ IU/mL was adopted in 2019.

Results: Infant vaccination for HBV was introduced in Armenia in 1999 and coverage reached 96.5% for the birth dose and 93.2% for the third dose (2021). In addition, children born from HBsAg-positive mothers also received HBIG from 2021. Treatment with nucleoside analogues, include crucial preventive treatment in pregnant woman with HBV DNA $\geq 200,000$ IU/mL not covered by the state.

22 years old female, HBV-infection diagnosed on 18 week of first pregnancy. Take into account quantitative PCR HBV DNA on 28 week of pregnancy 255.326.321 IU/mL, HBeAg+, TDF was started and continuing up to 12 week after delivery with withdraw according to guidelines. Two years after became pregnant second time, preventive treatment with TDF was restarted.

Conclusions: Development of the guidelines and state program on antiviral prophylaxis for PMTCT of HBV-infection in Armenia is important part of elimination strategy. Guidelines should clarify the statement on continuing TDF in women of reproductive age without interruption after 12 weeks from delivery.

Abstract Submission No. 100601

P-0082

Low level of soluble PD-1 is associated with HBsAg loss in Peg-IFN α -treated patients with CHB

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Background: It is still suboptimal to achieve loss of hepatitis B surface antigen (HBsAg loss) in chronic hepatitis B (CHB) patients after pegylated interferon alpha (Peg-IFN α)-based treatment, due to the impaired HBV-specific immunity. Herein, we assessed whether repeated soluble programmed cell death-1 (sPD-1) as a novel biomarker could improve the identification of HBsAg loss.

Methods: Virologic and immunological biomarkers were examined dynamically in CHB patients who had previously been treated with 48 weeks of NAs followed by 48 weeks of Peg-IFN α . We associated changes in sPD-1 with serial quantitative measurement of HBsAg (qHBsAg), quantitative HBeAg (qHBeAg), HBV-DNA, and alanine aminotransferase (ALT) at the Peg-IFN α start, 12-week, 24-week and 48-week follow-up.

Results: Of 229 CHB patients prospectively enrolled, there were 91 participants with HBsAg loss at 48 weeks. The sPD-1 level was significantly associated with qHBsAg ($p < 0.0001$). Compared with higher sPD-1, lower sPD-1 was associated with HBsAg loss ($p < 0.0001$). A decline in sPD-1 concentration occurred in both groups, but HBsAg loss was more commonly observed in individuals demonstrating greater declines in sPD-1 levels at 12 weeks. The sPD-1 level at 24 weeks was more closely related to HBsAg loss at 48 weeks, with AU-ROCs of 0.756 (0.512-0.882, $p < 0.001$).

Conclusions: The decreases in sPD-1 during Peg-IFN α treatment were associated with HBsAg level and loss, suggesting its role as a possible predictive biomarker.

Abstract Submission No. 100639

P-0083

Preventing mother-to-child transmission of hepatitis B virus with tenofovir alafenamide fumarate

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Background: Safety and efficacy on tenofovir alafenamide fumarate (TAF) for preventing mother-to-child transmission of HBV are limited.

Methods: In this nationwide multi-center cohort study (2nd analysis), chronic HBV-infected pregnant women with HBV DNA levels $> 200,000$ IU/mL and hepatitis B e antigen (HBeAg) positive were enrolled in nine hospitals in China. All the mothers were given TAF from gestational weeks 27-29 to delivery and followed until postpartum month six. Infants received immunoprophylaxis and were followed up after completion of hepatitis B vaccination. [ClinicalTrials.gov Identifier: NCT05177926].

Results: 197 pregnant women were enrolled up to January 1, 2023 and 104 pregnant women completed the study. The mean age, gestational week at delivery, alanine aminotransferase (ALT) level, and viral loads at treatment initiation were 28.8 years, 38.8 weeks, 18.2 U/L, and 7 log₁₀ IU/mL, respectively. At delivery, 89.1% (156/175) of the mothers achieved HBV DNA $< 200,000$ IU/L. None achieved HBsAg loss or HBeAg loss during the follow-up period. 3.0% (5/167) and 58.6% (85/145) mothers had abnormal ALT levels ($> 1 \times \text{ULN}$) at delivery and postpartum, respectively. Blood creatinine and urea nitrogen levels were within normal range before and after TAF treatment among the mothers. All newborns were given birth dose of hepatitis B vaccine and hepatitis B immune globulin. All the infants tested negative for HBsAg. Body weight, height, and head circumferences were comparable to national standards for physical development.

Conclusion: Antiviral prophylaxis with TAF during pregnancy is effective and safe for chronic HBV-infected mothers and their infants within 28 weeks of follow up postpartum.

Abstract Submission No. 100643

P-0084

IrAEs Occurrence is The Risk Factor for HBsAg Increase and HBV Reactivation in Cancer Patients

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Background: Previous studies have indicated the potential of PD-1/PD-L1 inhibitors in the treatment of HBV infection. Since phase III clinical trials in this area have not yet been announced, more information may be obtained if we observe the changes in serum HBsAg and HBV-DNA levels in HBsAg-positive cancer patients receiving PD-1 inhibitors.

Methods: To explore the impact of PD-1 inhibitor combinational therapies on Serum HBsAg and HBV-DNA levels and investigate the incidence of HBsAg loss, HBV reactivation (HBVr), and immune-related adverse events (irAEs), a retrospective study including 1195 HBsAg-positive cancer patients who received PD-1 inhibitors between July 2019 and June 2023 was undertaken. The risk factors associated with significant HBsAg fluctuations and HBVr were identified through univariable and multivariable analysis.

Results: 180 patients were eligible in this study (Fig 1). With concurrent use of antiviral agents, serum HBsAg levels decreased ($P<0.0001$) in 129 patients and increased ($P=0.033$) in 51 patients (Fig 2A), with 7 patients (3.89%) achieved HBsAg loss. HBV-DNA levels were kept undetectable, remained stable at a low level, or decreased in most of the enrolled patients (92.78%). When divided patients into different subgroups, significant HBsAg decreases were discovered in low baseline HBsAg group ($P=0.023$), HBeAg-seronegative group ($P=0.033$), non-irAEs occurrence group ($P=0.045$) and liver cancer group ($P=0.047$) (Fig 2B-2I). However, 11 patients and 36 patients experienced HBVr (6.11%) and irAEs (20%), respectively, which could lead to discontinuation or delayed use of PD-1 inhibitors. Besides, HBeAg-seropositive ($P=0.01$) and irAEs occurrence ($P=0.02$) were identified as independent risk factors for significant HBsAg increase, irAEs occurrence ($P=0.01$) was identified as the only independent risk factor for HBVr.

Conclusion: PD-1 inhibitors combined with antiviral agents may exert therapeutic potential for chronic HBV infection, attention also should be paid to the risk of significant HBsAg increase, HBVr, and irAEs caused by PD-1 inhibitor combinational therapy.

Abstract Submission No. 100644
P-0085

ALTERATION OF FIBROSIS BASED ON FIBROSCAN IN CHRONIC HEPATITIS B PATIENTS AFTER THERAPY IN PALEMBANG

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Introduction: Chronic hepatitis B virus infection is a major global health problem. This infection lead to progressive liver fibrosis. Hepatitis B treatment using Tenofovir, suppressed replication which will improve the degree of fibrosis. The non-invasive method (fibroscan) useful for diagnosing liver fibrosis in chronic hepatitis B.

Objective: The study aimed to assess the degree of liver fibrosis using fibroscan and changed in viral load number after receiving nucleoside therapy as a treatment evaluation tools.

Material and Method: This is a retrospective longitudinal study using repeated measurements. The subjects were 52 patients received nucleoside analogs (Tenofovir). This research conducted at Mohammad Hoesin General Hospital January to April 2023. The data obtained from secondary data, analyzed using Wilcoxon test.

Results: A total of 52 participants, 33 participants male (63.5%) and the rest were female. The lowest pre-treatment fibroscan value in this study was 4.20 kPa with a maximum of 69.5 kPa, while post-treatment with tenofovir, the minimum fibroscan value was 4.30 kPa and a maximum of 30.90 kPa. The minimum amount of HBV DNA viral load pre-treatment is 3×10^0 iu/ml and a maximum of 8.52×10^6 iu/ml, while

in post-treatment minimum viral load value is 0 with a maximum of 7.38×10^6 iu/ml.

The Wilcoxon test at the end of the study showed there is a significant changes in the fibroscan value and viral load among the participants ($p<0.0001$).

Conclusion: There is significant improvement in the fibroscan values and viral load after Tenofovir therapy.

Keywords: Fibrosis, Chronic Hepatitis B, HBV DNA Viral Load, Nucleoside Analogs

Abstract Submission No. 100682
P-0086

Effect of therapy in liver biopsy-proven inactive carrier CHB patients with nucleos(t)ide analogues

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Aims: It is controversial to initiate antiviral treatment for inactive carrier(IC) chronic hepatitis B(CHB) patients. Our objective was to analyze the efficacy of nucleos(t)ide analogs(NAs) antiviral treatment in liver biopsy-proven IC patients.

Methods: This retrospective cohort included 238 liver biopsy-proven HBeAg-negative CHB patients, with alanine aminotransferase (ALT) less than twice the upper limit of normal(ULN). Patients were divided into IC (n=77), mildly active (MA;n=23) and immune active (IA;n=138), according to baseline ALT and liver biopsy results.

Results: Of the enrolled patients, 52.10% were male with a mean age of 40.86 years. The virological response and HBsAg decrease rates were 93.55% and 22.58%, respectively, in IC-phase treated patients, whereas the proportions of virological response and HBsAg decrease were 100% and 50%, respectively, in MA-phase treated patients, which showed no difference with the 96.49% virological response and 33.33% HBsAg decrease rates in IA-phase treated patients. Additionally, there was no significant difference proportions of persistence of normal ALT and persistence of normal LSM between treated group and untreated group among the three groups.

Conclusions: NAs showed similar short-term effect in IC-phase patients, MA- and IA- phase patients. Further data in long-term outcomes for each subgroup in this cohort will be important.

Abstract Submission No. 100683
P-0087

TAF in CHB patients with Advanced Fibrosis and Partial Virologic Response to Nucleos(t)ide

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Background/Aim: The strategy for patients with partial response to nucleot(s)ide analogue (NUC) remains uncertain. It raised the aim of investigating tenofovir alafenamide (TAF) switching in chronic hepatitis B (CHB) patients with advanced fibrosis and partial response to other NUCs.

Patients and Methods: CHB patients with advanced fibrosis who were currently on NUC therapy (other than TAF) for >52 weeks with detectable HBV DNA were enrolled. Enrolled CHB patients on NUC were switched to TAF 25 mg once daily. This is an interim analysis of 96 weeks of TAF treatment. The efficacy and safety of TAF and metabolic parameters on treatment were evaluated at week 48, 72 and 96.

Results: Sixty-six patients, including 47 (71.2%) on entecavir, 13 (19.7%) on TDF and 6 (9.1%) on other NUCs, were enrolled (median 56 years, 35 [53%] male). Forty-five patients had completed the 96 weeks treatment of TAF. Thirty-one (47%) patients were HBeAg positive and the median HBsAg titer was 1803 IU/mL at enrollment. The median HBV DNA level declined from 74.5 IU/mL at enrollment to 72th, and 96th week with HBV DNA th, and 6.2 kPa at 96th week of TAF. The median body weight (BW) mildly increased from 63.3 kg to 64.5 kg at 48th, and decreased to 62.4 kg at 96th week. For patients of baseline BMI <23.5, BW increased from 52.7 kg to 56.5 kg at 48th, and 54.0 kg at 96th week. However, the increase in BW was not observed in patients with BMI ≥23.5 kg/m². Controlled attenuation parameter (CAP) changed from 239 dB/m to 242 dB/m at 48th, and 232 dB/m at 96th week. The HBsAg titer declined from 1803 IU/mL at enrollment to 1179 IU/mL at 48th, and 1368 IU/mL at 96th week. The median serum creatinine and eGFR levels were stable. The number of adverse events were small, and majority were considered unrelated to TAF treatment. Seven patients early terminated including five patients due to personal reason, and 2 patients died due heart attack and necrotizing fasciitis, respectively which were not related to TAF treatment.

Conclusion: TAF effectively suppresses viral replication and prevents progression of fibrosis in CHB patients with advanced fibrosis and partial virologic responses to other NUCs.

Abstract Submission No. 100688

P-0088

Machine learning for predicting postpartum liver function abnormalities in CHB pregnant women

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Background and objectives: A certain percentage of pregnant women with chronic hepatitis B (CHB) infection, with or without nucleoside analogs interventions, have hepatitis flares, or even severe disease in the postpartum period. The aim of this study was to develop a predictive model for distinguishing whether a pregnant woman will develop liver function abnormalities after childbirth or not.

Methods: We included 725 pregnant women in this study and developed two predictive models using machine learning techniques:

Extreme Gradient Boosting (XGBoost) and logistic regression. These models aimed to predict pregnant women who would have ALT levels exceeding 40 U/L within one year after childbirth. We assessed the established models using out-of-sample validation by splitting the sample into training and testing sets in a 3:1 ratio.

Results: Out of 725 patients, 21.8% (158) developed abnormal liver function after childbirth. Key predictors of postpartum abnormal liver function included pre-delivery HBeAg status, ALT, GGT, TBA, HBcAb, and HBV DNA levels. The XGBoost model outperformed the traditional logistic regression model in distinguishing between the abnormal and normal liver function groups in both the training and validation sets (AUC, Training set: 0.824 vs. 0.728; Validation set: 0.758 vs. 0.722).

Conclusions: Compared to traditional logistic regression models, the XGBoost model demonstrated superior performance in identifying pregnant women with CHB at risk of postpartum liver function abnormalities. This suggests that machine learning techniques have the potential to enhance the development and validation of predictive models in hepatitis B research.

Abstract Submission No. 100698

P-0089

Influence of Hepatitis B Family History on Antiviral Efficacy in Pregnant Women

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Objective: To explore whether hepatitis B pregnant women with or without family history have differences in the distribution of the five items of hepatitis B, and to explore whether family history is an independent influencing factor of antiviral therapy during pregnancy, so as to provide theoretical reference for early clinical treatment of hepatitis B, so as to prevent the occurrence of hepatocellular carcinoma and cirrhosis.

Methods: 410 pregnant women with hepatitis B who met the inclusion criteria were collected from the Obstetrical Clinic of the Affiliated Hospital of Nanjing University of Chinese Medicine, 352 of whom had a family history, 303 (86.5%) of whom had a hepatitis B mother, 29 of whom had a hepatitis B father, 35 of whom had no family history, and 23 of whom were unknown. The indicators of hepatitis B, HBV DNA, blood routine, and liver function of the two groups of cases were retrospectively analyzed. The collected data was analyzed using SPSS22.0 statistical software.

Results: The decline rate of HBsAg in the antiviral period of pregnant women with family history was faster than that of those without family history ($p < 0.005$).

Conclusion: 1) 352 pregnant women with HBV infection had a family history of hepatitis B; 2) Among pregnant women with a family history, HBsAg showed a rapid decrease in antiviral efficacy.

Abstract Submission No. 100705

P-0090

Noninvasive index of initiation for antiviral therapy in CHB patients under 30 years with normal ALT

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Aims: To investigate the noninvasive indicators of indications for antiviral therapy in chronic hepatitis B virus (HBV) infection patients under 30 years old with normal alanine aminotransferase (ALT) under the guidance of liver pathology.

Methods: A retrospective analysis was performed for the clinical data of 144 chronic HBV infection patients underwent liver biopsy with age ≤ 30 years old and ALT $\leq$ upper limit of normal (ULN). Univariate and multivariate binary logistic regression analyses were used to screen out the influencing factors for the initiation of antiviral therapy; the receiver operating characteristic (ROC) curve was plotted to evaluate the diagnostic efficiency of each indicator in determining the need for antiviral therapy in chronic HBV infection patients.

Results: Of all 144 patients, 47 (32.64%) had marked liver damage and thus needed active antiviral therapy. The multivariate analysis showed that HBeAg (odds ratio [HR] = 0.585, 95% confidence interval [CI]: 0.452-0.757, $P < 0.05$), albumin (HR = 0.894, 95% CI: 0.805-0.993, $P < 0.05$), and liver stiffness measurement (LSM) (HR = 1.479, 95% CI: 1.177-1.857, $P < 0.05$) were independent influencing factors for the initiation of antiviral therapy. The ROC curve showed that only LSM predicted the need for antiviral therapy with an area under ROC curve (AUC) > 0.5 , which was 0.628 (0.525-0.730). Taking LSM ≥ 6.15 kPa as the bound values, the sensitivity, specificity, accuracy, positive predictive value and negative predictive value were 40.4%, 84.5%, 63.5%, 72.3% and 58.6%, respectively.

Conclusions: LSM could diagnose the stage of liver injury for chronic HBV infection patients with age ≤ 30 years old and ALT $\leq$ ULN.

Abstract Submission No. 100718
P-0091

The Impact of CHB with MASLD on the Progression of Liver Fibrosis

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Background: Chronic hepatitis B (CHB) is often concurrent with metabolic abnormality-related fatty liver disease (MASLD), yet there is limited natural history data on this combined dual disease. Therefore, we explored the impact of CHB with MASLD on the progression of liver fibrosis.

Methods: This retrospective study collected patients admitted to Beijing Ditan Hospital from 2009 to 2015. Based on MASLD presence or absence, patients were divided into CHB with MASLD and CHB alone. Liver biopsies were performed at admission and one year later. Baseline characteristics and laboratory examinations were analyzed using SPSS software.

Results: 90 untreated CHB patients were included, among which 33 patients were in the CHB with MASLD group and 57 in the CHB alone group. One year later, the fibrosis progression rates were 22.7% and 34.8% ($p = 0.207$). Stratified analysis of the 33 patients with CHB and MASLD showed that 12 patients (36.4%) had alleviation of MASLD, while 21 patients (63.6%) continued to have concurrent MASLD. Among the 57 patients with CHB alone, 11 patients (19.3%) developed new-onset MASLD, while 46 patients (80.7%) remained with CHB alone. Compared to CHB alone patients, the fibrosis progression rates

after one year were 18.2% and 23.8% vs 34.8% ($P = 0.287$ and $P = 0.369$) (Fig).

Conclusion: For untreated CHB patients, the presence and changes of MASLD may not have a significant impact on the progression of hepatic fibrosis. However, due to the limited study duration and small sample size, these conclusions require further validation.

Abstract Submission No. 100735
P-0092

Efficacy and Safety of Tenofovir Alafenamide in Treatment-Naïve and Experienced CHB Patients

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Background: This study aims to explore the efficacy and safety of tenofovir alafenamide (TAF) in the treatment of chronic hepatitis B (CHB) patients in Southern China, both treatment-naïve (TN) and treatment-experienced (TE).

Methods: We collected data from 268 CHB patients who received TAF at Shenzhen Third People's Hospital from January 2019 to July 2021. We assessed virological, biochemical, and serological responses at 12 months of TAF treatment, as well as the impact on renal function, calcium-phosphorus metabolism, and lipid profiles.

Results: The TN group included 158 patients, achieving a 77.2% rate of undetectable HBV DNA and a 93.0% rate of ALT normalization at 12-month. The TE group included 110 patients, with an HBV DNA undetectable rate of 97.3% and ALT normalization rate of 92.7% at 12-month. Notably, 32 patients with suboptimal or low viremia experienced substantial improvements in virological response upon switching to or adding TAF. At 12-month, there were no significant changes in SCr, eGFR, serum Ca²⁺, and serum Pi- levels. Among 55 patients with renal dysfunction who switched to TAF, eGFR levels for CKD stage 2 patients increased from 79.34 (75.84, 84.09) ml/min/1.73m² at baseline to 82.60 (74.78, 89.68) ml/min/1.73m² at 12-month ($P < 0.05$). LDL-C and TG levels increased in the TN group, while TC, LDL-C, and TG levels increased in the TE group, but all increases remained within the normal range.

Conclusion: In both TN and TE CHB patients, TAF demonstrated robust virological response rates and ALT normalization rates with a good safety profile.

Abstract Submission No. 100736
P-0093

Altered Gut Microbiota on Entecavir Efficacy in Chronic Hepatitis B: A Cross-Sectional Study

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Background: Despite undergoing nucleos(t)ide analogue antiviral therapies, many patients with chronic Hepatitis B (CHB) fail to attain

optimal viral and immunological control. Prior research has suggested that shifts in gut microbiota may be a contributing factor to these suboptimal treatment outcomes. However, much of this evidence is derived from limited-scale animal studies, lacking substantial support from clinical data.

Methods: In this study, we conducted a cross-sectional study on a cohort of ninety CHB patients undergoing standard entecavir treatment. Gut microbiota composition was analyzed based on 16S rRNA sequencing across various strata of infection status, which included high/low levels of HBsAg (threshold was set to 1,000 IU/mL, denoted as S1, S0) and with/without of HBeAg seroconversion (denoted as E0, E1).

Results: Significant variances were observed in the microbial composition among patients with different infection statuses. At the phylum level, the E0S0 cohort had a higher proportion of Firmicutes and a lower proportion of Bacteroidota compared to the E1S1 cohort. Within the same S0 population, the E0 group showed a significant decline in the proportion of Proteobacteria. Similarly, among the E0 group, the proportion of Actinobacteriota was notably elevated in the S0 patients. Distinct differences were also observed at the class, order, and family taxonomic ranks.

Conclusion: Within the milieu of chronic HBV infection, the host's gut microbiome could serve as a pivotal factor impacting treatment efficacy or assessing disease prognosis. These findings may indicate the potential role of host-microbiome mechanisms of immune interactions in shaping long-term disease outcomes.

Abstract Submission No. 100761

P-0094

Prevalence of hep B reactivation in patients receiving non-rituximab immunosuppressive therapy.

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Background: Hepatitis B virus reactivation (HBVr) may develop in resolved HBV infection patients receiving chemotherapy. Risk of HBVr is perceived to be higher with haematological malignancy but this could be due to the use of stronger immunosuppressive therapy. Non-rituximab agents carry a lower risk of HBVr. We study the risk of HBVr in resolved HBV infection patients receiving non-rituximab therapy.

Method: Data of patients with resolved HBV infection receiving non-rituximab therapy who were seen in the hepatitis B immunosuppression clinic in Singapore General Hospital between March 2014 and May 2022 was retrospectively collected. HBVr is defined as detectable HBV DNA from previously undetectable DNA.

Results: A total of 111 resolved HBV infection patients who were initiated on non-rituximab chemotherapy did not receive chemoprophylaxis. There were 65(58.6%) females, with a median age of 63 (IQR 13). The most commonly use chemotherapy agent was alkylating agent (45.9%) and cytotoxic agent (39.6%). 9(8.1%) patients developed HBVr, none developed hepatitis B flare. All 9 patients had low HBV DNA load <200 IU/ml at reactivation. 3 patients required Entecavir due to rising HBV DNA load. Male, older age and lower baseline anti-HBs level were not associated with a higher risk of HBVr. 2(13.3%) patients with haematological condition developed HBVr, versus 7(7.3%) in other conditions (p=0.35).

Conclusion: Risk of HBVr is low in resolved HBV infection patients receiving non-rituximab chemotherapy. Close monitoring for reactivation is a feasible strategy in these patients.

Abstract Submission No. 100835

P-0095

Enhancing HBV Screening and Monitoring with Electronic Alerts

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BACKGROUND: Hepatitis B virus (HBV) reactivation is critical for patients undergoing systemic chemotherapy or immunosuppressive therapy. Reactivation of HBV can lead to severe hepatitis, sometimes with fatal consequences. Despite existing clinical guidelines recommending HBV screening and HBV-DNA monitoring, adherence remains suboptimal. To address this gap, we implemented an electronic alert system that prompts pre-treatment HBV screening and in-treatment HBV-DNA monitoring. Our study aimed to evaluate whether this alert system could improve guideline adherence and enhance patient management.

METHODS: The electronic alert system was introduced in our hospital in February 2020. We retrospectively analyzed data from 4943 patients treated between July 2014 and February 2022. We compared the rates of HBV screening and HBV-DNA monitoring before and after implementing the alert system.

RESULTS: Following the alert system implementation, there were notable improvements in HBs antigen measurement rate (from 96.2% to 98.6%), HBs antibody/HBc antibody measurement rate (from 82.8% to 88.9%), and HBV-DNA monitoring rate (from 56.1% to 82.2%). Subsequently, twenty-three patients undergoing HBV-DNA monitoring tested positive and received a prompt referral to a hepatologist for initiation of nucleotide analogues. **CONCLUSION:** Electronic alert systems play a crucial role in enhancing the management of HBV reactivation in patients receiving systemic chemotherapy and immunosuppressive therapy by facilitating guideline-directed HBV screening. These systems contribute to better patient outcomes by identifying at-risk individuals promptly.

Abstract Submission No. 100857

P-0096

The impact of steatosis and steatohepatitis in chronic hepatitis B patients: A longitudinal study

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Background: The evidence of the fibrotic effect of NAFLD or NASH in patients with chronic hepatitis B (CHB) remains controversial.

Methods: A retrospective cohort study on a liver biopsy population of treatment-naïve CHB patients was aimed to compare the cumulative liver cirrhosis incidences for 3 groups according to the NAFLD activity score (NAS): patients without steatosis, patients with simple steatosis and patients with steatohepatitis.

Results: Among the 695 CHB patients, 152 patients were found with steatosis (NAS score 1-2) and 91 patients were found with steatohepatitis (NAS score 3-8). Eighty patients developed cirrhosis, with a

median follow-up period of 58 months (IQR: 27-96). The 5-year cirrhosis incidences were 11.7% in patients without steatosis, 17.1% in patients with steatosis (Log rank $P = 0.181$) and 31.8% in patients with steatohepatitis ($P < 0.001$). The 10-year cirrhosis incidences were 16.6%, 30.2% (Log rank $P = 0.035$) and 44.8% ($P < 0.001$) in the 3 groups, respectively. The presence of simple steatosis and steatohepatitis was associated with higher risks of cirrhosis than the absence of steatosis in CHB patients (hazard ratio [HR] = 1.59, 95% confidence interval [CI]: 1.03-2.47, $P = 0.037$; HR = 3.09, 95% CI: 1.98-4.84, $P < 0.001$). A similar trend was found in the subgroup who received antiviral treatment within 6 months after liver biopsy.

Conclusions: Comorbidity with NAFLD, especially NASH, promotes the development of cirrhosis over a long-term follow-up in CHB patients. And simple steatosis might cause the difference in a relatively longer period of time.

Abstract Submission No. 100887
P-0097

Comparison of renal events during potent antiviral treatment in patients with chronic hepatitis B

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Background: Renal dysfunction is a major safety concern for patients with chronic hepatitis B (CHB) during long-term nucleos(t)ide analogues (NAs) therapy. We aimed to explore the association between potent NA treatment [entecavir (ETV), tenofovir disoproxil fumarate (TDF), tenofovir alafenamide (TAF)] and the risk of renal dysfunction for patients with CHB.

Methods: This retrospective study enrolled 2155 CHB patients who were treated with ETV ($n=1417$), TDF ($n=498$), or TAF ($n=240$) in Taipei Veterans General Hospital between January 2011 and March 2022. In a 3-year follow-up, the primary outcome was renal dysfunction, which was defined as estimated glomerular filtration rate decreased $>30\%$, or a chronic kidney disease stage worsen ≥ 2 stages compared to baseline.

Result: During NA therapy, the crude incidence rates of renal dysfunction were 4.42 (95% confidence interval CI 3.71-5.28), 3.85 (95% CI 2.79-5.32), and 4.84 (2.61-9.00) per 100 person-years in the ETV, TDF, and TAF groups, respectively. A multivariate analysis showed the independent risk factors for renal dysfunction were older age, history of stroke, lower serum albumin level, higher Charlson Comorbidity Index, higher fibrosis-4 score, and diuretics use, but not NA regimens. The adjusted hazard ratios (aHR) of renal dysfunction among these three NAs were as follows: TDF vs. ETV 1.406; 95% CI 0.950-2.081, $p=0.088$; and TAF vs. ETV (0.910; 95% CI 0.471-1.758, $p=0.778$), respectively.

Conclusion: There were no significant differences in the risk of renal dysfunction among patients using ETV, TDF and TAF.

Abstract Submission No. 100903
P-0098

Therapeutic Options for Entecavir-treated Chronic hepatitis B Patients with Low-level Viremia

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Objective: The aim of this study was to compare the efficacy of switching to TAF monotherapy with combination of entecavir with IFN treatment in entecavir-treated CHB patients with LLV.

Methods: This was a retrospective cohort study. Patients with CHB, treated with oral entecavir for more than 48 weeks between December 2018 and December 2021 at Beijing You'an Hospital, Capital Medical University, who had continuously detectable HBV DNA levels but less than 2000 IU/mL, were included. These patients were divided into TAF monotherapy group (TAF group) and entecavir combined with IFN group (IFN group). They were followed for 48 weeks. The therapeutic efficacy of the different therapies was analyzed.

Results: A total of 105 LLV patients, including 67 males and 38 females, were included. 65 patients (61.9%) were in the TAF group and 40 patients (38.1%) in the IFN group. The CVR rates at 48 weeks in the IFN group were similar to those in the TAF group, with no statistically significant difference (75.0% vs. 75.4%, $P = 0.999$). The degree of decline in HBV DNA at 48 weeks compared to baseline was also similar between the two groups, with no statistically significant difference (192 ± 421 vs. 142 ± 309 , $P = 0.487$). The HBeAg clearance rates at 48 weeks for the TAF and IFN groups were 20.0% (4/20) and 17.1% (6/35), respectively, with no statistically significant difference ($P = 0.792$).

Conclusion: For entecavir-treated CHB patients with LLV, switching to TAF monotherapy demonstrated comparable efficacy to entecavir combined with IFN treatment.

Abstract Submission No. 100915
P-0099

Risk factors for liver inflammation or fibrosis in HBeAg-positive indeterminate phase CHB Patients

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Objectives: To analyze the risk factors of advanced liver inflammation or fibrosis in HBeAg-positive hepatitis B indeterminate phase Patients with normal ALT

Methods: A retrospective study of 72 liver biopsy-proven patients were divided into mild (Metavir stage <2) and severe (Metavir stage ≥ 2) inflammation groups (48 cases vs. 24 cases) or fibrosis groups (44 cases vs. 28 cases).

Results: Logistic regression analysis identified three independent predictors of advanced inflammation: HBV DNA, ALT, and LSM. For each one-unit increase in the values of the above indicators, the probability of significant inflammation of liver tissue increases by 2.568 times, 9.2% and 75.3%. The AUC of above indicators in diagnosing advanced liver inflammation were 0.701, 0.662, and 0.661, respectively. The cutoff values of above indicators, were 7.81 IU/mL, 29.5 U/L, and 8.05 kPa respectively. The accuracy of the above three indicators combined diagnosis was the highest ($AUC = 0.87$), which was higher than the AUC of the indicators diagnosing advanced liver inflammation individually. Family history of hepatitis B and LSM were independent risk factors of advanced liver fibrosis. The risk of advanced liver fibrosis in patients with family history of hepatitis B

was 8.135 times higher than that without. For each one-unit increase in LSM was associated with a 48.5% increase in the risk of advanced fibrosis. The cutoff value of LSM was 8.05kpa.

Conclusion: HBV DNA, ALT, LSM and Family history might be important clues for us to identify immune-Active CHB from immune-tolerant CHB.

Abstract Submission No. 100918
P-0100

Risk factors for liver inflammation or fibrosis in HBeAg positive uncertain phase CHB Patients

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Objectives: To analyze the risk factors of advanced liver inflammation or fibrosis in HBeAg-positive hepatitis B indeterminate phase Patients with normal ALT

Methods: A retrospective study of 72 liver biopsy-proven patients were divided into mild (Metavir stage <2) and severe (Metavir stage ≥2) inflammation groups (48cases vs. 24cases) or fibrosis groups (44 cases vs.28cases).

Results: Logistic regression analysis identified three independent predictors of advanced inflammation: HBV DNA, ALT, and LSM. For each one-unit increase in the values of the above indicators, the probability of significant inflammation of liver tissue increases by 2.568 times, 9.2% and 75.3%. The AUC of above indicators in diagnosing advanced liver inflammation were 0.701, 0.662, and 0.661, respectively. The cutoff values of above indicators, were 7.8lgIU/ml, 29.5U/L, and 8.05kpa respectively. The accuracy of the above three indicators combined diagnosis was the highest (AUC = 0.87), which was higher than the AUC of the indicators diagnosing advanced liver inflammation individually. Family history of hepatitis B and LSM were independent risk factors of advanced liver fibrosis. The risk of advanced liver fibrosis in patients with family history of hepatitis B was 8.135 times higher than that without. For each one-unit increase in LSM was associated with a 48.5% increase in the risk of advanced fibrosis. The cutoff value of LSM was 8.05kpa.

Conclusion: HBV DNA, ALT, LSM and Family history might be important clues for us to identify immune-Active CHB from immune-tolerant CHB.

Abstract Submission No. 100920
P-0101

Distributional characteristics of HCV genotyping in HIV/AIDS population in Yunnan , China

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Objective: To understand the distribution characteristics of HCV genotypes in the HIV and hepatitis C virus (HCV)-infected population at the antiretroviral clinic of Yunnan Provincial Infectious Disease

Hospital, and to provide a basis for individualized treatment of HIV/HCV patients.

Methods: Clinical data of 232 HIV/HCV patients in the antiviral outpatient clinic of Yunnan Provincial Infectious Disease Hospital were collected from January 2022 to July 2023, and their HCV genotypes were detected.

Results: HCV genotyping was completed in 232 cases (95.47%), and four HCV genotypes (type 1, type 2, type 3, type 6) and nine gene subtypes (1b, 2a, 3a, 3b, 6a, 6n, 6u, 6v, 6xa) were detected. There were 95 cases of gene type 3b (40.95%), 64 cases of gene type 3a (27.59%), 34 cases of gene type 1b (14.66%), 22 cases of gene type 6n (9.48%), 6 cases of gene type 6a (2.59%), 4 cases of gene type 6xa (1.72%), 3 cases of undetectable type (1.29%), 2 cases of gene type 2a (0.86%), and Gene 6u type 1 (0.43%), Gene 6v type 1 (0.43%). Hepatitis C genotyping of HIV/HCV co-infected patients with different routes of infection showed statistically significant differences ($X^2=45.29$, $P<0.001$).

Conclusion: The distribution of HCV genes in HIV/HCV co-infected patients at the Antiviral Clinic of Yunnan Infectious Diseases Hospital was diverse, with type 3a and 3b as the main prevalent strains, and the route of infection was predominantly among intravenous drug addicts. The progression of liver fibrosis or cirrhosis was more pronounced in the HCV gene type 3b.

Abstract Submission No. 100933
P-0102

Effect of IFN-based Therapy in CHB Patients with Low-Level Viremia (OASIS project subgroup analysis)

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Background: Chronic hepatitis B patients with low-level viremia (LLV, HBV DNA <2,000 IU/mL) have higher risk for cirrhosis and hepatocellular carcinoma. However, evidence on optimizing therapeutic regimens for LLV remains limited.

Method: This analysis drew upon subgroup data from a multi-center, prospective real-world study (OASIS Project) from China, focusing on LLV patients at baseline. Virological and serological responses were assessed at 48 weeks of follow-up and were compared using chi-square tests.

Results: A total of 1640 LLV patients were categorized into five groups—A (Maintaining the same NAs, n = 489), B (switching to another NAs, n = 38), C (Maintaining the same NAs & adding PegIFNα, n = 892), D (switching to another NAs & adding PegIFNα, n = 77), and E (Ceasing NAs and switching to IFN monotherapy, n = 144). Group B had the highest CVR rate (76.9%) while Group E had the lowest (42.5%). The rates in Groups A (63.8%), C (60.6%), and D (62.5%) were similar. The differences among five groups were not significant ($p = 0.069$). However, IFN outperformed NAs regarding HBsAg seroconversion. (15.8% vs. 3.4%, $p < 0.001$).

Conclusions: For LLV patients, PegIFNα-based therapy had limited benefit in achieving CVR, but outperformed NAs regarding functional cure.

Abstract Submission No. 100939
P-0103

48 weeks outcome of switching from ETV to TAF in chronic hepatitis B patients

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Background: Real world data showed that switching from entecavir (ETV) to tenofovir alafenamide fumarate (TAF) could effectively improve viral suppression. However, long term outcome regarding to HBsAg level changes is uncertain.

Methods: In this single-center, prospective study, we enrolled patients who received ETV treatment for over 48 weeks at our hospital from 2015 to 2021. Eligible patients started treatment with TAF (TAF group) or continued ETV therapy (ETV group) for another 48 weeks according to their willing. The primary goal was to investigate 48 weeks outcome of HBsAg changes. Data on liver and renal function were also collected.

Results: 54 patients were enrolled, among whom 27 switched to TAF and 27 continued ETV treatment. Median age, gender, duration of prior ETV treatment, HBsAg level are listed in table 1. Patients in both groups exhibited a favorable virological response prior to treatment modification (HBV DNA < 50 IU/mL). TAF group exhibited a significant reduction in HBsAg level compared to ETV group after 48 weeks. ALT and eGFR were slightly improved in both group but without significance (Figure 1).

Conclusions: Patients with CHB can achieve improved reduction of HBsAg by Switching ETV to TAF, which may have significance of being foundation of HBV cure in the future.

Abstract Submission No. 100945

P-0104

TDF vsTAF on Risk of Osteoporotic Fracture in Patients with Chronic Hepatitis B

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Background: As tenofovir disoproxil fumarate (TDF) requires long-term use, a reduction in bone density should be considered a possibility when treating chronic hepatitis B (CHB) patients with aging and systemic diseases. Patients treated with tenofovir alafenamide (TAF) have improved bone mineral density loss compared to patients treated with TDF. Although improvements in bone density caused by TAF have been reported, studies on the actual reduction of fractures are insufficient. Therefore, we aimed to evaluate the impact of TAF on the risk of osteoporotic fractures in comparison with that of TDF.

Methods: A retrospective cohort study was conducted on 32,582 CHB patients who had been initially treated with TDF or TAF between

November 2017 and December 2020, using the national claims data of the Health Insurance Review and Assessment Service. The numbers of patients treated with TDF and TAF were 20,877 and 11,705, respectively. The annual fracture rate per 100 patients in each group was calculated, and the Cox proportional hazard ratio (HR) was analyzed after applying inverse probability treatment weights (IPTW) for both groups. **Results:** Among 32,582 patients, the average age was 47.8±11.2 years, 64.5% were men, and the follow-up period was 24.4±11.6 months. The incidence of osteoporotic fractures was 0.78 and 0.49 per 100 person-years in the TDF and TAF groups, respectively. After application of IPTW, the HR was 0.68 (95% confidence interval 0.55–0.85, p-value=0.001).

Conclusion: TAF-treated CHB patients had a significantly lower risk of osteoporotic fracture than that of TDF-treated patients.

Abstract Submission No. 100948

P-0105

SLC22A1 predicts the outcome of Pegylated IFNα-based treatment for HBeAg-negative CHB patients.

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Background: Pegylated IFNα-based treatment is the most common therapy for HBeAg-negative chronic hepatitis B patients to pursue clinical cure, but there is great heterogeneity in efficacy among different populations. SLC22A1 belongs to solute carrier family, specially expressed on the basolateral membrane of hepatocytes and its relationship with CHB has not been reported. We aim to explore the correlation between SLC22A1 and curative effect of pegIFNα-based treatment.

Methods: CHB patients whose HBeAg were negative, HBV DNA < 100 IU/mL, HBsAg < 1200 IU/mL and treated with peg-IFNα combined with nucleoside analog or not for at least 48 weeks were included. Their plasma at baseline, 12 weeks and 24 weeks after treatment was quantitatively detected for SLC22A1 by ELISA and their clinical data was analyzed together.

Results: A total of 128 patients whose age, sex and quantitative HBsAg at baseline were matched were included in this analysis, 65 uncured and 63 cured after 48-week treatment. The plasma SLC22A1 was higher in group cured than in group uncured at 12-week ($p < 0.0001$) and 24-week ($p < 0.0001$). The level of SLC22A1 increased in group cured with treatment, whereas stayed unchanged in group uncured (figure1). For the prediction of HBsAg clearance, AUROC of SLC22A1 at baseline, 12-week and 24-week were respectively 0.5495 ($p = 0.3345$), 0.7979 ($p < 0.0001$), 0.9148 ($p < 0.0001$) (figure 2).

Conclusions: The plasma SLC22A1 is involved in the outcome of peg-IFN-based treatment for HBeAg-negative chronic hepatitis B patients. The elevation of SLC22A1 during treatment predicts a higher clinical cure rate.

Abstract Submission No. 100980

P-0106

Effects of PegIFNα and NAs on Liver Fibrosis in CHB Patients (OASIS Project Subgroup Analysis)

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Background: The debate persists regarding whether PegIFN α is superior to Nucleos(t)ide Analogues (NAs) in improving liver fibrosis. This analysis aims to evaluate the liver fibrosis progression using liver stiffness measurements (LSM) offered by transient elastography (TE) examination.

Methods: This analysis was conducted in the data from a multicenter, prospective real-world study (OASIS project) in China. Patients were categorized into five groups with LSM of 7.3, 9.7, 12.4, and 17.5 kPa as thresholds. Changes in LSM across categories were defined as fibrosis regression or progression, while changes in the same category as indetermination. Comparisons were conducted using Chi-Square test, one-way ANOVA, and Kruskal-Wallis (K-W) test.

Results: A total of 331 patients who underwent TE examination at baseline and 48-week follow-up were included. At 48 week, the proportion of patients with fibrosis regression in IFN group was slightly lower than NAs group, but not statistically significant (20.0% vs. 24.6%, $p=0.499$). Similar conclusions were drawn in both HBeAg(+) (29.1% vs. 33.3%, $p=0.647$) and HBeAg(-) (19.0% vs. 23.5%, $p=0.492$) subgroups. Further analysis of the PegIFN α sub-group revealed that patients with fibrosis progression had a less decline in ALT ($p=0.024$) but a similar decline in HBsAg ($p=0.961$) from baseline to the 48-week follow-up.

Conclusion: PegIFN α and NAs showed similar efficacy in improving liver fibrosis in CHB patients. Patients receiving PegIFN α treatment with inadequate ALT reduction are more likely to experience fibrosis progression, suggesting hepatic inflammation factors may play a more significant role than virological factors in the progression of fibrosis.

Abstract Submission No. 101040

P-0107

Need of Treatment Modification in Entecavir Partial Virologic Responders with High Viral Load

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Background: The antiviral efficacy of ETV in chronic hepatitis B (CHB) patients with baseline high viral load (HVL) may be limited by insufficient response. Current guidelines suggest continuing an initial drug or adding another potent agent in the presence of partial virologic response (PVR) in CHB patients receiving entecavir (ETV). However, supporting data which one would be preferred are still limited. This study is aimed to evaluate the outcome of extended ETV monotherapy in CHB patients with HVL and/or PVR, and to propose a management strategy according to the antiviral response.

Methods: A total of 197 treatment naïve CHB patients who newly started ETV 0.5mg were included. Antiviral responses were compared between HVL ($\geq 8 \log_{10}$ IU/mL) and non-HVL group up to 120 months.

Results: Overall, 95 and 102 patients were included in the HVL and non-HVL group, respectively. Mean HBV DNA at baseline was 7.70 ± 0.45 and $5.58 \pm 1.04 \log_{10}$ IU/mL in HVL and non-HVL group. Virological response (VR) (HBV DNA < 20 IU/mL) was achieved in 65.9%, 79.2%, 83.9% and 82.7% of HVL patients and in 93.3%, 96.3%, 97.1% and 96.7% of non-HVL patients at months 24, 36, 60 and 120 respectively. Compared with non-HVL group, HVL group showed lower cumulative virologic response during 120 months of therapy ($P=0.001$). Antiviral resistance to ETV

(rtS202G+rtM204V+rtL180M) was developed in 4 of 127 HVL group patients (4.2%). The 75 (83.3%) and 49 (53.3%) patients showed PVR at month 6 and 12 in HVL group, respectively. The multivariate analysis showed that having HVL at baseline along with PVR at 6 months (Odds ratio, 0.12; $p = 0.01$) was a significant factor for VR at the 60-months. However, the rates of biochemical responses and HBeAg seroconversion were similar between the HVL group and non-HVL group.

Conclusions: Patients with baseline HVL and PVR at month 12 are exposed to risk of resistance to ETV and insufficient treatment response rates. We suggest CHB patients with baseline HVL and PVR need to modify a treatment strategy during ETV therapy.

Abstract Submission No. 101049

P-0108

No TAF resistance in adult, HBeAg +/- patients with CHB infection after treated with TAF to 8 years

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Background and Aims: We have previously shown no resistance to TDF after 8 years, and TAF resistance hasn't been detected after up to three years of treatment in CHB patients. Here we present annual resistance surveillance results from years 3 through 8 of TAF treatment.

Methods: Two randomized, double-blind, active-controlled trials assessed TAF treatment of HBeAg-negative and HBeAg-positive CHB participants over 8 years. Sequence analysis of the pol/RT region was conducted annually for participants experiencing a viral breakthrough, blip, or persistent viremia with HBV DNA ≥ 69 IU/mL those discontinuing with HBV DNA ≥ 69 IU/mL. Participants with substitutions at conserved pol/RT sites or polymorphic residues were phenotyped against TAF.

Results: Out of 1298 participants, the percentage qualifying for resistance annually from Year 3 to Year 8 remained low (range 1.7 – 8.4%). Those qualifying for sequencing showed progressively declining proportions with persistent viremia with only 3 persistently viremic participants by Year 8. Their baseline viral load was $> 10^8 \log_{10}$ IU/mL and declined over time but did not reach 69 IU/mL. During the 5-year open-label period where all participants received TAF, conserved site substitutions in the HBV viral pol/RT were observed in 13 participants. Polymorphic site substitutions in ≥ 2 participants were observed at various time points.

Conclusion: No resistance to TAF was detected in adult CHB participants with positive or negative HBeAg who received TAF therapy for up to 8 years. These findings support TAF as a long-term viral suppressive therapy for CHB infection regardless of HBeAg status.

Abstract Submission No. 101050

P-0109

Metabolic Effects and Cardiovascular Risks of Antiviral Treatments in Chronic Hepatitis B Patients

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Introduction: Antiviral treatments for chronic hepatitis B (CHB) have been known to have different metabolic effects. This study aimed to reveal whether TAF-induced dyslipidemia and atherosclerotic cardiovascular disease (ASCVD) risks are significant in CHB patients.

Methods: This study used 15-year historical cohort including CHB patients in Korea and consisted of two parts: the single-antiviral and switch-antiviral study. In the single-antiviral study, Metabolic profiles and estimated ASCVD risks were compared longitudinally using propensity score matching (PSM). In the switch-antiviral study, pairwise analyses were conducted in patients who switched NAs to TAF or from TAF.

Results: In the single-antiviral study, body weight and statin use significantly differ between groups before PSM. Linear regression model was then utilized for adjusting major confounders after PSM. Changes in total cholesterol were significantly different (-2.57 mg/dL/year in the TDF-only group and +2.88 mg/dL/year in the TAF-only group; $P=0.002$ and $P=0.02$, respectively). In the TDF-only group, HDL cholesterol decreased as well (-0.55 mg/dL/year; $P<0.001$). The TAF-only group had the greatest increase in ASCVD risk, followed by the TDF-only and non-antiviral groups. In the switch-antiviral study, patients who switched from TDF to TAF had a higher total cholesterol after switching (+9.4 mg/dL/year) than before switching (-1.0 mg/dL/year; $P=0.047$).

Discussion: TAF was associated with increased total cholesterol, whereas TDF was associated with decreased total and HDL cholesterol. Both TAF and TDF increased ASCVD risks, and statin use might mitigate these risks. Dyslipidemia and its associated outcomes should be monitored with preventive treatment with statins in CHB patients.

Abstract Submission No. 101053

P-0110

Bone and Renal Safety of TAF at 8 Years in CHB Patients with Underlying Risk Factors for Use of TDF

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Background: Current guidelines recommend tenofovir alafenamide (TAF) or entecavir for patients with risk factors for tenofovir disoproxil fumarate (TDF)-associated toxicities. We evaluated the safety of TAF, including in patients switched from TDF to TAF, with TDF-related bone and/or renal risks per EASL guidelines.

Methods: In two similarly designed Phase 3 studies, HBeAg-positive ($N=873$) and HBeAg-negative ($N=425$) patients were initially randomized to TAF 25 mg vs TDF 300 mg for up to 3 years, followed by open-label TAF. Safety data covered bone and renal parameters over 8 years in subsets with/without TDF risk factors: age >60 y, osteoporosis, eGFR <60 mL/min, urine albumin-to-creatinine ratio >30 mg/g, or serum phosphorus <2.5 mg/dL.

Results: Of 1298 patients, 239 (18%) had ≥ 1 risk factor. Baseline demographics were similar between treatment groups: 29% with age >60 y, 60% male, 40% with eGFR <90 mL/min, and 6% and 36% with osteoporosis at hip and spine, respectively. TAF-treated patients with risk factors showed greater eGFR decline at Year 8 (-8.3 vs -4.6 mL/min) compared to those without. In the TDF→TAF groups, a greater degree of recovery was noted in those with risk factors switched at Year 2 vs Year 3. In the TAF group, hip BMD decline was small at Year 8 regardless of risk factors. A sustained reversibility of TDF-associated bone loss was indicated. Consistent changes were seen in proteinuria markers and serum bone biomarkers.

Conclusion: Long-term TAF treatment showed favorable renal and bone tolerability in patients with/without baseline risk factors for TDF use supporting guideline recommendations.

Abstract Submission No. 101054

P-0111

Impact of long-term treatment with TAF or after switch from TDF on HCC incidence in CHB Patients

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Background: Antiviral therapy reduces HCC risk in CHB patients, particularly with TDF or entecavir. TAF is a first-line recommended treatment for CHB with comparable efficacy to TDF with higher ALT normalization and no resistance. We evaluated HCC incidence and risk at 8 years (y) in CHB patients treated solely with TAF or initially with TDF and then switched to TAF.

Methods: In two similarly designed Phase 3 studies, HBeAg-positive ($n=859$) and -negative ($n=439$) CHB patients were randomized to TAF 25 mg or TDF 300 mg for up to 3y (double-blind phase), followed by open-label TAF through Y8. HCC was assessed by local standards of care and by hepatic ultrasonography. Three validated models (REACH-B, aMAP, and mPAGE-B) were utilized to assess HCC risk.

Results: Through Y8, HCC was diagnosed in 21/1298 patients. Eight HCC cases were in cirrhotic patients. Median time to HCC onset was 729 days. Advanced age, male gender, and cirrhosis were more common in HCC, proportionately, more HCC patients were HBV genotype C and had BL HBV DNA 6 to ≤ 8 log₁₀ IU/mL. With treatment over 8y, by REACH-B, HCC incidence was significantly reduced ($P<0.0001$). Of patients predicted to be low risk for HCC at BL, nearly all remained low risk at Y8, and substantial proportions estimated to be medium or high risk shifted to a lower risk at Y8.

Conclusion: CHB patients treated with TAF alone or switched from TDF to TAF for up to 8 y showed reduced HCC risk compared to predictions.

Abstract Submission No. 101061

P-0112

Long-term efficacy of final 8 years of TAF Ph3 studies in CHB patients

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Background and Aims: In 2 similarly designed double-blind (DB), randomized (2:1), Phase 3 studies (Study 108 in HBeAg-negative patients [N=425] and Study 110 in HBeAg-positive patients [N=873]), tenofovir alafenamide (TAF) demonstrated noninferior efficacy relative to tenofovir disoproxil fumarate (TDF) in the blinded assessments. After completing up to 3 years (yr) of DB treatment, all patients were eligible to receive open-label (OL) TAF through week 384 (yr 8).

Method: Efficacy was assessed for each study by missing equals excluded (M=E) approach of the full analysis set and included serial assessments for viral suppression (HBV DNA < 29 IU/mL), ALT normalization by 2018 AASLD criteria, serologic responses, and fibrosis change by serum FibroTest. Resistance analyses, including deep sequencing of HBV pol/RT (at baseline and annually), for those with virologic breakthrough/blip, persistent viremia, or treatment discontinuation with viremia were performed.

Results: Of 1298 randomized and treated patients, 1157 (89%; 775 TAF; 382 TDF) entered the OL phase, including 180 and 202 TDF-treated patients who began OL TAF at week 96 (TDF-OL TAF 6 yr) or week 144 (TDF-OL TAF 5 yr) based on timing of a protocol amendment. Overall, 974 (75%) participants completed OL study treatment. The most common reasons for discontinuation were withdrawal of consent, loss to follow-up, or investigator discretion.

Conclusion: After 8 yr of treatment with TAF or up to 6 yr after switch from TDF, virologic suppression rates remained high across all groups; up to 33% achieved HBeAg/HBeAb seroconversion, while HBsAg loss was low (≤5%).

Abstract Submission No. 101065
P-0113

Safety profile of final 8 years of TAF Ph3 studies in CHB patients

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Background and Aims: In 2 similarly designed double-blind (DB), randomized (2:1), Phase 3 studies (Study 108 in HBeAg-negative and

Study 110 in HBeAg-positive patients), tenofovir alafenamide (TAF) demonstrated noninferior efficacy with superior renal and bone safety compared to tenofovir disoproxil fumarate (TDF) at week 96. After completing DB treatment, all patients were eligible to receive open-label (OL) TAF through year 8.

Method: In a pooled analysis, treatment-emergent AEs, serious AEs (SAEs), discontinuations, and laboratory abnormalities were assessed in patients who received OL TAF. Changes from baseline in estimated GFR and changes in hip and spine bone mineral density (BMD) were assessed.

Results: Overall, 974 (75%) participants completed OL study treatment. The overall incidence of patients experiencing AEs was similar among groups. Rates of Grade 3/4 AEs and AEs leading to discontinuation (D/C) were low and similar among groups. Few Grade 3/4 AEs or SAEs were related to the study drug. Overall, the most common Grade 3/4 lab abnormalities (>2%) were increased amylase (TAF 1.9%, TDF-TAF 2.7%), creatine kinase (TAF 1.4%, TDF-TAF 2.1%), fasting cholesterol (TAF 1.4%, TDF-TAF 2.9%), fasting LDL (TAF 5.9%, TDF-TAF 8.0%), and urine glucose (TAF 5.2%, TDF-TAF 2.7%). After experiencing declines in eGFR_{CG} and hip/spine BMD with TDF treatment in the DB phase, renal and bone outcomes improved following the switch to OL TAF with minimal change through year 8.

Conclusion: Long-term TAF treatment was safe and well tolerated, with minimal changes in eGFR_{CG} and BMD occurring over 8 years.

Abstract Submission No. 101107
P-0114

Prognostic analysis of CHB cirrhotic patients with hypoviremia based on a high-sensitivity assay.

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OBJECTIVE: To explore the clinical prognosis of patients with hepatitis B cirrhosis hypoviremia treated with NUCs.

Methods: Patients with hepatitis B cirrhosis treated with NUC were collected from 2020 to 2022 at Taiyuan No.3 hospital and were divided into group 1 low viremia group (HBV DNA 10–2000 IU/ml), group 2 below the lower limit of detection (HBV DNA <10 IU/ml), and group 3 undetectable target group by high sensitivity test. The patients were followed up for 48 weeks to observe the incidence of cirrhosis-related complications and HCC.

Results: 251 patients with NUC (ETV, TDF, and TAF) treated with hepatitis B cirrhosis were in group 1, 107 in group 2, and 119 in group 3. New cirrhosis-related complications occurred in all three groups, and the number of new cases of hypersplenism, ruptured esophagogastric fundal varices bleeding, portal vein thrombosis, and hepatorenal syndrome was not statistically significant. However, the number of new esophagogastric fundal varices was statistically significant, and the highest rate was observed in group 2.38 (15.14%) of people who developed HCC (group 1: 4 cases; group 2: 16 cases; group 3: 18 cases; and among them, 7 died). There was no statistically significant difference in the incidence of HCC or mortality among the groups with different DNA loads. Even in those with a complete virologic response, cirrhosis-related complications or even hepatocellular carcinoma may occur.

Conclusion: It is important to determine whether cirrhotic patients have achieved a complete virological response through high-sensitivity HBV DNA testing to actively control disease progression.

Abstract Submission No. 101108
P-0115

Hepatic Histologic Status and Pathologic Diagnosis in HBV Carriers with Normal or Mildly Elevated ALT

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OBJECTIVE: To analyze the hepatic inflammation and fibrosis and clinical diagnosis in HBV carriers with normal or mildly elevated alanine aminotransferase (ALT) levels.

Methods: Thirty-seven HBV carriers (DNA-positive) with normal or mildly elevated ALT levels who underwent hepatic puncture biopsy at Taiyuan No.3 Hospital from April 2020 to October 2022 were retrospectively collected to clarify the diagnosis and fibrosis, as well as the degree of inflammation in the patients.

Results: The 37 HBV carriers were aged (36.27±12.54) years, with ALT (36.89±23.20) IU/ml and a male/female ratio of 1.31/1. The stage of liver fibrosis ranged from S0-S4, with a predominance of S0-S1 in 20 cases (54%), and there were 17 patients with S ≥ 2 (46%), with S2 in 10 cases (27%), S3 in 3 cases (8%), and S4 in 4 cases (11%); liver inflammatory activity was graded between G0-G4, with G0-G1 predominating in 29 cases (78%) and G ≥ 2 in 8 patients (22%). A liver puncture definitively diagnosed 31 cases of chronic hepatitis B and 6 cases of cirrhosis.

Conclusion: Most of the HBV carriers with normal or mildly elevated ALT levels had varying degrees of liver fibrosis and liver inflammation, and some had reached cirrhosis. It is recommended to improve the histopathological examination of the liver in order to assess the indications for antiviral therapy and avoid delay in treatment.

Abstract Submission No. 101163

P-0116

Hydroxychloroquine Reduced the Risk of Hepatocellular Carcinoma in patients with HBV infection

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Background: Chronic hepatitis B virus (HBV) infection is one of the leading causes of hepatocellular carcinoma (HCC) worldwide. Hydroxychloroquine (HCQ) is a medication used to treat autoimmune disorders and recent studies have suggested that it may also have anticancer properties based on autophagy and non-autophagy mechanisms. This study investigates the correlation between HCQ use and the risk of hepatocellular carcinoma in patients with chronic HBV infection.

Method: HBV infected patients were enrolled from Taiwan's National Health Insurance Research Database (covering January 1, 2006, to December 31, 2016). The association between HCQ use and HCC risk was evaluated using the Kaplan-Meier method and Cox proportional hazards regression

Results: 434,690 HBV patients were enrolled and individual matching with 1:10. Among 3,871 patients using HCQ (defined as ≥ 28 cumulative defined daily doses [cDDD]), 39 developed HCC. Comparatively, among 38710 patients not using HCQ (≤ 28 cDDDs), 795 were diagnosed with HCC. HCQ use by HBV patients showed a significantly reduced HCC risk with an adjusted hazard ratio (aHR) of 0.47 (95% CI, 0.32~0.69). Furthermore, no observable dose-response relationship between HCQ use and HCC risk.

Conclusion: HCQ use appears to lower the risk of HCC among patients with HBV infection, suggesting potential benefits in preventing HCC in this population. Further research is necessary to confirm these findings and underlying mechanisms.

Abstract Submission No. 101208

P-0117

Abnormal rate of renal function index and the related risk factor in chronic hepatitis B patients

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Background: To investigate the abnormal rate of renal function index and related potential risk factors in CHB patients with or without antiviral treatment of nucleos(t)ide analogues.

Methods: Collected clinical data of CHB patients with urinary β2 microglobulin detection, including demographic characteristics, HBV DNA, ALT, AST, total bilirubin, direct bilirubin, urea nitrogen, creatinine, cholesterol, triglyceride, high density lipoprotein, low density lipoprotein, liver imaging and other routine tests from June 2022 to June 2023 in Shanghai Eastern Hepatobiliary Surgery Hospital. The normal of urinary β2 microglobulin is defined as < 0.173, and the normal of eGFR is defined as ≥ 90ml/min. Abnormal renal function index proportion and related risk factors were analyzed.

Results: 500 CHB patients were enrolled, aged 44.7±10.8 years, 67.2% were male, 57.2% were treated with antiviral drugs, and 52.2% had HBV-related family history. 28.8% patients with fatty liver, 35.0% with liver fibrosis, and 13.2% with cirrhosis. 43.2% patients with eGFR < 90ml/min, and 56.2% patients with abnormal rate of urinary β2-GM. There was no significant difference in the abnormal rate of urinary β2-GM between the untreated group and the antiviral treatment group (54.2% vs. 57.7%, P=0.25). Abnormal rate of β2-GM after more than one year ETV treatment was 54.6%. In the TE group, 56.4% patients with eGFR ≥ 90ml/min had abnormal urinary β2-GM.

Conclusion: Urinary β2-GM has a higher proportion of diagnosis than eGFR for renal injury in CHB patients. Male patients with CHB need to pay more attention to monitoring renal function and use antiviral regimens with renal safety profile.

Abstract Submission No. 101209

P-0118

Abnormal rate of renal function index and the related risk factor in chronic hepatitis B patients

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Background: To investigate the abnormal rate of renal function index and related potential risk factors in CHB patients with or without antiviral treatment of nucleos(t)ide analogues.

Methods: Collected clinical data of CHB patients with urinary $\beta 2$ microglobulin detection, including demographic characteristics, HBV DNA, ALT, AST, total bilirubin, direct bilirubin, urea nitrogen, creatinine, cholesterol, triglyceride, high density lipoprotein, low density lipoprotein, liver imaging and other routine tests from June 2022 to June 2023 in Shanghai Eastern Hepatobiliary Surgery Hospital. The normal of urinary $\beta 2$ microglobulin is defined as <0.173 , and the normal of eGFR is defined as ≥ 90 ml/min. Abnormal renal function index proportion and related risk factors were analyzed.

Results: 500 CHB patients were enrolled, aged 44.7 ± 10.8 years, 67.2% were male, 57.2% were treated with antiviral drugs, and 52.2% had HBV-related family history. 28.8% patients with fatty liver, 35.0% with liver fibrosis, and 13.2% with cirrhosis. 43.2% patients with eGFR < 90 ml/min, and 56.2% patients with abnormal rate of urinary $\beta 2$ -GM. There was no significant difference in the abnormal rate of urinary $\beta 2$ -GM between the untreated group and the antiviral treatment group (54.2% vs. 57.7%, $P=0.25$). Abnormal rate of $\beta 2$ -GM after more than one year ETV treatment was 54.6%. In the TE group, 56.4% patients with eGFR ≥ 90 ml/min had abnormal urinary $\beta 2$ -GM.

Conclusion: Urinary $\beta 2$ -GM has a higher proportion of diagnosis than eGFR for renal injury in CHB patients. Male patients with CHB need to pay more attention to monitoring renal function and use antiviral regimens with renal safety profile.

Abstract Submission No. 101281

P-0119

Circulating Capsid-Antibody Complex

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Background: It was reported that the naked capsids exist as capsid-antibody-complexes (CACs) in the circulation of patients with chronic hepatitis B (CHB). The previous studies have shown that CACs were involved in HBV infection induced hepatic injury. The purpose of this study was to investigate the correlation between CACs with hepatic inflammation and its clinical significance as a novel marker of hepatic inflammation.

Methods: This study included 611 CHB patients (untreated cohort: 316 cases, liver biopsy cohort: 260 cases, therapy cohort: 35 cases). The levels of serum CACs were determined based the semi-quantitative method established by our group. The differences between groups of CACs levels and their correlation with key clinical indicators were analyzed.

Results: Firstly, the serum CACs levels increased significantly in hepatitis phases ($p < 0.0001$). Further analysis of liver biopsy cohort showed serum CACs levels in G ≥ 2 group was higher than that in G < 2 group ($p < 0.0001$), and positively correlated with G grade, ALT, AST and GGT. ROC curves indicated that CACs ($AUC=0.686, P=0.01$) have higher diagnostic accuracy in indicating hepatic inflammation than ALT, HBcAb and HBV DNA. In addition, CACs identified hepatic inflammation in CHB patients with normal ALT ($AUC=0.638, p=0.035$). Finally, serum CACs levels in CHB patients decreased gradually and positively correlated with ALT and HBV DNA during treatment.

Conclusions: Taken together, CACs can be a novel marker for hepatic inflammation, especially for CHB patients with normal ALT, which can effectively supplement the existing clinical noninvasive hepatic inflammation indicators.

Abstract Submission No. 101306

P-0120

State of Fibrosis Following NA Therapy In Patient With Chronic HBV Infection in Mongolia

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Background: The high prevalence of hepatitis B virus among the population of Mongolia has become a public health problem. Chronic hepatitis B causes cirrhosis, which can progress to HCC. Alcohol abuse, obesity, and hepatitis B and C are the main causes of cirrhosis.

Purpose: To compare fibrosis before and after NA therapy with the Elastography device in patients with B virus infection.

Methods: A comparative study of progression of liver fibrosis before and during the NA therapy in patient with chronic HBV infection. Out of 1100 patients undergone NA treatment, 207 people were eligible for the study because of lack of elastography data. But out of those 96 patients fulfilled our inclusion criteria. 72 patients had taken TAF and 24 patients had taken Entecavir.

Results: 49.4% of patient who took TAF had an increase in stiffness, 40.7% decreased, and 9.9% had no change. 50% of patient who took Entecavir had an increase in stiffness after treatment, 42.9% decreased, and 7.1% showed no change. The mean duration of the drug intake was 12 months.

Conclusion: Fibrosis regression was common in many other HBV treatment studies. But in our study fibrosis progression was observed in higher rates than those of regressed. We think it might be due to short observation period, or because NAs do not clear HBsAg, or because some patients were taking alcohol during the treatment, or inflammation did not stop during the treatment

Abstract Submission No. 101311

P-0121

Efficacy of TMF combined with Peg-IFN for treatment-naïve chronic hepatitis B: a real world study

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Background: Selection of nucleos(t)ide analogues (NAs) is crucial for improving cure rates in chronic hepatitis B. This study evaluated the effectiveness of Tenofovir amibufenamide (TMF) combined with pegylated interferon (Peg-IFN) compared to tenofovir disoproxil fumarate (TDF)+ Peg-IFN and Entecavir (ETV)+ Peg-IFN in treatment-naïve patients.

Methods: 251 treatment-naïve patients with chronic hepatitis B received NAs and Peg-IFN for at least 24 weeks. They were divided into

TMF + Peg-IFN, TDF + Peg-IFN, and ETV + Peg-IFN groups. The primary endpoint was HBsAg clearance at 24 and 48 weeks.

Results: Among the 251 participants, 60 achieved HBsAg clearance at 24 weeks, with 16 in TMF + Peg-IFN, 25 in TDF + Peg-IFN, and 19 in ETV + Peg-IFN. At 48 weeks, 159 participants were included, with 30 in TMF + Peg-IFN, 50 in TDF + Peg-IFN, and 34 in ETV + Peg-IFN achieving clearance. The type of NA medication did not significantly affect clearance rates at 24 weeks ($P=0.315$) and 48 weeks ($P=0.439$) after adjusting for age, gender, and baseline HBsAg levels.

Conclusions: TMF, TDF, and ETV combined with Peg-IFN show comparable efficacy in achieving HBsAg clearance in treatment-naïve patients with chronic hepatitis B.

Abstract Submission No. 101375

P-0122

Prevalence of Fibrosis and Steatosis in newly diagnosed asymptomatic Hepatitis B and C patients

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Background and Aims: Chronic HBV and HCV can present with liver steatosis and advanced fibrosis due to infection itself or metabolic comorbidity. We aimed to determine prevalence of hepatic steatosis and fibrosis in asymptomatic HBV and HCV at presentation using Fibroscan.

Methods: Consecutive patients ($n=383$) with newly diagnosed HBV ($n=323$) or HCV ($n=60$) underwent Fibroscan (ECHOSENS 630 Xpert) at presentation. Patients with hepatic decompensation, chronic kidney disease, HIV, alcohol abuse and pregnancy were excluded. F0, F1/F2, F3 and F4 fibrosis was defined as LSM values <6 kPa, 6-8 kPa, 8.1-12.5 kPa and >12.5 kPa respectively. Steatosis severity; S1(mild), S2 (moderate) and S3 (severe) was defined as CAP values 222-246 dB/m, 247-273 dB/m and ≥ 274 dB/m respectively.

Results: Details of liver stiffness and steatosis is mentioned in Table. Among 12 patients with HCV and F4 fibrosis, 5 had severe and 4 had moderate steatosis. Presence of metabolic syndrome was not associated with greater steatosis ($p=0.137$) and fibrosis ($p=0.158$) in HCV cases. Among 17 patients with HBV and F4 fibrosis, 8 had severe and 2 had moderate steatosis. Presence of metabolic syndrome was associated with greater steatosis ($p<0.001$) and fibrosis ($p=0.001$) in HBV.

Conclusions: In newly diagnosed patients with chronic viral hepatitis, metabolic syndrome correlates with fibrosis and steatosis in HBV, but not in HCV.

Abstract Submission No. 101420

P-0123

FUNCTIONAL AND MORPHOLOGICAL ABNORMALITY OF LIVER AMONG DIABETIC PATIENTS WITH VIRAL HEPATITIS

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Background: The management of chronic liver disease depends on the degree of liver fibrosis. Materials and methods: We collected 320 serums samples of DM, HCV (-) and DM, HCV (+) different groups. It was a matched population based case control study which included 123 adults, aged 28-80 years old who diagnosed DM in MJH.

Results: There were 350 patients in immunology: anti-HCV 32.34% of the patients were diagnosed with Hepatitis B and C, 26.83% of were infected with HCV, 4.94% were infected with HBV, and 0.57% were infected with both HCV and HBV in immunology: anti HCV 29.37 $\pm$ 18.9; HBsAg 590.134 $\pm$ 1013.7; M2BPGI 2.24 $\pm$ 2.2. relationship of fibrosis test associated with DM, HCV (-) and DM, HCV (+) patients. HCV (+), diabetes patients; M2BPGI and NAFLD fibrosis score was 0.7 unit higher than HCV (-), DM. DM. M2BPGI was decreased by 16.1% in HCV (+), diabetes patients; group after the treatment. Despite, the M2BPGI was dropped by 4.7% in HCV (+), non-DM.

Discussion: 1. In our study population, 32.34% of the patients were diagnosed with Hepatitis B and C, 26.83% of viral hepatitis patients were infected with HCV, 4.94% were infected with HBV, and 0.57% were infected with both HCV and HBV 2. DM, HCV (+) the indicators of liver fibrosis such as fibroscan, M2BPGI were higher than in people with DM, HCV (-). 3. M2BPGI was decreased by 19.4% in HCV (+), DM; group after the treatment. Despite, the M2BPGI was dropped by 6.6% in HCV (+), non-DM. Top of Form

Abstract Submission No. 101447

P-0124

Comparison of Tenofovir Alafenamide and Entecavir Therapy in Patients with Severe Acute Hepatitis B

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Background and aims: Treatment of Acute Hepatitis B is mainly supportive. However, antivirals may be warranted in certain situations such as severe acute hepatitis. Real-world data regarding efficacy of Tenofovir alafenamide (TAF) compared to Entecavir (ETV) for Severe AVH-B is lacking. We aimed to retrospectively compare the efficacy of the two antivirals.

Methods: Patients with severe acute hepatitis who were found to have IgM Anti HB core positive in the past 2 years were included and data retrieved from EMR. Patients were categorised into two groups, TAF and ETV group. Follow up data was assessed.

Results: Twenty patients were diagnosed with Severe Acute Hepatitis-B. Of them 11 patients received Tenofovir alafenamide (25mg/day) and 9 patients received Entecavir (0.5mg/day). After 4 weeks of treatment, the TAF treatment group exhibited a significantly decline in HBV DNA viral load ($P=0.029$). The mean duration for undetectable DNA were comparable (39.2 $\pm$ 12.5 days (TAF) vs 56.8 $\pm$ 18.4 days (ETV), $P=0.46$). The seroconversion (HBsAg loss) was significantly faster with TAF (96.5 $\pm$ 20.5 days vs 140.5 $\pm$ 25.4 days, $P=0.04$).

Conclusion: This real-world retrospective study showed that TAF is more effective than ETV in reducing viral load and achieving faster seroconversion in patients with severe acute hepatitis B.

Abstract Submission No. 101451

P-0125

Liver cirrhosis with gastric adenocarcinoma a patient case report

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The prevalence of gastric cancer is higher people with liver cirrhosis than people without liver cirrhosis. The contributing factors include stomach ulcers, gastropathy, zinc deficiency, alcohol and tobacco use, and *Helicobacter pylori*. By preventing or reducing the intake of these factors, the development and progression of cancer can be prevented. Scientists are also investigating whether hepatitis B virus (HBV) infection may be a risk factor for not only liver cancer but also gastric cancer. How to reduce the risk of stomach cancer in people with cirrhosis? is still a serious problem. Patient 37 years old, male presented with symptom of poor appetite, fatigue in our hospital. In 2006, hepatitis B and D viruses was diagnosed and he regularly took vemlidy once a day. He smokes 10 cigarettes a day for 20 years. On gastroscopy 2.0*2.0 cm ulcerative-infiltrative lesion in posterior wall of the cardia. Biopsy was taken. Biopsy result poorly differentiated adenocarcinoma, *helicobacter pylori* is positive. He underwent open total gastrectomy Roux Y D2 dissection surgery. Cirrhosis was diagnosed by taken biopsy from the liver during surgery. A patient's symptom had decreased and he was discharged 7 days later. HBV-DNA was 863700. He was taken vemlidy (tenofovir alafenamide) medicine once a day for 6 months, HBV-DNA 18500. For patients with gastric cancer and liver cirrhosis with Child-Pugh depending on the stage, it is necessary to choose the right treatment option

Abstract Submission No. 101466

P-0126

eALT-F: a new method to identify patients with HCC from ultra-high HBV viral load population

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Background: Ultra-high viral load HBV belongs to the immune tolerance (IT) stage and is associated with an increased risk of hepatocellular carcinoma (HCC) occurrence. The purpose of this study was to investigate the clinical features of individuals with ultra-high HBV viral load and created a novel chronic hepatitis B (CHB) staging method that can help identify patients with medium to high HCC risk more effectively.

Methods: In total 2118 patients with HBV DNA > 1x10⁷ IU/ml who visited in Peking University People's Hospital between January 2010 and March 2023 were enrolled retrospectively.

Results: In the overall patients, more than one-third of the patients were under 30 years old (40.1%), furthermore, a small proportion of older people (>60 years) also have ultra-high HBV viral load (4.3%). 9.1% and 6.7% individuals with ultra-high HBV viral load showed FIB-4>3.25 and aMAP≥50, respectively. In the traditional stages of CHB, which based on HBeAg and ALT (an upper limit of normal

(ULN) ALT level at 40 IU/L for both men and women), we found no matter in which phases, there was a certain proportion of patients at risk of developing HCC (4.1%, 6.4%, 25.0% and 20.3%). However, in the new "eALT-F" stages, which were based on HBeAg, ALT (the ULN of ALT level at 30IU/L for men and 19IU/L for women) and/or FIB-4 levels (>1.45), aMAP≥50 was only observed in chronic hepatitis patients with positive or negative HBeAg (6.4% and 22.1%).

Conclusion: The "eALT-F" staging method, based on HBeAg, ALT and/or FIB-4 levels was more effective in identifying medium to high-risk patients with HCC from patients with ultra-high HBV viral load than the traditional staging method.

Abstract Submission No. 101477

P-0127

Impact of Antiretroviral Therapy on Liver Enzymes in HIV Patients in WRH, Nepal

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Background: Antiretroviral therapy (ART) has been a remarkable achievement in treating HIV disease, but it may also exacerbate liver disease. Monitoring the viral load and CD4 counts of HIV patients is crucial in evaluating the outcome of ART. This study aimed to assess the level of liver enzymes in HIV patients, taking into consideration the effect of comorbidities and different drug therapies.

Methods: A pre-post study was conducted on 250 HIV patients at the Western Regional Hospital, an ART center of Nepal, before and after the ART. Laboratory variables, ART use, viral load and CD4 count were obtained at baseline and over 18 months of the period. Various statistical tests were used to analyze based on the nature of data.

Results: Among 250 patients, 120 (48%) were males and 130 (52%) were females with a median age of 40. ART was initiated to 44 (17.6%), 45 (18.0%), 160 (64%) and 1 (0.4%) patients of clinical stage I, II, III and IV as categorized by WHO respectively. Statistical significance ($p<0.05$) was found for the reduction of viral load, increase in CD4 count and as well as for elevation of liver enzymes after receiving ART whereas statistical insignificance ($p>0.05$) was observed with various comorbidities and as well as with difference in therapy either efavirenz or nevirapine among drugs.

Conclusions: It was observed that the elevation of the liver enzyme occurs with antiretroviral therapy though comorbidities associated with HIV and efavirenz or nevirapine based therapy were observed to not affect the elevation of liver enzymes.

Abstract Submission No. 101482

P-0128

Renal and Bone Safety Between Tenofovir Alafenamide and Entecavir in treatment-naïve CHB patients

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Background: To investigate the safety of renal and bone of tenofovir alafenamide (TAF) and entecavir (ETV) in treatment-naïve CHB patients in clinical practice.

Methods: In this prospective study, 95 treatment naïve CHB patients were randomly assigned to 25mg TAF (n=45) or 0.5mg ETV (n=50) during August 2019 to June 2020. Renal and bone biomarkers, including bone mineral density (BMD), serum phosphorus, 25-hydroxyvitamin D₃, serum creatinine, urine α 1-MG/Cr, Urine b2MG/Cr, urine

retinol-binding protein (RBP), cystatin C(CysC), urine β -NAG were collected at baseline, week 48 and week 96. The primary endpoint was the proportion of patients who had abnormal renal or bone function at week 96.

Results: At baseline, there was no significant difference in mean age, cirrhosis, renal and bone biomarkers between the two groups (Table 1). At week 96, TAF group had significantly lower rate of abnormal urine α 1-MG/Cr (5.3% vs 25.6%, $P=0.014$), β -NAG (7.9% vs 30.8%, $P=0.011$), CysC (6.1% vs 10.5%, $P=0.026$) compared with ETV group. TAF group tended to show a lower abnormal rates in serum creatinine (7.9% vs 12.8%, $P=0.479$). In hip and spine BMD measurements, the percentage of low bone mass of TAF was numerically lower than ETV (11.8% vs 21.7%, $P=0.412$). The proportion of patients with HBV DNA <20 IU/mL was 97.8% (44/45) in TAF group and 96.0% (48/50) in ETV group. The differences in the rates of normal alanine aminotransferase were similar at week 96 of treatment in patients receiving TAF and ETV (97.8% vs. 100%).

Conclusion: In this study, TAF demonstrated better safety of renal tubular function over ETV in treatment-naïve CHB patients, which might relates to long safety of bone.

Abstract Submission No. 101571

P-0129

Role of HBsAg levels during the different natural phases of chronic h

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Aims: Baseline HBsAg level is a potential predictive factor for antiviral response. However, potential diagnostic value of HBsAg levels to distinguish the different natural phases of CHB infection has not been well illustrated owing to the dynamic changes of HBV DNA and ALT. Therefore, we aimed to elucidate the role of HBsAg levels during the different natural phases of CHB patients mainly infected with HBV-genotype C (HBV-C) in China.

Methods: Seven hundred and seven chronic HBV-infected patients who were treatment-naïve and all underwent liver biopsy were analyzed in a cross-sectional study. Patients were classified into four phases based on liver biopsy: hepatitis B e antigen (HBeAg)-positive chronic HBV infection (n=214), HBeAg-positive chronic hepatitis B (n=116), HBeAg-negative chronic HBV infection (n=199) and HBeAg-negative chronic hepatitis B (n=178). HBsAg was quantified and correlated with HBV-DNA and clinical parameters within each phase.

Results: The median HBsAg levels in four phases were 4.58 log₁₀ IU/mL, 3.97 log₁₀ IU/mL, 3.34 log₁₀ IU/mL and 3.54 log₁₀ IU/mL, which were significantly different between each phase ($P<0.05$). HBsAg levels showed a significant correlation with the levels of HBV DNA, HBeAg, ALT and LSM ($P<0.001$) in both HBeAg-positive phases, while HBsAg levels only significantly correlated with age in both HBeAg-negative phases ($P<0.001$). AUCs of HBsAg and HBeAg cut-off of 4.35 log₁₀ IU/mL and 3.03 log₁₀ S/CO for differentiation inactive patients from HBeAg-positive phases, while LSM was higher diagnostic value with cutoff of 7.7 kPa and 6.1 kPa for diagnosis of active patients in HBeAg-positive and HBeAg-negative phase.

Conclusions: HBsAg levels differed significantly during the phases of chronic HBV infection and could predict HBeAg-positive chronic HBV infection patients mainly infected with HBV-C, all of which might better help to manage of chronic HBV-infected patients with HBV-C.

Abstract Submission No. 101572

P-0130

Role of DNA in Simplified Hepatitis B Treatment Criteria in a Resource-Limited Asian Country

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Background: Hepatitis B is still the leading cause of HCC and cirrhosis in Filipinos. Criteria to start antivirals evolve to consider resource limitations, especially when diagnostics, including DNA, limit linkage to care. The 2021 Philippine criteria for antivirals include at least reactive HBsAg with cirrhosis or DNA >2000 IU/mL with elevated ALT. **Methods:** Data from 573 HBsAg+ individuals from the “Early Cancer Detection in the Liver of Filipinos with Chronic Hepatitis B using AI-driven integration of clinical and genomic biomarkers (CANDLE Study)” were analyzed. Patients were classified by whether they satisfied criteria for treatment. Clinical, laboratory and ultrasound data were analyzed.

Results: The cohort was predominantly (82.2%) HBeAg negative (Figure 1). In treatment naïve patients meeting treatment criteria 27.13 % had a Fibrotest of $\geq F2$ vs 2.59% in those not meeting treatment criteria (Figure 3). There was significant steatosis at baseline (27.57 % by ultrasound, 45.2% by Steatotest) in the entire cohort (Figure 2). In patients with elevated ALT, 48.17% had DNA <2000 IU/mL. Among patients with elevated ALT but low DNA, 83.67% had steatosis by ultrasound and/or steatotest and 31.58% had alcohol intake at least once a week.

Conclusions: Data from our study may support simplification of treatment criteria for CHB in our population. We propose that DNA levels are integral to determining treatment eligibility for Filipinos with Hepatitis B. Our data suggests that steatotic liver disease from metabolic dysfunction and alcohol may be significant contributors to underlying liver disease and need diagnosis and management together with CHB.

Abstract Submission No. 101601

P-0131

Detection of preS1 with monoclonal antibodies during chronic hepatitis B virus infection

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Measurement of hepatitis B surface antigen (HBsAg) is essential in managing chronic hepatitis B virus (CHB) infection and achieving HBsAg loss is considered a goal in CHB treatment. HBsAg consists of three different surface envelope proteins, large- (LHBs), middle- (MHBs), and small-HB (SHBs) surface proteins. However, in clinical practice it is not common to evaluate each of these HB components separately. Recently, the measurement of preS1, a component of LHBs known for its essential role in HBV entry, has been found to have a

significant role in CHB. In this study, we investigated preS1 expression using seven monoclonal antibodies (mAbs) and examined their antigenicity, as well as its application in clinical settings. We found that preS1 expression remained consistent, regardless of HBsAg levels and different genotypes in CHB patients, in contrast to what was observed in SHBs. The epitopes of the seven mAbs were concentrated within the aa33–47 region of preS1, and their antigenicity was significantly reduced by an aa45F substitution. Interestingly, the expression of preS1 decreased when switching from entecavir to tenofovir alafenamide fumarate, which was different from the behavior of HBsAg or other HBs proteins. These results suggest that the region within preS1 is preserved across different genotypes and is independent of HBsAg levels, highlighting its vital role in the HBV infection cycle.

Abstract Submission No. 101616

P-0132

The Long-term safety of antiviral treatment for infants born to mothers infected with hepatitis B

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Background: We designed this study to evaluated the long-term physical and intellectual development of the children born to the mother who received antiviral treatment during pregnancy.

Methods: 154 children were delivered to 153 mothers with chronic hepatitis B infection, included from 2009 to 2020. The normal children were randomly selected as blank control group, and the growth and intellectual development of children in the experimental group and blank control group were compared. Adverse maternal events during pregnancy and at postpartum and infants' congenital anomalies were evaluated.

Results: Before delivery, almost all mothers were negative for HBV DNA, and no mother has severe ALT flare, the peak level was 93 U/L. No severe maternal abnormalities were observed. 7 months postpartum, 154 children were tested HBsAg and HBV DNA, none of them were positive. No congenital anomalies or severe adverse events were observed at delivery. Most of children' physical development is with the normal range, only two child whose body mass index-for-age (BAZ) lower than 2 SD had mild low Zn and Insulin-like growth factor 1 (IGF-1), respectively. 35 children in experimental group and 19 children in blank control group accomplished Raven's standard progressive matrices, there was no difference between the experimental group and the blank control group.

Conclusions: Receive antiviral treatment during pregnancy is effective and safe to mothers and infants. The data of long-term follow-up indicates that the children born to the mother receive antiviral treatment have normal physical and intellectual development.

Abstract Submission No. 101642

P-0133

Vemlidy Tx Effectiveness in Tx-naïve, CHBV AAPI Adults With ALT <2x ULN and Significant Fibrosis in a Community-Based Clinical Setting

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Background & Aims: Chronic Hepatitis B virus (CHB) remains a significant infection in the US despite excellent viral suppression drugs. Although guidelines suggest that treatment of CHB starts when the ALT level is >2x the ULN, there is a group of patients with normal ALT but have significant fibrosis who may benefit from treatment. We investigated the use of antiviral therapy in a community dwelling group of patients with CHB, normal ALT but with significant fibrosis.

Methods: This cohort study was comprised of 67 Asian adults (age ≥ 18), who were CHB treatment-naïve, had a detectable viral load (DNA > 2000 IU/ml), had an ALT level < 2x ULN as defined by the AASLD guidelines (ULN ALT is ≤ 35 U/L for males and ≤ 25 U/L for females) and had F2/F3 fibrosis as measured by transient elastography (TE). Each patient receiving TAF underwent liver cancer screening, TE, and had lab work drawn (XXX) at study baseline, q6 months for 36 months, and at end of study. Primary endpoint was the proportion of patients achieving complete HBV DNA suppression, HBeAg seroconversion in eAg positive patients, HBsAg seroclearance, developing anti-HBs, and improvement in liver fibrosis (one stage improvement on TE).

Results: Average age was 56.4 ± 10.1 years, 61.2% were men with an average BMI median of 24.1 kg/m² (range 22.3–25.7). Majority were Asian (98.5%), 13.4% had diabetes, median FIB-4 score was 1.207 (IQR 1.45–1.8), 91% had shear wave elastography readings of ≤ 8.7 kPa, 13% were HBeAg positive, with a median estimated glomerular filtration rate (eGFR) of 94.1 mL/min (84–104), 54.3% had evidence of osteopenia, and median duration on TAF was 3.4 years (3.3–3.7). Average follow-up was 3.3 years. Over almost 5 years of follow-up the trend for mean-log HBV DNA decreased from baseline average value of 4.7 to 1.1 at last visit (P < 0.0001) after adjusting for age, sex, diabetes, and hypertension using generalized linear re-modeling. Over 4 years of follow-up, there was no statistically significant change in elastography elasticity (~7.7 kPa). HBsAg seroclearance rate was 0%. HBeAg seroconversion rate was 1 at 12 months. Rate of developing anti-HBs was 1; however, subsequent labs showed the patient as non-immune. No significant changes in BMD (P = 0.94) were found. Mean eGFR showed a decrease from mean baseline 94.1 ± 14.1 to 89.9 ± 18.6 (P = 0.011) at last visit.

Conclusions: The use of TAF for CHB in Asian Pacific Islanders reveals promising outcomes, including significant reductions in mean-log HBV DNA levels over almost 5 years. However, concerns arise regarding the lack of significant changes in elastography elasticity, a 0% HBsAg seroclearance rate, and a decline in mean eGFR, necessitating ongoing monitoring. These findings highlight the need for further research to elucidate the long-term impact of TAF treatment on liver fibrosis, renal function, and immune responses, underscoring the importance of comprehensive patient management in CHB.

Abstract Submission No. 101672

P-0134

Natural course of HBV-infection in Armenia

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Background: According to a summary of the key outcomes of a HBV burden analysis in Armenia undertaken by the Center for Disease Analysis Foundation, in collaboration with field expert, the prevalence is expected to decrease from 1.6% in 2018, to 1.3% by 2030. In the

absence of implementation of the WHO elimination program, HBV-associated mortality, decompensated cirrhosis and HCC will increase by 4-6% by 2030.

Material: In 75 patients with chronic HBV infection (48% men), from 5 to 74 years old (40.7 ± 14.5), HBV DNA viral load (VL) was checked by *Abbott Real-Time PCR*, quantitative HBsAg (qHBsAg) *ARCHITECT*, *Abbott* (>0.05 IU/mL). Fibrosis was determined by non-invasive methods Fibrotest or/and Fibroscan.

Results: VL ranged from <10 to 75,669,100 IU/ml, qHBsAg ranged 1-124924 IU/mL. In 12.3% HBsAg-positive patients HBV DNA was undetectable, VL <200 was detected in 22.8%, $>200,000$ in 15.8% patients (characteristics of patients with VL $>200,000$ IU/ml in Tab.1). HBeAg-positive status in 5 patients, HDV infection was diagnosed in 2 patients with high HDV RNA VL and an extremely low HBV DNA. Liver fibrosis was $<F2$ in 75.9%, $F2$ in 6.4%, $F3$ in 3.2 %, and $F4$ in 14.5%. Decompensated cirrhosis was observed in 5 patients: two with HDV-infection; one with HCV-co-infection and HCC; another has Budd-Chiari syndrome. 11 (15%) patients are receiving antiviral therapy with tenofovir alafenamide.

Conclusion: In the majority of patients with chronic HBV infection, fibrosis stage was below 2 and the level of viral load varied from 2000 to 20000. The presence of comorbid conditions or co-infection negatively affected the natural course of the disease.

Abstract Submission No. 101713

P-0135

Durability of Virological Response with generic Tenofovir Disoproxil Fumarate in Chronic Hepatitis B

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Background: Though CHB patients require lifelong use of nucleot(s)ide analogues, it is reimbursed for a limited period in Taiwan, causing treatment discontinuations. Switching the treatment to low-cost generics post-reimbursement discontinuation can help prolong treatment and maintain the durability of viral response.

Methods: In this study, the durability of virological response (measured using virological recurrence and HBV-DNA levels) in patients who received generic TDF (Ricovir®; study group) for 24 weeks after switching from the branded TDF (Viread®) was evaluated. The results were compared with the historical control group who received Viread® for more than one year till reimbursement cessation.

Results: The study included 20 eligible CHB patients each in the study group and the control group. No patients in the study group experienced a virological recurrence at any treatment visit. At week 24, the rates of virological recurrence of HBV in the control group were significantly higher as compared to the study group. (30% vs 0%; $p=0.020$) Only the control group (13 patients) had detectable HBV-DNA levels at week 24 (65% vs 0%; $p<0.001$). Two mild adverse events (AEs) were reported in the study group, which were considered not related. No deaths, serious AEs, or treatment discontinuations occurred during the study. Treatment with the study group was well tolerated with 99.4% median study drug compliance.

Conclusion: This study's results conclude that generic TDF (Ricovir®) was effective and safe in maintaining the HBV virological response.

Abstract Submission No. 101740

P-0136

The Role of Serum pgRNA Dynamics in Predicting HBeAg seroconversion during Pregnancy and Postpartum

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Background: HBeAg seroconversion and HBV flares have been associated with changes in the immune system during pregnancy and postpartum. Serum pgRNA serves as a viral marker for assessing treatment response and disease flares. This study objective was to assess the predictive capability of pgRNA dynamics in determining HBeAg seroconversion in HBeAg-positive pregnant women.

Methods: This prospective study included pregnant chronic HBV carriers who were HBeAg-positive and had HBV DNA $\geq 5 \log_{10}$ IU/ml. These individuals received antiviral prophylaxis from 24-28 weeks of gestation. Serum and plasma samples were regularly collected and quantitatively analyzed to observe the dynamics changes of serum pgRNA and to evaluate the relationship between pgRNA and HBV DNA, HBeAg, ALT, CD4 and CD8.

Results: In this study, of 106 pregnant women with HBeAg-positive who received TDF median treatment duration of $15.96 (\pm 2.38)$ weeks were followed up until 48 weeks postpartum. Out of the 33 (31.13%) individuals who experienced HBV flares and necessitated re-antiviral therapy, 14 (42.42%) patients demonstrated concurrent serological conversion. The levels of serum pgRNA exhibited dynamic fluctuations during pregnancy and postpartum. There was an observed association between serum pgRNA and HBV DNA at baseline ($P < 0.05$), but this correlation ceased to exist following TDF treatment. Furthermore, a correlation was observed between serum pgRNA and HBeAg, and pregnant women with HBV pgRNA levels below 100 exhibited a higher likelihood of experiencing seroconversion ($p < 0.05$).

Conclusions: The extent of HBV replication and flares can be better comprehended by assessing the level of pgRNA, which can serve as an biomarker for predicting HBeAg seroconversion.

Abstract Submission No. 101750

P-0137

Safety and Efficacy of TAF in HBV PMTCT <st

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Background: There is limited available data regarding the safety and efficacy of Tenofovir alafenamide fumarate (TAF) for pregnant women and fetus, despite its potential interference with the mother-to-child transmission of Hepatitis B virus (HBV). This study aims to investigate and compare the clinical effectiveness and safety of TAF and

tenofovir disoproxil fumarate (TDF) in preventing mother-to-child transmission of HBV among Chinese pregnant women with HBV infection.

Methods: There were 96 cases of pregnant women with HBV and their newborns in the study, which employed a retrospective cohort study design.

Results: Compared to TDF in pregnant women with HBeAg-positive, TAF was more effective in reducing serum HBV-DNA levels. Neither TAF nor TDF elicited intrauterine infections in neonates. There were no statistically significant disparities observed among pregnant women in rates of HBeAg seroconversion, ALT flare, cesarean section, postpartum hemorrhage, prematurity, or congenital malformations. There were no notable disparities observed in the development and complications of infants.

Conclusion: TAF exhibited a significant capacity to decrease the peripheral blood HBV-DNA level in pregnant women with a high hepatitis B virus load, consequently reducing the risk of mother-to-child transmission of the virus compared to TDF. TAF antiviral therapy is recommended for pregnant women in the middle and late trimesters who have a high hepatitis B virus load.

Abstract Submission No. 101754
P-0138

Effectiveness of an Alert System for Medical Records and iTACT-HBcrAg to Prevent HBV Reactivation

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Aim: To prevent HBV reactivation by immunosuppressive agents and anticancer agents, we established an electronic medical record alert plus direct message (DM) system and introduced a highly sensitive quantitative HB core-associated antigen test (iTACT-HBcrAg) for rapid diagnosis of HBV reactivation. We evaluated the effectiveness of the monitoring system in our hospital.

Methods: (1) We confirmed the status of cases in which the display alert was overridden. (2) We studied de novo reactivation cases from March 2020 to December 2022. (3) Stored sera from patients who met the criteria for nucleic acid analog (NA) agent administration (HBV-DNA ≥ 1.3 LogIU/mL) during reactivation monitoring were measured with iTACT-HBcrAg.

Results: (1) In 2021 and 2022, the number of invalidated alert cases was 2836 (37%) and 2586 (30%), respectively. 167 (25%) out of 668 cases sent DM were appropriately addressed; for HBs antigen-positive cases, all cases were appropriately addressed after DM was sent. (2) From March 2020 to December 2022, 17340 cases (3272 cases) of HBV-DNA were measured, of which 17 were HBsAg negative and HBcAg positive and 17 were de novo reactivations requiring treatment. (3) Of the 6 cases requiring treatment and using iTACT-HBcrAg, HBcrAg was detected earlier than PCR in two cases, three cases were positive concurrently with PCR, and one case was determined to be positive earlier by PCR.

Conclusions: The promotion of testing using DM for alert-overridden cases was effective. In addition, iTACT-HBcrAg may be a potential alternative to the PCR method for reactivation monitoring.

Abstract Submission No. 101759
P-0139

Hypomethylation of IL-22R1 predicts prognosis in acute-on-chronic hepatitis B liver failure

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Aims: To evaluate the methylation level of IL-22R1 promoter in acute-on-chronic hepatitis B liver failure and determine its predictive value for prognosis.

Methods: 107 patients with ACHBLF, 79 with chronic hepatitis B (CHB), and 48 healthy controls (HCs) were retrospectively enrolled. Real-time quantitative polymerase chain reaction (RT-qPCR) was used to detect the expression pattern of IL-22R1 in ACHBLF in peripheral blood mononuclear cells (PBMCs), IL-22R1 methylation level in PBMCs was detected by MethyLight.

Results: The level of IL-22R1 mRNA in patients with ACHBLF was significantly higher than that in patients with CHB ($p < 0.001$) and HCs ($p < 0.0001$). IL-22R1 promoter methylation levels were significantly lower in patients with ACHBLF than in those with CHB ($p < 0.0001$) and HCs ($p < 0.0001$). Meanwhile, the PMR value of IL-22R1 was notably negatively correlated with the mRNA expression level ($r = -0.356$, $p < 0.001$). At the same time, the level of IL-22R1 promoter methylation was also an independent factor in the development of ACHBLF. When the IL-22R1 promoter methylation level was used to diagnose ACHBLF, its detective value was superior to the MELD score, especially 1-month.

Conclusions: IL-22R1 methylation levels had better diagnostic value in predicting 1-month mortality in ACHBLF and it may become a promising non-invasive novel predictive biomarker for predicting the short-term prognosis of patients with ACHBLF.

Abstract Submission No. 101778
P-0140

Epidemiology and clinical features of acute hepatitis B and Delta in Mongolia

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Objective: To investigate the clinical and laboratory features and the rate of development to chronic infection in patients with acute hepatitis B and delta in adult patients.

Materials and methods: A total of 182 patients with acute hepatitis B (AHB) and acute hepatitis Delta (AHD) were enrolled and followed-up 12 months in this study. They admitted to the acute viral hepatitis unit at NCCD between January 2016 and January 2018. All participants provided written informed consent and the study had been fully explained and agreed. All laboratory tests were performed using standardized laboratory procedures at NCCD.

Results: A total of 182 participants enrolled, 59.3% were male. 105 patients were diagnosed with acute hepatitis B (AHB), five patients were diagnosed with HBV/HDV co-infection, and 72 patients were diagnosed with acute HBV/HDV super-infection on chronic hepatitis B. Mean age was 25.2 ± 6.1 years in AHB group, 30 ± 7.6 years in HBV/HDV super-infection group and 28.4 ± 2.2 years in HBV/HDV co-infection ($p = 0.0001$). In patients with AHB and HBV/HDV co-

infection, the clinical symptoms completely disappeared and liver function tests returned to normal. Although, changes in liver function test findings were statistically significantly different comparing to other groups ALT (85.5 ± 125.8 ; 18.2 ± 36 vs 13.8 ± 6.5 ; $p=0.0001$), AST (63.4 ± 67.1 ; 18.9 ± 19.2 vs 19.7 ± 9.6 ; $p=0.0001$) by final follow-up.

Conclusion: 6.7% of patients with acute hepatitis B virus infection, 40% of patients with HBV/HDV co-infection and 93.3% of patients with HBV/HDV super-infection developed chronic infection. In patients with AHB and HBV/HDV co-infection, the clinical symptoms and liver function tests were completely cleared.

Abstract Submission No. 101790

P-0141

A long-term observation of TAF switching for chronic hepatitis B virus infection

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Tenofovir alafenamide fumarate (TAF) had been available as anti-viral treatment for hepatitis B virus (HBV) infection. TAF monotherapy has been also considered as switching from entecavir (ETV), tenofovir (TDF) or two nucleos(t)ide analogues (NAs) combination. TAF is expected in HBsAg decrease and serum phosphorus (P) increase but is concerned in cholesterol metabolism. In present study, we retrospectively evaluated long-term changes in HBsAg, eGFR, serum P and cholesterol in patients with TAF switching. 68 patients with TAF switching was included to present study. 39 males, median age of 63 years old, 60 patients with HBeAg-negative and 10 with HCC history were included. Median observation period was 35 months from TAF switching in present study. 45 with ETV, 3 with TDF and 18 with 2 NAs combination were administered as previous therapies. After TAF switching, the control of HBV-DNA was good, and significant alterations in renal function or serum P were not found. Regarding with HBsAg decrease, HBsAg was decreased at only 24 months after TAF switching in overall cohort (pre 1875, 24 months 1588 IU/mL, $p<0.05$), and significant HBsAg decreases was not found at other time points (3, 6, 12, 35, 48 and 60 months after TAF switching). However, significant HBsAg decrease was found in patients with HBsAg<100 before TAF administration (28.5, 24.0, 24.0, 21.6, 16.0, 1.84 and 0.07 IU/mL at 0, 6, 12, 24, 36, 48 and 60 months after TAF switching, respectively). HBsAg loss was found in 3 patients in present study. As for cholesterol, no clinically significant changes were found after TAF switching. Good tolerability was observed with no adverse events after TAF switching. TAF is a useful NA for chronic HBV infection as a candidate of NA switching with good anti-viral effects and safety profiles.

Abstract Submission No. 101797

P-0142

TAF use among individuals with HBV with decompensated liver disease

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Background: Among patients with hepatitis B virus (HBV) with decompensated liver disease (DLD), 5-year survival ranges from 15-35%. Tenofovir alafenamide (TAF) is a highly effective front-line treatment

for HBV. We utilized electronic medical records (EMR) to describe outcomes among those who initiated TAF following DLD.

Methods: A retrospective cohort study was conducted using Health-Verity US EMR data (01Oct2015 – 31Dec2022). Adult individuals were identified for inclusion through ICD-10 claims for HBV and DLD. Exclusion criteria included evidence of HIV/HCV/HDV, HCC or LTx prior to cohort entry, or evidence of TAF treatment or ≥ 30 days of other nucleos(t)ide analog treatment in the 90 days prior to cohort entry. Follow-up was censored at TAF discontinuation or end of data availability.

Results: Among 23,076 individuals with HBV and evidence of DLD, $n=455$ met all inclusion/exclusion criteria and were treated with TAF. Incidence of HCC and LTx during TAF treatment was 1.46 ($n=6$) and 4.55 ($n=18$) per 100 person-years, respectively (mean follow-up 340.7 days [SD 379.0]). For $n=14$ individuals with available labs, mean ALT changed from 81.9 at baseline to 21.0 – 31.9 U/L at timepoints between 90 and 365+ days after TAF initiation; changes were also observed for mean bilirubin (2.0 to 0.7 – 1.6 mg/dL). Mean albumin and sodium remained stable in normal ranges, creatinine results were mixed.

Conclusions: This study presents early data on outcomes following TAF treatment among those with HBV-related DLD. Follow-up time was limited but changes in laboratory measures suggest a positive benefit to continuous TAF exposure.

Abstract Submission No. 101852

P-0143

Incidence of Osteopenia and Osteoporosis in Chronic Hepatitis B Patients: A South Korea Cohort Study

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Background: Chronic hepatitis B (CHB) patients have higher osteoporosis/fracture risks, but hepatologists have low awareness of metabolic bone diseases in CHB patients. Bone health assessment may be beneficial in evaluating/monitoring treatment plans for CHB patients. We report the epidemiology and risk factors associated with osteopenia/osteoporosis in CHB patients in South Korea.

Methods: This retrospective cohort study included patients ≥ 19 years who underwent bone mineral density (BMD) testing ≥ 2 times between 2005–2021 at Severance Hospital. Demographic factors/comorbidities for CHB and non-CHB patients were propensity-matched at a 1:4 ratio. Cox proportional hazards regression models were used to estimate hazard ratios (HR; 95% confidence intervals [CI]) for assessing osteoporosis risk.

Results: Incidence of osteopenia/osteoporosis in CHB/non-CHB patients was 25.8% and 28.7%, respectively. After propensity-matching, 275 CHB patients (mean age: 57.8 years) and 1,100 non-CHB patients (mean age: 57.9 years) with normal BMD in the first BMD test were analyzed. In the second BMD test, 73.8%/24.7%/1.5% of CHB patients and 70.7%/26.5%/2.8% of non-CHB patients had normal BMD/osteopenia/osteoporosis, respectively. Osteoporosis risk factors (HR [95% CI]) in CHB patients were age (1.00 [1.00–1.00]), body mass index (BMI) ≥ 25 (0.65 [0.50–0.84]), chronic kidney disease (2.10 [1.50–2.80]), and proton pump inhibitor use (0.78 [0.62–0.99]). There was no significant difference between the cumulative hazard for patients with/without CHB (Figure 1).

Conclusion: CHB patients showed similar osteopenia/osteoporosis risks compared to non-CHB patients. Further studies of bone disease in CHB patients may encourage closer monitoring and elucidate factors that impact bone health in CHB patients.

Abstract Submission No. 101887
P-0144

Virological Response at 12 Months Predicts Lower HCC Risk in Genotype D Chronic Hepatitis B Patients

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OBJECTIVES: Recent studies have suggested that achieving normal serum ALT levels after antiviral treatment for chronic hepatitis B (CHB) is linked to a decreased likelihood of liver-related complications.^{1,2,3} Nevertheless, these studies predominantly included CHB patients with genotype C. It is still uncertain whether earlier normalization of ALT levels is associated with a lower risk of hepatocellular carcinoma (HCC) in patients with CHB.

METHODS: A total of 774 CHB patients who were predominantly genotype D, without a history of HCC, and who were treated with NAs for more than 1 year from 2007 to 2022, were included from two district hospitals in Istanbul, Turkey. Normal ALT was defined as ≤ 35 U/L (men) and ≤ 25 U/L (women), and virological response (VR) as serum hepatitis B virus DNA <15 IU/mL.

RESULTS: The median age was 46.8 years (18–77), and 64.5% of the patients were male. During the median 5.8 years of treatment, 43 (5.6%) patients developed HCC. The baseline characteristics are summarized in Table 1. ALT normalization occurred in 63% of patients at 1 year and 62.8% of patients at 2 years and was not associated with HCC risk in time-dependent Cox analyses. Patients who achieved VR at 12 months had a significantly lower HCC risk than patients without VR at 12 months (HR 0.48; p 0.034) (Figure 1). Male sex, age, cirrhosis at baseline, and VR at 12 months were independent risk factors for hepatocellular carcinoma (Figure 2).

DISCUSSION: In patients with CHB treated with entecavir or tenofovir, VR at 12 months, but not ALT normalization, was independently associated with a lower HCC risk in patients with predominantly genotype D CHB.

Abstract Submission No. 101893
P-0145

NUC discontinuation outcomes in chronic hepatitis B in xalnesiran containing arms

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Background: There is a lack of consensus on Nucleos(t)ide analogues (NUC) discontinuation and restarting criteria in trials exploring novel finite duration regimens for chronic hepatitis B (CHB). We report the criteria and outcomes from xalnesiran (a small interfering ribonucleic acid) containing therapies in the PIRANGA phase 2 study (NCT04225715).

Methods: Virologically-suppressed CHB participants were randomized into study arms (see table) for 48 weeks of treatment and 48 weeks of follow-up. Participants stopped NUC if the end-of-treatment (EOT) or follow-up visits showed: ALT <1.25 baseline, AND HBV DNA <20 IU/mL, AND negative HBeAg, AND HBsAg loss or HBsAg <100 IU/mL with ≥ 1 log₁₀ IU/mL decline from baseline. Participants who discontinued NUC were followed up every 2 weeks for 12 weeks and 4 weekly thereafter. Participants with HBV DNA levels >20 and $>2,000$ IU/mL were followed up every 2 weeks and weekly. NUC was restarted if pre-defined criteria were met.

Results: At 24 weeks post-EOT, 55/124 (44%) participants met NUC stopping criteria and 36 stopped NUC. 14/36 (39%) experienced virological relapse (HBV DNA >2000 IU/mL) and in 6/14 (43%) participants ALT was elevated. Maximum ALT was <2 ULN, 6–8 ULN, and 23 ULN in 3, 2, and 1 participants, respectively. 13/36 (36%) participants met criteria to restart NUC and all achieved virological suppression and ALT normalization. 14/124 (11%) participants had HBsAg loss at 24 weeks post-EOT, 10 of which met NUC stopping criteria and 6 remained HBsAg negative off NUC. One additional participant had HBsAg loss after NUC discontinuation.

Conclusion: NUC discontinuation was safely managed with close monitoring and pre-specified stopping/restarting criteria.

Abstract Submission No. 101925
P-0146

Prediction of fibrosis stage using HBsAg quantification in CHB patients with HBeAg-positive

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Background: It is often difficult to undergo liver biopsy and antiviral therapy in the optimal timing in chronic hepatitis B (CHB) patients with HBeAg-positive including immune-tolerant phase (IT).

Methods: This study enrolled 866 HBeAg-positive patients who underwent liver biopsy without antiviral therapy. We aimed to predict liver fibrosis progression based on HBsAg levels, stratified by IT or immune-active (IA) phases.

Results: 68 cases (7.9%) were classified as IT stage, and 798 cases (92.1%) were classified as IA stage. The distribution of liver fibrosis stages was F1 38%, F2 28%, F3 20%, and F4 14%, respectively. The median HBsAg levels by liver fibrosis stage were F1: 4.26 log IU/mL, F2: 3.91, F3: 3.60, and F4: 3.32, showing a trend toward lower HBsAg levels as the stage progressed (P-trend <0.001). The median HBsAg level by stage was 4.26 log IU/mL for IT and 3.83 for IA (P <0.001). When the cutoff was HBsAg level = 10,000 IU/mL or higher, the capability to predict fibrosis below F1 in the IT stage was 86% sensitivity, 63% specificity, 72% positive predictive value, and 80% negative predictive value. Similarly, the sensitivity was 63%, specificity was 70%, positive predictive value was 54%, and negative predictive value was 77% in the IA stage.

Conclusion: An inverse correlation was found between liver fibrosis progression and HBsAg levels. HBsAg levels were useful for predicting minimal fibrosis stage patients in the IT stage.

Abstract Submission No. 101956
P-0147

Evaluation of Sequential Therapy Peg-IFN and NA Compared to Monotherapy in CHB Patients

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Aims: CHB remains a significant global health issue that can result in the development of liver cirrhosis and HCC. It is crucial to monitor patients with CHB infection to identify any changes in the disease's progression, such as HBsAg seroconversion. While NA is known for effectively suppressing viral load, its long-term use poses a high risk of resistance. Therefore, an alternative treatment approach could involve adding an immunomodulator. This study aimed to evaluate the response at the end of sequential therapy (NA and Peg-IFN) compare with monotherapy in suppressing HBsAg.

Methods: A systematic search through Pubmed, Scopus, Cochrane Library, and EBSCO was conducted to find this topic. The studies were selected and critically appraised.

Results: In a study by Zhang et al. (2019), it was found that the early combination therapy resulted in a significantly higher proportion of patients with a reduction of HBsAg levels by more than 1500 IU/mL (61/108, 56.5%) compared to the NA monotherapy group (63/151, 41.7%). This suggests that the combination therapy may be more effective in reducing HBsAg levels. Similarly, Heng Chi (2017) observed a greater decrease in HBsAg levels in patients receiving peginterferon add-on therapy compared to those on NA monotherapy from week 0 to week 48. (-0.40 vs. -0.15 log IU/mL; $P = .005$). These findings indicate that the addition of peginterferon to the treatment regimen may lead to better outcomes in terms of HBsAg reduction.

Conclusions: Sequential therapy (NA and Peg-IFN) can be effectively made HBsAg loss and seroconversion.

Abstract Submission No. 102009
P-0148

Streamlined vs Traditional Treatment eligibility criteria using Chronic Hepatitis B Treatment Phase

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Background: Hepatitis B treatment criteria rely on indirect measures of risk factors for disease severity including ALT, DNA, eAg status. Fibrosis information may not always be available, especially in the Philippines. Traditionally, patients in the immune active and immune reactivation phase are deemed treatment eligible. In 2021, the Philippines expanded its treatment criteria to include individuals with ALT elevation and DNA > 2000 IU/mL.

Methods: Data from 390 treatment naïve HBsAg+ individuals from the "Early Cancer Detection in the Liver of Filipinos with Chronic Hepatitis B using AI-driven integration of clinical and genomic biomarkers (CANDLE Study)" were analyzed. Patients were classified by phase of infection. Clinical and fibrosis data, which was measured

by Fibrotest, was analyzed.

Results: Using traditional criteria, 15.6% of these HBsAg + individuals were deemed treatment-eligible (HBeAg + Immune active and HBeAg – Reactivation phase), 22.9% of these individuals had Fibrotests of $\geq F2$. 17.86% of the population met streamlined Philippine criteria for treatment and 34.2% of these individuals had Fibrotest of $\geq F2$. Streamlined criteria increased the patients eligible for treatment from 15.6% to 17.86%.

32.9% of the individuals were in the gray zone/ indeterminate phase (see table) and of this population 7.7% had F2 or higher in the indeterminate phase, 2.3% cirrhosis, 0.78% HCC.

Conclusions: Streamlined criteria using DNA and ALT level may increase the number of patients treated for Hepatitis B, including those with significant fibrosis. A significant proportion of individuals are indeterminate phase and these may include individuals with significant liver disease.

Abstract Submission No. 102027
P-0149

Management of CHB patients outside the guidelines: insights from real word data in Egypt

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Current antiviral therapies play a crucial role in achieving long-term suppression of HBV replication, which prevents disease progression and reduces the occurrence of HCC. Despite these remarkable benefits, a mere 2.2% (6.6 million) of chronic hepatitis B (CHB) patients globally received treatment in 2019 [1]. This alarming treatment gap can be attributed to restrictive nature of clinical practice guidelines, which often necessitate liver biopsies or persistent elevations in ALT levels and HBV DNA > 2000 IU/mL for treatment initiation [2]. Since 1998, we have adopted a "treat-all" approach, aiming to provide compelling evidence supporting the advantages of early treatment for CHB patients.

Methods: We conducted a retrospective analysis of data from 1226 CHB patients managed between January 1998 and December 2020 at the Egyptian Liver Research Institute and Hospital (ELRIAH) and the Association of Liver Patients Care (ALPC) in Mansoura, Egypt. Comprehensive clinical and laboratory parameters were collected before initiating antiviral treatment and subsequently at 6-month intervals, following a standardized protocol. Patients were categorized into two groups: group A, comprising those with initial HBV DNA levels below 2000 IU/mL, and group B, consisting of patients with initial HBV DNA viremia exceeding 2000 IU/mL.

Results: Our findings demonstrate that 28.3% patients with an initial HBV DNA level below 2000 IU/mL (group A) had significant liver fibrosis (F3,F4) compared to 18.4 % among patients with higher initial HBV DNA viremia (group B). Also incidence of HBsAg loss was significantly higher in group A (4.2%) compared to group B (1.3%). ($P < 0.002$).

Conclusion: We advocate for a shift towards a more inclusive and proactive approach in managing CHB patients, with a focus on early treatment initiation to prevent disease progression, reduce the occurrence of cirrhosis, and potentially achieve functional cures.

Abstract Submission No. 200072
P-0150

CORRELATION OF FIB3 INDEX WITH FIB4, FIBROSCAN AND M2BPGI IN DETERMINING FIBROSIS IN CHB PATIENTS

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Background: Chronic hepatitis B (CHB) infection poses a significant global health burden, frequently leading to advanced liver fibrosis; hence, early detection is crucial.^{1,2,3} Several non-invasive methods including the Fib-3 index, Fib-4, transient elastography (FibroScan), and the M2BPGi assay, have been developed to evaluate liver fibrosis.^{3,4,5} However, the correlation among these methods in predicting advanced fibrosis in CHB patients remain an area of ongoing research. This study aimed to evaluate the correlation between the Fib-3 index and established non-invasive fibrosis assessment tools (Fib-4, FibroScan, and M2BPGi) in determining the occurrence of advanced fibrosis in patients diagnosed with chronic hepatitis B.

Methods: A retrospective analysis was conducted, comprising 37 CHB patients. Clinical data, serum biomarkers, Fib-3 index, Fib-4 scores, TE measurements, and M2BPGi values were collected and analyzed. Correlation analyses were performed to assess the relationships between Fib-3, Fib-4, FibroScan, and M2BPGi values using Spearman's rho.

Results: This investigation revealed a significant and positive relationship between the Fib-3 index and Fib-4 ($r = 0.626$, $p < 0.01$), as well as with FibroScan ($r = 0.681$, $p < 0.01$), in the identification of advanced fibrosis among individuals diagnosed with CHB. However, while a positive association was observed between the Fib-3 index and M2BPGi, the statistical analysis indicated a lack of significance ($r = 0.210$, $p = 0.213$).

Conclusion: The findings support the utility of the Fib-3 index as an effective non-invasive method for identifying advanced fibrosis in CHB patients, particularly in concordance with Fib-4 and FibroScan assessments.

Abstract Submission No. 200138
P-0151

Hepatitis B associated with severe COVID-19: A nationwide cohort study in Sweden.

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Background: A comprehensive understanding of the association between individuals with chronic hepatitis B and risk for severe Coronavirus Disease 2019 (COVID-19) is lacking. This study, utilizing nationwide data from Swedish healthcare registers, assesses the

association between chronic Hepatitis B and severe COVID-19 outcomes, defined by the need for hospitalization or death due to COVID-19.

Method: Analysing a cohort of 1,057,174 individuals with laboratory-verified SARS-CoV-2 infections from February 2020 to April 2021, we identified chronic Hepatitis B cases based on specific diagnosis codes, stratifying them into those without cirrhosis and those with cirrhosis/decompensation diagnoses. Multivariable logistic regression analyses considered age, sex, comorbidities, COVID-19 vaccination, region of birth, income, and education.

Result: This study indicates a higher risk of severe COVID-19 in individuals with chronic Hepatitis B (adjusted odds ratio [aOR] 1.24, 95% confidence interval [CI] 1.10-1.40). Stratified analyses revealed increased risks for both chronic Hepatitis patients without cirrhosis (aOR 1.18, CI 1.04-1.34) and those with cirrhosis (aOR 2.46, CI 1.55-3.89). Although the chronic Hepatitis B cohort did not show a significant overall increase in COVID-19-related deaths, patients with complications exhibited a higher, albeit nonsignificant, risk (aOR 2.35, CI 0.92-5.20).

Conclusion: This nationwide study in Sweden underscores the heightened risk of severe COVID-19 in individuals with chronic Hepatitis B, particularly those with liver cirrhosis. Geographic and socioeconomic factors contribute to outcome variations, emphasizing the need to consider hepatitis B status in COVID-19 risk assessment. Future research should validate these findings, considering evolving SARS-CoV-2 variants and increased vaccination coverage.

Abstract Submission No. 200186
P-0152

Risk factors for hepatitis B virus reactivation in patients with hematological malignancies

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Background: Medical advances lead to accurate diagnosis of malignancies and use of efficient immunosuppressive therapies. Patients with viral hepatitis receiving chemotherapy are at risk of developing viral reactivation. Complete evaluation of viral hepatitis serologic status is necessary in oncological patients.

Methods: We performed a retrospective observational study, in which we included patients with hematological malignancies and positive serological markers for hepatitis B virus infection (HBV) recorded in a Romanian tertiary hospital between 2007 and 2023. Clinical, biological and treatment-related data were collected. We analyzed patient characteristics and risk factors for HBV reactivation (HBVr) using SPSS Statistics (version 23).

Results: We included 68 patients, 47 males (69%) with a median age of 58 years (IQR: 54-68) and 21 women (31%) with a median age of 61 years (IQR: 58-65.5). Six patients were co-infected with hepatitis C virus. Most common hematological malignancies in the enrolled patients were non-Hodgkin lymphoma (56%) and chronic lymphocytic leukemia (29.4%). Most patients (87%) received chemotherapy. Half of the patients had rituximab in their treatment regimen. HBVr occurred in 23 patients (33.8%). Among them, 4 patients (17.4%) died. All patients with HBVr received chemotherapy. We found that HBVr was correlated with the median length of time since the diagnosis of the hematological malignancy and with the number of chemotherapy cycles. The median number of cycles for patients with HBVr was 6, compared to 3 in patients without HBVr ($p = 0.001$).

Conclusions:

Approximately 1/3 of patients receiving chemotherapy developed HBV reactivation and it correlated with the number of administered cycles.

Abstract Submission No. 200189

P-0153

Reactivation of hepatitis B virus following immune checkpoint inhibitors

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Background: The risk of reactivation of hepatitis B virus (HBV) during and after immune checkpoint inhibitor (ICIs) is not well known yet. We conducted a multicenter retrospective study to evaluate the risk and characteristics of HBV reactivation in patients with solid cancers receiving ICIs.

Methods: Cohort1) HBsAg-positive patients treated with ICI therapy for solid tumors at a Japan Society of Hepatology-accredited facility were retrospectively analyzed with or without HBV reactivation. Cohort2) Cases of HBV reactivation defined as the detection of HBV DNA among HBsAg-negative but HBcAb-positive patients treated with ICIs were collected and analyzed.

Results; Cohort1) A total of 314 patients with solid tumors who were HBsAg-positive and treated with ICIs were enrolled. Of these, 14 (4.4%) had an elevation of ≥ 1.0 logIU/ml, of which 7 (2.2%) met the criteria for reactivation of AASLD. The median time to reactivation was 334 days, and significant risk factors for reactivation were the presence of concomitant chemotherapy, chemotherapy use prior to ICI treatment, prolonged steroid use, and no prophylactic administration of a nucleic acid analog. Cohort2) Seven cases of HBV reactivation after ICIs in HBsAg-negative and HBcAb-positive patients were observed. Six of the 7 patients were treated with concomitant chemotherapy or pretreatment chemotherapy. 1 patient had acute liver injury.

Conclusions: HBV reactivation can occur not only in HBsAg-positive but also HBsAg-negative patients with solid tumors receiving ICIs. To prevent HBV-related hepatitis, Antiviral prophylaxis may be useful for HBsAg-positive patients, whereas HBV DNA monitoring is necessary in HBsAg-negative but HBcAb-positive patients receiving ICIs.

Abstract Submission No. 200266

P-0154

Antiviral therapy reduces the risk of HCC recurrence after resection/ablation in chronic hepatitis B

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Introduction:

Hepatocellular carcinoma (HCC) is the fifth most common malignancy worldwide, 60% of cases are attributable to chronic hepatitis B (CHB). The long term success of curative resection or ablation for early HCC (Barcelona Stage A or 0) is limited by high rates of recurrence in 38.6-78%. HBV suppression with antivirals can decrease the incidence and recurrence rate of HBV related HCC. This study reviews the relationship between antiviral therapy, HBV DNA levels, and the rate of recurrence post resection/ablation in a New Zealand between 2003-2023

Methods: Patients with HBV associated HCC who had surgical resection or ablation were identified from the database of the NZ Liver Transplant Unit, a national referral centre for HCC care, between 2003 and 2023. Patients were retrospectively analyzed and their outcomes compared using Cox regression analysis

Results: A total of 343 patients were assessed between 2001 and 2023, 216 underwent resection, 127 underwent ablation. The 5 year recurrence rate is 55.1%.

Suppressed HBV viral load at the time of resection/ablation is associated with improved recurrence free survival Hazard ratio 0.65 (P<0.05, 95% CI 0.1-0.876)

Patients established on antiviral treatment had a significantly reduced rate of HCC recurrence aHR 0.69 (95% CI 0.5-0.94).

Commencement of antiviral therapy after resection/ablation did not significantly affect recurrence aHR 1.26 (95% CI 0.92-1.74)

Discussion: Patients with HBV DNA suppression at the time of treatment had a significant reduction in the rate of recurrence of HCC after resection/ablation. Being established on antiviral therapy is associated with a reduction in the rate of recurrence, however the survival benefit was not demonstrated in our study. Treatment after HCC treatment did not show any change in the rate of recurrence.

Abstract Submission No. 100310

P-0155

Prevalence and genotype distribution of HCV among general population of Arkhangai province, Mongolia

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Background: Globally, an estimated 58 million people have chronic hepatitis C virus infection, with about 1.5 million new infections occurring per year. Hepatitis C virus (HCV) is one of the major causes of liver cirrhosis and hepatocellular carcinoma (HCC) in Mongolia. We aimed to investigate the population-based prevalence of HCV infection and genotype distribution among 2128 apparently healthy populations in Arkhangai province in Mongolia.

Methods: Between May 2022 and August 2023, sera from 2128 residents of Arkhangai province were collected by two-stage cluster random sampling, and anti-HCV was tested. Anti-HCV-positive samples were tested for HCV RNA by reverse transcription polymerase chain reaction, and HCV genotype was determined.

Results: The mean age of the subjects was 56.5 ± 14.8 years, and 1170 (54.98%) were male. Overall, the prevalence of anti-HCV was 17.8% (378/2128) and HCV RNA was detected in 283 subjects (13.3%). Among 283 HCV RNA-positive samples, 278 (98.23%) were classified into genotype 1b, three were genotype 1a and two were genotype 2a. The HCV genotype 2a isolates were obtained from a 54-year-old male and a 60-year-old female who resided in rural areas of Arkhangai provinces. The highest rate of HCV infection was among the 40-59 age group ($p < 0.001$).

Conclusions: Approximately 13.3% of apparently healthy population had detectable HCV RNA in Arkhangai province, and the predominant genotype of HCV was 1b. Our experience in Arkhangai, demonstrates that through commitment of provincial public health departments, massive screening of populations at risk groups for HCV infection is feasible in resource limited settings.

Abstract Submission No. 100626
P-0156

Molecular and Evolutionary Analysis of HCV genotypes in Mexico

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Hepatitis C virus (HCV) represents a significant global health challenge despite treatment options. The seven genotypes (1-7) and more than 70 sub-genotypes have a global distribution. Although the virus's origin remains unknown, the potential introduction into different regions is often linked to historical events. This study aimed to ascertain the timeline of arrival of the main HCV sub-genotypes in Western Mexico.

In this cross-sectional study, 135 HCV sequences were analyzed. Sanger sequencing and phylogenetic analysis (MEGA11) were performed. Nucleotide substitution models were computed using the jModeltest, yielding GTR + I + G. Models were assessed with strict and relaxed molecular clocks using 500,000,000 MCMC chains in BEAUti and BEAST. Results and common ancestor dates were determined with Tracer v1.5 and FigTree v1.4.0

HCV genotype 1a predominated in 54.1%, followed by 1b (14.1%), 2a (2.2%), 2b (16.3%), and 3a (13.3%). The Most Recent Common Ancestor (MRCA) for HCV sub-genotype 1a was dated to 1977 (95%CI = 1930-2003), while sub-genotype 1b MRCA was 1913 (95%CI = 1759-2008). Sub-genotypes 2a/2b had an estimated MRCA in 1998 (95%CI = 1979-2010), and sub-genotype 3a MRCA was estimated as in 1965 (95%CI = 1916-2010). The introduction of sub-genotypes 1a and 3a may be linked to the Vietnam War, whereas sub-genotype 1b with WWI. Both events are related to the post-war migration of veterans to Mexico, tainted blood transfusions, and the current increase in injection drug use. Further molecular-evolutionary studies are required to monitor emerging strains or the decrease of the prevalent genotypes due to elimination strategies.

Abstract Submission No. 101182
P-0157

Identifying mitochondria-related genes that contribute to hepatocarcinogenesis after HCV elimination

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Background: To elucidate the mechanism of carcinogenesis after SVR, we performed a comprehensive gene expression profiling.

Methods: RNA-seq analysis was performed on background liver tissue from thirteen patients who developed HCC after SVR with IFN and underwent surgical resection at the collaborating institution (HCC group) and from ten patients who underwent liver biopsy 1 year after achieving SVR with DAA and have not developed hepatocarcinoma to date (non-HCC group). We then examined the differences in gene expression between the HCC and non-HCC groups. We also performed an integrated analysis using RNA-seq data from public databases on HCC cases with persistent HCV infection and HCC cases with non-B non-C liver disease. In addition, we performed RNA-seq analysis using liver-derived Huh7 cells prepared (1) before HCV infection, (2) 4 days after infection, (3) 7 days after HCV elimination by DAA in (2), and (4) 10 more days after drug-free from (3).

Results: Comparative analysis identified an increase of 771 genes and a decrease of 303 genes in the background liver tissue of the HCC group compared to the non-HCC group as differentially expressed genes ($|\log_2 \text{Fold change}| \geq 1$, $\text{FDR} < 0.01$). The large number of decreased DEG were related to mitochondrial metabolic function. On the other hand, among the increased DEG, we identified the MRP1 gene, which was particularly highly expressed in adjacent liver tissue of HCC cases after HCV elimination compared to other etiology, and it has been reported to regulate the overall morphology of mitochondria. As for *in vitro* experiments using HCV-infected cells, gene ontology analysis showed that genes related to mitochondrial organization, including MRP1 gene, were significantly upregulated after HCV elimination compared to HCV-infected cells.

Conclusion: Mitochondrial dysfunction due to abnormal MRP1 gene expression was suggested as a molecular mechanism contributing to hepatocarcinogenesis in the adjacent liver tissues after HCV elimination. MRP1 expression may be a predictive marker for HCC.

Abstract Submission No. 101808
P-0158

Immune Enhancement by the Hepatoprotective Temulawak Rhizome in The of Liver Disease in Hepatitis C

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Temulawak is one type of plant native to Indonesia and is quite popularly used treatment of hepatic diseases. One of the hepatic diseases is hepatitis c caused by the HBV virus so substances that can inhibit HBV gene expression and replication using hepatoprotective substances are needed. The aim is to describe Temulawak phytochemicals that have hepatoprotective effects against the hepatitis c virus. This study uses

qualitative and quantitative research with methods derived from secondary data. The subjects in the hepatoprotective effect were male Sprague Dawley rats, 3-4 months old, weighing 150-200 grams made in 5 groups. The phytochemical contains polyphenol and flavonoid compounds in the form of curcuminoids and curcumin analogs. There are essential oils consisting of d-camfer, cyclo isoren, mirsen, tumerol, xanthorrhizol, zingiberen, zingiberol. The hepatoprotective activity of temulawak can be caused by free radical capture and antioxidant activity resulting from the presence of polyphenol and flavonoid compounds and other substances in the temulawak rhizome. Curcumin can also increase glutathione S-transferase (GST), and inhibit several pro-inflammatory factors such as nuclear factor- κ B (NF- κ B) and profibrotic cytokines so that inflammatory by-products are reduced. Animal models showed that rats given temulawak rhizome decoction induced by aspirin decreased levels with a dose of 2.6 g/kgBB and 5.2 g/kgBB liver damage. Other clinical results showed that curcumin at high doses (1000-2000 mg/day) did not harm the body. Temulawak rhizome with phytochemical content of polyphenols, flavonoids, and other substances has a hepatoprotective effect so that it can be used as an alternative hepatoprotection in Hepatitis C patients.

Abstract Submission No. 200079
P-0159

Diagnostic Performance of the Genedrive HCV in Hemodialysis Setting at Cipto Mangunkusumo Hospital

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Background/Aim: Genedrive is a diagnostic tool to detect HCV viral load qualitatively. Genedrive is one of the point of care diagnostics is essential to detect and treat hepatitis C virus in single visit. The potential use of Genedrive is in remote area and in key population. The World Health Organization is targeting to eliminate hepatitis by 2030, which decreasing infections by 90%, and deaths by 65%. Chronic kidney disease(CKD) patients on hemodialysis are among the population at risk of being infected of hepatitis C due to nosocomial transmission. Therefore, there it is a need for simple, handy and cost-effective examination of such as Genedrive. This study aimed to assess the diagnostic accuracy of Genedrive HCV detection in Hemodialysis setting. **Methods:** This study used a *cross-sectional* design. Genedrive results were evaluated in 64 chronic kidney disease on hemodialysis at Cipto Mangunkusumo Hospital, Jakarta. ROC analysis conducted to assess significant hepatitis C among chronic kidney disease on hemodialysis. **Results:** The calculated detection limit of Genedrive was 3.1×10^3 IU/mL. Genedrive HCV assay showed 93.3% sensitivity, 91.2% specificity, 92% negative predictive value, and 93% positive predictive value to detect HCV, 10.60 positive likelihood ratio, and 0.073 negative likelihood ratio.

Conclusion: *Point of care test* could contribute to the elimination hepatitis C. Genedrive is a part of point of care and could be a simple, portable, accurate, and reliable method for detect hepatitis C with chronic kidney disease on hemodialysis.

Abstract Submission No. 100110
P-0160

Safety and Efficacy of DAAs for Hepatitis C Patients with and without malignancies

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Background: DAAs reimbursement is approved in Taiwan to all hepatitis C patients with HCV RNA positive. However, combination of antiviral and cancer treatment can be a concern. Hepatitis C patients with malignancy who receive DAAs would be considered at higher risk for adverse events than those without malignancy. This issue should be clarified for this particular population.

Aim: This study is to assess the safety and efficacy of Direct Antiviral Agents for Hepatitis C in patients with and without malignancies.

Method: Patients who had received DAA treatment from January 2020 to December 2022 in our hospital were enrolled. The data was divided into two groups, including hepatitis C patients with and without malignancies.

Results: The total HCV case number is 927, in which 149 (16.1%) hepatitis C patients with malignance underwent oncology treatment. The major cancer type is Hepatobiliary and Pancreas (43.6%), followed by Head and Neck (16.1%). The median age was 67 in cancer group and 62 in non-cancer group. 94% had completed DAA treatment in cancer group vs. 97.6% in non-cancer group ($p=0.032$). The major reason of incomplete DAA treatment was death 11.4% in cancer group and 1.2% in non-cancer group ($p<0.001$). Per-protocol analysis SVR (100%) in cancer group and 99.2% in non-cancer group ($p=0.6$). Furthermore, intention to treat SVR was 87.2% vs. 95.0% ($p<0.001$) in cancer group and non-cancer group.

Conclusion: The combination of HCV antiviral therapy and oncology treatment can be feasible in clinical practice if cancer stage is considered. Although the rate of complete DAA seems lower in cancer group, most oncologic patients were well tolerated and acceptable for HCV elimination.

Abstract Submission No. 100118
P-0161

Factors influencing patients' intention to seek HCV treatment: experience from a medical center

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Background: DAAs for hepatitis C patients with HCV RNA positive are covered by Taiwan's NHI budget. However, most patients did not actively seek out medical options and must be recalled for HCV treatment by a healthcare professional.

Aim: This study is to examine the factors that may influence patients' awareness and desire to receive HCV treatment.

Method: People who received blood tests for C screening between January 2020 and June 2023. Five hundred and nineteen patients with chronic hepatitis C were enrolled. Data were analyzed and divided into two groups, including those who desire to take DAAs and those who did not. A standardized questionnaire was used to collect data on the reasons for not taking DAA medication.

Results: 51.6 percent of women and 48.4 percent of men participated in the survey. The most common causes for lack of therapy were symptoms free (43.0percent). Secondly, patients were unaware of the necessity for treatment (42.6percent). Thirdly, patients were unaware of the current treatment policy and continued to fear IFN-based treatment (16.4%). In the group that had no desire for treatment, 76.6 percent had been living with HCV for more than five years and median age was 62. In contrast, 92 percent of patients in the treatment group were notified of their anti-HCV status within a year, the median age was 64.

Conclusion: Most individuals with HCV are asymptomatic, so their liver illness might be neglected, placing them at risk for disease progression. Thus, strategies should be implemented to increase patient treatment uptake.

Abstract Submission No. 100121

P-0162

Efficacy and Safety of DAAs in Elderly Chronic Hepatitis C patients with Moderate Renal Impairment

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Background: Limited data for Direct-acting antiviral drugs (DAAs) in old age or renal impairment. Aim: to investigate the efficacy and safety of DAAs in Chronic hepatitis C (CHC) elderly patients with moderate renal impairment.

Methods: Sofosbuvir/Daclatasvir for 12 weeks was investigated in 4 groups each was 85 patients.

Results: Age and estimated Glomerular Filtration Rate (eGFR) mean±SD were: G1 (70.2±6.4 years and 52.1±2.9 mL/min/1.73m²), G2 (70.5±6.8 and 37.5±4.4), G3 (45.2±7.3 and 39.5±4) and G4 (41.1±10.1 and 96.8±21.8) respectively. No significant difference among groups in the clearance of HCV (98.8, 97.6, 96.5 and 100%, respectively) with total success rate of 98.2%. Insignificant higher adverse effects was noticed, except deterioration of kidney function which was significantly higher in Group 2 (20, 60, 38 and 2 patients, respectively; p<0.001). Five patients (4 in G2 and one in G3) developed deteriorated GFR (<30 mL/min) and Sofosbuvir dose was decreased to 200 mg/day, but none needed dialysis and they recovered to >30 mL/min during the follow up. Independent predictors of deterioration of kidney function were age >59.5 years, Creatinine >1.55 mg/dL and eGFR <48 mL/min/1.73m².

Conclusion: Old age or moderate renal impairment doesn't affect DAAs high cure success rate. Deterioration of kidney function could happen if old age with baseline moderate renal impairment. We think it is important to introduce DAAs to CHC patients as a curative therapy regardless of old age or moderate kidney diseases, but with strict follow up of their renal function and adjustment of Sofosbuvir dose if needed.

Abstract Submission No. 100123

P-0163

DAAs Effects on the Glycemic Control and Lipid Profile in Diabetic patients with Chronic Hepatitis C

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Background: Chronic hepatitis C (CHC) is associated with increased incidence of type 2 diabetes.

Aim: to assess Direct Acting Antiviral Drugs (DAAs) effects on CHC diabetic patients.

Methods: One hundred fifty one diabetic CHC naive non-cirrhotic patients on diet modification or oral anti-diabetic medications were treated with Sofosbuvir 400mg and Daclatasvir 60mg for 12 weeks. The following labs were reviewed: Fasting blood sugar (FBG), hemoglobin A1C (HbA1C), Fasting Insulin, Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), Low-density lipoprotein (LDL), Triglycerides and Cholesterol.

Results: Mean age 52.7±3.2 years, 53% females. Body weight has a significant positive correlations with FBG, HbA1c and HOMA-IR (p=0.039, 0.012 and <0.001 respectively). Overall sustained virologic response (SVR) after DAAs treatment was 98.7%. Those who achieved SVR had significant improvements in the followed labs (before and after treatment mean±SD and p value): FBG: 157.9±18.1, 121.3±11.5 mg/dL, <0.001; HbA1C: 8.3 ±2.1, 6.5±1.5, <0.001; Fasting Insulin: 7.1±2.1, 5.4±2.3 µIU/mL, <0.001; HOMA-IR: 2.8±0.8, 1.8±0.6, <0.001; LDL: 129.6±18.2, 125.9±16.2 mg/dL, <0.001; Triglycerides: 177.6±40.6, 172.9±41.1 mg/dL, 0.004; Cholesterol: 207.5±31.6, 202.7±28.2 mg/dL and <0.001 respectively).

Conclusion: Our data shows that presence of diabetes doesn't worsen DAAs high cure success rate. The significant improvement of glycemic control, insulin resistance and lipid profile in those achieved SVR make it possible to hypothesize that clearance of HCV in diabetic patients could improve the glucose and lipid homeostasis control.

Abstract Submission No. 100132

P-0164

Safety and effectiveness of DAA treatment for children and adolescents with AHC in China

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Objectives: Based on the safety and efficacy of several interferon-free DAA regimens in children and adolescents with chronic HCV, several DAAs were approved for treatment of hepatitis C virus (HCV)-infected children 3 years of age and older; however, the real-world data is limited. We aim to assess the safety and effectiveness of DAAs in acute HCV-infected Chinese children and adolescents.

Methods: This observational study included 26 acute hepatitis C children aged 3 to <18 years old or weighing >35 kg from 2018 to 2019. Co-infection with HBV and patients with malignancy are excluded.

Results: All 26 children were type 1B, with a mean age of 7.04 years, 14 boys and 12 girls, and the incubation period of HCV infection was 70±22 days, which was longer than that of adults. Based on the patients' ALT, HCV-RNA quantification, and willingness to treat, 11 patients with lower ALT received DAA antiviral therapy (5 for 3-6y; 3 for 7-12y, 4 for 12-17y). The treatment regimen was SOF/LDV for 4 children and SOF/VEL for 7 children, with dosages based on the children's age or weight. SVR12 and SVR24 were 100%. 15 patients with high ALT levels were untreated. Among them, 2 lost contact and 1 did not achieve HCV-RNA clearance at 36 weeks of follow-up, while all the other 12 children achieved spontaneous HCV-RNA clearance. No serious adverse events were reported.

Conclusions: Treatment with the SOF-based regimen was well tolerated in Chinese children and adolescents with acute HCV, with 100% SVR12 and negligible side effects.

Abstract Submission No. 100133
P-0165

High efficacy of interferon-free therapy for acute hepatitis C in China

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Background: Recently, clinical trials investigating the benefit of IFN-free direct-acting antivirals treatment for acute HCV infection have been conducted. Based on the results of the cost-effectiveness analysis, DAAs should be initiated early in acute HCV infection, prior to spontaneous viral clearance. However, real-world data is limited. We aimed to evaluate the effectiveness and safety of DAA treatment regimens in the setting of AHC.

Methods: In this observational study, we enrolled 129 acute HCV patients from 2018–2019. The primary efficacy outcome was the proportion of patients with SVR12. Others were the safety and tolerability of DAA treatment.

Results: Treatment was initiated in 129 patients with AHC (median age 47.0 years; 66 males; 63 females). All had genotype GT-1b and had no HIV or HBV co-infection. Some of the 129 patients had less severe symptoms, including malaise (64, 49.61%), loss of appetite (57, 44.19%), and yellowing of urine (32, 24.81%). According to patients' characteristics, 76 patients started treatment in the first four weeks (76/129, 58.91%), 27 patients started treatment between four and eight weeks (27/129, 20.93%), and 26 patients started treatment between eight and thirty-six weeks (26/129, 20.15%); following 15%, the following DAA regimens were prescribed: daclatasvir/yasunaprevir (6.2%; 8/129), sofosbuvir/radipavir (3.1%; 4/129), ombitasvir/paritaprevir/ritonavir (16.2%; 21/129), grazoprevir/elbasvir (59.6%; 77/129) and sofosbuvir/velpatasvir (14.7%; 19/129). All AHC patients achieved a SVR12. Adverse events associated with DAA were rare.

Conclusions: Interferon-free DAA regimens can achieve 100% SVR12 in AHC patients with a favorable safety profile if treatment durations similar to CHC are used.

Abstract Submission No. 100147
P-0166

Expanding screening for hepatitis C in DM patient via the assistance of an auto-run alert program

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In the era of HCV micro-elimination, an efficient HCV screening and treatment strategy is crucial, particularly when targeting high-risk populations such as individuals with diabetes mellitus (DM). Previous studies have shown that DM patients have double the prevalence of anti-HCV antibodies compared to the general population. Additionally, treating HCV can improve blood sugar control in DM patients.

To address this, we implemented an auto-run alert program within our Hospital Information System (HIS) to assist metabolic specialists in identifying DM patients who had not undergone HCV screening during outpatient clinic visits. This program also facilitated related serological examinations for HCV screening, with automatic result reporting. Upon confirmation of hepatitis C infection, another auto-run

transfer program streamlined the process of referring patients directly to hepatologist outpatient clinics for further evaluation and treatment. Following the implementation of this screening program, the anti-HCV screening rate among DM patients in our hospital dramatically increased from 35.8% to 85.6% within a six-month period. Out of 4,729 individuals who participated in the screening program, 97 patients (2.1%) tested positive for anti-HCV antibodies. Subsequently, 47 HCV patients were successfully referred to hepatologists, and 26 of them (55.3%) tested positive for HCV RNA. All of these patients received direct antiviral agents with a complete treatment course. This study demonstrates the effectiveness of an efficient auto-run alert HCV screening program implemented via the HIS in a medical center. It significantly improved the screening rate in a specific population, and the transfer program provided a convenient method to facilitate HCV treatment.

Abstract Submission No. 100178
P-0167

Sofosbuvir/Viplateasvir/Vosigrivir Retreatment of Hepatitis C Failed a NS5A-containing DAAs Regimen

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About 5–10% of patients treated with DAAs containing NS5A inhibitors cannot achieve a sustained virological response. Retreatment of patients with DAA failure could be challenging, as emergence of resistance-associated substitutions (RASs) in HCV non-structural (NS) regions can negatively impact on the chances of SVR. We report two cases of failed treatment of DAAs containing NS5A inhibitors who received SVR after 12 weeks of treatment with the Sofosbuvir/Viplateasvir/Vosigrivir regimen.

Case 1, male, 31 years old, with chronic hepatitis C, genotype 6a, took oral Sofosbuvir/Velpatasvir 1 tablet/d, once a day for 12 weeks. 18 months later, after treatment, HCV RNA is 9.8×10^5 IU/mL. He took Sofosbuvir/Viplateasvir/Vosigrivir 1 tablet/day for 12 weeks. SVR12 was obtained.

Case 2, male, 56 years old, chronic hepatitis C, genotype 2a. He took oral Sofosbuvir/Viplateasvir 1 tablet/day for 12 weeks. 2 years later, after treatment, HCV RNA is 7.77×10^6 IU/mL. He took Sofosbuvir/Viplateasvir/Vosigrivir 1 tablet/d + ribavirin for 12 weeks. SVR12 was obtained.

Sofosbuvir/velpatasvir/voxilaprevir is approved for retreatment of patients with HCV and a previous failure on direct-acting antivirals (DAAs). The two cases we reported showed the use of Sofosbuvir/Viplateasvir/Vosigrivir combined with or without ribavirin therapy for patients who failed DAA treatment with NS5A inhibitors is effective and well tolerated. This group of cases represents an effective re-treatment program with good curative effects and few side effects.

Abstract Submission No. 100186
P-0168

Effectiveness and safety of GLE/PIB for hemodialysis patients with hepatitis C

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Background/Aims: Glecaprevir/pibrentasvir (GLE/PIB) is a pan-genotypic regimen for the treatment of hepatitis C virus (HCV) infection.

GLE and PIB are direct acting antiviral (DAA) agents that can be used for patients with chronic renal failure who are on hemodialysis (HD) and those with HCV genotype 2 infections.

Material and Methods: The subjects comprised patients with genotype 1 and 2 (six each) and one unknown genotype patient in whom GLE/PIB therapy. The mean HCV RNA amount prior to treatment initiation was 4.81 (2.1-6.5). The administration periods were 8 and 12 weeks (n = 9 and 4, respectively).

Results: Twelve patients received all the doses orally while an increase in total bilirubin (T-BIL) caused administration to be discontinued in one patient. HCV RNA at week 4 after treatment initiation became undetectable in 11 (91.6%) of the 12 patients. All patients achieved rapid viral response (RVR).

Conclusion: The results suggest that GLE/PIB can also be safely administered to HD patients. However, the usefulness and safety need to be further studied by examining more cases.

Abstract Submission No. 100196

P-0169

An in-hospital Hepatitis C elimination model

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Background: Hepatitis C has become a serious global public health problem. But the diagnosis rate and the treatment rate are only 32.7% and 11% in China, which needs to be improved. In this study, we screened all antibody-positive patients in the electronic medical record, and telephoned track for HCV RNA testing and patient treatment to improve the in-hospital HCV RNA testing rate and treatment rate.

Methods: The HCV elimination model was an in-hospital hepatitis C screening program and initiated by the infection department in the No2. people's hospital of Fuyang city. The nurse screened daily inpatients and outpatients with antibody-positives in the electronic medical system and was responsible for reminding the physician to test HCV RNA by phone every day, as well as tracking the full treatment and follow-up course.

Results: A total of 2,296 patients were HCV antibody-positive, 1,836 patients had HCV RNA testing, 317 patients were HCV RNA-positive, and 259 patients were treated in the hospital. Before and after the HCV elimination model, HCV RNA detection was 64% and 80%, treatment rate was 61% and 82%, respectively. 75% (44/59) of untreated patients were in the non-infection department. All 258 patients treated achieved SVR12 100%.

Conclusions: In-hospital elimination with screening and telephone tracking patients with HCV antibody-positives is effective in improving HCV RNA testing and treatment rates, which improves the HCV elimination.

Abstract Submission No. 100198

P-0170

A new model of HCV elimination with Township Health Centers in China

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Background: In China, most patients with hepatitis C are elderly and living at isolated villages, It's hard for them to seek medical care because the designated hospitals always are in cities over long distances. The study aimed to establish an innovative model of HCV elimination with Township Health Centers (THC), which is currently the first THC model in China.

Methods: The Xiaonan Centers for Disease Control (CDC) chose Dougang THC, in a high prevalence town of hepatitis C, for the hospital screening high risk population, e.g., older than 45 years of age, previous surgery, risky offering blood, with free HCV antibody and HCV RNA assay. Meanwhile, Dougang THC utilized the HCV Ab(+) data from 2004-2021 in the Xiaonan CDC database to call back and offer free HCV RNA assay. The patients with HCV RNA+ could start antiviral therapy and received reimbursement for DAA in 3 working days at this hospital.

Results: A total of 75280 cases with high risk were screened from 2022.8-2023.8, of which 6776(9.0%) cases were HCV Ab(+), 331 (4.9%) cases were HCV RNA (+). 4376 cases with HCV Ab(+) in CDC database, 401 cases dead, 2043 cases lost or refused to follow-up, 1932 cases came back to hospital, of which 1748 (90.5%) cases were HCV Ab(+), and 249 (14.2%) were HCV RNA (+). 411 (70.8%) cases started antiviral therapy, 96.6%(397/411) patients achieved SVR12.

Conclusions: The HCV THC model of screening, treatment, and reimbursement at local THC was an effective way. Expanding this model may accelerate HCV elimination.

Abstract Submission No. 100199

P-0171

Simplify CHC Treatment: SOF-based treatment regimens in CHC patients with untested genotypes

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Background: Four liver conferences advocated for a simplified treatment without testing for genotype in CHC patients before treatment. Simplifying treatment could reduce the burden on patients. This study observes the feasibility and efficacy of SOF-based treatment regimens in patients with untested genotypes.

Methods: 36 CHC patients diagnosed in the No. 2 People's Hospital of Fuyang City from Oct. 2022 to Jul. 2023 were retrospectively observed with no genotype detection, and the follow-up time was optimized with 28 tablets of medication dispensed at the beginning of the treatment, 56 tablets of medication dispensed at the 4th week, and telephone tracking of patients with untimely follow-up at the 12th and 24th weeks. The treatment regimen was 12W SOF-based, Sofosbuvir/Velpatasvir in 20 patients (72%), including 8 patients with decompensated cirrhosis and hepatocellular carcinoma all in combination with ribavirin 12W, and ledipavir/sofosbuvir treatment in 10 patients (28%), with follow-up SVR12.

Results: At baseline, 36 patients had a mean age of 62 years and HCV RNA level of 6.70×10^6 IU/ml; 18 patients (50%) were male; 9 patients (50%) had compensated cirrhosis, decompensated cirrhosis and hepatocellular carcinoma; and 7 patients (19%) had HIV co-infection. A follow-up rate was 100% (36/36), 94% (34/36), and 93% (14/15), respectively at 4, 12, 24 weeks. SVR12 was 100% (14/14).

Conclusion: A simplified treatment without genotype testing and optimized follow-up is simple and feasible in the management of patients with chronic hepatitis C. It reduces the economic burden on patients, and SOF-based regimens can achieve high SVR12.

Abstract Submission No. 100206
P-0172

The efficacy and safety of SOF-based treatment regimens in elderly patients with chronic hepatitis C

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Background: Population pharmacokinetic analysis in HCV patients showed that age did not have a clinically relevant effect on the exposure to sofosbuvir, GS-331007, ledipasvir or velpatasvir. However, there are few real world data on elderly patients. Our study was designed to observe the efficacy and safety of SOF-based treatment regimens in elderly patients with CHC.

Methods: We retrospectively analyzed patients with chronic hepatitis C aged 60 years or older who were diagnosed in the NO.2 people's hospital of Fuyang City from January to March this year. These patients received sofosbuvir/velpatasvir or ledipasvir/sofosbuvir for 12 weeks. Cirrhosis patients were treated with ribavirin. Routine blood, liver and renal functions, HCV RNA were monitored at baseline, 4, 8, 12 and 24 weeks.

Results: A total of 54 elderly patients were enrolled. At baseline, the mean age was 70 years and HCV RNA was 5.26×10^6 IU/ml, 22 patients (39%) were male, 22 patients (41%) were GT1b, 10 patients (19%) were GT2a, 22 patients (41%) were undetected genotypes. 30% patients (16/54) had compensated cirrhosis, decompensated cirrhosis and HCC. 20 patients (37%) had one complication, 11 patients (20%) had two complications, 7 patients (13%) had three or more complications. Before and after treatment, ALT was 93 U/L and 22 U/L, eGFR was 113 ml/min and 110 ml/min, respectively. SVR12 was 98% (53/54). The reported adverse reactions in patients were: fatigue(6%), nausea(4%), diarrhea(2%). No serious adverse events, discontinuations or deaths were found during treatment.

Conclusions: SOF-based treatment regimens can achieve high SVR12 and good safety in elderly patients.

Abstract Submission No. 100211
P-0173

HCV Elimination: Reengagement of In-hospital Hepatitis C patients to Improve Linkage to Care rate

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OBJECTIVE: Through reengagement of In-hospital Hepatitis C patients, to understand their awareness of diagnosis and treatment, strengthen disease education, and improve patients' knowledge of hepatitis C disease and treatment compliance.

METHODS: Hospitalized patients with HCV RNA-positive from 2013 to 2023 in a tertiary hospital in Jiangxi, China, were retrieved through the electronic case system, specialists from infectious disease department called the patients/patients' relatives by telephone to know the patients' current situation, their awareness of Hepatitis C and their willingness of further diagnosis and treatment.

RESULTS: 247 patients were retrieved from the electronic case system and followed up. 66 patients were diagnosed by hepatologist. 36.43% of the patients (n=90) could not be contacted by phone. Of the 157 patients who had been contacted, 21 had died, cause of death were hepatitis C cirrhosis in decompensated stage (n=3), hepatocellular carcinoma (n=6), and other diseases (n=12); 38.05% of the patients (n=94) were aware of their condition, of which 88 had completed hepatitis C treatment, 85 patients were treated by DAA regimen; 48 patients were unaware of their hepatitis C condition, after educating about the hepatitis C treatment and health insurance policy, 41.66% (20/48) were willingness to go to the hospital for treatment.

CONCLUSION: Reengagement of in-hospital hepatitis C patients, could strengthen the referral to infectious disease department, improve the rate of linkage to care and follow-up, which were not only helpful to improve patients' knowledge and compliance with hepatitis C, but also an effective measure to clear hepatitis C in the hospital.

Abstract Submission No. 100212
P-0174

Exploring in-hospital referral model for HCV screening and management

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Aim: To support WHO's goal of HCV elimination by 2030, A tertiary hospital in Jiangxi, China, carried out an in-hospital hepatitis C early warning and referral program to improve the effectiveness of HCV diagnosis and treatment.

Methods: The in-hospital hepatitis C early warning and referral program included: (1) a dedicated specialist contacted the care physician of HCV antibody-positive patient to test HCV RNA; (2) a mobile Wechat group to communicating the HCV RNA positive result; (3) the specialist in charge of patients' consultation, referral, treatment, and follow-up.

Results: The program was initiated in June 2022. 76 215 cases (from Jan. 2021 to May. 2022) and 73 389 cases (from Jun. 2022 to Jun. 2023) of our hospital were screened for HCV antibody. HCV antibody positivity rates before and after the program were 0.45% (342/76215) and 0.58% (428/73389), respectively. 86.99% patients that HCV antibody positive distributed at non-infectious departments, the top three were cardiovascular department (20.87%), nephrology (8.13%), and neurology (4.88%). HCV RNA positivity rates were increased from 33.71% (64/192) to 36.67% (66/180) after initiation the program. The treatment rates were increased from 10.93% (7/64) to 36.36% (24/66). 83.33% (20/24) patients from non-infectious departments were treated, the reasons for not treating were death (n=2), malignant tumor (n=2) and cost of treatment (n=14). 93.54% (n=29) were treated with SOF/VEL. The overall SVR rate was 98%.

Conclusion: The practical model for HCV in-hospital elimination program, increase the rate of diagnosis and treatment of in-hospital hepatitis C patients, and enhanced the awareness of hepatitis C.

Abstract Submission No. 100213
P-0175

The efficacy and safety of sofosbuvir/velpatasvir in patients with chronic HCV/HIV coinfection

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Background: There are multiple complications and DDI in patients with chronic HCV/HIV coinfection. Our study aimed to access the efficacy of sofosbuvir/velpatasvir and DDI during the treatment in these patients.

Methods: We retrospectively analyzed patients with chronic HCV/HIV coinfection receiving sofosbuvir/velpatasvir 12 weeks treatment from 2017 to 2019 in Lixin County People's Hospital. Blood routine, liver and renal function, HCN RNA and CD4 were detected at baseline, 12W and 24W. DDI in different drugs was also observed.

Results: A total of 95 patients were included. At baseline, 92 patients (97%) had history of selling blood. The mean age was 57 years, HCV RNA was 1.02*10⁷ IU/ml, ALT was 63 U/L and CD4 was 488/ul. 48 patients (51%) were male. 16 (17%) GT1b, 7 (7%) GT2a, 72(76%) undetected genotype. 19 (20%) with cirrhosis. The count of combined with gastritis, hypertension, cardiovascular and vascular disease, other diseases were 16 (17%), 26 (27%), 27 (28%), 18 (19%). All treated Patients achieved SVR12 99% (94/95). 27 patients (28%) took antacids, PPI or EFV, which reduced the concentration of sofosbuvir/velpatasvir, but did not affect the SVR12. 79 patients(82%) took TDF-based regimens, which increased tenofovir exposure and renal function need to be detected during the treatment. Before and after treatment, Cr 62umol/L and 64umol/L remained stable. BUN 5.5mmol/L and 6.2mmol/L were within the normal range. There were no discontinuations or deaths due to the effects of DDI in all treated patients.

Conclusions: Sofosbuvir/velpatasvir provide high rates of SVR and well tolerated in Chronic HCV/HIV coinfection patients.

Abstract Submission No. 100215

P-0176

Multi-Party Cooperation for HCV Elimination

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Background: Screening HCV patients with a previous stockpile, especially with high prevalence in the remote mountainous region is necessary for HCV elimination. To assess the untreated rate of patients in the CDC database and follow-up DBU patients with DAA treatment.

Methods: Screening patients who were definite in the CDC database from 2004 to 2022 in the townships of Anhui. The local community health service centers extracted HCV RNA and sent blood samples to Lixin County People's Hospital. The CDC noticed patients with HCV RNA positive by phone in 3 rounds and tracked them to the designated hospital for treatment.

Results: A total of 850 patients were tested for HCV RNA; 171 patients (20%) were positive. 154 patients (90%) had a history of selling blood. The mean age was 63 years, and the mean HCV RNA was 2.93*10⁶ IU/ml. 85 patients (50%) received sofosbuvir/velpatasvir or ledipavir/sofosbuvir regimens and all treated patients achieved 100% SVR12. Tracking untreated 86 patients, 36 patients (42%) had a willingness to be treated but hadn't initiated therapy, 34 patients (39%) couldn't get in touch. 4 patients (5%) worked away from home. 4 patients (5%) due to economic difficulties. 5 patients (6%) due to old age (mean age 78Y). 2 patients (2%) had a low level of HCV RNA and retest was negative. 1 (1%) died.

Conclusions: Screening the past stock patients through CDC cooperation with designated hospitals and communities is effective for eliminating HCV. However, the treatment rate was low. Further follow-up with untreated patients is needed.

Abstract Submission No. 100233

P-0177

Huge improvement of HCV-positive ITP after treatment of DAA: a report of an unusual case

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A 45-year-old female with a history of immune thrombocytopenia purpura visited our gastroenterology outpatient department due to easy bruising over limbs and trunks. The diagnosis of immune thrombocytopenia was made by obstetrician and hematologist during prenatal examination about 8 years ago. IVIG and steroid therapy were ever given during the pregnancy 8 years ago, and the platelet count ever elevated to 30x10³/μL from the baseline of 4x10³/μL. However, the platelet count soon back to the range of 4x10³/μL ~ 10x10³/μL if hold IVIG and steroid therapy.

This time, she was referred to gastroenterology outpatient department from Hematologist due to HCV-positive finding during the treatment course of IVIG and steroid therapy. Poor response of treatment for thrombocytopenia by Hematologist, the platelet count only maintained the level of 4x10³/μL ~ 6x10³/μL after IVIG and steroid therapy. After referral to gastroenterology outpatient department, the workup of Hepatitis C virus was done. HCV viral load showed 3481305 IU/mL, and genotyping revealed type 1a. Sonography showed mild fatty liver (score=1), without the finding of splenomegaly. Direct-acting antiviral agent of Maviret (glecaprevir/pibrentasvir) was prescribed for this patient, the following of platelet count showed huge improvement of immune thrombocytopenic purpura at the stage of end of treatment response (EOT) and sustained virological response (SVR). Compared with the past treatment experience of chronic hepatitis C virus, peginterferon and ribavirin were contraindicated among the group of HCV-positive thrombocytopenia. Direct-acting antiviral agents offer better choice of antiviral therapy in the group of HCV-positive thrombocytopenia.

Abstract Submission No. 100240

P-0178

HCV Micro elimination in Huadu District, Guangzhou, China

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Background: We analyzed the data on hepatitis C screening, diagnosis, and treatment in Huadu to further improve the working mode of HCV elimination.

Methods: HCV elimination in Huadu was carried out in close cooperation with the Center for Disease Control and Prevention of Huadu District, the People's Hospital of Huadu District (the only assigned hospital for HCV treatment in Huadu) and 17 community health centers. We conducted telephone follow-up and recall back, improved the

HCV elimination process intra hospital, and targeted special population.

Results: 1. Telephone follow-up of newly reported hepatitis C patients in 2022-2023 in Huadu was conducted from March 2023, 397 patients were followed up, with a follow-up rate of 84.11%. The treatment rate of diagnosed Hepatitis C patients increased from 68.82% in 2022 to 76.43% in 2023. 2. As the assigned hospital, our hospital has continuously improved the HCV elimination process since 2021, and the treatment rate of hepatitis C patients in our hospital has increased significantly from 50% in 2020 to nearly 80% in 2022 (close to the WHO target). 3. There are 44 registered methadone patients in the district, 15 have tested HCV RNA (+), and by 6th October 2023, 8 patients had started treatment. (Details See Table 1 and Figure 1)

Conclusions: HCV elimination in Huadu has achieved preliminary results, and the treatment rate has been steadily improved. Screening should be expanded, and countermeasures should be improved according to the reasons for not starting antiviral therapy.

Abstract Submission No. 100256

P-0179

Eradication of Hepatitis C virus from interferon to DAA in jailed prisoners.

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Totally 530 male prisoners received anti-HCV therapy, 175 interferon and 355 DAA, all IDU, aged 42.7 ± 6.9 years. The distribution of genotype was 1a/ 1b / 2 / 3 / 6 / mixed infection: 27.2/ 16/ 8.1/ 21/ 24.6/ 2.8 (%) respectively. Co-infection with HBV, HIV, and HBV/HIV was 10%(54/530), 12.6%(67/530), 1.9%(10/530). The duration of PEGRIB is 6 months or 12 months by response guide, the AE was common 60%, the interrupt of treatment or follow-up was high 21.1% (12.5 % early release, 8.5% intolerance) due to the long period of treat and follow up. The overall sustained viral response (SVR24) for those completing full dose and at least one dose PEGRIB is 87.6 % (121/138) and 71.4% (125/175). The SVR of HBV co-infection is not different from HCV mono-infection (90% vs. 89.9%) but SVR is lower in HIV co-infection (71.4% vs. 89.9%). The duration of DAA(Epclusa/Harvoni/Maviret/Zepatier: 117/92/135/11) is 8-16 weeks and AE is minor including skin rash/itching, fatigue, headache and insomnia at 8.8% (31/355). Due to early release, one prisoner interrupted DAA therapy and 12 prisoners missed SVR check-up due to early release or transferring. The SVR12 is 99.4% (340/342) on complete follow-up and 95.8% (340/355) on intention to treat. Two failed SVR is genotype 3 treated with epclusa treatment. One mortality is decompensated hepatitis and it was not reverse after DAA treatment. The SVR of DAA treatment is extremely excellent as 100% in the co-infection with HBV/HIV.

Abstract Submission No. 100287

P-0180

Epidemiological characteristics of genotype distribution in 1,342 HCV infections in eastern China

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Background: To analyze the distributions and clinical characteristics of HCV genotypes in 1,342 patients of the designated hospitals in Ningbo City, Zhejiang Province, China.

Methods: From April 2011 to December 2021, 1342 CHC patients were included in Ningbo No. 2 Hospital and Ningbo Fourth Hospital. The distribution of HCV genotypes in patients with different detection time, age, and infection route were analyzed.

Results: The top three genotypes were genotype 1 (49.11%), genotype 6 (19.97%), and genotype 3 (15.50%). The number (the proportion) of HCV genotypes detected increased year by year, reaching a peak (14.31%) in 2020. Genotype 1 predominated every year, however, after 2015, the proportion of type 3 and types 6 showed an overall increasing trend. The male to female ratio was 1.21: 1. The patients were mainly young and middle-aged (>20-60 years old) (87.85%). The composition ratios of type 1, type 2, type 3 and type 6 were the highest in the >50-60 years old group (64.42%), the ≥61 years old group (16.13%), the >30-40 years old group (26.01%), and the >30-40 years old group (26.59%), respectively. the non-young/middle-aged group (≤20+≥61 years old) There were 345 cases with definite infection route. The top three infection routes were intravenous drug addiction, with a history of paid blood donation, unsafe acupuncture, injection, and oral treatment. There were statistically significant differences in age and gender of patients with different infection routes ($F = 16.761$, $P < 0.001$). Patients with intravenous drug addiction had the lowest age and the highest male composition ratio, and the differences were statistically significant compared with other groups ($P < 0.05$). The first two infection routes of patients with type 1 were hemodialysis and paid blood donation, of patients with type 3 were unsafe sex and intravenous drug addiction, of patients with type 6 were unsafe acupuncture, injection, and oral treatment, and intravenous drug addiction.

Conclusions: The distribution of HCV genotypes in the designated hospitals in Ningbo City, Zhejiang Province, China is diverse. Genotype 1, 6 and 3 are the top three genotypes. There are differences in age, gender, and infection routes among patients with different genotypes.

Abstract Submission No. 100295

P-0181

Chronic kidney disease is associated with hepatitis C infection in patients with Type 2 diabetes

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Background: Hepatitis C virus (HCV) infection can induce insulin resistance, and patients with Type 2 diabetes mellitus (T2DM) have a higher prevalence of HCV infection. HCV can induce renal insufficiency, but the association between HCV and severity of chronic kidney disease (CKD) in T2DM remained unclear.

Methods: From March 2022 to May 2023, 4402 T2DM patients in Taipei Veterans General Hospital were prospectively enrolled into the in-hospital referral program for HBsAg and anti-HCV antibody

screening. The clinical features of patients with HBV and HCV infection were compared. Factors associated with anti-HCV (+) were analyzed.

Results: Among 4402 T2DM patients, the prevalence of HBsAg-positive and anti-HCV-positive were 8.0% and 2.4%, respectively. Anti-HCV-positive patients had older age and worse renal function, while HBsAg-positive patients had higher ALT level. The prevalence of anti-HCV (+) were 1.8%, 2.3%, 2.6%, 3.5%, and 7.8% in CKD stage 1, 2, 3, 4, and 5, respectively ($p = 0.014$). Independent factors associated with anti-HCV (+) were age > 65 y/o, CKD stages, and urine albumin-creatinine ratio > 300 . For patients with T2DM more than 10 years, the proportion of CKD stage 1 were 26.9%, 16.7%, and 0% in patients with HCV RNA undetectable, after anti-viral treatment (interferon or DAAs) > 3 years, and after anti-viral treatment ≤ 3 years, respectively ($p = 0.038$).

Conclusions: The prevalence of anti-HCV antibody seropositivity increases with the severity of CKD in patients with T2DM. Patients who achieve virological response earlier have a higher proportion of maintaining in early-stage CKD.

Abstract Submission No. 100296

P-0182

Comorbidities in HCV-infected Patients: Data from the National Viral Hepatitis Registry in Russia

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Background: Chronic hepatitis C infection is recognized as a risk factor for extrahepatic comorbidities. There were no studies on comorbidities in HCV-infected population of Russia.

Materials and Methods: In this retrospective cross-sectional study, we extracted and analyzed adult patients' data on comorbidities from the National Registry of Viral Hepatitis which included more than 300 000 HCV-infected patients. Patients' inclusion criteria were age of >18 , untreated chronic hepatitis C confirmed with positive test for anti-HCV antibody and RNA of hepatitis C virus, availability of data on co-morbidities status. The statistical analysis was descriptive.

Results: 233 167 patients were enrolled from 25 regions of Russia. The overall rate of comorbidities was 11.1% including metabolic disorders (0.02%), diabetes mellitus (0.27%), ischemic heart disease (0.06%), cerebrovascular diseases (0.05%), arterial hypertension (0.34%), renal failure (0.01%), gastrointestinal diseases (0.26%), neoplasms other than liver cancers (0.13%), mental and behavioral disorders (0.03%), chronic infection and infestation (3.22%), HIV-coinfection (6.70%), alcohol and drug abuse (1.0% and 7.5%, correspondingly). Other comorbidities were not reported. Compared with published data, rates of comorbidities in our study are underestimated. Compared with the general study population, the HIV-coinfected patients group included more men, were younger and showed 4.4-times higher rate of drug abuse.

Conclusions: The most common comorbidity in HCV-infected patients in our study was HIV-infection. This should be taken into consideration for appropriate and early testing for HIV of patients with chronic hepatitis C. Rates of other comorbidities were low, and it may reflect the possibility of underdiagnosed or underreporting to the registry.

Abstract Submission No. 100311

P-0183

Efficacy and safety of LED/SOF treatment patients with HCV in Arkhangai province of Mongolia

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Background: Ledipasvir/sofosbuvir (LDV/SOF) shows high efficacy and safety in patients with genotype 1-hepatitis C virus (HCV). We aimed to investigate the efficacy and safety of LDV/SOF in real-world patients in Arkhangai province of Mongolia.

Methods: Between 2017 to 2022, 7 (0.6%) and 1113 patients (99.4%) with genotype 1a and 1b HCV, respectively, were treated with a fixed-dose tablet containing 90 mg ledipasvir and 400 mg sofosbuvir for 12 weeks, and 14 patients (1.25%) with previous experience of interferon (IFN)-based treatment.

HCV RNA was measured at 4, 12, and 24 weeks after the first dose to determine rapid virologic response, end of treatment response (ETR), and sustained virologic response at 12 weeks after end of treatment (SVR12).

Results: Most patients ($n=1,113$; 99.4%) achieved ETR and SVR12 without virologic relapse. Patients with genotype 1a showed low rates of ETR and SVR12 in only 5 patients (71.4%). There was no significant difference in SVR12 rate between patients regardless of IFN experience ($n=14$; 1.25%), cirrhosis ($n=290$; 25.9%), HCV RNA $>6 \times 10^6$ IU/mL ($n=193$; 17.23%). No severe adverse events (AEs) were reported, and there was no dose reduction or interruption due to AE. The most common AEs were headache ($n=110$; 9.8%), fatigue ($n=81$; 7.2%), abdominal discomfort ($n=65$; 5.8%).

Conclusions: LDV/SOF showed high efficacy and safety for patients with genotype 1, especially 1b HCV, in Arkhangai province, Mongolia.

Abstract Submission No. 100312

P-0184

Early occurrence HCC after DAA treatment with HCV infected cirrhotic patients in Mongolia

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Background: Hepatocellular carcinoma (HCC) represents a serious complication of HCV-related cirrhosis. Hepatitis C virus (HCV) is one of the major causes of liver cirrhosis and hepatocellular carcinoma in Mongolia. New direct-acting antivirals (DAA) cure HCV infection in over 96% of patients in Mongolia. The aim of this study was to evaluate the early occurrence of HCC in cirrhotic patients treated with DAA. **Methods:** We analyzed 300 consecutive with chronic hepatitis C patients, without HCC, who were treated with DAA, and followed for 48 weeks.

Results: DAA therapy induced sustained virological response in 99% of patients in Mongolia. During 48-week follow-up, HCC was detected in 17 patients of 300 patients (5.7%, 95% CI: 5.2-9.8). Child-Pugh Class B, more severe liver fibrosis, lower platelet count was

significantly associated with HCC development, at univariate analysis. At multivariate analysis, Child-Pugh class ($p=0.03$, OR: 4.65, 95% CI: 1.28–13.5) and resulted independently associated with HCC development.

Conclusions: In 17 patients (5.7%) with liver cirrhosis develops of HCC after HCV treated with DAA in Mongolia. For these reasons, all cirrhotic patients should be closely monitored and followed during and after antiviral therapy.

Abstract Submission No. 100335

P-0185

Evaluating utilization and management of comedications for DDIs among HCV patients initiating DAAs

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Background and Aims: This analysis compared rates and management of comedications with drug-drug interactions (DDI) risk among patients initiating direct-acting antiviral (DAA) treatment with sofosbuvir/velpatasvir (SOF/VEL) or glecaprevir/pibrentasvir (GLE/PIB) for chronic hepatitis C (HCV).

Method: Adults initiating SOF/VEL or GLE/PIB from July 2016–April 2020 were identified from US administrative claims data. All DDI comedications associated with GLE/PIB and SOF/VEL and DDI comedication severity were from the Liverpool HEP Drug Interactions Database. DDI comedication discontinuation, dose decrease, and change to medication with no DDI risk were measured in the subset of patients.

Results: Among 4,528 patients, 66.6% of GLE/PIB initiators and 43.7% of SOF/VEL initiators had any baseline DDI comedication use ($p < 0.01$). Compared with SOF/VEL initiators, GLE/PIB initiators had higher baseline rates of DDI comedication severity. DDI comedication use decreased during DAA treatment but remained higher in GLE/PIB initiators ($p < 0.01$). 979 GLE/PIB and 658 SOF/VEL initiators used prevalent DDI comedications in the 90 days pre-index. Those GLE/PIB vs SOF/VEL initiators had similar mean age, proportions of female and commercially insured patients, and lower baseline compensated cirrhosis. A higher proportion of GLE/PIB initiators discontinued at least 1 DDI comedication before initiating DAA treatment ($p < 0.01$). During DAA treatment, GLE/PIB initiators had higher rates of dose decrease ($p = 0.026$) and change to medication with no DDI risk ($p = 0.014$).

Conclusion: Use of DDI comedications was identified among a substantial proportion of patients, with higher rates in GLE/PIB initiators.

Abstract Submission No. 100336

P-0186

Concomitant use of PPI and SOF/VEL: Evidence from Clinical trials and Real-World data

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Background: Literature and product labels suggest velpatasvir bioavailability may be reduced when administered concomitantly with a proton pump inhibitor (PPI). We aimed to determine the clinical relationship between PPI use and sustained virologic response rates (SVR) in patients treated with sofosbuvir/velpatasvir (SOF/VEL) for chronic hepatitis C virus (HCV) infection.

Method: Retrospective and descriptive analysis of data from patients treated with SOF/VEL for 12 weeks with and without concomitant use of PPIs and participating in Phase 2/3 RCTs and RWD studies. Main variables collected for this analysis consisted of SVR12 and relapse rate.

Results: 546 patients with PPI use were identified and the control group without PPI use was 5,201.

In RCT, patients receiving PPI and SOF/VEL were mainly male, GT3 in 56% and cirrhotic in 35%. Most patients participating in RCT (66%) continuously used PPI during the 12-week course of treatment with SOF/VEL. Overall SVR12 in PPI users was 97%, comparable to non-PPI users (97%). SVR12 in GT3 patients was 96%, in F4 was 94%. In GT3 plus F4 patients, SVR12 was 96%. In RWD, patients receiving PPI and SOF/VEL were male (54%), GT3 in 25% and cirrhotic in 29%. Overall SVR12 in PPI users was 99%, comparable to non-PPI users (99%).

Conclusion: In RCTs and RWD, the single-tablet regimen of SOF/VEL for 12 weeks was effective in patients with concomitant PPI use. These data support the use of SOF/VEL according to labeled recommendations with respect to co-administration of PPIs and other acid reducing agents.

Abstract Submission No. 100337

P-0187

Finding undiagnosed Hepatitis C cases: using machine learning

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Background and Aim: Undiagnosed Hepatitis C Virus (HCV) is a major public health concern in the US. Gilead's FIND-C program enables to efficiently screen and identify undiagnosed HCV patients. The initial step for FIND-C was development of a high-precision machine learning (ML) algorithm, followed by partnership with a US-based health system for assessing improvement in the screening to diagnosis ratio (SDR) and user adoption. Validation of the algorithm using real-world health system data is necessary.

Method: This study involved development of an ML algorithm using a large-scale US dataset consisting of deidentified electronic health records (EHR); the cohort for model development included 295,512 patients (HCV-positive: 50,726; HCV-negative: 245,236), using 32 clinical (diagnoses, treatments, procedures), demographic, and social determinants of health variables. The model's precision was optimized and model performance was evaluated in a health system having viral infectious disease as a core focus and sufficient digital capabilities for model integration. The test dataset contained 26,154 patients (HCV-positive: 4,848; HCV-negative: 21,306).

Results: Performance of the model algorithm trained on EHR data was: AUROC: 95%, Precision: 93%, Recall: 50%. Using health system test data, we found AUROC: 86%, Precision: 91%, Recall: 30%.

Conclusion: Effective implementation of the HCV patient identification solution can provide a resource-efficient, expedited identification of undiagnosed HCV patients, thereby serving as a catalyst for

universal screening guidelines and a scalable solution for achievement of global elimination goals.

Abstract Submission No. 100360
P-0188

SOF/VEL Effectiveness in Treating Chronic Hepatitis C Genotype 3: A Real-World Study in Xinjiang.

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Objective: This study aimed to assess the effectiveness and safety of sofosbuvir/velpatasvir(SOF/VEL), with or without ribavirin(RBV), in treating chronic hepatitis C(CHC) genotype 3(GT3) individuals.

Methods: Totally 230 patients diagnosed with CHC GT3 were included and received treatment at two hospitals in Xinjiang from June 2018 to March 2023. Patients with CHC and CC received SOF/VEL treatment for 12 weeks, while those previously treated with interferon plus ribavirin(PR) and DCC patients were treated with SOF/VEL for 24 weeks or SOF/VEL plus RBV for 12 weeks. Comprehensive assessments including high-sensitive HCV RNA levels, liver and renal function, abdominal ultrasound examinations were conducted. The primary endpoint was the sustained virologic response at 12 weeks post-treatment(SVR12).

Results: The mean age was 43.31±11.18 years, consisting of 66.5%(153/230) male. Among these, 137 cases(59.6%) were of GT3a, while 93 cases(40.4%) were of GT3b. Within the cohort, 44 cases(19.1%) presented with compensated cirrhosis(CC), 3 cases(1.3%) had decompensated cirrhosis(DCC), 33 cases(14.3%) were co-infected with HCV/HIV, 6 cases(2.6%) exhibited HBV/HCV co-infection, and 2 cases(0.9%) had HBV/HCV/HIV co-infection. Overall, the SVR12 was 99.6%(229/230) including 100% SVR12 rates for GT3a(137/137) and 98.9% for GT3b(92/93). Only one patient experienced relapse due to the poor adherence. Notably, SVR12 rates for CC and DCC patients were both 100%, and SVR12 rates for HCV/HIV, HBV/HCV, and HBV/HCV/HIV co-infections were all 100%. The overall safety profile was favorable, with no treatment discontinuations due to adverse events.

Conclusion: SOF/VEL monotherapy or combined with RBV demonstrated highly effective and well-tolerated in treating with CHC GT3, including those with cirrhosis, in Xinjiang, China.

Abstract Submission No. 100361
P-0189

Prevalence of Naturally Occurring Hepatitis C Virus Resistance-Associated Substitutions in Korea

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This study aimed to investigate the prevalence of naturally occurring resistance-associated substitution (RAS) of hepatitis C virus (HCV) in Korean patients by next-generation sequencing.

Patients with chronic HCV infection were prospectively enrolled from March 2020 to July 2022 and treated with direct-acting antivirals. Sera were collected at baseline, at the end of treatment, and 12 weeks after treatment. Whole genome sequencing for HCV was performed to analyze RAS by next-generation sequencing.

A total of 263 patients (median age 62, male 129) were enrolled and successfully treated with DAA. HCV RAS was analyzed from the baseline sera of 71 patients (genotype 1b 39, genotype 2 33). For genotype 1b, RAS was detected in 48.7% (19/39); NS3 in 41.0% (16/39), NS5A in 15.4% (6/39), NS5B in 28.2% (11/39), respectively. Among NS3 RASs, Y56F was most frequently detected (23.1%), followed by Q80H/L (20.5%) and S122G/T (17.9%). Among NS5A RASs, Y93H was most frequently detected (10.3%), followed by L31M (2.6%) and R30Q (2.6%). Among NS5B RAS, C316N was most commonly seen (23.1%), followed by L159F (2.6%) and S556G (2.6%). For genotype 2, NS3 RAS was detected in 24.2% (8/33), but no RAS was found in NS5A and NS5B.

This study revealed the baseline prevalence of NS3, NS5A, and NS5B RAS of HCV in Korean patients for the first time. Knowledge of baseline RAS of HCV could help guide DAA treatment for difficult-to-treat patients.

Abstract Submission No. 100369
P-0190

Relink Model of Hepatitis C Elimination among HCV/HIV-coinfected Patients

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Background: Luyi is a city with high prevalence of AIDS in North China, where the prevalence of HCV infection was high among HIV-infected populations. HIV patients were previously managed by the Luyi Centers for Disease Control (CDC) and followed up regularly twice a year, but there were not any HCV screening and treatment for this population. This study aimed to evaluate the innovative relink HCV elimination model of undiagnosed hepatitis C patients identification and activation in HIV population.

Methods: Luyi County People's Hospital collaborated with local CDC. CDC utilized the database of HIV population with or without HCV antibody data for HCV Ab and HCV RNA confirmation from 2022.5, they offered free HCV antibody and HCV RNA assay at fixed follow-up points without recall efficiently. All the patients with HCV RNA+ were transferred to the Infection Disease Department of Luyi Country People's Hospital, where physicians conducted disease education and initiated antiviral therapy after critical assessment of disease and DDIs.

Results: A total of 667 HIV-infected patients were screened for HCV RNA confirmation at fixed follow-up points from 2022.5-2023.7, of which 233 (34.9%) cases were HCV Ab(+), 81(12.1%) cases were HCV RNA (+). 77.8% (63/81) patients initiated antiviral therapy, 4 subjects lost to follow-up, 1 subject relapsed, 1 subject had breakthrough due to irregular dose, overall 57 patients achieved 98.4%(57/63) SVR rate.

Conclusions: It was an effective model of undiagnosed hepatitis C patient identification and activation in HIV population, which could be scalable to accelerate HCV elimination in China.

Abstract Submission No. 100379

P-0191

HCV Elimination Pilot Program in Hospital to Support Hepatitis C Elimination 2030

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BACKGROUND: To support the WHO 2030 hepatitis C elimination goal, Xiangya Hospital Central South University joined the HCV elimination pilot program of the China Hepatitis Prevention and Control Foundation (CHPCF)'s "Hepatitis C-Free Hospitals Initiative".

METHODS: The program was initiated in March 2023 in Xiangya Hospital Central South University, and was led by the Infectious Diseases Department, with the participants of the Medical Department, Information Department, and Blood Transfusion Department. A review of hepatitis C antibody or RNA data was conducted twice a week, and patients with antibody or RNA positive were followed up by telephone. Additionally, infectious disease specialists educated medical staff on HCV screening and diagnosis, recommending RNA testing for antibody-positive patients and antiviral therapy for RNA-positive patients.

RESULTS: From March to August 2023, a total of 625 HCV antibody-positive patients were enrolled, with 316 undergoing RNA testing. The RNA testing rate increased from 39.0% (Mar. 2023) to 59.0% (Aug. 2023). Notably, 83% of antibody-positive patients were from non-infectious departments, mainly gastroenterology and hepatic surgery department. Among 229 RNA-positive patients, 160 (69.9%) patients received DAA treatment. For patients not receiving antiviral therapy, 46% couldn't be contacted, 14% had other illnesses and 14% refused treatment.

CONCLUSION: Since initiating the in-hospital HCV elimination pilot program, the rate of RNA testing for HCV antibody-positive patients has significantly increased. Most hepatitis C patients are from non-infectious departments. Going forward, we'll strengthen collaboration between infectious and non-infectious departments to improve hepatitis C patient screening and referral.

Abstract Submission No. 100397

P-0192

Hepatitis C Elimination Model in Taiwan's rural Community Care Home

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Background and Aims: Yunlin and Chiayi counties and cities are high-prevalence areas for hepatitis C in Taiwan, with an antibody-positive rate of 7.3%. The Hepatitis care team of the Chiayi Hospital

proactively screened residents of 22 community care homes (CAHs) to eliminate hepatitis C.

Methods: Since 2017, the Taiwanese government has complied with financial resources for free hepatitis C screening and cure programs. From September 2021 to December 2022, An HCV elimination program was planned and implemented for a total of 450 residences of 22 CAHs based on the paradigm of integrated care. The positive cases of HCV screening were then sent to the Chiayi Hospital for further tests and then treated antiviral medications, prospectively, delivered by Chiayi Hospital.

Results: Among the 353 aged 45-79 residents, 320 (91%) participated in this HCV screening program. The number of positive cases of HCV Ab and HCV-RNA was 48 (15%) and 23 (7%), respectively. Among the confirmed cases, 20 people received HCV antiviral medication treatment, while 3 of them people did not receive any treatment due to death or unwillingness to be treated. The average age of cases receiving DAA treatment was 59 years; the treatment rate was 83%; the complete treatment rate, follow-up rate, and SVR rate was all 100%.

Conclusions: This innovative model of providing institutionalized resident HCV screening and treatment through an integrated mechanism of organization and delivery integration revealed conclusive results of a hepatitis screening rate of $\geq 60\%$ and a hepatitis C treatment completion rate of $\geq 90\%$.

Abstract Submission No. 100410

P-0193

Assessing Liver Fibrosis in Patients with Chronic Hepatitis C Genotype 6 Treated with Ledvir

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Hepatitis C virus (HCV) is an important health problem globally. If left untreated, there is a risk of progression to cirrhosis, hepatocellular carcinoma and death.

Aims: Assessing liver fibrosis (LF) in patients with HCV treated with Ledvir.

Method: The prospective cohort study was conducted on 54 patients with HCV genotype 6 who were treated with Ledvir (Ledipasvir/Sofosbuvir 90mg/400 mg) orally once a day for 12 weeks at Cam Khe Clinic from 4/2019 to 9/2023. LF was evaluated using the METAVIR scoring system, by Fibroscan. Quantification of HCV RNA using HCV RNA real-time PCR method. Evaluate treatment response at week 4 after starting treatment, week 12 and 24 after end of treatment (EOT).

Results: Virologic response rate at 4 weeks of treatment was 96.3% and sustained virological response at 12 weeks was 98.1%. LF from 11.6 kPa before treatment, to 10.1 kPa at EOT, 9.3 kPa at week 12 after EOT and 8.2 kPa at week 24 after EOT. The proportion of F4 patients before treatment was 25.9%, at EOT was 18.5% and week 24 after EOT was 14.8%. F0-F1 group at the time before treatment was 37.0%, and increased to 55.6% at EOT and 74.1% at week 24 after EOT. Factors related to LF response are: overweight, initial fibrosis and AST activity ($p < 0.01$). Side effects of the drug include: nausea and headache.

Conclusions: The level of LF improvement gradually increased in patients with HCV treated with Ledvir over time: EOT, week 12 after EOT and week 24 after EOT.

Abstract Submission No. 100412
P-0194

Epidemiology and countermeasures on hepatitis C among pregnant women in China from 2018 to 2020

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Objective: This study aim to investigate the hepatitis C virus (HCV) infection status of pregnant women in Nanjing of East China.

Methods: We carried out HCV antibody(HCV-Ab) screening for pregnancy women in 5 tertiary hospitals between 2018 and 2020. Positive patients were transferred to designated hospitals for re-examination and confirmation. 55359 pregnant women who underwent HCV infection testing were consisted in this study, follow-up cohort was established to conduct questionnaire surveys, pregnancy management, delivery, and infant monitoring.

Results: 101 of the 55,359 pregnant women were HCV-Ab(+), with a positive rate of 0.18%. The average age of 101 HCV-Ab(+) pregnant women was 30.20 ± 5.17 years, 81 primiparas and 20 multiparous women. Among the 101 HCV-Ab(+) pregnant women, 83 had chronic infection in the past, 7 had virus clearance before pregnancy, 75.24%(76/101) were HCV-RNA(+). The postpartum hemorrhage rate in the HCV-RNA(+) group was higher than that in the HCV-RNA(-) group (94.74% vs 5.26%, $P=0.014$). There was no significant difference in the rate of cesarean section and premature birth between the two groups. Both perinatal death($n=2$) and mother-to-child transmission ($n=2$) occurred in the HCV-RNA(+) group, but the difference was not statistically significant, which was related to the lower incidence.

Conclusion: Anti-HCV prevalence was moderate in pregnant women in Nanjing of East China. However, pregnant women with HCV RNA(+) have a higher rate of postpartum hemorrhage, and there is a possibility of infant death and mother-to-child transmission of HCV. Routine screening for HCV and DAAs treatment before pregnancy are encouraged.

Key words: hepatitis C virus; pregnant women; pregnancy outcome

Abstract Submission No. 100432
P-0195

Hepatitis C elimination experience of HCV infected patients in methadone clinic

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Aim: This study aims to evaluate the efficacy and safety of hepatitis C patients receiving SOF/VEL treatment in a methadone clinic.

METHODS: Chronic hepatitis C patients (receiving methadone substitution therapy at the methadone clinic) treated at the Infectious Department of Xi'an Central Hospital from Jan. 1, 2023 to Jun. 1, 2023 were enrolled. All of them received SOF/VEL ± RBV treatment for 12 weeks and were followed up to assess the efficacy and safety.

RESULTS: A total of 77 patients treated with SOF/VEL ± RBV were enrolled in the study, the baseline characteristics of the patients were: 74.02% were males ($n=57$), mean age was 53.49 years. Genotypic distribution of GT3a was 66.23% ($n=51$), GT3b 11.69% ($n=9$), GT6a 12.99% ($n=10$). Baseline HCV RNA level was 8.91×10^6 IU/mL, ALT

level was 94.33 ± 63.78 U/L, Fibrotest value was 13.71 ± 5.17 kPa, 16.89% ($n=13$) combined compensated cirrhosis, 11.69% ($n=9$) combined decompensated cirrhosis, 11.69% ($n=9$) combined fatty liver, and 2 cases combined HCC. 61 out of 77 patients underwent DAA treatment, the rate of SVR12 was 97.37% (37/38), SVR12 in compensated cirrhosis was 100% (13/13), and 88.89% (8/9) in decompensated cirrhosis patients. The patients were well tolerated with no drug-related SAEs.

We also found that half of the patients were unable to follow up regularly as recommended, after the telephone reminders by nurses, the follow up rate increased from 49.18% to 62.30%.

CONCLUSION: Hepatitis C patients in methadone outpatient clinics on SOF/VEL treatment can achieve high SVR rates, and the adherence of this population needs more attention.

Abstract Submission No. 100433
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Hepatitis C Screening and Patient Disease Knowledge Questionnaire in a Drug Rehabilitation Center

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AIM: This study was designed to determine the prevalence of HCV infection through centralized screening in a rehabilitation center, get disease awareness and the mental health situation of these high-risk populations.

METHODS: This study was conducted from April 2023 to June 2023 at a drug rehabilitation center in Lantian District, Xi'an. Participants were screened for HCV antibodies, HCV RNA, and genotype. A questionnaire on hepatitis C disease awareness and the SCL-90 evaluation was distributed.

RESULTS: 127 people were screened, of which 79.53% were male ($n=101$), 60.63% of the screened individuals were aged 45-59 yrs. Majority had a history of alcohol consumption (85.83%), and smoking (94.49%). The HCV antibody positivity rate was 49.61% ($n=63$), of which 58 cases tested positive for HCV RNA, with a mean HCV RNA level of 6.24×10^6 IU/mL, and the genotype results were GT1b 1.72% ($n=1$), GT2a 8.62% ($n=5$), GT3a 62.07% ($n=36$), GT3b 13.79% ($n=8$), GT6a 10.34% ($n=6$), untyped 3.45% ($n=2$). 38.10% of the patients with hepatitis C had clinical symptoms (including malaise, nausea, abdominal pain, abdominal distension, etc.). The results of the disease questionnaire showed only 14.29% correct responses. The results of the SCL-90 evaluation showed abnormal scores in 2/3 of the respondents, suggesting the need for further assessment of the mental health status of patients with hepatitis C.

CONCLUSION: Our study shows that there is a high prevalence of HCV in the population of drug rehabilitation centers, and this population has low disease awareness and poor mental health, which needs to be given more attention.

Abstract Submission No. 100434
P-0197

HCV prevalence among male inmates in the compulsory drug rehabilitation center in Qinghai, China.

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Background: The prevalence of hepatitis C virus (HCV) infection is notably higher among individuals who engage in intravenous drug use (IDU) and those in prisons compared to the general population. These vulnerable groups are pivotal in achieving the WHO's 2030 goals for HCV micro-elimination.

Objective: Our study aimed to ascertain the prevalence of HCV antibodies (HCV-Ab) and HCV RNA among incarcerated males within a compulsory drug rehabilitation center.

Methods: A total of 287 inmates were assessed, a fingerstick sample was obtained and subjected to HCV antibody rapid diagnostic test (RDT), immediately followed by a reflect HCV RNA test, for HCV-Ab positive inmates, venous blood sample were collected and sent for laboratory HCV RNA and genotype.

Results: All incarcerated individuals had a history of intravenous drug use (IDU), and the shared use of razors in the drug rehabilitation center contributed to potential HCV transmission. The prevalence of HCV-Ab among these inmates was approximately 43% (123 out of 287). Among the 112 HCV-seropositive individuals tested for HCV RNA, 92 (82.14%) were found to be HCV RNA positive. A total of 86 samples were qualified for genotyping, the most common genotype was GT3b (52.3%, n=45), followed by GT3a (29%, n=25), GT1b (8.1%, n=7), GT6a (5.8%, n=5), GT2 (3.5%, n=3) and GT1a (1.3%, n=1).

Conclusions: The prevalence of HCV infection among male inmates in the drug rehabilitation center was alarmingly high. Future efforts should focus on developing appropriate elimination strategies, which may include non-specialists' involvement and nurse participation, training programs, and mentorship initiatives, to facilitate effective linkage to care.

Abstract Submission No. 100483
P-0198

Surveillance of the Safety and Effectiveness of Glecaprevir/Pibrentasvir in Korean Patients with CHC

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Hepatitis C virus (HCV) infection is a leading cause of chronic liver disease. Previous clinical trials demonstrated that

glecaprevir/pibrentasvir (G/P) treatment is effective and well-tolerated among patients with chronic hepatitis C (CHC), although data in real-world clinical settings is limited. This prospective, multicenter, post-marketing surveillance study (NCT03740230) evaluated the safety and efficacy of G/P in Korean patients with CHC in real-world settings. The study included participants aged ≥ 12 years with CHC who received G/P in South Korea (January 2021 to January 2023) for 8, 12, or 16 weeks according to approved local labels. Of 1,674 participants evaluated for safety, mean (SD) age was 59.54 (± 12.17) years, and 52.93% were female; 18.58%, 28.61% and 7.89% had liver cirrhosis, liver impairment, and renal impairment, respectively. Adverse events (AEs) and treatment-related AEs (TRAEs) occurred in 11.23% and 5.91% of participants, respectively; serious AEs and serious TRAEs occurred in 1.43% and 0.12%, respectively, and unexpected TRAEs and unexpected serious TRAEs occurred in 3.05% and 0.06%, respectively. Among participants evaluated for efficacy, 98.77% achieved sustained virological response 12 weeks post-treatment (SVR12) and 98.36% achieved end-of-treatment response. SVR12 rates were similar regardless of HCV genotype, presence/absence of liver cirrhosis or renal impairment, prior CHC treatment, and age group. Treatment breakthrough and post-treatment virologic relapse occurred in 1.07% and 1.00% of participants, respectively. G/P was well-tolerated and effective in Korean patients with CHC regardless of HCV genotypes in real-world settings. No new safety signals were observed regardless of age group and presence of hepatic or renal impairment.

Abstract Submission No. 100486
P-0199

HCV Micro-elimination in Community-based<st

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Background: There are no reports on the prevalence of HCV among Ex-Drug Users (EDUs) from CDRCs in China. This study aimed to assess the prevalence of HCV in EDUs and establish a linkage-to-care model for this population.

Methods: This prospective study planned to conduct HCV screening in 10 CDRCs in Shunde, Guangdong Province. EDUs who enrolled in the study were required to complete a questionnaire and undergo finger-stick anti-HCV testing. Blood samples were collected for HCV RNA testing for the people with the HCV-Ab(+) at the same time. HCV RNA-positive patients were recalled by phone and referred for treatment.

Results: From June to October 2023, a total of 86 EDUs from four CDRCs were screened; all underwent finger-stick anti-HCV testing. The average age was 47 years, 88% were male, 100% were anti-HIV-negative, 88.5% had a middle school education or below, and 50% were people who had previously injected drugs (ex-PWID). The HCV antibody positive rate was 51.1% (44/86), with a high rate of 88.4% (37/43) among ex-PWID and 25% with liver cirrhosis (11/44). The HCV RNA positivity rate was 72% (31/43), with one patient currently undergoing direct-acting antiviral (DAA) treatment and not testing. The successful referral rate for treatment was 41.9% (13/31), with 11/13 referrals completed within 2 weeks and 9/13 patients already started DAA treatment.

Conclusion: This is the first report on the prevalence of HCV among the EDUs from CDRCs in China. The high prevalence of HCV in this population requires our attention, and linkage-to-care will continue in the remaining 6 CDRCs.

Abstract Submission No. 100499
P-0200

HCV High Prevalence in Psychiatric Inpatients: An Opportunity for Enhanced Screening and Treatment

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Background: The data of HCV prevalence among psychiatric inpatients in China is limited. This study aims to evaluate uptake of HCV testing and treatment among psychiatric inpatients.

Methods: Cross-sectional study, 2508 psychiatric inpatients admitted to Yangjiang Public Health Hospital from January 2018 to June 2023 were enrolled, and their HCV antibody and RNA testing results were analyzed.

Results: Among the 2508 patients, 1491 (59.4%) were male, with a mean age of 42 years (range: 10-107 years), and 1736 (69.2%) were diagnosed with schizophrenia. In this cohort, 2488 (99.2%) underwent HCV antibody screening, and 65 (2.6%) tested positive. The HCV antibody positivity rate was 4.0% (59/1472) in males and 0.6% (6/1016) in females. 56.9% (37/65) of patients underwent HCV RNA testing, while the rest were lost to follow-up after discharge. HCV RNA testing revealed a positivity rate of 78.3% (N=29), with 8 cases testing negative (including 4 previously treated patients). Among the 29 HCV RNA-positive patients, 6 received direct-acting antivirals (DAA) treatment and achieved sustained virologic response (SVR); 10 inpatients were preparing to start DAA treatment, and the remaining 13 discharged patients were being recalled for referral.

Conclusion: Psychiatric inpatients exhibit a high prevalence of HCV, with a higher proportion in males than females. The relatively low treatment rate in the past can be attributed to the psychiatric adverse effects of interferon-based therapies on psychiatric patients. With a safer and more effective profile of DAAs, there is an opportunity to enhance HCV screening and treatment within the psychiatric inpatient setting.

Abstract Submission No. 100571
P-0201

LSM after oral antivirals effectively predict the risk of HCC in patients with chronic hepatitis C:

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Background: Hepatocellular carcinoma (HCC) can still occur in patients with chronic hepatitis C after achieving a sustained virologic response (SVR) with direct-acting antiviral (DAA) therapy. Therefore, we aimed to identify parameters related to HCC development and validate the performance of these parameters and HCC prediction models.

Methods: This retrospective cohort study included 3,357 patients with chronic hepatitis C from 10 tertiary hospitals who were treated with DAA and achieved SVR.

Results: During a median follow-up of 3.2 years, 190 (5.7%) patients developed HCC at a median of 4.86 years (incidence rate 1.690/100 patient-years). LSM gradually improved from baseline to SVR and 1 year after SVR (all $P < 0.05$). In the multivariate analysis, LSM at SVR

and 1 year after SVR were significantly associated with the occurrence of HCC (all $P < 0.05$). LSM at SVR and 1 year after SVR could better predict HCC risk than baseline LSM (c-index: 0.733, 0.758, and 0.793 at baseline, SVR, and 1 year after SVR, respectively), and the highest c-index was observed at 1 year of follow-up. Low-risk patients (LSM < 10 kPa) using LSM values at 1 year after SVR (76.4%) showed an incidence risk of 0.5 incidence rate/100 patient-years. When classifying the low-risk group using a cut-off value of 8 or 10 kPa in LSM at 1 year after SVR, even patients with advanced chronic liver disease before treatment showed an HCC risk of less than 1 incidence rate/100 patient-years.

Conclusions: LSM after achieving SVR effectively assesses the risk of developing HCC.

Abstract Submission No. 100574
P-0202

HCC risk scores assess the risk of HCC in CHC patients without advanced fibrosis after DAAs

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Background: The current guidelines recommend lifelong ultrasound surveillance for chronic hepatitis C patients with advanced fibrosis or cirrhosis after achieving SVR with DAA therapy. However, there are limited studies on the risk of HCC in patients without advanced fibrosis. Therefore, we aimed to identify high risk group for HCC development using HCC prediction models.

Methods: This study included 1,839 chronic hepatitis C patients without advanced chronic liver disease from 10 tertiary hospitals who were treated with DAA. Advanced fibrosis was defined as LSM ≥ 10 kPa, FIB-4 > 3.25 , or APRI ≥ 1.5 at baseline. The predictors of HCC occurrence and predictive ability of HCC risk scores were assessed.

Results: During a median follow-up of 2.8 years, 28 (1.5%) patients developed HCC at a median of 2.77 years. The mean age was 56 years, and 852 (46.3%) patients were male. When the patients were divided into HCC and non-HCC groups, patients who developed HCC during follow-up were significantly older, and had lower platelet count and albumin level before antiviral treatment. In addition, patients who developed HCC had a higher FIB-4 score ($P < 0.001$). Comorbidities, such as diabetes and hypertension, were more common among patients with HCC than those without HCC ($P < 0.05$). In multivariate analysis, old age, platelet count, albumin level, and sodium level before treatment were significantly associated with the occurrence of HCC (all $P < 0.05$). The high-risk group defined by previously published HCC prediction models showed a significantly high HCC occurrence. This finding was observed in most validated HCC prediction models including aMAP and mPAGE-B, and the incidence of HCC ranged from 1.5% to 7.4% at 3-years and from 3.8% to 24.2% at 5-years at SVR in high-risk patients (Table and Figure). HCC rarely occurred during the first 5-years of follow-up in low and intermediate-risk patients defined by HCC risk scores.

Conclusion: HCC risk models effectively assess the risk of HCC in chronic hepatitis C patients without advanced fibrosis after achieving SVR. Therefore, even in patients without advanced liver fibrosis before treatment, surveillance should be considered if they are included in the high-risk group of the HCC prediction model.

Abstract Submission No. 100584
P-0203

The challenge of a recall programme from a community-based hepatitis C screening campaign

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Background: We assessed the proportion of participants who obtained linkage to care (LTC) since the end of the screening campaign and examined various factors affecting LTC in these participants. The effectiveness of recall intervention for the non-LTC population and its barriers were analyzed.

Methods: We initiated an HCV patients recall program to identify the HCV participants who might not be treated after the HCV screening campaign. A program staff recalled HCV participants who lost to follow-up through the telephone from March 2019 to June 2019. They were informed of HCV treatment's importance, availability, and safety. **Result:** Among 185 HCV-infected participants, a total of 91 participants were tried to be contacted in the recall program. The subsequent follow-up results were as follows: 33 (36.2%) persons could not be reached because of incorrect telephone number and non-response, 3 (3.3%) persons died, 3 (3.3%) persons' anti-HCV became negative, 15 (16.5%) persons had LTC in CGMH, 15 (16.5%) persons had LTC in other hospitals, and 22 (24.2%) persons did not LTC. At the end of the recall program, 127 (69.8%) persons had LTC. The proportion of LTC increased by 10.9%.

Conclusion: The associated factors affecting LTC included older age, living in a rural area, being unaware of their HCV infection, and having no health insurance. After a community screening campaign, 59 % of participants with anti-HCV positive had LTC. The recall program can increase by 11 %. However, there were still 30% of HCV participants who couldn't be linked to care.

Abstract Submission No. 100591
P-0204

ACCURACY OF THE APRI SCORE TO ASSESS THE PRESENCE OF CIRRHOSIS IN HCV-INFECTED PATIENTS

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Background: According to WHO guidelines aspartate aminotransferase-to-platelet ratio index (APRI) is recommended as the preferred non-invasive test (NIT) to assess for the presence of cirrhosis (APRI score >2 in adults) in resource-limited settings. The results of NITs may be impacted by intercurrent diseases (alcoholic hepatitis, HIV-infection, use of drugs and traditional herbal medicines etc.) that may falsely increase or decrease the scores. The impact of different comorbidities on the diagnostic accuracy of the APRI score has not been fully evaluated.

Methods: 588 HCV-infected patients from 18 to 83 years old (age 53.8±12.1) involved in the study. According to the state program for the treatment of chronic HCV-infection with directly acting antiviral agents, all anti-HCV antibody positive patients for inclusion in program subsequently should be checked on HCV-RNA by PCR and liver

fibrosis stage with liver fibrosis stage determined by Elastography or APRI, FIB-4 calculation.

Results: From 588 patients with chronic HCV-infection liver fibrosis stage determination by APRI calculation was done in 454 patients (77%). APRI≥2 observed in 59 patients (6.6%), among them 21 without liver cirrhosis (36%), 25 with Child-Pugh A (42%), 13 with Child-Pugh B liver cirrhosis (22%). On the other hand among 395 patients with APRI<2 in 12 patients (3%) was diagnosed liver cirrhosis: 6 with Child-Pugh A, 5 with Child-Pugh B and 1 with Child-Pugh C liver cirrhosis.

Conclusions: In 36% of patients despite absence of liver cirrhosis APRI was 2 and above. Misdiagnosis of advanced liver fibrosis can influence on efficacy of treatment and lifelong follow-up on HCC.

Abstract Submission No. 100614
P-0205

Prognosis after SVR of chronic hepatitis C patients treated with Glecaprevir/Pibrentasvir treatment

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Aims: Direct-acting antiviral (DAA) therapy can cure chronic hepatitis C (CHC), and glecaprevir/pibrentasvir (GLE/PIB) was introduced to Korea in 2018. A good prognosis is expected in patients who achieved sustained virologic response (SVR) after DAA treatment. However, information about the prognosis of Korean CHC patients who achieved SVR after GLE/PIB treatment is still limited. We aimed to investigate the prognosis of these patients.

Methods: This is a multicenter prospective observational study. The CHC patients achieved SVR after GLE/PIB treatment were enrolled and final follow-up date was June 2023. The primary end-point was hepatocellular carcinoma (HCC) occurrence. At last one time in a year, we checked about this end-point.

Results: Total 361 patients were included in this analysis and mean follow-up duration was 23.9 months. Male was 159 patients (44.0%) and median age was 59 years. Genotypes were 1 (131, 36.3%), 2 (223, 61.8%), 3 (5, 1.4%) and 6 (2, 0.6%). Cirrhosis was 85 patients (23.5%) and significant alcohol intake prevalence was 60 (16.6%). Mean Child-Pugh score was 5.2 and HCC occurrence cases were 8 patients (2.2%) for up to 4 years. HCC patients all had cirrhosis prevalence (100% vs. 21.8%, p<0.001), older age (68 years vs. 59 years, p=0.025), higher APRI (2.0 vs. 0.4, p<0.001) and FIB-4 (7.2 vs. 2.0, p<0.001). Cox regression analysis showed APRI over 0.714 (p=0.045), FIB-4 over 5.778 (p=0.005) were significant risk factors for HCC occurrence. Recurrence or reinfection occurred in 2 patients (0.6%) at 21 and 22 months after SVR each.

Conclusion: The prognosis of patients achieved SVR after GLE/PIB treatment was generally good. However, HCC risk was not completely removed especially in patients with high APRI or FIB-4 score. Recurrence or reinfection is also possible. Therefore, regular follow-up surveillance is still warranted.

Abstract Submission No. 100615

P-0206

Prognosis after SVR of chronic hepatitis C patients treated with Elbasvir/Grazoprevir treatment

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Aims: Direct-acting antiviral (DAA) therapy can cure chronic hepatitis C (CHC), and elbasvir/grazoprevir (EBR/GZR) was introduced to Korea in 2017. A good prognosis is expected in patients who achieved sustained virologic response (SVR) after DAA treatment. However, information about the prognosis of Korean CHC patients who achieved SVR after EBR/GZR treatment is still limited. We aimed to investigate the prognosis of these patients.

Methods: This is a multicenter prospective observational study. The CHC patients achieved SVR after EBR/GZR treatment were enrolled and final follow-up date was June 2023. The primary end-point was hepatocellular carcinoma (HCC) occurrence. At last one time in a year, we checked about this end-point.

Results: Total 127 patients were included in this analysis and median follow-up duration was 34.3 months. Male was 60 patients (47.2%) and median age was 60 years. Genotypes were 1b (125, 98.4%), 2 (1, 0.8%), and 4 (1, 0.8%). Cirrhosis was 39 patients (30.7%) and significant alcohol intake prevalence was 14 (11.0%). Mean Child-Pugh score was 5.1 and HCC occurrence cases were 2 patients (1.6%) for up to 5 years. HCC patients all had cirrhosis prevalence (100% vs. 21.8%, $p=0.093$), higher APRI (2.5 vs. 0.4, $p=0.001$) and FIB-4 (10.1 vs. 2.1, $p=0.002$). Recurrence or reinfection case was not observed.

Conclusion: The prognosis of patients achieved SVR after EBR/GZR treatment was generally good. However, HCC risk was not completely removed especially in patients with high APRI or FIB-4 score. Therefore, regular follow-up surveillance is still warranted for advanced fibrosis cases

Abstract Submission No. 100629

P-0207

PLATELET LYMPHOCYTE RATIO (PLR) AS A PREDICTOR OF LIVER FIBROSIS IN HCV-HIV COINFECTION PATIENTS

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Background: HCV and HIV coinfection is associated with higher HCV RNA values compared to HCV monoinfection. HIV infection causing impairment of immune responses that impact HCV clearance. Platelet lymphocyte ratio (PLR) acts as a potential prognostic indicator in chronic diseases such as HCV and HIV, which is related to the disease progression and prognosis. This study aimed to determine the accuracy of PLR on liver fibrosis in HCV-HIV co-infected patients at Mohammad Mohammad Hoesin Hospital Palembang (RSMH).

Methods: This is an analytic observational study, on 38 HCV-HIV coinfecting patients at the Internal Medicine Clinic at RSMH from March 2022 to February 2023. Statistical analysis used diagnostic test with SPSS version 25.

Results: From the study, it was found that 78.9% ($n=31$) subjects were male, with homosexuality as the highest risk factor (39.5%). It was also found a total of 17 subjects (44.7%) had liver cirrhosis. The mean PLR value within the cirrhosis group was 169.8. The mean PLR value within the non-cirrhosis group was 190.8. PLR with a cut off value of 70 had a sensitivity of 29.4%, specificity of 80.9%, NPV of 58.6%, PPV of 55.5%, and accuracy of 57.8%.

Conclusion: PLR ratio with a value of less than 70 has the potential to predict the incidence of cirrhosis in HCV- HIV coinfecting patients at RSMH Palembang.

Keywords: Hepatitis C; HIV; PLR; HCV RNA

Abstract Submission No. 100633

P-0208

Questionary of Chronic Hepatitis C among Residents in Guangzhou in 2023

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Background: The level of awareness among residents regarding knowledge of chronic hepatitis C (CHC) has a significant impact on the management of this disease and the data is limited in China.

Methods: We organized community consultation and conducted face-to-face questionnaires to assess the general public's knowledge level of CHC. The data were also analyzed.

Results: From May to October 2023, 402 CHC questionnaires were collected from five ordinary communities, one leisure club, and one foot bath center in Guangzhou. The residents generally believed that hepatitis C can be transmitted through blood (70.65%), but only about one-third to one-half of the residents were aware of the high-risk behaviors, mother-to-child transmission, and sexual transmission of hepatitis C. Over 40% of the respondents were unable to identify the high-risk behaviors for hepatitis C infection, and approximately 20% of the residents mistakenly believed that hepatitis C can be transmitted through daily life activities. The average awareness rate of whether hepatitis C can cause severe outcome was only 56.22%. The awareness rate among individuals aged 18 to 30 was 66.94%, which was higher than other age groups ($P<0.05$). The awareness rate among individuals with a college education or above was 78.33%, which was higher than other educational levels ($P<0.05$). Over half of the participants unsure or believe that hepatitis C is incurable. (Table 1)

Conclusion: The awareness rate of CHC knowledge among the surveyed individuals was low, with insufficient or even incorrect understanding of the transmission routes, treatment, and prognosis of hepatitis C.

Abstract Submission No. 100686

P-0209

DAA improved treatment access and outcome in chronic hepatitis C patients undergoing hemodialysis

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INTRODUCTION: Treatment of Hepatitis C virus (HCV) is important to prevent nosocomial transmission and extrahepatic complications in chronic hepatitis C (CHC) patients undergoing hemodialysis (HD). The impact of treatment access to direct-acting antiviral (DAA) in CHC patients undergoing HD remained unclear in Singapore.

METHOD: We retrospectively reviewed all CHC patients undergoing HD in our hospital during the pre-DAA era (<2014), restricted DAA era (2014-2017) and unrestricted DAA era (2018-2022). Study outcomes include the rate of HCV treatment and SVR12.

RESULT: A total of 378 patients underwent HD during the pre-DAA (7.7%), restricted DAA (43.7%) and unrestricted DAA (48.6%) era. The overall seroprevalence and viremic prevalence was 10.9% and 7.5%, respectively. From pre-DAA to restricted DAA and post-DAA era, the introduction of DAA significantly increased the treatment rate (25% vs 70% vs 100%, $p=0.005$) and SVR12 (0% vs 85.7% vs 100%, $p=0.005$). Improving DAA access allowing more HD patients with advanced fibrosis (FIB4>3.25) to be treated (14.8% vs 37.0% vs 48.1%, $p=0.074$). The HCV viremic prevalence in patients undergoing dialysis had declined, but remained substantial (14.3% vs 6.3% vs 7.3%, $p=0.324$).

CONCLUSION: Improving DAA access had improved the treatment rate and SVR12 of CHC patients undergoing HD. Our findings suggest HCV screening and linkage to care remained relevant among patients undergoing HD.

Abstract Submission No. 100687

P-0210

DAA treatment did not reduce mortality in chronic hepatitis C patients undergoing hemodialysis

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INTRODUCTION: Current guidelines recommend urgent HCV treatment among patients undergoing HD. However, HD patients often had multiple comorbidities and reduced survival. We aim to determine if direct-acting antiviral (DAA) treatment improve the survival in HCV patients undergoing HD.

METHODS: We retrospectively reviewed all patients undergoing HD between 2012 to 2022 in our hospital. Cox-regression was used to estimate the predictors of the survival in HD patients, with or without DAA treatment.

RESULTS: 375 patients (mean age 64 years old, 64% male) underwent HD from 2012-2022. Metabolic comorbidities were common (T2DM in 15.7%, hypertension 86%, dyslipidemia 71.2%, IHD 54.9%, prior stroke in 14.7%).

The overall HCV seroprevalence and viraemic prevalence was 10.9% ($n=41$) and 7.5% ($n=28$), respectively. Three patients (1%) developed HCV after dialysis initiation. The commonest genotype was genotype 3 (51.9%), 39% already had liver cirrhosis upon initiation of dialysis.

Twenty (77.8%) received DAA treatment. Overall SVR was 90.0% (16/18), with no treatment-related complications reported.

Over a median follow-up of 54 months (IQR: 24-86), 37.9% had demise, 9.6% lost to follow-up. Hepatocellular carcinoma (HCC) developed in 0.8% (all having baseline liver cirrhosis). Overall mortality was not influenced by the HCV treatment, presence of liver cirrhosis, or HCC ($p>0.05$ for all); however, mortality increases with IHD (HR: 1.7, 95%: 1.7-2.5, $p=0.018$), prior stroke (HR: 1.9, 95%CI: 1.2-2.8, $p=0.003$), and older age (HR: 1.0, 95%CI: 1.0-1.1, $p<0.001$). The commonest cause of death was cardiovascular-related death (20.3%), only 2.1% demised from liver-related death.

CONCLUSION: HCV treatment with direct-acting antiviral is safe and efficacious, but did not reduce mortality in patients undergoing HD.

Abstract Submission No. 100719

P-0211

The efficacy of SOF/VEL in patients with chronic hepatitis C virus genotype 6 infection

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Background: The hepatitis C virus (HCV) genotype (GT) is mainly GT 1b and the proportion of GT 6 is small in the world. But GT 6 is relatively difficult to treat among all GTs. Our aim is to evaluate the efficacy of sofosbuvir/velpatasvir (SOF/VEL) in patients with chronic HCV GT 6 infection.

Methods: We retrospectively analyzed patients with chronic HCV GT 6 infection from July 2018 to May 2023. All patients received SOF/VEL for 12 weeks, and patients with liver cirrhosis were combined ribavirin. Routine blood, liver and renal functions, HCV RNA were monitored at baseline, 4, 8, 12 and 24 weeks.

Results: A total of 163 patients were enrolled. The mean age was 60.58 ± 12.70 y, 107 cases were male (65.64%), the median HCV RNA was 2.75×10^6 IU/ml, and the proportion of cirrhosis was 5%. At the end of treatment, the proportion of normalized ALT was 94.34% (150/159). RVR, ETVR, SVR12 was 96.93% (158/163), 100% (163/163) and 99.20% (122/123), respectively.

Conclusions: SOF/VEL achieved high virological response and ALT normalization rate in patients with chronic HCV GT 6 infection.

Abstract Submission No. 100764

P-0212

Real-World Data with Pangenotypic Direct-Acting Antivirals: Preliminary Results of the SVR10K Study

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Background: A previous real world data analysis demonstrated high effectiveness of sofosbuvir/velpatasvir (SOF/VEL) in > 6,000 HCV patients from 12 clinical cohorts across Australia, Canada, Europe & USA. Expanding this research initiative to include even more patients from additional geographical areas will allow to show SOF/VEL effectiveness across multiple diverse populations & the evaluation of HCV patient characteristics from Western countries, Asia, Middle Eastern and Latin-American regions.

Methods: This real-world analysis includes patients ≥ 18 years treated with SOF/VEL without RBV for 12 weeks, as decided by the treating HCP, from 7 sites across Hong Kong, Mexico, Sweden, Spain, Taiwan, and the United Arab Emirates. Age, sex, treatment experienced (TE), cirrhosis stage (no decompensated included), genotype, coinfections, time to treatment initiation (TTI) from HCV diagnosis, and SVR (4/12/24) were analyzed.

Results: Overall, 4,679 patients were included, 51% of them from Asian countries. Median age was 56.9 [IQR 46-66], where males 59%, and age > 50 years in 68%. Genotype 3 was present in 25%, F4 21%, TE 5%, while HIV, HBV and HDV coinfection was reported in 4.7%, 4.3%, and 0.1%, respectively. The TTI was available in 74%, with 17% having ≤30 days. In terms of effectiveness, SVR was achieved in 98.4% of the treated population, 99% for Asian countries.

Conclusions: Results on treatment effectiveness in these new geographies did not differ from real world studies of patients in the Western countries, reinforcing that HCV treatment guidelines are globally applicable, and supporting the efficacy of pDAA therapy.

Abstract Submission No. 100854
P-0213

Simplified Hepatitis C diagnosis on outpatient care for people living with HIV/AIDS

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Background: The simplification of current hepatitis C (HCV) diagnostic algorithms and service delivery is very crucial to achieving the WHO goal by 2030. To increase timely diagnosis and improve the linkage to care in people living with human immunodeficiency virus (PLWH), HCV reflex testing and a call-back strategy was implemented in an outpatient-clinic of a territorial hospital in Southwest China.

Methods: The pilot study was conducted in two phases. In Phase 1 (Jan 2022 ~ Oct 2022), the traditional approach to HCV diagnosis including at least 3 visits was adopted. In Phase 2 (Dec 2022 ~ Jul 2023), reflex testing for HCV RNA and genotype was implemented which only required one visit to confirm HCV diagnosis.

Results: In phase 1, totally 1689 PLWH were included during 10-month study period. With close follow-up by coordinating nurses, 93 anti-HCV positive patients came back for HCV RNA testing and the RNA diagnostic rate was only 71.5% (93/130). In phase 2, totally 4020 PLWH were included during 9-month period. The patients of Phase 2 with the “one-visit for diagnosis” strategy, the RNA diagnostic rate increased to 100% (465/465). Compared with the Phase 1, the mean time from screening to treatment initiation was shorter from 144 days (144.47±47.29) to 61 days (61.46±25.59), $p < 0.01$.

Conclusion: The application of the reflex testing significantly increased HCV diagnosis rate and efficiently improved the HCV care cascade efficiently in the HIV outpatient clinic. The simplified HCV diagnosis and treatment strategy could be scaled up for HIV services in China.

Abstract Submission No. 100928
P-0214

Follow-up of HCV reinfection in HCV with Methadone-Maintenance treatment: Four consecutive years

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Treatment of HCV infection in patient with Methadone Maintenance Treatment (MMT) is not easy. The reinfection rate in this group is also high and it's difficult in following reinfection rate. We share an experience of following-up of reinfection of HCV patient with MMT for four consecutive years.

Method: In 2020, we began to cooperate with the psychiatrist to incorporate anti-HCV core antigen with routine blood tests during regular outpatient follow-up of patient with MMT. We used anti-HCV core antigen as an indicator of reinfection and calculated the number of HCV reinfection.

Result: The number of participants in the first to fourth years were 94, 109, 141 and 141. New cases of HCV patient with MMT was decreased year by year, with 55 new cases in the second year, 37 new cases in the third year, and 31 new cases in the fourth year. The reinfection number in the first to fourth years were 5, 0, 4 and 1, and the reinfection person-year rate in the first to fourth years were 3.2/person-year, 2.0/person-year, 1.6/person-year and 1.1/person-year. The reinfection patient-year rate was decreased gradually.

Discussion: After 4 consecutive years of follow-up, we found that the reinfection person-years rate has decreased year by year, from 3.2/person-year to 1.1/person-year. The number of new cases of HCV patients with MMT has also decreased, which can prove that MMT patient with HCV infection can be eliminated by DDA treatment. The cooperation with psychiatrist for following HCV reinfection rate makes it easier and more effective.

Abstract Submission No. 101015
P-0215

Characteristics and factors of HIV/HCV in southwest China

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Objective: To analyze the characteristics of hepatitis C virus (HCV) infection in people living with hiv (PLWH), and to provide reference for the prevention and treatment of HCV in PLWH.

Methods: From January 2022 to July 2023, HIV /AIDS patients in Yunnan Infectious Disease Hospital were selected as the study subjects. A cross-sectional survey was conducted to collect demographic information, HCV antibody screening rate, HCV RNA screening rate, infection positive rate, infection route, biochemical indicators, liver fibrosis, treatment and other data. Differences in characteristics between

HIV mono-infected patients and HIV/HCV co-infected patients were analyzed.

Results: A total of 7413 PLWH outpatients were under treatment and management, and 5709 of them were screened. The HCV antibody test rate was 77.01% (5709/7413), and the HIV/HCV antibody positive rate was 10.42% (595/5709). The detection rate of HCV RNA was 86.72%(516/595). FIB-4 score > 3.25 was 37.93% (88/232). There were significant differences in age and transmission route between HIV mono-infected patients and HIV/HCV infected patients ($P < 0.001$).

Conclusions: The positive rate of HCV antibody was high in HIV infected people, and most of them were male, 40-49 years old and intravenous drug users. HIV co-infection was older and more likely to be infected through injection drug use. Patients with HIV/HCV co-infection have a higher proportion of progressive liver fibrosis and more severe liver fibrosis, and are more likely to develop liver cirrhosis. Therefore, early screening, early diagnosis and early treatment of hepatitis C in HIV/HCV co-infection population are recommended.

Abstract Submission No. 101098
P-0216

Barriers to Hepatitis C Treatment in South Korea: A Cascade of Care Analysis

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Background: The HCV care cascade plays a crucial role in improving treatment rates. This study aims to examine the cascade of care for chronic hepatitis C patients in South Korea and identify factors impeding treatment.

Methods: We conducted an analysis using data from the Korea Disease Control and Prevention Agency, which registered 8,810 patients with chronic hepatitis C in 2019. We collected and analyzed baseline characteristics, income levels, healthcare facility utilization, actual treatment status, comorbidities, and laboratory test results.

Results: The proportions of patients diagnosed at primary, secondary, and tertiary healthcare facilities were 26%, 53%, and 21%, respectively. Among all diagnosed patients, 41% did not receive actual treatment. Treatment rates were 11.5% at primary healthcare facilities and 47.3% and 59.4% at secondary and tertiary healthcare facilities, respectively, for patients diagnosed at these respective levels. Among patients diagnosed at primary healthcare facilities, 60% were referred to higher-level facilities, and 80% of those referred received treatment. Treatment rates did not significantly differ by region, but the lowest income group (below 25%) exhibited lower treatment rates. However, income level did not show a proportional relationship with treatment rates. Treatment rates were also lower for elderly patients, those with underlying comorbidity, and patients with liver cirrhosis.

Conclusion: Treatment uptake for chronic hepatitis C in South Korea falls below optimal levels, posing a challenge to achieving the goal of HCV elimination. Efforts are needed to address barriers that reduce treatment rates and improve the cascade of care for HCV patients.

Abstract Submission No. 101105
P-0217

Morbidity and mortality after direct-acting antivirals in patients with chronic hepatitis C

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Background: Treatment of hepatitis C with direct-acting antivirals (DAAs) results in permanent viral clearance (SVR) in the vast majority of patients with chronic hepatitis C (CHC). The aim of this study was to assess long-term liver-related outcomes and mortality after DAA treatment.

Methods: This multicenter, retrospective cohort study consisted of 3,128 consecutive adult CHC patients without decompensated cirrhosis who were treated with all-oral DAAs. After excluding patients who did not achieve SVR, 3,024 were included in this study (2,691 non-HCC experienced, 333 HCC experienced). Primary endpoints were the occurrence or recurrence of hepatocellular carcinoma (HCC), mortality, and the cause of death.

Results: The median follow-up durations were 6.6 and 6.3 years for the non-HCC and HCC experienced groups, respectively. Although the cumulative de novo HCC incidence rates were longitudinally increased (3-year, 4.0%; 5-year, 5.6%; 8-year, 7.0%), those of the recurrence rates reached a plateau in 3-5 years (3-year, 50.4%; 5-year, 59.1%; 8-year, 62.0%). None of the patients aged under 50 ($n=377$) developed de novo HCC. Even in patients without cirrhosis, the 8-year cumulative de novo HCC incidence increased with age (age 50-59, 1.8%; age $\geq$ 60, 5.5%; age $\geq$ 75, 8.7%) (log-rank test: $P<0.001$). The 3-year, 5-year, and 8-year survival rates for patients with HCC were 85.2%, 74.6%, and 67.4%, respectively. 74% of the deaths were caused by liver-related complications. For patients in the non-HCC group, 72% of the deaths were caused by non-liver-related complications.

Conclusion: DAA treatment improves liver-related morbidity and survival. Patients aged over 60 should be considered for long-term HCC surveillance.

Abstract Submission No. 101129
P-0218

Elimination of Hepatitis C Virus in a Hemodialysis Unit in Cipto Mangunkusumo Hospital

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Hepatitis C in hemodialysis patients remains a global health problem, and the biggest risk factor is caused by nosocomial transmission. In the era DAA eliminating HCV in hemodialysis unit become more feasible. In HD unit at Cipto Mangunkusumo hospital we perform program for eradication of HCV. DAA treatment in special population as in HD unit is important to achieve WHO goal for hepatitis C elimination by 2030, assuming a 90% reduction in new cases of chronic hepatitis C and a 65% reduction in hepatitis C deaths. The research aims to achieve a therapeutic sustained virological response (SVR) for all patients. The study design was a prospective cohort. The outcome studied was SVR12. We treat with two types of DAA within two periods of time. In period 1, 45 patients treated with grazoprevir/elbasvir. While in period 2, there were 9 patients treated with grazoprevir/elbasvir and 2 patients with sofosbuvir/daclatasvir, due to relaps and no respon with previous treatment. A total confirmed of 56 HCV patients were enrolled. The DAA treatment initiation rate and completion rate were

100%. All patients in period 1 were treatment naïve, while in period 2 there were 9 patients treatment naïve and 2 patients re-treatment. SVR 12 in period 1 achieved in 43 out of 45 (96%). While, in period 2 SVR12 rate 11 out of 11 (100%). The elimination of HCV infection in our HD patients was successful. The most important strategy is to detect patient with a valid method, then treat and re-treat them at the same time.

Abstract Submission No. 101178

P-0219

Nomogram for Hepatocellular Carcinoma Risk Prediction in Chronic Hepatitis C Patients

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Aim: To detect risk factors to predict the risk of developing hepatocellular cancer (HCC) among hepatitis C virus (HCV) patients after antiviral treatments and to develop nomograms to indicate the development of HCC.

Methods: 618 patients with chronic HCV infection treated with interferon (IFN)-based and direct-acting antiviral agents (DAA) were included in the study. Cox's multivariable model was used to predict HCC, followed by a nomogram to assess individualized risk

Results: The average age of Chronic HCV patients at diagnosis was 53.5 ± 15.1 years. The average follow-up period of the patients was 107.6 ± 48.3 months. During follow-up, 32 patients developed HCC (median duration 51 months). Three variables were independently associated with HCC formation: ferritin level (above 24.7750 ng/ml), platelet (PLT) count (below 143,500/ml), and aspartate aminotransferase (AST) value (above 43.5 IU/L). to be.

Conclusion: These nomograms may be a visualization risk model that can provide personalized prediction of long-term outcomes for HCV-associated HCC patients.

Abstract Submission No. 101183

P-0220

Glecaprevir/Pibrentasvir improves fibrosis after SVR and during long-term follow-up.

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Background and Aim: Chronic hepatitis C (CHC) has been a significant contributor to advanced liver diseases, such as liver cirrhosis and hepatocellular carcinoma (HCC). The advent of direct-acting antiviral agents (DAAs), particularly pangenotypic DAAs like glecaprevir/pibrentasvir and sofosbuvir/velpatasvir, has revolutionized CHC treatment. Fibrosis plays a crucial role in disease progression post sustained virologic response (SVR). This study focuses on analyzing fibrosis improvement after SVR in patients treated with glecaprevir/pibrentasvir. **Method:** This single-center retrospective cohort study reviewed patients undergoing glecaprevir/pibrentasvir treatment. SVR evaluation was conducted 12 weeks post-treatment by checking HCV RNA. Fibrosis assessment occurred through fibroscan before treatment, at the SVR time point, and annually thereafter.

Results: Out of 264 patients treated with glecaprevir/pibrentasvir, with an average age of 59.2 years and a female dominance of 79.8%, 31.1%, 66.7%, 1.5%, and 0.8% had genotypes 1, 2, 3, and 6, respectively.

Sixty-one patients had liver cirrhosis, and 237 were treatment-naïve. A remarkable 98.5% of patients achieved SVR, with only 5 patients diagnosed with HCC during the follow-up period. Liver stiffness decreased from 6.3 kPa to 5.6 kPa at SVR ($p = 0.0004$). After a long-term follow-up of at least 1 year, liver stiffness further decreased from 7.1 kPa to 5.0 kPa ($p < 0.0001$).

Conclusion: Glecaprevir/pibrentasvir not only proved effective in treating CHC but also demonstrated significant improvement in liver fibrosis over the long term.

Abstract Submission No. 101254

P-0221

Risk factor for hepatoma in chronic kidney disease patients with HCV infection after DAA treatment

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Background: Hepatitis C virus (HCV)-infected individuals treated with direct-acting antivirals (DAAs) are at risk for hepatocellular carcinoma (HCC) after achieving sustained virological response (SVR). This study explored the risk factors for HCC in chronic kidney disease (CKD) patients with HCV infection receiving DAA therapy.

Methods: From March 2014 to December 2021, 738 patients with HCV-positive CKD who were regularly followed up at Kaohsiung Chang Gung Memorial Hospital for DAA treatment were included in the study.

Results: 738 patients with anti-HCV positive CKD patients were included in this study. Of these 738 patients, 542 patients who had achieved SVR without HCC before DAA treatment were analyzed. Univariate analysis showed that age (≥ 70.5 years), AFP (≥ 20 ng/ml) and cirrhosis were risk factors for the development of hepatocellular carcinoma. Multivariate analysis showed that cirrhosis only (HR: 4.34, 95%CI: 1.42-13.27, $p=0.01$) was an independent risk factor for the development of HCC.

Conclusion: In HCV-infected patients with CKD, cirrhosis was an independent risk factor for new HCC after DAA treatment.

Abstract Submission No. 101300

P-0222

Investigation and analysis of hepatitis C virus infection for hemophiliacs in Mainland China

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Background and Aims: To investigate the prevalence of hepatitis C virus (HCV) infection in a neglected hemophiliacs cohort in Mainland China.

Method: Hemophilia patients in ten regional and local hemophilia centers were recruited to conduct an online questionnaire-based survey to preliminarily identify those with suspicious signs and symptoms from HCV infection. After that, HCV IgG antibody kits were disseminated for self-detection in these high-risks. HCV RNA detection, liver function evaluation and HCV genotyping were conducted based on the HCV-antibody screening results. The classification, age and geographical characteristics of hemophilia were analyzed.

Results: The positive rate of anti-HCV was 5.92% (61/1030) in a total 1030 hemophilia patients, with breakdown of 5.93% (50/843) and 6.40% (11/172) in hemophilia A and B, respectively (statistically significant difference, $P < 0.001$). The anti-HCV positivity rate in hemophilia patients born before 1993 (year from when blood products were mandated for HCV screening) was significantly higher than that from patients born after 1993 (13.50% (54/400) vs. 1.11% (7/630), $p < 0.001$). Variance in HCV-antibody results from geographic distribution was not identified ($P = 0.5119$). Further diagnosis using HCVRNA quantification confirmed 24.59% (15/61) was current HCV infection, with a median HCVRNA at 1.06×10^6 IU/ml. Subgroup analysis revealed HCVRNA positivity in hemophilia A was 22.00% (11/50), while in hemophilia B was relatively higher 36.36% (4/11), with statistical significance ($P = 0.0442$). HCVRNA was negative in all seven hemophiliacs born after 1993 while conversely 27.78% (15/54) in whom were born before 1993 ($p < 0.05$).

Conclusion: Confirmed HCV infection rate in hemophilia population demonstrated an unsurprisingly higher prevalence than that from general population with in Hemophilia B higher than in hemophilia A. Year of born before or after 1993 in hemophiliac patients might be potential risk factor in our cohort and there is no geographic distribution bias. The lower percentage of HCV RNA (+) from those HCV antibody(+) may warrant further investigation before optimal HCV screening strategy in hemophiliacs could be shaped.

Abstract Submission No. 101313

P-0223

Short term observation of fibrosis in patients who had HCV eradication therapy using non-brand DAAs

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Background: Chronic hepatitis C can cause both liver cirrhosis and HCC. Fibrosis stage was assessed before and after HCV eradication.

Methods: A comparative study of changes in the degree of liver fibrosis measured before and after non-brand DAA treatment in patients with chronic HCV. Of 251 patients who received antiviral C therapy, 230 patients met our study criteria. 123 patients 24 patients took Ledvir and 107 patients took Hepcinat DAAs respectively.

Results: Fibrotouch (Elastography) was used in patients treated with Ledvir DAAs. 100% reduction in stiffness was observed, with 43 patients (34.9%) had a reduction within grade F4, 21 patients (17%) had a reduction from F4 to F3, and 19 patients (15.4%) had a reduction from F4 to F2. 18 patients or 14.6% were downgraded from F4 to F1, 6 patients were downgraded from F3 to F2 or 4.8%, and 14 patients were downgraded from F3 to F2 or 11.8%.

100% reduction in fibrosis was observed in patients who received Hepcinat DAA. Fibrosis was reduced in 32 patients or 29.9% within the F4 stage, 21 (19.6%) patients were reduced from F4 to F3 grade or, 25 patients or 23.3% were reduced from F4 to F2 stage. There were 29 patients or 27.1% who were reduced from F4 to F1.

Conclusion: When combined 75 patients or 35.7% were reduced within the F4 stage, 42 (20%) patients were reduced from F4 to F3; 44 patients or 20.9% patients from F4 to F2, and 47 (22.3%) patients were downgraded from F4 to F1.

Abstract Submission No. 101360

P-0224

The Role of NLR and HCV RNA in HIV-HCV Coinfection after DAA therapy

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Background: Hepatitis C is an inflammatory disease of the liver caused by Hepatitis C Virus (HCV) infection. Neutrophil Lymphocyte Ratio (NLR) is one of significant inflammatory markers. The amount of HCV RNA *Viral Load* which combines neutrophils is an active inflammatory component and lymphocytes as a regulatory and protective component in one parameter. Research on the relationship between NLR and HCV RNA in patients with HIV HCV co-infection is still limited. This study aims to determine the relationship between NLR and HCV RNA in HCV co-infected HIV patients who received DAA therapy at Mohammad Hoesin Hospital Palembang.

Methods: This study was an analytical observational study with a Cohort design with 38 subjects of HCV co-infected HIV patients who sought treatment at the outpatient clinic at Mohammad Hoesin Hospital Palembang in March 2022 – February 2023. Data were obtained through recording from medical records. Data were categorical and tested by Spearman correlation method using SPSS version 25.0 for windows application.

Results: The mean NLR of HCV co-infected HIV patients before receiving DAA therapy at RSMH Palembang was 1.97 and the high HCV RNA *Viral Load* was 4.31×10^5 /mm³. The correlation test results showed a p value = 0.000 with an r value = 0.709 for the correlation between NLR and HCV RNA values in patients who had not started DAA therapy p value = <0.005 with an r value = 0.603 for the correlation between NLR and HCV RNA values in patients who had received 12 weeks of DAA therapy.

Conclusion: This study shows there is a significant strong correlation between NLR and HCV RNA values in HCV co-infected HIV patients before and after receiving DAA therapy at Mohammad Hoesin Hospital Palembang.

Abstract Submission No. 101479

P-0225

The Incidence and Care Cascade of the Hepatitis C Virus in Korea

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Background/Aims: The 2030 hepatitis C virus (HCV) elimination targets of the World Health Organization are an 80% reduction in incidence and 65% reduction in mortality compared to the 2015 rates. However, information on the nationwide incidence and treatment rates of HCV infection are limited. We aimed to investigate the nationwide incidence and status of the care cascade for HCV infection in Korea.

Methods: This study used data from the Korea Disease Control and Prevention Agency linked with the data of the Korea National Health Insurance Service. Linkage to care was defined as visiting hospitals twice or more due to HCV infection within 1.5 years of the index date.

The treatment rate was the number who had been prescribed antiviral medication within 1.5 years from the index date out of patients newly diagnosed with HCV.

Results: The new HCV infection rate was 17.2 per 100,000 person-years ($n=8,810$) in 2019. The number of new HCV infections was the highest in patients aged 50 to 59 years ($n=2,480$), and the new HCV infection rate significantly increased with age ($p<0.001$). Among newly infected patients with HCV, the linkage to care rate was 78.2% (78.2% men, 78.2% women) and the treatment rate was 58.1% (56.8% men, 59.3% women) within 1.5 years.

Conclusions: The new HCV infection rate was 17.2 per 100,000 person-years in Korea. It is necessary to continuously monitor the incidence and care cascade of HCV to establish proper strategies to reach the goal of HCV elimination by 2030.

Abstract Submission No. 101575

P-0226

Risk factors for developing hepatocellular carcinoma after eradication of hepatitis C virus

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Background: Although almost patients with hepatitis C virus (HCV) can achieve a sustained virologic response (SVR) with direct-acting antiviral agents (DAA), a few patients develop hepatocellular carcinoma (HCC) after SVR.

Methods: In 1609 patients who achieved SVR after administration of DAA for HCV, without a history of HCC, hypovascular tumors, and HBV co-infection, we investigated the risk of developing HCC after DAA-SVR each aMAP risk score.

Results: HCC developed in 111 patients during an average observation period of 57.2 months. The 5-year cumulative HCC development rate was 7.1% in all patients, and 11.2%, 2.9%, and 0%, for high-risk (>60), medium-risk (50-60), and low-risk (<50) group, respectively ($p<0.001$). In medium and high-risk groups, Cox proportional hazard analysis showed male, liver cirrhosis, aMAP score >64 , and albumin at the end of treatment (EOT-Alb) <3.8 g/dL and alpha fetoprotein at EOT (EOT-AFP) <5.2 ng/mL were associated with the development of HCC. In the high-risk group, when the sum of these factors was 0-1, 2-3, and 4-5, the 5-year cumulative HCC incidence was 2.2%, 7.0%, and 31.4%, respectively ($p<0.001$). On the other hand, in the medium-risk group, only EOT-Alb and EOT-AFP were extracted, and the 5-year cumulative HCC development rates for 0, 1, and 2 factors were 1.5%, 6.4%, and 20.0%, respectively ($p<0.001$).

Conclusions: During approximately 5 years of follow-up, there were no HCC development in the aMAP low-risk group. In the medium and high-risk groups, further stratification of HCC risk was possible by combining aMAP score, EOT-Alb, and EOT-AFP.

Abstract Submission No. 101605

P-0227

The efficacy and safety of 12W treatment with SOF/VEL in patients with chronic HCV/HIV coinfection.

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Background: There are multiple complications and DDI in patients with chronic HCV/HIV coinfection. Our study aimed to access the efficacy of sofosbuvir/velpatasvir and DDI during the treatment in these patients.

Methods: We retrospectively analyzed patients with chronic HCV/HIV coinfection receiving sofosbuvir/velpatasvir 12 weeks treatment from 2017 to 2019 in Lixin County People's Hospital. Blood routine, liver and renal function, HCV RNA and CD4 were detected at baseline, 12W and 24W. DDI in different drugs was also observed.

Results: A total of 95 patients were included. At baseline, 92 patients (97%) had history of selling blood. The mean age was 57 years, HCV RNA was 1.02×10^7 IU/ml, ALT was 63 U/L and CD4 was 488/uL. 48 patients (51%) were male. 16 (17%) GT1b, 7 (7%) GT2a, 72(76%) undetected genotype. 19 (20%) with cirrhosis. The count of combined with gastritis, hypertension, cardiovascular and vascular disease, other diseases were 16 (17%), 26 (27%), 27 (28%), 18 (19%). All treated Patients achieved SVR12 99% (94/95). 27 patients (28%) took antacids, PPI or EFV, which reduced the concentration of sofosbuvir/velpatasvir, but did not affect the SVR12. 79 patients(82%) took TDF-based regimens, which increased tenofovir exposure and renal function need to be detected during the treatment. Before and after treatment, Cr 62umol/L and 64umol/L remained stable. BUN 5.5mmol/L and 6.2mmol/L were within the normal range. There were no discontinuations or deaths due to the effects of DDI in all treated patients.

Conclusions: Sofosbuvir/vepatasvir provide high rates of SVR and well tolerated in Chronic HCV/HIV coinfection patients.

Abstract Submission No. 101645

P-0228

The prognostic value of soluble biomarkers in hepatitis B-related hepatocellular carcinoma patients

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Background & Aims: Soluble (s) immune checkpoints (ICs) are functional parts of membrane ICs. Clinical studies have evaluated their prognostic values in cancers. However, few studies were conducted in patients with hepatitis B-related hepatocellular carcinoma (HBV-HCC). We aimed to clarify the prognostic value of sICs in HBV-HCC and develop a random survival forest (RSF) model to predict the overall survival (OS).

Patients and methods: We profiled the plasma levels of 14 sICs in healthy controls (HC) ($n=20$), chronic hepatitis B (CHB) group ($n=20$), chronic hepatitis B cirrhosis (HBV-LC) group ($n=20$), and HBV-HCC group ($n=196$) using a multiplex Luminex Immunoassay. Flow cytometry was performed from HBV-HCC group ($n=80$). HBV-HCC group ($n=196$) were divided into training and validation sets. We also evaluated the predictive efficacy and analyzed the correlations of sICs with clinical parameters and membrane ICs.

Results: sICs level in HBV-HCC were elevated compared with HC. The areas under the receiver operating characteristic values of 1-, 2- and 3-year survival predicted by the RSF model were 0.96, 0.85, and 0.82 in training set and were 0.91, 0.79, and 0.71 in validation set. The model can adapt to different distributions of events and clinical staging systems. Soluble TIM-3 has the strongest correlation with clinical indicators, reflecting the severity of hepatocyte injury, persistent inflammation and immunosuppression.

Conclusion: RSF model can predict the OS of HBV-HCC patients. sTIM-3 is of interest in reflecting clinicopathologic and immunologic features in HBV-HCC.

Keywords: HBV-HCC; soluble immune checkpoints; RSF model; OS.

Abstract Submission No. 101656
P-0229

DAA treated HCV patients over 75 yr have a similar prognosis with non-HCV individuals.

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Aim: To clarify the significance of treatment for elderly HCV cases

Methods: The subjects were 218 HCV cases aged 75 years or older (DAA group) and 519 HCV antibody-negative and HBs antigen-negative cases (health checkup group) who had physical checkups in our institute since January 2015. The background of each group was 80.5 (75-96) / 75 (75-89) years of age, 84 (38.5%) / 319 (61.5%) male, 147×10³ /μl (19-341) / 214×10³ /μl (47 -341) platelets, ALT 24 IU/l (6-120) / 19 IU/l (4- 118), Fib4 index 3.52 (0.81-38.38) /1.92 (0.50-11.67), 27 (12.4%) / 0 with previous liver cancer.

Results: The cumulative survival rate of DAA overall was 92.2%/85.2 % at 3/5 years, 97.0%/94.6% in the group without liver cancer and 60.0%/24.1 % in the group with pre-existing liver cancer, with significantly worse prognoses in the group with pre-existing liver cancer (P<0.001). The health checkup group was 97.7%/95.4%, with a predominantly poor prognosis for DAA overall (P<0.001), but no significant difference was found between the group with no liver cancer and the group with liver cancer (P=0.280). A gender-matched propensity score analysis showed similar results (P=0.191).

Conclusion: DAA treatment of HCV in patients over 75 years of age with no history of liver cancer eliminates HCV and offers a prognosis equivalent to that of HCV-negative cases undergoing health checkups.

Abstract Submission No. 101671
P-0230

Interim results of an automated electronic alert system for the micro-elimination of hepatitis C

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Background: This study aimed to evaluate the effectiveness of integrating an automated electronic medical record (EMR)-based alert system for the micro-elimination of the hepatitis C virus (HCV) in a tertiary referral center.

Methods: The analysis included 2,234 patients who tested positive for HCV antibodies between 2009 and 2022. Starting from June 2021, an EMR-based alert system was implemented.

Results: Out of the 172,241 patients who underwent anti-HCV testing, 2,234 patients (1.3%) tested positive for anti-HCV. After excluding patients previously diagnosed with HCV and those with a follow-up duration of less than 2 days, 2,033 patients were included in the analysis. Before the introduction of the automated EMR-based alert system, 60.7%(1077/1773) of the patients underwent HCV RNA testing

following the initial positive anti-HCV result. Among them, 48.1% (518/1077) were confirmed to have HCV infection. Notably, 3.1%(20/638) of patients who did not undergo the HCV RNA confirmatory test within our hospital were diagnosed with HCV elsewhere. Among 198 patients who had not undergone HCV RNA test before EMR-based alert system and had been followed up after alert system, 31.3%(62/198) were tested following the alert notification, resulting in confirmation of 12 new HCV infections. After incorporating an EMR-based alert system, 66.9%(174/260) of anti-HCV-positive patients were ordered an HCV RNA test, with 27.6%(48/174) confirmed cases.

Conclusions: The integration of an EMR-based alert system for HCV microelimination improved RNA testing rates in new anti-HCV positive patients and diagnosis of previously missed HCV infection in a hospital-based setting.

Abstract Submission No. 101855
P-0231

Clinical manifestations of Cryoglobulinemia in chronic hepatitis C patients

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Introduction: Hepatitis C virus (HCV) infection is the most common cause of liver transplantation worldwide. Hepatic steatosis is another major liver manifestation which is associated with metabolic factors. Cryoglobulinemia is one of the important extrahepatic manifestations in chronic hepatitis C (CHC) patients.

Aims: To study the clinical association between cryoglobulinemia and steatosis of liver in CHC patients,

Patients and Methods: We enrolled 904 patients with CHC in a tertiary Medical Center in Southern Taiwan. The clinical and laboratory data were collected. The cryoglobulinemia were tested and the liver steatosis was determined by the fibroscan CAP values.

Results: There are 390 (43.1) males with a mean age of 60.9±12.1 years. The positive cryoglobulinemia was found in 367 (40.6%) patients. Compared to patients without cryoglobulinemia, patients with cryoglobulinemia were significantly older (P=0.028), had significantly higher percentages of male gender (P=0.001), cirrhosis (P=0.013), lower levels of CAP (P=0.047), HbA1C (P=0.001), platelet (P=0.005), TG (P<0.001), and higher levels of kPa (P=0.005) and HDL-C (P=0.02) in multivariate analyses. In multivariate analyses, gender, cirrhosis (all P<0.005), HCV RNA level, and HbA1c, TG level (both P<0.001) were factors significantly associated with cryoglobulinemia.

Conclusions: Cryoglobulinemia and steatosis were found in 40 % and 41% of CHC patients, respectively. Cryoglobulinemia was associated with gender, cirrhosis, HCV RNA level and metabolic factors but not liver steatosis.

Abstract Submission No. 101862
P-0232

Antaitasvir plus Yiqibuvir for treatment of chronic hepatitis C virus infection: a phase 2/3 study

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BACKGROUND: This phase 2/3 study is to evaluate the efficacy and safety of antaitasvir (NS5A inhibitor) plus yiqibuvir (NS5B polymerase inhibitor) in Chinese subjects with HCV genotype 1, 2, 3, or 6 including previously treated with interferon or untreated subjects, and those with compensated cirrhosis or without cirrhosis.

METHODS: In phase 2, approximately 120 subjects received 100 mg or 200 mg antaitasvir plus 600 mg yiqibuvir once daily for 12 weeks. In phase 3, approximately 400 subjects were enrolled in a 3:1 ratio to receive 100 mg antaitasvir/600 mg yiqibuvir or placebo for 12 weeks. Subjects in placebo group switched to receive antaitasvir/yiqibuvir for 12 weeks as the extended treatment. The primary endpoint was sustained virologic response 12 weeks after the end of treatment (SVR12).

RESULTS: A total of 442 subjects received at least one dose of 100 mg antaitasvir plus 600 mg yiqibuvir, and 420 (95.0% [95% CI: 92.6%-96.9%]) subjects achieved SVR12. The SVR12 of subjects with HCV genotype 1, 2, 3, or 6 were 99.1% (212/214), 99.1% (105/106), 77.8% (49/63) and 91.5% (54/59) respectively. The majority of TEAEs were mild to moderate in intensity. No patient prematurely discontinued the study treatment due to TEAEs, and no death was reported. None of serious AE was judged to be related to the study treatment.

CONCLUSIONS: Treatment with the pan-genotypic regimen of antaitasvir plus yiqibuvir for 12 weeks was highly effective and safe in subjects infected with HCV.

Abstract Submission No. 101949

P-0233

Factors associated with non-response to antiviral therapy in hepatitis C in Kazakhstan.

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From 2011 in Kazakhstan, antiviral therapy for CHC has been reimbursed, with nearly 99% of patients with SVR. The aim of the study is to identify the risk factors associated with the absence of a virological response to standard therapy with direct-acting antiviral agents from 2017 in the Republic of Kazakhstan.

This multicenter retrospective case-control study, spanning 14 regions in Kazakhstan, focused on CHC patients over 18 years old. The study included those who hadn't undergone prior antiviral therapy or hadn't achieved virological response (VR) after treatment with DAAs since 2018.

Examining 812 patients, the study categorized them into case (absence of VR to DAAs) and control (achieved sustained virological response, SVR) groups. Most patients were men aged 40 and above, with a significant number being men (62.32%) and Asians (66.13%).

Analyzing risk factors, the study identified various associations with the absence of VR, including stomach ulcers ($p=0.0266$), HIV ($p=0.0279$), overweight/obesity ($p=0.0045$), arterial hypertension ($p=0.0057$), chronic kidney disease ($p=0.0169$), hepatocellular carcinoma ($p=0.0327$), alcohol abuse ($p=0.0003$), prior antiviral therapy with Peg interferon/Ribavirin ($p=0.0005$), genotype 3 of hepatitis C virus ($p<0.0001$), stage 4 fibrosis ($p<0.0001$), prescribed antiviral therapy regimen ($p<0.0001$), duration of CHC before AVT ($p=0.0057$), known AVT duration ($p<0.0001$), and patient adherence ($p<0.0001$).

The study concludes by emphasizing the intricate interplay of demographic, clinical, virologic, host, and pharmacological factors in CHC patients' response to antiviral therapy.

Abstract Submission No. 101953

P-0234

Change of alfa-fetoprotein after DAA therapy in HCV patients and risk of hepatocellular carcinoma

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A retrospective study of the change of serum alfa-fetoprotein before and after treatment by Sofosbuvir-based regimens in patients without hepatocellular carcinoma was conducted. The cases of newly diagnosed hepatocellular carcinoma were evaluated. 483 patients received antiviral therapy and followed after 12 weeks after therapy. The mean age was 59.6 years old, and the female patients were predominant (52.4%). The medications were Sofosbuvir/Velpatasvir (62.1%), Sofosbuvir/Ledipasvir (28.2%), Sofosbuvir (8.9%), Sofosbuvir and Daclatasvir (0.8%), added ribavirin (15.3%). The duration was 12 weeks. There were patients with interferon-experienced (10.6%), liver cirrhosis (26.5%), diabetes (18.6%), uremia (1%), and HBV carrier (5.8%). The rate of SVR was 98.6%. After a mean follow-up of 33.7 months, 21 patients (4.3%) developed hepatocellular carcinoma. The pre-treatment serum alfa-fetoprotein was $>7\text{ng/ml}$ in 123 patients (25.4%), $>10\text{ng/ml}$ in 91 patients (18.8%), or $>15\text{ng/ml}$ in 47 patients (9.7%). After therapy, the level decreased to $<7\text{ng/ml}$ in 105 patients (86.1%). The risk of HCC development was 0% in pretreatment AFP >7 to posttreatment <7 ; 13.3% in AFP persistent in pre- and posttreatment >7 , but decreasing ($P<0.01$); 100% in AFP persistent in pre- and posttreatment >7 , and increasing ($P<0.01$); 15.4% in pretreatment AFP <7 , increasing to posttreatment >7 ($P<0.01$); 3.9% in AFP persistent <7 in pre- and posttreatment ($P=0.04$). The patients with persistent elevation of AFP before and after treatment had a higher risk of HCC development. The risk was lowest in patients with pre-treatment high AFP, then reduced to the normal range.

Abstract Submission No. 101989

P-0235

8-week glecaprevir/pibrentasvir for challenging hepatitis C patients with PHT or active HCC

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Background: The efficacy of 8-week glecaprevir/pibrentasvir (G/P) therapy in treating treatment-naïve chronic hepatitis C patients with compensated cirrhosis is already established. This study aims to evaluate the effectiveness and safety of the 8-week G/P treatment in patients with more advanced liver diseases, including active hepatocellular carcinoma (HCC) and portal hypertension (PHT).

Methods: The data of patients who received an 8-week course of G/P therapy at a single institute between August 2018 and May 2023 were retrospectively reviewed. Patients diagnosed with PHT or those with active HCC not in complete remission during their G/P treatment were selected for the analysis. Criteria for PHT were one or more of the following: presence of gastroesophageal varices, liver stiffness measurements (LSM) exceeding 20 kPa via transient elastography, or LSM of 15–20 kPa coupled with a platelet count under 110 K/ μ L. We assessed the sustained virological response (SVR12) at 12 weeks post-therapy as the primary endpoint, alongside safety profile evaluations.

Results: A total of 42 patients were enrolled, with a median age of 75.8 years; of these, 28 had PHT and 20 had active HCC. All patients (100%) achieved SVR12. During treatment, seven patients (16.7%) required hospitalization due to adverse events unrelated to G/P therapy. Four patients (9.5%) temporarily developed Grade 3 hyperbilirubinemia, with two cases linked to HCC radiotherapy. None had premature treatment termination, hepatic decompensation, or death.

Conclusion: The 8-week G/P regimen is highly effective and safe for challenging chronic hepatitis C patients, including elderly patients with PHT or active HCC.

Abstract Submission No. 200053

P-0236

HCV genotype and clinical features with 595 HIV/HCV co-infected patients

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Objective: To analyze the HCV genotyping and clinical characterization of 595 cases of HIV/HCV co-infected patients in antiretroviral outpatient clinic of Yunnan Provincial Infectious Disease Hospital, and to provide reference for the prevention and treatment of HIV/HCV.

Methods: The HIV/AIDS patients attending the clinic from January 2022 to July 2023 were selected for the study, and a cross-sectional survey was used to collect basic information, HCV antibodies, HCV RNA, HCV genotype and biochemistry.

Results: Screening 5709 patients with HIV infection, HCV antibody positive rate of 10.42% (595/5709); HCV RNA detection rate of 86.72% (516/595), HCV RNA positive rate of 47.09% (243/516). 95.47% of HCV RNA positive completed HCV genetic testing, of which the proportion of each type is: type 1b (14.66%), type 2a (0.86%), type 3a (27.59%), type 3b (40.95%), type 6 (14.66%), and unidentified type (1.29%). The rate of FIB-4 score > 3.25 was 37.86% among HCV RNA-positive patients. The difference in HCV genotypes in the route of infection was statistically significant ($P < 0.05$), and the FIB-4 indexes of the genotypes 3a, 3b were higher than those of the other genotypes, and the difference in the comparison of the two genotypes were all statistically significance (all $P < 0.01$).

Conclusion: HCV antibody and HCV RNA positivity rates are high in HIV-infected populations, and HCV genotypes 3b and 3a are the main prevalent strains, with a high percentage of progressive liver fibrosis

occurring. In the population of people with HIV and HCV, early hepatitis C screening, diagnosis, and treatment are crucial.

Abstract Submission No. 200099

P-0237

Post-treatment occurrence of serum cryoglobulinemia in chronic hepatitis C patients

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Background: Persistent cryoglobulinemia after completion of antiviral treatment is an important consideration of clinical management in chronic hepatitis C patients. We aimed to investigate the occurrence of serum cryoglobulinemia in chronic hepatitis C patients without cryoglobulinemia at the initiation of antiviral treatment.

Methods: Totally 776 patients without cryoglobulinemia were assessed for serum cryoglobulinemia after completion of anti-HCV treatment. Serum cryoglobulinemia precipitation was assessed both initiation and completion of the treatment and analyzed for the clinical, laboratory factors associated with chronic hepatitis C.

Results: One hundred eighteen percent (118) of patients were checked for serum cryo-precipitation after completion of the treatment and 8 patients (4.6%) were positive for serum cryoglobulinemia. In multivariate analysis, liver cirrhosis (Odds Ratio [OR]–17.86, 95% Confidence Interval [95% CI]–1.79–177.35, $p = 0.014$) and other organ cancer (OR–25.17 95% CI–2.59–244.23, $p = 0.005$) were independently and significantly associated with positive cryoglobulinemia 3 months after antiviral treatment.

Conclusions: Three months after the antiviral DAA therapy had concluded, eight patients checked positive for cryoglobulinemia, representing a 6.7% prevalence. Further investigation into the causes of positive cryoglobulinemia after DAA antiviral therapy is warranted.

Abstract Submission No. 200185

P-0238

Efficacy of Sofosbuvir, Velpatasvir and Ribavirin in prior DAA experienced patients in Myanmar

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Background: Treatment options for DAA experienced hepatitis C patients are limited in Myanmar as Sofosbuvir, Velpatasvir, Voxilaprevir regimen and Glecaprevir and Pibrentasvir regimens are not available. This study is aimed to evaluate the efficacy of Sofosbuvir (SOF), Velpatasvir (VEL) and Ribavirin (RBV) in treatment-experienced HCV patients.

Methods: Twenty patients with HCV relapse from prior DAA treatment from Yangon Specialty Hospital were given SOF/VEL/RBV regimen for 24 weeks. The primary end-point was sustained virological response at 12 weeks post-treatment (SVR12).

Results: Age of the patients varied from 35 to 70 years (mean age – 53.75 years $\pm$ 8.4 and 65% (13/20) were female. Age of the patients

varied from 35 to 70 years with mean age of 53.75 years $\pm$ 8.4 and 65% (13/20) were female. Baseline APRI scores ranged from 0.2 to 7.6. Mean HCV RNA was 1.13×10^6 IU/ml. Ten patients had done genotyping (70% Genotype 3b, 20% 6a and 10% 1a). Seventeen patients received prior treatment with Sofosbuvir and Daclatasvir, one with Sofosbuvir and Ledipasvir and two with SOF/VEL regimen. Sixty-five percent (13/20) of patients had liver cirrhosis including 4 decompensated patients. Three patients had evidence of HCC before initiating treatment. One patient had HBV co-infection and three had HIV taking Tenofovir/Lamivudine/Dolutegravir. Nineteen patients (95%) achieved SVR12. Treatment failure was observed in the patient with HCC and received prior SOF/VEL treatment.

Conclusion: SOF/VEL/RBV regimen for 24 weeks is effective in difficult-to-treat DAA experienced patients and is a feasible option in a resource limited country like Myanmar.

Abstract Submission No. 200274
P-0239

SOF/VEL/VOX in hepatitis C patients with previous DAA failure

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Objective To evaluate the efficacy and safety of sofosbuvir/vipataivir/VOX (SOF/VEL/VOX) in real-world patients with hepatitis C virus (HCV) infection who have failed previous direct antiviral therapy (DAA). **Methods** A multicentered retrospective study included chronic hepatitis C patients who had previously failed DAA antiviral therapy and were treated with SOF/VEL/VOX (400mg/100mg/100mg/ tablet, 1 tablet/day) for 12 weeks from June 2020 to Mar 2023. Sustained virological response (SVR12) was observed 12 weeks after the end of treatment, and biochemical changes and adverse reactions were assessed to evaluate the safety of the drug. **Results** A total of 18 patients were enrolled, including 12 patients with non-cirrhosis, 6 patients with compensatory cirrhosis, and 4 patients with two or more previous DAA treatment failures. 18 patients (18/18, 100%) achieved SVR12. Among the 18 enrolled patients, 10 reported adverse events during treatment, the most common adverse events were pruritus and nausea. There were 11 adverse events in the drug-related treatment period, and 1 patient had serious adverse events, and no adverse events resulted in drug discontinuation or patient death. **Conclusion** SOF/VEL/VOX has a higher rate of SVR12 in salvage therapy for chronic hepatitis C patients who have failed DAA treatment in the past, and is well tolerated and safe.

Abstract Submission No. 100097
P-0240

Clinical and histological variants of HBV and HDV infection

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Background and Aims: Timely detection of patients with chronic HBV and HDV infections is complicated by the fact that their clinical manifestations are not typical for viral hepatitis. All this greatly complicates the possibility of diagnosing chronic viral hepatitis and prevents the identification of patients infected with HBV and HDV. The aim of the study was to identify the relationship between clinical manifestations and the histological picture of liver damage in HBV and HDV infection.

Methods: A comprehensive clinical and laboratory examination of 41 patients with chronic HBV and HDV infection was carried out, of which 12 had HBV infection and 29 HDV infection. Clinical, biochemical, serological, molecular-biological, instrumental research methods were used.

Results: In patients with chronic HDV infection, the disease had severe clinical symptoms compared with HBV infection. Out of 12 patients with HBV infection, clinical diagnoses did not coincide with histological ones in 2 (16.7%) cases. Due to the paucity of clinical symptoms of the disease, chronic hepatitis B was diagnosed, but liver biopsy revealed liver cirrhosis. Of the total number of patients with HDV infection, there was a discrepancy between the clinical diagnosis and the histological diagnosis in 7 (24.1%) patients with liver cirrhosis. Of these, in 5 (17.2%) patients, histological examination revealed chronic hepatitis with minimal activity (F0-1), in 2 (6.9%) patients - chronic hepatitis with moderate activity (F1-2).

Conclusions: The intensity of clinical manifestations was not in all cases combined with morphological changes. With minor clinical manifestations, pronounced morphological changes are sometimes observed.

Abstract Submission No. 100183
P-0241

Epidemiological prevalence and clinical characteristics of Hepatitis Delta in Xinjiang Region

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Objective: This study aimed to examine the epidemiological prevalence and clinical characteristics of hepatitis delta virus (HDV) infection among chronic hepatitis B (CHB) patients in the Xinjiang region.

Methods: A cross-sectional study was conducted at a single center, enrolling a total of 1,100 HBsAg-positive patients attending at the Hepatology Department of Traditional Chinese Medicine Hospital Affiliated to Xinjiang Medical University between December 15, 2022, and June 30, 2023. All participants underwent testing for HDV antibodies and HDV RNA.

Results: Among the participants, 23 cases (2.09%) and 13 cases (1.18%) were positive for HDV-IgG and HDV-IgM, respectively. 14 cases (1.27%) were positive for HDV-RNA, all of which were classified as HDV genotype 1. The average age of these cases were 46.83 $\pm$ 7.9 years, with 11 (47.82%) being of Kyrgyz ethnicity. Additionally, 18 cases (78.26%) presented with liver function abnormalities, 17 cases (73.91%) exhibited progressive liver disease, including 16 cases (69.57%) with cirrhosis and 1 case (4.35%) with hepatocellular carcinoma (HCC). Autoimmune hepatitis (AIH) was observed in 4 cases (17.39%), and the coexistence of AIH was identified as an independent risk factor for disease progression.

Conclusion: The prevalence rate of HDV serological markers and HDV-RNA in this single center study in Xinjiang were 2.09% and 1.27%, respectively, with all cases belonging to HDV genotype 1. A higher incidence of HDV infection was observed in patients with abnormal liver function and progressive liver disease, underscoring the importance of targeted screening and diagnosis for such individuals.

Abstract Submission No. 100418
P-0242

Efficacy of Pegylated IFN- λ and IFN- α Treatments on HBV and HDV Infections in Humanized Mice

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HDV decline kinetics under pegylated IFN- λ therapy in chronic HDV-infected patients were dramatically higher compared to pegylated IFN- α therapy. The goal of this study was to investigate viral kinetics during IFN treatment in humanized mice.

Thirteen mice were treated twice weekly with 30 μ g/kg of either IFN- α or IFN- λ ; for either 12 weeks or 13 weeks. Ten mice were coinfecting with HBV and HDV, and 3 were superinfected. HBV DNA, HDV RNA, hAlb, and HBsAg levels were measured.

Baseline HBV DNA, HDV RNA, hAlb, and HBsAg levels had a median of 8.8 log IU/mL, 9.8 log IU/mL, 6.9 log ng/mL and 4.0 log IU/mL, respectively. Regardless of type of IFN, HDV RNA had a longer delay in decline than HBV DNA, with medians of 3 weeks and 1 day, respectively. Thereafter, mice treated with IFN- α experienced a significantly greater decline in HBV DNA, HDV RNA, and HBsAg, at weeks 9, 6, and 5, respectively, until end of treatment (EOT). The magnitude of decline from baseline to EOT for HBV DNA was significantly greater than that of HDV RNA, with medians of 1.55 and 0.79, respectively.

IFN- α was more effective than IFN- λ in decreasing HBV DNA, HDV RNA, and HBsAg during treatment in humanized mice that lack of an adaptive immune response, suggesting that IFN- α induces stronger innate immune responses than IFN- λ . The greater decline in HDV under IFN- λ compared to IFN- α in patients, may suggest a role of the adaptive immune response that needs to be investigated in future studies.

Abstract Submission No. 100511
P-0243

Sero-prevalence and genotype distribution of HDV among 67 HBsAg-positive pregnant women in Cambodia.

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Background and Aims: Globally, about 5% of people living with chronic Hepatitis B Virus (HBV) have Hepatitis Delta Virus (HDV) and is prevalent in HBV-endemic regions like Cambodia. The main epidemiological challenge is the disparity in HDV prevalence data due to the inaccessibility of standardized inexpensive tests. We developed an in-house Direct Enzyme Immuno-Assay (ELISA) method for detecting Anti-HDV among 67 HBsAg-positive pregnant women from Siem Reap, Cambodia. We estimated the prevalence of HDV and identified the HDV genotype.

Method: The developed in-house direct ELISA was compared with a commercial HDV assay by testing on 91 stocked samples containing anti-HDV positives. The in-house Direct ELISA was then used to analyze anti-HDV status in 67 pregnant women from Cambodia. HDV RNA was detected, and genotypes identified in anti-HDV positive samples.

Results: The sensitivity and specificity of the In-house direct ELISA against the Commercial ELISA were 96.55% and 98.39%, respectively. Anti-HDV was detected in 4(4/67) samples by the in-house Direct ELISA method, giving a prevalence of 5.97% (95% CI:1.65-14.59). Of the anti-HDV positive samples, 2(2/4) had detectable HDV RNA, both were classified as HDV genotype 1.

Conclusion: The prevalence of Anti-HDV among 67 HBsAg-positive Cambodian pregnant women was 5.97% with genotype 1 being the predominant strain. The In-House Direct ELISA proved effective as a screening method, with implications for diagnosis and treatment.

Abstract Submission No. 100518
P-0244

Healthcare resource utilization & costs of HDV vs HBV mono-infection across disease states from Spain

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Background: Concurrent infection of hepatitis delta virus (HDV) and hepatitis B virus (HBV) results in the most severe viral hepatitis. This retrospective study compares healthcare resource utilization (HCRU) and costs of HDV infection vs HBV mono-infection by disease states in Spain.

Methods: Adult patients with HDV or HBV (≥ 1 ICD-9/10-CM diagnosis code) between 01/01/2000 and 12/31/2019 (study period) were identified in the Spanish National Health System's Hospital Discharge Records Database. Patients initially diagnosed between 01/01/2001 and 12/31/2018 and with continuous enrollment for ≥ 12 months pre- and post-diagnosis were selected. Mean per patient per year (PPPY) HCRU and costs were compared within subgroups of liver disease severity. Descriptive statistics were summarized; comparisons were made via generalized linear models.

Results: Significantly more patients with HDV vs patients with HBV only had compensated cirrhosis (CC; 25.4% vs 9.5%, $P < .0001$) or decompensated cirrhosis (DCC; 51.6% vs 20.6%, $P < .0001$). Patients with HDV spent significantly less time in each liver disease state than patients with HBV only. Mean (SD) days spent in hospital was longer for patients with HDV vs HBV only, particularly due to CC (6.6 [2.7] vs 4.3 [1.8], $P = .04$), DCC (11.7 [4.7] vs 6.9 [3.8], $P = .03$), and liver transplantation (11.8 [3.0] vs 9.1 [3.4], $P = .04$). Mean pharmacy,

inpatient, outpatient, and total costs PPPY were significantly higher for those with HDV vs HBV only and increased with disease state severity.

Conclusion: These findings underscore the need for effective screening, diagnosis, and treatment of HDV to help reduce the clinical and economic burden of disease.

Abstract Submission No. 100519
P-0245

Disease progression among insured hepatitis delta virus infected patients in the United States

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Background: Concurrent infection of hepatitis delta virus (HDV) and hepatitis B virus (HBV) results in the most severe viral hepatitis. Herein, the rate of disease progression in a matched cohort of adults with HDV and HBV mono-infection were compared.

Methods: Commercially insured adult patients diagnosed with HDV or HBV from 1/1/2006–12/31/2021 (study period) were identified via PharMetrics database. The index date was the first claim of HDV or HBV diagnosis between 1/1/2007–12/31/2020. Patients were required to have ≥12 months of continuous enrollment pre-index and 1-day post-index date. Disease progression (baseline to next disease state) was assessed using Kaplan-Meier curves of propensity score-matched patients and multivariable Cox-proportional hazard regression model. Disease states include non-cirrhotic, compensated cirrhosis (CC), decompensated cirrhosis (DCC), and hepatocellular carcinoma (HCC).

Results: Of 291,482 patients, 116,370 met inclusion criteria and were propensity score-, age- and gender-matched, leading to 5,620 individuals each in HDV and HBV mono-infection cohorts. A total of 32% HDV and 36% HBV mono-infection patients had ≥10 years of follow-up. Compared with the HBV mono-infection cohort, patients with HDV demonstrated a higher rate of progression from non-cirrhotic disease to CC, DCC, and HCC (all $P < 0.05$) and were at higher risk of transitioning from non-cirrhotic disease to CC (HR: 1.54, 95% CI: 1.38–1.73, $P < 0.001$), DCC (HR: 1.60, 95% CI: 1.46–1.75, $P < 0.001$), and HCC (HR: 1.62, 95% CI: 1.24–2.12, $P = 0.015$).

Conclusion: These findings underscore the need for earlier identification, diagnosis, and treatment of HDV to mitigate future disease progression and burden of disease.

Abstract Submission No. 100670
P-0246

Screening of HDV-RNA presence in seminal fluid and cervical swab samples from HDV infected patients

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The sexual transmission of HDV is largely speculative. There is a very limited number of studies showing solid evidence for sexual transmission of HDV. The aim of this study is to screen the presence of HDV-RNA in male seminal fluid and female cervical swab samples. Our study was conducted for a total of 61 participants, which included 31 males and 30 females. Viral RNA was isolated from the blood, seminal fluid, and cervical swab samples from the respective participants. RT-PCR analysis of HDV-RNA was done for all samples isolated from blood, seminal fluid, and cervical swab samples. The results were expressed as statistical points including odds ratios (OR), Pearson's chi-squared test with Yates' continuity correction, and correlation coefficient (R^2). HDV-RNA detection rate is different for the samples from male and female. In the male cohort, 48.38% of seminal fluid samples were positive whereas 80% were positive for cervical swab samples from the female cohort. The data shows a statistically significant difference between genders for the presence of HDV-RNA in seminal fluid and cervical swab (OR=0.234, 95% CI= 0.749-0.7306). Also, Pearson's chi-squared test showed that there is a sufficient association between the degree of infectiousness and gender (5.3079, $df = 1$, p -value = 0.02123). A significant correlation was found between blood HDV-RNA quantity and HDV-RNA presence status in cervical swab samples ($R^2=0.7769$). However, no such significant correlation was found for males ($R^2=0.0163$). Overall, these findings provide substantial evidence of the potential risk of sexual transmission of HDV for each gender.

Abstract Submission No. 100700
P-0247

Development of chemiluminescence based quantitative ELISA assay for detection of anti-HDV Ag

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Background: Development of diagnostic assays for HDV is very limited due to its disproportional prevalence worldwide. There is no commercially available quantitative anti-HDV ELISA kit.

Aim: In this study, we have developed a chemiluminescence-based quantitative ELISA using the chemical immobilization method, that enhances the sensitivity and specificity of a diagnostic test.

Method: Recombinant His-tagged S-HDAg antigen was produced in *E.coli* and purified by Ni-NTA chromatography. The purified S-HDAg was immobilized on the polystyrene plate with APTES for the construction of the ELISA kit. A series of experiments were done to determine the optimal assay condition. The standard polyclonal anti-HDV antibody samples were prepared from HDV-infected human serum and used as standards in quantification analysis. To determine the characteristics of the assay, serum samples from 247 people including 120 patients with HDV/HBV infection (HDV RNA and HBsAg positive), and 127 healthy people (Anti-HCV and HBsAg negative) were analyzed.

Result: In the frame of the applied settings, the optimal ELISA assay parameters are: serum dilution 1:10, secondary Ab dilution 1:60000, 20 min incubation at 37°C, 1 min luminescence reaction and 30 min total test duration. The calibration curve was generated from serially diluted standards (20, 10, 5, 1, 0.1, 0.01 µg/ml $R^2=0.9851$). The ROC analysis shows the confidence of the assay (optimal cut-off point=5.62 µg/ml, AUC=0.9968, 95%CI 0.9932 to 1.00005 ($p < 0.001$). The

specificity, sensitivity and LOQ were calculated (96.85 %, 96.67 %, 3.52 µg/ml).

Conclusion: The ELISA assay developed by chemical immobilization shows confidence in quantitative analysis of HDV-Ab.

Abstract Submission No. 100817

P-0248

Efficacy & safety of bulevirtide in combination with pegylated interferon α -2a in patients with CHD

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Background: Bulevirtide (BLV) is approved for chronic hepatitis delta (CHD). Phase 2 MYR204 evaluated the safety and efficacy of BLV (2 and 10mg) with/without pegylated interferon α -2a (pegIFN) in patients with CHD and compensated cirrhosis (CC).

Methods: Based on CC status, 174 patients were randomized (1:2:2:2) to receive (A) pegIFN for 48 weeks (Wks); (B) BLV 2mg + pegIFN; (C) BLV 10mg + pegIFN for 48 Wks, then BLV 2 or 10mg monotherapy for 48 Wks; or (D) BLV 10mg for 96 Wks. The primary endpoint was sustained virologic response (SVR) at Wk24 (SVR24) after EOT (end of treatment) defined as undetectable hepatitis delta virus (HDV) RNA with comparison between Arms C and D.

Results: Overall, 35% had CC, mean liver stiffness was 13.1 (7.72) kPa, mean HDV RNA was 5.3 (1.2) log₁₀ IU/mL, mean alanine aminotransferase (ALT) was 114.0 (94.8) U/L, 28% were on nucleos(t)ide analogue therapy, and 48% were IFN experienced. SVR24 was achieved by 17% (Arm A), 30% (Arm B), 46% (Arm C), and 12% (Arm D) ($P = 0.0003$; Arm C vs D) (Table). ALT normalization and composite endpoint at Wk24 after EOT were superior with BLV 10mg + pegIFN vs monotherapy. Hepatitis B surface antigen loss was observed in the combination groups. Adverse events (AEs) observed for the BLV + pegIFN arms were similar to pegIFN monotherapy. Six patients (3%) discontinued treatment (unrelated to BLV).

Conclusions: Combination therapy was effective and well tolerated. Longer-term data will help define durability of BLV + pegIFN for CHD.

Abstract Submission No. 100824

P-0249

Impact of reflex testing on the delta hepatitis burden in the United States

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Background: Chronic infections by the hepatitis delta virus (HDV) cause the most severe form of viral hepatitis. Undiagnosed patients face a high risk of liver complications that could be reduced with earlier treatment. The objective of this analysis was to assess the impact of double reflex HDV testing compared to current practice on HDV-related morbidity and mortality in the United States.

Methods: A model combining a decision tree of the HDV screening cascade in patients with hepatitis B virus (HBV) with a previous Markov cohort model reflecting disease progression in HDV patients was developed. Model inputs were based on literature reviews, real-world data, and expert consensus. Two scenarios were compared: one reflecting current HDV screening rates, and the other reflecting double HDV reflex testing for diagnosed HBV patients. The model then estimated the number of diagnosed HDV patients and the incidence of liver morbidity and mortality over a 5-year period.

Results: In the United States, implementing double reflex testing among all patients with HBV would increase the number of treated HDV patients by 1,617% (7,361 vs 429 in double reflex testing vs current scenario). Over a 5-year period, increased rates of HDV diagnosis and treatment would reduce rates of compensated cirrhosis (−4%), decompensated cirrhosis (−23%), hepatocellular carcinoma (−18%), liver transplant (−22%), and liver-related mortality (−21%).

Conclusions: Implementing double reflex testing for HDV among all patients with HBV would greatly increase the number of HDV patients treated, thus substantially reducing HDV burden in United States within the next five years.

Abstract Submission No. 100846

P-0250

THE PREVALENCE OF HEPATITIS DELTA VIRUS IN EASTERN PROVINCE MONGOLIA

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Background: Hepatitis delta virus (HDV) poses a significant global threat to liver health, leading to increased morbidity and mortality. This study aimed to assess the prevalence of HDV infection in individuals who tested positive for hepatitis B surface antigen (HBsAg) residing in Dornod province, located in Eastern Mongolia.

Methods: A total of 86 HBsAg-positive individuals underwent anti-HDV testing using radioimmunoassay. Those who tested positive for anti-HDV were further examined for HDV-RNA levels through polymerase chain reaction (PCR).

Results: Among the participants, 58 were male (68 %) and 28 were female (31.9%). The average age was 42.8 ± 7.5 years (ranging from 19 to 64 years), 73% of patients (62 out of 86) tested positive for anti-HDV. Among these 62 individuals, 100% were found to be positive for HDV-RNA. The mean HDV-RNA level was 1,884,574 IU/ml. This indicated a chronic HDV infection rate of at least 73% within the entire study group (62 out of 86). Moreover, 46 patients (54%) in the study group were diagnosed with cirrhosis. The prevalence of anti-HDV sero-positivity and the presence of HDV RNA were higher among those with cirrhosis (45 out of 53%). The patients with HDV-RNA

positivity higher ALT levels (94 U/L) compared to those without HDV-RNA.

Conclusion: This study showed a high prevalence of hepatitis delta virus infection among HBsAg-positive patients in Eastern Mongolia. These findings underscore the need for increased vigilance and tailored management strategies for HDV-infected individuals in this region.

Abstract Submission No. 100979
P-0251

Development and validation of an algorithm for identifying HDV RNA+ patients

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Background: There is a large gap in correctly identifying patients with hepatitis D virus (HDV) using (non-laboratory) real-world data. The objective was to develop and validate an algorithm to identify HDV RNA+ patients.

Methods: HDV status was identified by HDV RNA test results from HealthVerity claims data and linked with laboratory data of hepatitis B virus (HBV) diagnosed patients. Data was divided into training and test data (80/20 split). During training, algorithms were developed and scored via 10-fold cross-validation, where the lowest sum of scores indicated the best performing algorithm which were further tested using testing data. Variables included in the algorithms were: age and gender, diagnosis of HBV/HDV, hepatitis-related complications, and use of hepatitis-related therapies. Algorithms were scored based on accuracy, positive predictive value (PPV), sensitivity, and specificity. Algorithms were further validated using TriNetX Dataworks data.

Results: The generalized linear model with elastic net regularization (GLMNET) model performed the best while outperforming the diagnoses-based algorithms. In the testing data, accuracy, PPV, sensitivity, and specificity for GLMNET versus diagnosis-based algorithm were 0.96 versus 0.95, 0.79 versus 0.69, 0.58 versus 0.58, and 0.99 versus 0.98, respectively. In the validation data, accuracy, PPV, sensitivity, and specificity for GLMNET versus diagnosis-based algorithm were 0.94 versus 0.93, 0.53 versus 0.41, 0.21 versus 0.34, and 0.99 versus 0.97, respectively.

Conclusions: This new claims-based algorithm can be used to identify HDV RNA+ patients in real-world databases, which in turn will enable the accurate generation of real-world evidence surrounding HDV.

Abstract Submission No. 101804
P-0252

The study of cirrhosis stage in patients with HBV infection and HBV/HDV co-infection in Mongolia

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Objective: Comparative study of cirrhosis stage in patients with HBV infection and HBV/HDV co-infection in Mongolia.

Materials and Methods: Our study continued from January 2018 to March 2020 and we measured liver fibrosis stage in patients with HBV infection and HBV/HDV co-infection using a FibroScan (kPa). In our study, in random sampling cases are selected 354 patients with HBV single infection and HBV/HDV co-infection. 177 of all patients have HBV/HDV co-infection. We selected parameters from patient medical histories in our study, such as serologic markers of HBV, quantification of HBV and HDV in serum samples, blood test, liver function test and liver fibrosis stage.

Results: 354 patients (169 men (47.7%) and 185 females (52.3%); range (18-75)) are participated in our study. According to the comparative study in laboratory tests, ALT level was HBV - 44 (36; 51.5) and HBV/HDV - 61 (39.8; 97.55). AST level was HBV - 39.1 (30; 83) and HBV/HDV - 50 (33.1; 77.8). The Platelet count was HBV - 193±66 and HBV/HDV 181±62.8. When we compared, liver fibrosis stages were HBV - F0 67 (37.9%), HBV/HDV - F0 57 (32.2%), HBV-F1 22 (12.4%), HBV/HDV-F1 17 (9.6%), HBV-F2 39 (22%), HBV/HDV F2 39 (22%), HBV-F3 29 (16.4%), HBV/HDV - F3 41 (23.2%), HBV - F4 20 (11.3%) and HBV/HDV - F4 23 (13%).

Conclusion: Aging can also increase the risks of liver cirrhosis. Our study shows that, the hepatitis is more severe in patients with HBV/HDV co-infection and the platelet count is more decreased.

Abstract Submission No. 101942
P-0253

Relationship of HDV Infection to Increased Risk of Cirrhosis and HCC in Chronic Hepatitis B Patients

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Aims: Chronic hepatitis B patients are at a high risk of developing severe complications, including hepatocellular carcinoma (HCC), which can be fatal. Hepatitis Delta Virus (HDV) is a single-stranded RNA virus that relies on HBV for its propagation. In several countries, a study aims to investigate the correlation between HDV infection and the increased risk of cirrhosis and HCC in patients with chronic hepatitis B.

Methods: This is a systematic literature review with the keywords "HDV Infection", "Cirrhosis", "HCC" and Chronic Hepatitis B Patients with a descriptive analysis research model.

Results: Study by Jang et al. (2021) showed that liver cirrhosis (HR/95%CI 9.98/5.11–19.46, $P < 0.001$) was responsible for HCC, and among patients with cirrhosis, HDV RNA positivity was associated with HCC (HR/95%CI 9.98/5.11–19.46, $P < 0.001$). In a study conducted by Romeo et al. (2009), they examined 299 patients infected with HDV over 28 years and found that HDV infection persistently led to cirrhosis and HCC at annual rates of 4% and 2.8%, respectively. Oyonsuren et al. (2006) conducted a retrospective investigation of 292 patients with chronic hepatitis and found that HDV coinfection was more strongly associated with HCC at a younger age compared to HCV mono-infection. Another study by Ji et al. (2012) revealed that out of 9,160 HBV patients, 650 had HDV co-infection over a period of 11 years, and HDV was identified as a strong risk factor for an increased risk of HCC.

Conclusions: The presence of HDV infection in chronic hepatitis B

patients is strongly associated with an increased risk of developing cirrhosis and hepatocellular carcinoma (HCC), emphasizing the need for management and control of HDV infection to reduce the occurrence of these complications.

Abstract Submission No. 100126
P-0254

Gilbert's syndrome and *UGT1A1* Gene Abnormalities IN Mongolians ARE WESTERN TYPE

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Hereditary abnormalities of the uridinediphosphoglucuronate-glucuronosyltransferase 1A1 (*UGT1A1*) gene are identified as a major cause of unconjugated hyper-bilirubinemia. Asian and Caucasian populations have different genetic profile for *UGT1A1* while abnormalities of the *UGT1A1* gene in the Mongolian population remains uninvestigated. **Methods:** Between 2007 to 2022, 12 in 110 Mongolian adults developed indirect hyperbilirubinemia. We genotyped the TATA box promoter region of the *UGT1A1* gene for the A(TA)₆TAA (6) or A(TA)₇TAA (7) promoter variant, and the coding region for nucleotide mutations (nt-211 G to A (G71R), nt-686 C to A (P229Q), nt-1091 C to T (P364L) and nt-1456 T to G (Y486D)).

Results: three patients were homozygous for the nt-211G>A mutation, three patients were heterozygous for the 6/7 promoter genotype and the nt-211G>A mutation, whereas six patients were with homozygous 7/7 genotype and were diagnosed with GS. The percentage of 7/7 genotype patients (50%) was comparable with Caucasian, African, and Indian populations but significantly higher than other Asian countries. We did not identify any Mongolian patients with nt-686 C to A, nt-1091 C to T, or nt-1456 T to G mutations, which are common in Asian countries but not in the Western population. One patient with homozygous nt-211G>A mutation developed severe indirect hyperbilirubinemia during the initial phase of the combined interferon and ribavirin therapy.

Conclusion: The prevalence of *UGT1A1* abnormalities in Mongolians is more similar to the Western population than the Asian population; whereas the high prevalence of nt-211G>A mutation is similar to Asians.

Abstract Submission No. 100210
P-0255

Clinical features of neurologic Wilson's disease without Kayser-Fleischer rings

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Background: Wilson's disease (WD) as a rare hereditary disease, remains a commonly misdiagnosed disease. We summarized the characteristics of neurologic WD patients without KF rings in a WD cohort.

Method: The enrolled neurologic WD patients were divided into two groups according to the presence of a KF ring. We compared demographic data, laboratory findings between the two groups.

Results: The neurologic WD patients were classified as positive

(n=195) or negative (n=54) for KF rings. The WD patients without KF rings have a significantly higher proportion of female than those with KF rings (27.8% vs. 20%, p=0.049). There was no significant difference in BMI (19.1±0.64 kg/m² vs. 19.6±0.36 kg/m²) and age of onset (19, range 14-22.25 years vs. 20, range 15-25 years) between patients without KF rings and patients with KF rings. 5.6% of WD patients without KF rings have family history of WD, and 4.1% in those with KF rings (p >0.05). Although there had no significant difference, a higher ceruloplasmin observed in neurologic WD patients without KF rings (40, range 20-80 mg/dl) compared to patients with KF rings (40, range 20-60 mg/dl). The 24-hour urinary copper excretion level was lowed in patients with WD without KF rings (3.96±0.23 μmol/24h) than patients with KF rings (4.03±0.26 μmol/24h). There were no significant difference in psychiatric symptoms between the two groups (16.7% vs. 22.6%, p >0.05).

Conclusions: The neurological WD patients without KF rings had a relatively distinct features. Further studies are warranted to explore the mechanisms of gender difference in neurological WD.

Abstract Submission No. 100258
P-0256

Common Presentation of a Rare Disease-Benign Recurrent Intrahepatic Cholestasis- A Case Report

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Benign recurrent intrahepatic cholestasis is a rare autosomal recessive disease, which usually presents with complain of recurrent jaundice with cholestatic pattern of liver function tests. Its diagnosis requires high degree of suspicion. It is a self-limiting disease and does not cause cirrhosis but increases the risk of hepatobiliary carcinomas. We had a case of 18 years old boy who presented to us in outpatient department, he was found to have BRIC on histo-pathological examination of liver biopsy sample and responded to Ursodeoxycholic acid. As only few cases of BRIC have been reported, this disease needs to be highlighted so that can be diagnosed earlier without proceeding for expensive investigations in limited resources area as in our case report.

Abstract Submission No. 100624
P-0257

Severe liver damage in LDLR T52T/ApoE3 genotype HCV patients consuming a hepatopathogenic diet

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Background: The outcome of HCV infection is modulated by genetic and environmental factors interacting with the virus, such as the low-density lipoprotein receptor (LDLR) and Apolipoprotein E (ApoE) associated with lipid metabolism. We analyzed the genetic profile, dietary habits, and liver damage in anti-HCV-positive Mexican-Mestizos.

Methods: This cross-sectional study included 152 anti-HCV positive patients, 110 were viral load (VL) + and 42 VL-. A medical-nutritional evaluation was registered. The genetic profile including LDLR/ApoE genotypes was assessed by allelic discrimination. Comparative statistics were performed between VL+ and VL- subjects.

Results: The patients (85F/67M) were 49.8±12 years old and had a body mass index of 27.7±5.4 kg/m². The patient's genetic background was consistent with the Mestizo ancestry with a high prevalence of Amerindian risk alleles. VL+ patients showed low levels of cholesterol, triglycerides, VLDL, LDL, compared to VL- ($p<0.001$), and had high ALT, AST, GGT ($p<0.001$), and low platelets ($p<0.001$). A 61.1% (58/95) of the VL+ patients had a high risk for fibrosis (FIB-4) and 35.7% (35/98) had severe fibrosis (APRI). A 10% (11/110) of the VL+ patients were TT LDLR/ApoE3 genotype carriers in which 90% (10/11) had moderate/severe damage compared to the C allele carriers (CC, CT), whereas the VL- patients showed 0% of the TT LDLR genotype ($p=0.035$). LDLR TT carriers consumed a hepatopathogenic diet high in saturated fatty acids compared to the CC+CT genotype carriers ($p=0.014$).

Conclusions: The presence of TT/ApoE3 genotype and consumption of a hepatopathogenic diet suggests that this genotype can be a useful genetic marker combined with nutrigenetic strategies to avoid liver damage.

Abstract Submission No. 100912
P-0258

Prevalence and Treatment Pattern of Wilson's Disease using Korean National Health Insurance Data

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Background: Wilson's disease (WD) is an autosomal recessive disorder in which copper accumulates in organs, particularly in the liver and central nervous system. This study aimed to investigate the prevalence, incidence, and treatment patterns of WD patients in South Korea.

Methods: National Health Insurance System (NHIS) claims data from 2010 to 2020 were analyzed. Patients with WD as a primary or additional diagnosis at least once were identified using the International Classification of Diseases (ICD)-10 disease code E83.0 and a record for a registration program for rare intractable diseases in South Korea.

Results: The average age- and sex-adjusted prevalence and incidence of WD between 2010 and 2020 were 3.06/100,000 and 0.11/100,000, respectively. The mean age of the patients with newly diagnosed WD was 21.0 ± 15.9 years. Among the 622 WD incident cases during the study period, 19.3% of the patients had liver cirrhosis and 9.2% had received liver transplantation. Psychological and neurological diseases were present in 40.7% and 48.1% of the patients, respectively. Regarding the diagnosis of WD, liver biopsy was performed in only 51.6% of new cases. D-Penicillamine, trientine, or zinc were prescribed in 81.5% of the incident cases, and the treatment uptake rates decreased with increasing age.

Conclusion: The prevalence of WD in South Korea is 3.06/100,00 and approximately 1,800 patients use medical services annually. A significant proportion of patients are diagnosed at the cirrhotic stage and not treated with Cu-chelating therapeutics, suggesting the need for early diagnosis and adequate treatment to improve prognosis.

Abstract Submission No. 101128
P-0259

Case series of C282Y mutation in the HFE gene in Turkey: Single-center experience

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BACKGROUNDS: Hereditary Hemochromatosis (HH) is an autosomal recessive disease characterized excessive iron accumulation in the body. Major C282Y mutation is detected very rarely in Turkish HH patients. We aimed to determine the clinical and demographic parameters of patients with the C282 Y mutation who are being followed at our center.

METHODS: Ten patients with C282Y mutation, being follow up at the Liver Diseases Follow-up Clinic of Ankara University Faculty of Medicine between 2015 and 2021, were retrospectively analyzed. Genomic DNA was isolated from whole blood containing EDTA by using genomic DNA isolation kit (Roche). The DNA region containing the HFE gene was amplified by PCR using appropriate primers. The amplified PCR products were sequencing using the BigDye terminator kit, ABI 310 Genetic Analyzer.

RESULTS: Seven patients (70%) were male, median age was 51.6 (27-73). Three (38%) patients had Diabetes Mellitus. The median hemoglobin, serum alanine aminotransferase, aspartate aminotransferase and gamma glutamyl transferase levels were 14.8mg/dL (12.3-17.4), 50 U/L (11-98), 40 U/L (16-104) and 55.0 U/L (10-226). Median transferrin saturation (TS) and ferritin values were 68% (40-95), and 2298 ng/mL (36-5264). AA homozygous and heterozygous mutations were identified in 60%, and 40% patients respectively. Two (20%) patients had cirrhosis and were C282 Y homozygous. A significant difference was found between the mean ferritin values and TS of those homozygous and heterozygous patients (3332ng/dl vs 766 ng/dL $p<0.001$), (77% vs.56%, $p<0.001$) as well as in AST (52 vs.35 IU/L, $p<0.001$), and ALT levels (60 vs. 39 IU/L, $p<0.001$). Iron accumulation in MRI was observed in 4 out of the 6 patients (67%) of whom 3 (75%) were homozygous. In 3 patients who underwent liver biopsy, iron accumulation was observed consistent with HH.

CONCLUSION: In our series, we have reported the largest cohort of C282Y mutations in Turkey. Notably, elevated liver function tests and increased iron parameters were more pronounced in patients with HH who had the C282Y homozygous mutation.

Abstract Submission No. 101860
P-0260

RISK AND COMPARATIVE ANALYSIS OF BLOOD PARAMETERS, ELASTOGRAPHY AND MRI IN THE DIAGNOSIS OF NASH

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BACKGROUND: Non-alcoholic fatty liver disease (NAFLD) is prevalent in 20-30% population undiagnosed and asymptomatic with 80% cardiovascular risk.

MATERIALS AND METHODS: 19 NAFLD patients, and various factors were considered, including BMI, hypertension (HTN), diabetes mellitus (DM), transient elastography (TE) with controlled attenuation parameter (CAP)(Fibroscan), proton magnetic resonance spectroscopy and liver biopsy.

RESULTS: Among the 19 subjects, all had a BMI above 27 kg/m², 42.1% had DM, and 26.3% had HTN. Biochemical analysis revealed that 57.89% had normal levels of AST and ALT, while 42.1% had elevated levels, with 62.5% of them having concomitant HTN or DM. Insulin-like growth factor levels are within normal range upto stage F3. Fibroscan results showed that all patients had CAP parameters exceeding 300 dB/m, indicating pronounced fibrosis (elasticity indices

exceeding 7.5 kPa). 14 patients out of 19, in whom MRI liver steatosis more than 9% were considered for liver biopsy. Biopsy was done in 50% patients out of 14, in 71.4% of whom the results of Fibroscan showed pronounced excess fibrosis F3 and pronounced steatosis S3.

CONCLUSION: obesity is the primary cause of NAFLD, followed by DM and HTN. Normal biochemical results do not exclude the diagnosis in high-risk groups, and screening with Fibroscan is recommended. Elevated AST and ALT values are sensitive indicators in patients with HTN or DM. Fibroscan is effective in the F2 stage, but it may overestimate the F3 stage. MRI/biopsy demonstrates higher diagnostic efficiency for steatohepatitis compared to Fibroscan.

Abstract Submission No. 200228
P-0261

Metabolomics of hepatoblastic nuclear degeneration

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Background: Hepatolenticular degeneration disease is an abnormal copper metabolism caused by autosomal recessive inheritance.

Aim: To analyze the significance of differential metabolites in patients with Wilson's disease and to analyze the most meaningful metabolism pathway, further elucidating the possible pathogenic mechanisms of hepatolenticular degeneration.

Method: The serum of patients were detected by UHPLC-Q Exactive Orbitrap HRMS.

Data Processing: The raw data files were preprocessed and imported into MetaboAnalyst4.0 software for principal component analysis (PCA) and partial least squares discriminant analysis (PLS-DA) to screen differential metabolites with variable important projection (VIP) greater than 1.

Result: 35 sera metabolites with significant differences were identified between the patients and the healthy control group. The compounds were compared with the online database and were not completely verified by the standard.

Three metabolic pathways with higher pathway impact are Porphyrin and chlorophyll metabolism, Arginine and proline metabolism, Taurine and hypotaurine metabolism. The pathogenesis of hepatolenticular degeneration might be related to the shortage of energy supply, the increase of oxygen free radicals production and the VII clearance of obstacles, and the abnormal ammonia metabolism.

Conclusion: Compared with controls, the metabolic profile of patients was altered obviously. Taurine, N-Methylphenylethanolamine and Ubiquinone-1 may serves as the marker metabolites in distinguishing patients from controls. The pathogenesis of WD may be related to the shortage of energy supply, oxidative stress, and the abnormal ammonia metabolism.

Abstract Submission No. 100294
P-0262

Deletion of ADAR2 ameliorates hepatic glycolipid metabolism disorder in diet-induced obese mice

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Non-alcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease worldwide. NAFLD and type 2 diabetes mellitus (T2DM) commonly coexist. Adenosine-to-inosine (A-to-I) editing, catalyzed by adenosine deaminase acting on RNA (ADAR) enzymes, is an important post-transcriptional modification of genome-encoded RNA transcripts. Three fundamentally related members of the ADAR family have been identified: ADAR1, ADAR2, and ADAR3. ADAR1 and ADAR2 are ubiquitously expressed, while ADAR3 is exclusively expressed in the brain. However, the functional role of ADAR2 in hepatic steatosis, particularly that in NAFLD, is unclear. In this study, ADAR2^{+/+}/GluR-B^{R/R} (wild type) mice and ADAR2^{-/-}/GluR-B^{R/R} (ADAR2 KO) mice were fed with standard chow or high-fat diet (HFD) for 12 weeks. ADAR2 KO mice exhibited protection against HFD-induced glucose intolerance, insulin resistance, and dyslipidemia. Moreover, ADAR2 KO mice displayed reduced liver lipid droplets in concert with decreased hepatic TG content, improved hepatic insulin signaling, better pyruvate tolerance, and increased glycogen synthesis. Glucose uptake in primary hepatocytes from ADAR2 KO mice was increased. Pyruvate-induced glucose release was reduced in primary hepatocytes from ADAR2 KO mice. Mechanistically, ADAR2 KO mitigated hepatic lipid production via AMPK/Sirt1 pathway. ADAR2 KO inhibited hepatic gluconeogenesis via the AMPK/CREB pathway and promoted glycogen synthesis by activating the AMPK/GSK3 β pathway. These results provided novel evidence that ADAR2 KO protected against NAFLD progression through AMPK signaling. 51 Inhibition of ADAR2 is a potential therapeutic target for NAFLD.

Abstract Submission No. 100494
P-0263

Lactobacillus Casei-Fermented *Amomum Xanthioides* Mitigates NAFLD in a High-fat Diet Mice Model

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Non-alcoholic fatty liver disease (NAFLD) is a substantial global health issue owing to its high prevalence and the lack of effective therapies. Fermentation of medicinal herbs has always been considered a feasible strategy for enhancing efficacy in treating various ailments. This study aimed to investigate the potential benefits of the *Lactobacillus casei*-fermented *Amomum xanthioides* (LAX) on NAFLD in a high-fat diet model. HFD-fed C57BL6/j mice were administered with 200 mg/kg of LAX or unfermented *Amomum xanthioides* (AX) or 100 mg/kg of metformin for 6 weeks from the 4th week. The 10-week HFD-induced alterations of hepatic lipid accumulation and hepatic inflammation were significantly attenuated by LAX dominantly (more than AX or metformin), which evidenced by pathohistological findings, lipid contents, inflammatory cytokines (TNF- α , IL-6 and IL-1 β), oxidative parameters (ROS and MDA), and molecular changes reversely between lipogenic (GPAM and SREBP-1) and lipolytic (PPAR- α and p-AMPK α) molecules in the liver tissues. In addition, the abnormal serum lipid parameters (triglyceride, total cholesterol and LDL-cholesterol) notably ameliorated by LAX. In conclusion, these findings support the potential of LAX as a promising plant-derived remedy for NAFLD.

Abstract Submission No. 100516

P-0264

Association of TNF- α gene polymorphisms with non-alcoholic fatty liver disease: A meta-analysisAlaa Abd El-Ghany Osman¹, Sally Waheed Elkhadry¹, Laila Shehata Dorgham¹¹Epidemiology and Preventive Medicine Department, National Liver Institute, Menoufia University, Egypt Shebin El Kom, Menoufia Egypt

Background: Nonalcoholic fatty liver disease (NAFLD) is one of the most prevalent liver diseases that is affected by various environmental and genetic factors. The association between tumor necrosis factor- α (TNF- α) gene polymorphism in regions -308G/A (rs1800629) and -238G/A (rs361525) and susceptibility to NAFLD is controversial. This meta-analysis evaluated the association between these TNF- α polymorphisms and NAFLD.

Methodology: A systematic search was conducted on PubMed, Cochrane Library, Scopus, Web of Science, and EMBASE databases to retrieve relevant studies published until March 29, 2023. Based on predetermined selection criteria, all eligible studies were included in the meta-analysis. Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated.

Results: Eleven studies with 1155 NAFLD cases and 1364 controls demonstrated the significant association between TNF- α rs1800629 polymorphism and NAFLD under the dominant model (GA/AA vs. GG) [OR = 1.27, 95% CI = 1.01–1.59, P = 0.04] and allelic model (G vs. A) [OR = 1.26, 95% CI = 1.03–1.54, P = 0.02]. Considering the TNF- α rs361525 polymorphism, nine studies including 904 cases and 848 controls suggested significant association under each of the dominant model [OR = 1.76, 95% CI = 1.14–2.71, P = 0.01] and the allelic model [OR = 1.66, 95% CI = 1.31–2.44, P = 0.01]. Subgroup analysis based on ethnicity suggested a significant association among Caucasians, while the evidence for both rs1800629 and rs361525 was insufficient among Asians.

Conclusion: This meta-analysis suggested that TNF- α gene polymorphism at positions -238 and -308 might be a risk factor for NAFLD.

Abstract Submission No. 100583

P-0265

Gender and Ethnic Disparities in Metabolic Dysfunction-Associated Steatotic Liver DiseaseElina Cho¹, Clarissa Elysia Fu², Mark Muthiah^{2,3,4}, Daniel Q Huang^{2,3,4}, Margaret Teng⁰, Cheng Han Ng^{2,3}, Nicholas Syn⁰

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Background: Metabolic-associated steatotic liver disease (MASLD) has been introduced as the new nomenclature to overcome the limitations of non-alcoholic fatty liver disease (NAFLD). While certain epidemiological data have been analyzed, there is limited evidence regarding gender and ethnic variations in MASLD. This study assesses the differences across gender and ethnicity on the prevalence,

associated risk factors and adverse outcomes in individuals diagnosed with MASLD.

Methods: Data retrieved from NHANES between 1999 to 2018 was analyzed. Prevalence, clinical characteristics, and outcomes were evaluated according to gender and ethnicity respectively. Adverse outcomes and mortality events were analyzed using multivariate analyses.

Results: An analysis from 1999 to 2018 revealed a significant increase in prevalence across Mexican Americans (APC +2.010%, p<0.001), other Hispanics (APC +2.116%, p=0.003), Caucasians (APC +1.236%, p=0.018), African Americans (APC +1.124%, p=0.006), and female gender (APC +0.984%, p=0.026), but not male gender. Females were at lower risk of all-cause (HR: 0.741, 95%CI: 0.679 to 0.807, p<0.001), CVD (SHR: 0.798, 95%CI: 0.685 to 0.929, p=0.004), cancer-related mortality (HR: 0.765, 95%CI: 0.654 to 0.895, p=0.001) as well as major adverse cardiovascular events and high-risk advanced fibrosis compared to males. Significantly, African Americans have the highest risk of all-cause and CVD-related mortality followed by Caucasians then Mexican Americans.

Conclusion: Gender and ethnic variations are similar amongst individuals diagnosed with MASLD and NAFLD. Whilst further studies are required to investigate the impact of MASLD beyond the United States population, this study strengthens the case for usage of MASLD without hindering ongoing developments based on NAFLD.

Abstract Submission No. 100653

P-0266

Hepatic steatosis characteristics in mouse models of NAFLD based on AI analysisXiaoxiao Wang¹, Yuyun Song¹, Rui Jin¹, Zilong Wang¹, Xiaohu Li¹, Qiang Yang², Xiao Teng², Fangfang Liu³, Nan Wu¹, Yandi Xie¹, Huiying Rao¹, Feng Liu¹

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Objective: This study aims to establish an artificial intelligence (AI) analysis method that based on SHG/TPEF technology to evaluate the characteristics of hepatic steatosis in mouse model with non-alcoholic fatty liver disease (NAFLD) automatically and objectively.

Methods: C57BL/6 mice were divided into 6 NAFLD model groups: Western diet (WD) group; WD + fructose drinking water (WDF) group; WDF + CCl₄ group; High fat diet (HFD) group; HFD plus fructose (HFDF) group; HFDF+CCl₄ group. Liver tissue and blood samples of mice were collected at different time points (0w, 8w and 16w) after modeling. All tissue sections were subjected to H&E and SHG/TPEF imaging. The changes of hepatic steatosis were analyzed by AI.

Results: Compared with 0w, according to AI analysis, the area and the number of fat vacuoles in each group, as well as the diameter of fat vacuoles and the number of fat droplets per unit area corresponding to the diameter of fat vacuoles, showed an increasing trend with the prolongation of modeling time, especially in WD and WDF groups. Meanwhile, compared with the 8W model, the above-mentioned steatosis characteristics in the 16W model increased significantly. Although the steatosis grade also showed a steady upward trend, there was no significant difference between the 8w and 16w using NASH CRN scoring method.

Conclusion: AI analysis based on SHG/TPEF image could quantify the dynamic changes of the area, number, and size of hepatic steatosis

automatically and objectively, making it more suitable for the evaluation of pre-clinical animal experiments.

Abstract Submission No. 100692
P-0267

BODY COMPOSITION OF MAFLD PATIENTS AND PREDICTORS OF SIGNIFICANT FIBROSIS

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Background: Body composition of MAFLD patients changes as they progress from fatty liver disease to advance fibrosis. Visceral adipose tissue (VAT) along with conventional factors like Diabetes, hypertension has been postulated to be the driver of fibrosis in these patients.

Aim: To study the body composition analysis using bioelectrical impedance (BIA), and finding out potential predictors of significant fibrosis by comparing clinical, laboratory and BIA parameters.

Methods: We enrolled 146 MAFLD patients, 69 had significant fibrosis (>F2, Group-A) and while 77 were without significant fibrosis (<F2, Group-B) along with 35 controls (Group-C). All underwent detailed clinical evaluation, FibroScan & Bioelectrical impedance analysis using four electrode BIA machine.

Results: Patients in Group-A were older in age (56.7 ± 10.8 vs 42 ± 11.6) years, had higher percentage of patients with diabetes mellitus (63.8 vs 35.1), hypertension (47.8 vs 28.6) had significantly higher visceral adipose tissue (VAT) percentage (18 ± 6 vs 15 ± 7), body water content percentage (53 ± 3 vs 51 ± 3), while Patients in Group-B had higher body mass index (Kg/m^2) (31.3 ± 5.3 vs 28.9 ± 4.9), total body fat percentage (32 ± 6.4 vs 28 ± 6), subcutaneous adipose tissue (SAT) percentage (28 ± 6 vs 22 ± 7) & bone mass (kg) (2.9 ± 0.7 vs 2.6 ± 0.7), insignificant but higher skeletal muscle percentage (35 ± 6 vs 33 ± 6) compared to Group-A. while Group-C had significantly lower total body fat percentage (24 ± 07), VAT% (09 ± 03), SAT% (18 ± 07) & higher muscle mass percentage (38 ± 04), bone mass (kg) (2.9 ± 0.38) compared to group A&B. Significant difference for hemoglobin (11.65 ± 2.09 vs 12.87 ± 1.67) gm/dl, platelets count (168 ± 66 vs 282 ± 72)/mm³, bilirubin (1.25 ± 1.04 vs 0.82 ± 0.48) mg/dl, protein (6.87 ± 0.82 vs 7.60 ± 0.48) gm/dl, albumin (3.51 ± 0.55 vs 3.94 ± 0.32) gm/dl levels & Hba1c level (6.87 ± 1.73 vs 6.23 ± 1.17) observed among group-A and B. Logistic regression analysis only VAT was significant predictor of fibrosis.

Conclusion: MAFLD patients with significant fibrosis compared to without significant fibrosis have older age, more likely diabetic and hypertensive with higher VAT, and higher water content, while patients without significant fibrosis has, higher BMI, total body fat%, SAT, muscle and bone mass.

Abstract Submission No. 100699
P-0268

Inter-cellular network analysis in tumor microenvironment during the progression of MASLD/MASH-HCC

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Immune checkpoint inhibitor (ICI) therapy is reportedly effective in several types of cancers. However, it has been reported that ICI therapy for MASLD/MASH-associated hepatocellular carcinoma (HCC) revealed little efficacy, suggesting that the anti-tumor immunity in the tumor microenvironment of MASLD/MASH-associated HCC might be distinct from other cancers. Therefore, clarifying the mechanism of MASLD/MASH-HCC pathogenesis and identifying novel therapeutic targets are anticipated. Although ICI therapy alone is not effective, combination therapy using ICI together with drugs targeting other cancer progression pathways might improve anti-tumor efficacy. In this study, to elucidate the tumor-promoting pathways in the MASLD/MASH-associated HCC, we tried to clarify the whole transcriptomic landscape of stromal cells and cancer cells in the tumor microenvironment of the MASLD/MASH-associated HCC. We performed single-cell RNA-seq on each cell type isolated from non-tumor and tumor tissues of 23 patients with non-viral HCC and the subsequent combined bioinformatics analysis using pseudotime analysis and interactome analysis to search for the tumor-promoting cell-cell interactions in the tumor microenvironment specific for non-MASLD-HCC and MASH-HCC during tumor progression. The results show the VEGFA-VEGFR2 interaction between cancer cells and endothelial cells in the non-MASLD HCC, which we think reasonable result that support the hyper-vascularity of HCCs and the effectiveness of VEGF inhibitors in clinical practice. On the other hand, in MASH-HCC specific interactome analysis, novel interactions were detected between the same cell types, suggesting that the molecular network is slightly different in MASH-HCC. We will present these unique interactions in the MASH-HCC and suggest the possibility for MASH-HCC treatment.

Abstract Submission No. 100763
P-0269

Prevalence of Depression in Chronic Liver Disease and its implications for Mortality

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Introduction: Depression is a pervasive mental health issue that often intersects with chronic health conditions, impacting individuals' overall well-being. This study explores the prevalence of depression in those with chronic liver disease (CLD) and its implications for mortality.

Methods: The current analysis uses data from the National Health Interview Survey 2005 to 2018. To account for inherent population sampling variance, the study uses survey analysis weightage for proper sample representation of the United States. Longitudinal survival was examined using survey weighted cox regression and competing risk mortality for cardiovascular and cancer related mortality.

Results: In total, 18,115 individuals were included in the study. Depression was identified to be in 1,144 CLD individuals. Individuals that were depressed were more likely to be older in age ($p < 0.001$),

females ($p<0.001$). Ethnicities, particularly a higher proportion of Asians, were more likely to be associated with depression ($p=0.003$). Interestingly, BMI and diabetes were not found to be significantly different between the two groups. Additionally, a higher proportion of depressed individuals were abstinent from alcohol use ($p<0.001$). In the analysis on overall mortality, individuals with depression were at a significantly higher risk of overall mortality (HR: 1.231, CI: 1.002 to 1.513, $p=0.047$) after adjusting for diabetes, smoking, ethnicities, region and alcohol use. This was similarly found in a competing risk analysis for cancer related mortality (SHR: 1.429, CI: 1.211 to 1.687, $p<0.001$) but not cardiovascular related mortality (SHR: 1.034, 0.738 to 1.450).

Discussion: The study reveals a substantial prevalence of depression in individuals with CLD and highlights its significant impact on overall mortality, particularly in the context of cancer-related mortality. These findings underscore the need for integrated healthcare strategies that address both mental and physical health in this population. Healthcare providers should consider these results when developing comprehensive care plans for individuals with CLD, recognizing the potential to improve their life expectancy and overall well-being.

Abstract Submission No. 100775
P-0270

Entacapone as an FTO Inhibitor: A Promising Repurposed Therapy for Steatotic Liver Disease

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Background and Objectives: Metabolic-associated steatotic liver disease (MASLD) is a prevalent chronic liver condition closely associated with metabolic disorders, including central obesity, dyslipidemia, hypertension, hyperglycemia, and persistent liver function abnormalities. The recently discovered Fat Mass and Obesity-Associated (FTO) gene has emerged as a genetic factor contributing to obesity. Nonetheless, the precise molecular mechanisms underlying the effect of FTO on obesity remain largely elusive. Recent insights from comprehensive genome-wide association studies have not only linked the FTO gene to human metabolic issues but also cancer, a condition closely tied to obesity. Furthermore, laboratory and computational investigations have shown that disrupting FTO's enzymatic activity of FTO leads to the dysregulation of genes involved in energy metabolism. In this study, entacapone, originally designed as a catechol-O-methyltransferase inhibitor for Parkinson's disease, was repurposed as an FTO inhibitor to treat MASLD in a mouse model.

Methods: Male C57BL/6/J mice were fed a high-fat and high-carbohydrate diet (HFHC) for 13 weeks to induce obesity. Subsequently, entacapone (at doses of 10 and 30 mg/kg body weight/day) or vehicle was administered intraperitoneally for 12 weeks. Fasting glucose levels, glucose tolerance, and insulin sensitivity were assessed. Liver histology, serum biochemical parameters, adiponectin levels, and hepatic FTO gene expression were evaluated using microscopy, ELISA, RT-qPCR, and immunohistochemical staining, respectively.

Results: The HFHC diet led to a significant increase in body weight and liver index scores compared to entacapone-treated mice ($p<0.0001$). The MASLD activity score (MAS) showed progressive increases ($p<0.0001$) associated with heightened steatosis, ballooning, and lobular inflammation in HFHC-fed mice. Additionally, periportal fibrosis was observed in the HFHC-fed mice. Impaired fasting glucose levels and glucose tolerance were evident after oral glucose testing. Key biochemical parameters, including alanine transaminase, aspartate transaminase, triglycerides, and total cholesterol, were significantly increased ($p<0.01$) in HFHC-fed mice. Serum adiponectin and FTO levels were significantly elevated ($p<0.0001$) in HFHC mice

compared to those treated with Entacapone. Immunohistochemical examination confirmed the increased nuclear expression of FTO in the livers of HFHC-fed mice, which decreased considerably following entacapone treatment. A progressive and significant ($p<0.0001$) increase in FTO gene expression was observed in the livers of HFHC-fed mice compared to that in treated mice.

Conclusion: This study revealed a progressive increase in FTO gene expression, elevations in crucial biochemical parameters, and a correlation with NAS scores as the disease progressed in HFHC-fed mice. Moreover, Entacapone treatment mitigated the progression of NAFLD in these animals, suggesting the potential repurposing of Entacapone for treating obesity and fatty liver disease.

Abstract Submission No. 100807
P-0271

RESMETIROM LOWERS LDL-CHOLESTEROL AND IMPROVES MASH IN A 3-WEEK MASH MOUSE MODEL

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Objectives: There is currently no marketed drug for the treatment of Metabolic Dysfunction-Associated Steato-Hepatitis (MASH). To expedite preclinical drug development, we have developed a mouse model fed a high fat/cholesterol/cholic acid diet with cyclodextrin in drinking water (HFCC+CDX diet) to favor hepatocyte cholesterol uptake and induce MASH within 3 weeks. To optimize future head-to-head comparison or drug combinations studies, we evaluated the efficacy of resmetirom, one of the most advanced drugs in clinical trials.

Methods: Male, 8-week-old, C57BL/6/J mice were fed the HFCC+CDX diet for 3 weeks. After 1 week, mice were randomized based on their plasma transaminases levels and body weight, then treated with vehicle or resmetirom 3 mg/kg. After 2 weeks of treatment, blood and liver were collected for biochemistry and histology analysis.

Results: Resmetirom did not alter transaminases levels but significantly reduces plasma total cholesterol and LDL-cholesterol levels (-27% and -37% respectively, both $p<0.001$ vs. vehicle). This LDL-lowering effect was associated with higher LDL-receptor (+39%) and lower apolipoprotein B (-17%) hepatic gene expression (both $p<0.01$). Resmetirom reduced hepatic triglycerides content (-25%, $p<0.01$) and significantly reduced NAFLD activity score through lower inflammation score ($p<0.01$), as well as lower IL-6 and IL-1b hepatic gene expression (both $p<0.05$). Resmetirom also showed anti-fibrotic effects as shown by a significantly lower % Sirius Red labelling.

Conclusion: Resmetirom lowers LDL-cholesterol, hepatic inflammation, and fibrosis in the 3-week MASH mouse model. This preclinical model will be useful to expedite preclinical drug development for the treatment of MASH.

Abstract Submission No. 100827
P-0272

Treatment with human placental extract ameliorates metabolic-associated fatty liver disease

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Background: Metabolic-associated fatty liver disease (MAFLD) is characterized by the intense deposition of fat globules in the hepatic

parenchyma. Uncontrolled MAFLD may develop into fibrosis, which could potentially progress to liver cirrhosis and hepatocellular carcinoma. We evaluated the effect of human placental extract (HPE) to prevent the progression of MAFLD to hepatic fibrosis and cirrhosis.

Methods: SHRSP5/Dmcr rats (spontaneously hypertensive rats/stroke prone) were fed a high-fat and cholesterol (HFC) diet for 4 weeks and screened for steatosis. A set of animals on HFC diet were treated with HPE (3.6 mg/kg body weight) subcutaneously thrice a week, and another set served as control. The animals were sacrificed at 12 weeks from the beginning of the experiment.

Results: The animals fed with HFC diet depicted well-developed fibrosis with bridging and early cirrhosis. Immunohistochemical staining for α -SMA and 4-hydroxy-2-nonenal (4-HNE) demonstrated activation of hepatic stellate cells and marked increase in lipid peroxidation, respectively. Staining for collagens type I and type III depicted marked deposition of newly formed collagen fibers in the hepatic parenchyma. Animals treated with HPE demonstrated significant reduction in biochemical and histopathological changes compared to the respective control group.

Conclusion: The results of the present study indicated that treatment with HPE could ameliorate MAFLD and might be suitable to use as a therapeutic agent to prevent the progression of steatosis to hepatic fibrosis and cirrhosis. Various cytokines, growth factors, anti-inflammatory agents, and antioxidant molecules present in HPE might contribute towards the amelioration of MAFLD.

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Abstract Submission No. 100863

P-0273

Macrophages release miRNA-enriched extracellular vesicles that are taken up by lipotoxic hepatocytes

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Introduction: Lipotoxicity and inflammation in the liver play a critical role in the development of nonalcoholic fatty liver disease (NAFLD). Extracellular vesicles (EVs) carry microRNAs (miRs) to modulate cellular crosstalk. Here, we investigated whether miR-223 can be transported from macrophages to lipotoxic hepatocytes via EVs.

Methods: To demonstrate that macrophages transfer EVs containing miR-223 to hepatocytes, we transfected macrophages with a Cy3-miR-223 mimic. Co-culture between the transfected macrophages and the palmitic acid induced-lipotoxic hepatocytes was performed on a transwell system for 24 hours, and miR-223 and its target genes in the hepatocytes was examined. EV uptake assay was also measured by labelling macrophage-derived EVs with MemGlow 488, and incubating them with lipotoxic hepatocytes. Low-density lipoprotein receptor (LDLR) in the lipotoxic hepatocytes was measured.

Results: We found that miR-223 was highly expressed in EV fractions from the transfected macrophages. Upon co-culture, the lipotoxic hepatocytes displayed Cy3 fluorescence and exhibited an increase in miR-223 levels and a decrease in miR-223 target genes, *FOXO3* and *TAZ*, as compared to the control group. Blocking EV secretion from macrophages with GW4869 led to reduced transfer of miR-223 to hepatocyte recipient cells. The MemGlow dye was transferred to lipotoxic hepatocytes when incubated with MemGlow-labeled EVs from macrophages. The results also suggested that LDLR played a partial role in facilitating EV uptake by lipotoxic hepatocytes.

Conclusions: Our results show that macrophages transfer miR-223 to lipotoxic hepatocytes predominantly by EV-dependent manner.

Abstract Submission No. 100898

P-0274

A Systematic Review for Adjusting High-fat/High-fructose Animal Models to Clinical Feature of NAFLD

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Background: The complexities of the etiology and pathophysiology of Non-alcoholic fatty liver disease (NAFLD) lead to difficulty in development of therapeutics. We aim to assess statistically the diet-related factors contributing to NAFLD progression using animal studies, which would inform both physicians and researchers for the management of patients and for their preclinical studies.

Methods: From both PubMed and Cochrane database, we searched NAFLD data through October 2022, focusing on high-fat, high-fructose diet (HFHFD) rodent model. We extracted the details for the compositions of diet and routes of intake, period of induction, and characteristics of rodents. And then, we conducted correlation analysis and multiple linear regression analysis among those variants.

Results: A total 161 data (116 articles) was final selected, which produced 14 independent variables. Unexpectedly, no variant significantly correlated with the progression of Non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH), while three factors were the key contributing factors in fibrosis progression under multiple regression analysis ($r = 0.717$, $p < 0.001$); as a relative portion by 40.2% of inducing period, 33.2% of fructose-derived calorie in the pellet, and 26.6% of the ratio of carbohydrate to fat in the pellet, respectively.

Conclusions: From current study, we confirmed the impact of fructose-rich diet in progression of NAFLD, especially by liver fibrosis, along with period of exposure. It would help us further to understand and design the strategy for clinical management and preclinical investigation of NAFLD in the future.

Abstract Submission No. 100899

P-0275

Identification of tumor-promoting secreted factors in the progression of steatosis-associated HCC

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Recently, the number of steatosis-associated hepatocellular carcinoma (HCC) patients has increased due to the expansion of the obese population worldwide. However, the details of the pathogenesis of steatosis-associated HCCs have not been fully understood, and thus the identification of molecules for appropriate diagnosis and therapeutic targets is an urgent issue. We previously identified that hepatic stellate cells (HSCs), which undergo cellular senescence due to obesity, provoke senescence-associated secretory phenotype (SASP) and secrete inflammatory cytokines, chemokines, and so on. We also previously

reported that senescent HSCs increase the production of PGE2 that suppresses the anti-tumor immunity by CD8+ T cells and IL-33 that stimulates ST2+ Tregs, creating a tumor-promoting microenvironment. However, other numerous secreted factors, which could be associated with the prognosis of steatosis-associated HCC, have not been cleared yet. In this study, we performed single-cell RNA-seq analysis on human non-viral HCC specimens and investigated which factors promote tumor progression by analyzing whole secreted proteins shown in the Human Protein Atlas focusing on the expressed genes of secreted factors from senescent HSCs. We narrowed the gene sets of secreted proteins using machine-learning that can determine how strongly each gene influences on the outcome of the disease, such as fibrosis or HCC, by changing parameters. Each identified gene can be applied to predict patients' prognosis by analyzing patients' real survivals. Our analysis will develop a potential analytical tool to identify a series of secreted factors that affect patients' prognosis. These factors could be utilized as prognostic markers of steatosis-associated HCCs.

Abstract Submission No. 100958
P-0276

Apolipoprotein J is associated with indole-mediated metabolism in hepatocytes

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Background: Indole, a metabolite derived from dietary tryptophan, is relevant to human non-alcoholic fatty liver disease (NAFLD) and shows potential in alleviating diet-induced NAFLD symptoms in mice. Indole is absorbed by hepatocytes and can be metabolized by the hepatic microsomal enzyme CYP2E1 (a member of the CYP450 family 2E) and the sulfotransferase enzyme SULT1A1 (a member of the sulfotransferase family 1A) to produce the uremic toxin indoxyl sulfate. Previous research from our group has demonstrated that Apolipoprotein J (ApoJ), a stress-induced molecular chaperone, plays a role in lipid-related metabolic disorders. This study aimed to investigate the relationship between indole levels and ApoJ content in hepatocytes and to explore the mechanisms by which ApoJ regulates the indole metabolic pathway in mice with diet-induced NAFLD.

Methods: To further examine how Apolipoprotein J specifically impacts liver metabolic function, we utilized iTRAQ quantitative proteomics analysis. We assessed the association between hepatic ApoJ levels and markers mediated by indole in the livers of diet-induced NAFLD mouse models. Additionally, in vitro experiments involved treating Huh7 cells with 400 μ M of indole for 24 hours, followed by western blot experiments to assess enzymes associated with indole.

Results: Our findings support the ability of ApoJ to induce hepatic damage and its association with the indole metabolic pathway and enzyme activation in hepatocytes. These modifications appear to be a result of the direct impact of metabolism on the liver.

Abstract Submission No. 100968
P-0277

Targeting Apolipoprotein J restores hepatic cholesterol balance via bile acid alternative pathway

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Background: Free cholesterol (FC) in the liver is crucially regulated through esterification to cholesteryl ester (CE) or conversion to bile acids (BA) to maintain hepatic cholesterol balance. Dysregulation of cholesterol balance can lead to metabolic-associated fatty liver disease (MAFLD). Previous research from our group revealed that targeting Apolipoprotein J (ApoJ) reduces hepatic cholesterol accumulation, in part, by inhibiting sterol-O acyltransferase 2 activity, thus preventing CE synthesis.

Methods: The mice were fed with high fat diet to induce MAFLD. The proteomic approach was applied to identify the pathways involved in hepatic pathogenesis. The metabolites in liver were analyzed by UPLC MS/MS.

Results: Previous research from our group revealed that targeting Apolipoprotein J (ApoJ) reduces hepatic cholesterol accumulation, in part, by inhibiting sterol-O acyltransferase 2 activity, thus preventing CE synthesis. In this study, we delved deeper into the role of ApoJ in hepatic cholesterol homeostasis using Omics approaches. Our findings demonstrated upregulation of CYP7B1, a key enzyme in the alternative pathway of BA synthesis, in these mice. Consequently, ApoJ knockout elevated Hepatic levels of primary bile acids, chenodeoxycholic acid (CDCA), and its secondary bile acid derivative, ursodeoxycholic acid (UDCA), synthesized through CDCA dehydroxylation.

Conclusions: These results suggest that ApoJ may serve as a potential therapeutic target for MAFLD by restoring the BA alternative pathway and maintaining hepatic cholesterol balance.

Abstract Submission No. 101034
P-0278

Strenuous Exercise Was Not Associated With Reduction of Fatty Liver in Adolescents and Young Adults

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Background: Hepatic steatosis, or fatty liver (FL), is a common cause of chronic liver disease. This study aims to determine the prevalence of FL in the younger population (ages 14-30 years) and determine risk factors for FL. Liver biopsy is the gold standard to diagnose FL. However, it entails risks and is costly. Transient elastography (TE) is a less expensive, noninvasive alternative. This study uses TE to measure hepatic steatosis and fibrosis.

Methods: Non-consecutive subjects, ages 14-30 years, were recruited from November 2022-September 2023 and underwent liver TE, using the Fibroscan 230 Echoscanner Paris, France. FL was defined as a Controlled Attenuation Parameter (CAP) score of ≥ 238 dB and significant fibrosis was defined as a fibrosis score of F2 or greater (≥ 7.5 kPa). Body mass index (BMI) was calculated. Weekly moderate to strenuous exercise, diet, alcohol intake, and demographics were self-reported.

Results: 59 out of 241 subjects (24.5%) had FL. On an unadjusted model, subjects who exercised for 2.5+ hours weekly had a lower prevalence of FL compared to subjects who exercised less than 2.5 hours weekly (41% vs 59% $p=0.039$). However, when adjusted for BMI, this association was no longer significant ($p=0.24$). FL prevalence was significantly associated with BMI (Underweight 0%, Normal weight 8.5%, Overweight 28.1%, Obese 83.3%).

Conclusions: BMI remains the main predictor of FL in our young subjects. Exercise is not an independent predictor of absence of FL.

Abstract Submission No. 101117

P-0279

Iron Overload Aggravates Liver Injury in Progression of Non-Alcoholic Steatohepatitis

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Background: Non-alcoholic steatohepatitis (NASH) is a progressive form of non-alcoholic fatty liver disease (NAFLD) that causes cirrhosis and hepatocellular carcinoma. Evidences from animal studies and NASH patients have demonstrated that iron overload is a hallmark of NASH. However, the impact of iron overload in the progression of NASH is still need further studied. The purpose of this study is to investigate the relation of iron overload with liver injury in various stages of NASH.

Methods: Various stages of NAFLD mouse model were established by feeding male C57BL/6 mice a methionine-choline deficient-diet for 4, 8 and 12 weeks, respectively. The liver iron content and serum biochemistry were detected. Liver histopathology assessment, including H&E, Oil-red O and Sirius red staining, were conducted. NAFLD Activity Score (NAS) was assessed based on the analysis of liver histopathology.

Results: The liver iron content was related with the level of serum ALP, AST, ALT, total bilirubin and direct bilirubin. When the iron content was increased, the serum markers of liver function were also elevated. The correlation coefficients were between 0.6 and 0.8. There was a positive correlation of hepatic iron content and NAS, with the correlation coefficients was 0.752. With the progression of NASH based on NAS, hepatic lipid peroxidation-associated malondialdehyde (MDA), which was the oxidative stress marker in ferroptosis, was also significantly elevated.

Conclusions: This study demonstrates that the hepatic iron overload related with the liver injury with the progression of NASH. It provides a potential direction for future research in NAFLD treatment strategies.

Abstract Submission No. 101124

P-0280

Regulation of BHMT by LRH-1 in methionine cycle of liver

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Betaine-homocysteine S-methyltransferase (BHMT), one of the most abundant proteins in the liver, is involved in the regulation of homocysteine metabolism. Generally, decreased BHMT gene expression leads to homocysteine accumulation in the liver, which can induce mitochondrial stress. However, the molecular mechanism of *Bhmt* transcription has not been elucidated. This study outlines the mechanism of *Bhmt* is mediated by liver receptor homolog-1 (LRH-1), and the effect of BHMT deficiency in liver causes methionine disorder. During fasting, both *Bhmt* and *Lrh-1* expressions increased in the liver of normal mice, but *Bhmt* expression was decreased in LRH-1 liver specific knockout (LKO) mice. In addition, the lipid peroxide content in the liver tissues of LRH-1 LKO mice was increased. Promoter activity analysis confirmed the binding of LRH-1 to a specific site at +131/+137 bp of the mouse *Bhmt* promoter. LRH-1 deficiency is associated with elevated reactive oxygen species (ROS) production, lipid peroxidation, and mitochondrial stress in hepatocytes. In conclusion, this study suggests that lack of LRH-1-mediated decrease in *Bhmt* expression, promotes triglyceride accumulation by increasing ROS

levels and inducing mitochondrial stress via disrupted methionine cycle. Understanding these regulatory pathways may pave the way for novel therapeutic interventions in metabolic disorders associated with hepatic lipid accumulation.

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Abstract Submission No. 101161

P-0281

Pharmacological Mechanism of Gegen-Qinlian in Preventing NAFLD

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Background: Traditional Chinese Medicine (TCM) has shown potential treatment to Non-alcoholic fatty liver disease. The study aims to use network pharmacology to explore the pharmacological mechanisms of Gegen Qinlian decoction (GQD) in treating NAFLD.

Methods: The study found four herbs' ingredients and targets from TCMID and PharmMapper to construct interaction networks. Microarray data from 87 NAFLD patients informed the protein-protein interaction (PPI) and molecular docking, which evaluated ingredient-target interactions.

Results: 619 differentially expressed genes were obtained through GeneCards and GSE151158 chip as the NAFLD target prediction dataset. By intersecting with the effective component target gene set of GQD, the drug treatment targets for NAFLD were identified as CASP8, CASP3, PLA2, BCL2, AHR, RELA, PPARG, IL6, MCL1, GABPA1. We constructed the drug-active component-target synergistic network to analyze the relationship among the drugs, active components, and targets for NAFLD disease. We found baicalein, β -sitosterol, and musk flavonoids were docked with the effective target points BCL2, PPARG, TGR5, NF- κ B, and MPK7 respectively by molecular docking. We fed the high-fat and high-fructose (HFHF) diet NAFLD mice models for 16 weeks, and the GQD group was orally administered for 8 weeks. In the GQD group, there was a significant improvement in the NAS score compared to the HFHF group ($P < 0.0001$), steatosis change ($P = 0.009$), lobular inflammation change ($P = 0.002$), ballooning change ($P < 0.0001$), and fibrosis improvement ($P = 0.018$). In terms of ALT and AST, the GQD group showed improvement compared to the HFHF group ($P = 0.0412$, $P = 0.0128$).

Conclusion: By network pharmacology and post-validation, GQD can improve histological changes in NAFLD.

Abstract Submission No. 101177

P-0282

miR-4449 modulates the progression of NASH-induced fibrosis by regulating the merlin-TAZ pathways.

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Background and Aim: While the majority of patients with non-alcoholic fatty liver disease (NAFLD) exhibit benign clinical courses, those with non-alcoholic steatohepatitis (NASH) accompanied by hepatic fibrosis experience poor prognoses compared to individuals with non-alcoholic fatty liver (NAFL) or NASH without hepatic fibrosis. This study aimed to investigate the role of miR-4449 in the progression of NASH-induced fibrosis.

Method: Liver tissue and sera were obtained from NAFLD patients who underwent liver biopsies at Korea University Guro Hospital. MicroRNA sequencing was performed using sera, and mRNA sequencing was conducted using liver tissue from patients with biopsy-confirmed NAFLD. In vitro lipotoxicity was induced in mouse hepatocytes (HepG2 and Huh7 cells) by treating them with palmitic acids (PA).

Results: A total of 24 NAFLD patients were recruited, with 15 having NAFL or NASH without fibrosis, and nine presenting with NASH accompanied by fibrosis. MiRNA sequencing analysis revealed significant differences in the expression levels of 31 miRNA sequences between the two groups, with miR-4449 exhibiting the most prominent upregulation in NASH-fibrosis compared to the NAFL or NASH without fibrosis group. PA treatment increased the expression level of miR-4449 in both supernatant and hepatocytes. Conversely, the expression of merlin, a potential target of miR-4449, decreased in PA-treated hepatocytes compared with vehicle-treated hepatocytes. Additionally, merlin expression levels significantly decreased in NASH patients with fibrosis compared to those without fibrosis.

Conclusion: MiR-4449 was found to regulate merlin expression and TAZ phosphorylation in hepatocytes during lipotoxicity. Thus, miR-4449 may serve as a promising novel therapeutic target in NASH-fibrosis.

Abstract Submission No. 101260

P-0283

Plasma and liver EFEMP1 are elevated in morbidly obese subjects with early fibrosis in MASLD

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Background: A quarter of adult population worldwide suffers from metabolic dysfunction-associated steatotic liver disease (MASLD). Fibrosis is the best predictor of liver-related risk in persons with MASLD. Using *in silico* methods, we discovered circulating biomarkers associated with fibrosis development and validated their specificity in a MASLD-biopsy proven cohort.

Methods: GSE125251 RNAseq dataset was re-analyzed using the bioinformatics pipeline by comparing F0-F1 (early fibrosis, n=139) vs. F2/F3-F4 (moderate/advanced fibrosis, n=67) liver transcriptomes in MASLD subjects. Differentially expressed genes (DEGs) were filtered, selecting only plasma-secreted protein-coding genes through an *in silico* funnel strategy. Expression of the best-ranked genes was analyzed in liver samples of a morbidly obese cohort (n=65) stratified according to fibrosis. Plasma levels of best candidates was assessed using ELISA.

Results: 106 DEGs were detected and 22 of them individuated as candidates coding for plasma-circulating proteins. The five best-ranked candidates were tested by qPCR (*EFEMP1*, *LTBP2*, *LUM*, *DPT*, *CCL20*). *EFEMP1* mRNA level was 1.11 ± 0.30 folds higher in F2/F3-

F4 than F0/F1 livers (p-value <0.005). Plasma EFEMP1 was also increased with fibrosis (21.85 ± 4.18 ng/mL in F2/ F3-F4 respect to 7.114 ± 1.26 ng/mL in F0-F1, (p-value <0.005).

Conclusion: EFEMP1 is a secreted ECM protein, expressed by fibroblasts, with a role in the maintenance of ECM stability. Our data indicates EFEMP1 plasma levels as a potential marker of hepatic fibrosis during MASLD.

Abstract Submission No. 101277

P-0284

Hypoxanthine plasma concentration changes in MASH and its role as a biomarker of steatohepatitis

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Background: Plasma hypoxanthine (HypX) was reported as a putative marker of Metabolic-Dysfunction Steatotic Liver Disease (MASLD). Here we aimed to characterize changes in HypX pool in blood, liver, and Visceral Adipose Tissue (VAT) by evaluating the main genes/enzymes involved in purine catabolism.

Methods: HypX concentration was quantified in plasma, liver, and VA tissues in 132 MASLD biopsy-proven subjects stratified in fatty liver (MASL) and steatohepatitis (MASH) using a fluorometric enzymatic method and also using HPLC in a subset of samples (n=40). Several clinical-biochemical-histological parameters were correlated with plasma and intracellular HypX levels. Expression for purine catabolism genes by qPCR and xanthine oxidoreductase (XDH) activity analysis was also performed.

Results: Plasma HypX was reduced in MASH patients (2.0 [IQR $1.16-3.0$] in MASL vs. 0.8 [0.5-1.9] in MASH, p-value <0.0001) both enzymatic and HPLC assessment. Plasma HypX receiver operating characteristics curve analysis demonstrated an accuracy of 0.75 for MASH diagnosis. Significant correlations among HypX levels and lobular inflammation ($\rho = -0.23$; $p = 0.010$), ballooning ($\rho = -0.48$; $p < 0.0001$), fibrosis ($\rho = -0.33$; $p = 0.0006$), GGT ($\rho = 0.18$; $p = 0.04$), and triglycerides ($\rho = 0.22$; $p = 0.017$) were observed. Changes in gene expression were significant only in VAT of MASH patients (XDH: 18.0 ± 13.2 MASL vs 1.5 ± 9.0 MASH; PNP: 0.3 ± 0.6 MASL vs. 1.3 ± 0.9 MASH; HPRT: 11.4 ± 13.7 MASL vs. 1.8 ± 6.2 MASH, all $p < 0.01$).

Conclusions: Plasma hypoxanthine could be used as a biomarker of steatohepatitis in MASLD. Our data indicate that VAT might contribute to the hypoxanthine pool changes observed in subjects with MASLD.

Abstract Submission No. 101377

P-0285

Investigating the Interactome of Apolipoprotein J under Lipid Stress

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Background: Previously, our group successfully identified the pathological role of Apolipoprotein J (ApoJ) in hepatic lipid deposition. When faced with nutrient overload, ApoJ stabilizes sterol-O acetyltransferase 2, promoting the synthesis of cholesteryl ester, while concurrently hindering lipophagy through its interaction with mTOR.

Given ApoJ's chaperone activity, it stands as a potential master regulator for maintaining intracellular homeostasis when cells encounter nutrient stresses. This study establishes an ApoJ interactome to gain a deeper understanding of the pathogenesis associated with ApoJ.

Methods: A flag-tagged ApoJ is utilized for immunoprecipitation-mass spectrometry (IP-MS) analysis. The immunoprecipitate undergoes LC/MS/MS analysis to identify the client proteins of the ApoJ chaperone. The pathways associated with ApoJ are identified through GO and KEGG analyses.

Results: A total of 1701 proteins were identified as putative client proteins of ApoJ. Among these, 114 proteins (Protein dataset 1) were exclusively detected in cells without lipid stress, whereas 45 proteins (Protein dataset 2) were specifically found in cells subjected to oleic acid treatment. Subsequent GO and KEGG analyses revealed that Protein dataset 1 is associated with proteasomal pathways and ubiquitination functions, while Protein dataset 2 encompasses proteins involved in autophagy, fibrosis, mitochondrial function, and the electron transport chain.

Conclusions: Our data suggest that ApoJ interacts with specific client proteins in response to nutrient stresses. Under nutrient stress conditions, ApoJ enhances the stability of client proteins associated with mitochondrial function, thereby promoting pathogenesis by inhibiting proteasomal and ubiquitination pathways.

Abstract Submission No. 101388
P-0286

The CHOL-to-CE conversion regulates cellular senescence in primary human hepatocytes with steatosis

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Background and Aims: Metabolic-associated fatty liver disease is long-term dysfunctional progression involving complex mechanisms and multiple factors, including aging. However, the changes of lipid metabolism in normal human hepatocyte remained uncovered using an *in vitro* model of aging. In this study, we monitored the lipid changes in association with young to senescence in primary human hepatocytes (PHH) by multi-omic analysis.

Method: The first, we characterized the phenotypes of senescent PHH and middle-aged mice with the cell-cycle biomarkers, and senescence phenotypes. Next, we analysed the changes of metabolic gene expression and lipid contents by integrated transcriptomic and lipidomic analyses. Finally, we investigated the pathogenic effects of cholesterol-to-cholesteryl ester (CE) remodelling in PHHs treated with the inhibitor, TMP-153 to block sterol O-acyltransferase (SOAT) activity.

Results: The PHHs were monitored the expression of senescent biomarkers, telomere length, DNA damage and lipid content, then classified into three stages by different passages, including young (P3~P5), early senescence (P7~P9) and late senescence (P11~P13). With transcriptomic analysis, the metabolic differentially expressed genes in senescent PHH were determined, revealing the genes (P8-vs.-P4 and P12-vs.-P8) in glycerolipids metabolism, glycerophospholipids metabolism and steroid biosynthesis. In lipidomic results, the percentage of glycerophospholipids was decreased in P8 PHHs but reversed in P12, meanwhile, those regulatory patterns for CE were mirrored. Finally,

the SOAT1 protein was decreased in PHHs during aging and the TMP-153-treatment promoted hepatic senescence and lipid accumulation.

Conclusion: Lipid metabolic modulation between cholesterol-CE might occur as the initial hepatic senescence and provide potential therapeutic targets for combating age-related hepatosteatosis.

Abstract Submission No. 101404
P-0287

The effects of senolytic drugs on primary human hepatocyte with lipid droplet accumulation

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Background and Aims: Metabolic-dysfunction associated fatty liver disease (MAFLD) is characterized by lipid accumulation, which might be accelerated by hepatic cellular senescence. In this study, we investigated the effects of senolytic drugs on primary human hepatocyte (PHH) with lipid droplet accumulation.

Method: First, the cultivated PHH was induced to lipid droplet accumulation with fatty acid overload and the changes of transcriptome were examined for 1 day or 3 days. Next, the effects of senolytic drugs, quercetin or curcumin were assessed.

Results: The lipid droplets consisting of increased triglyceride and cholesteryl ester were accumulated in oleic acid (OA)-treated PHH at day 1 and day 3 post-treatment. The differently expressed genes involved in cellular senescence were revealed in OA-treated PHHs with delayed time at day 3. Treatment with senolytic drugs reduced p16/p27 but not p53/p21 in a manner with the replicative senescent signaling pathways.

Conclusion: The senolytic drugs might be potentially effective in the development of therapeutic treatment for MAFLD.

Abstract Submission No. 101411
P-0288

Creation of humanized mice models of advanced SLD via patient-derived fecal microbiota transplants

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Background: Gut microbiota is increasingly recognized as a contributing factor in the etiology of steatotic liver disease (SLD). Humanized mice models can better understand the causal associations of gut microbiome and SLD pathology. The study aims to explore if a single gavage was sufficient for stable establishment of the humanized microbiota with advanced SLD histopathological features.

Methods: Six-week-old C57BL/6J male mice received either standard food and water (SF) or a high fat high cholesterol diet, and fructose and glucose water (HFHC). Mice were given 3 courses of 7 days of antibiotics (ampicillin, cefazolin, clindamycin, ertapenem, neomycin, vancomycin) for 3 weeks, then a single gavage of 100uL fecal microbiota transplant (10^9 CFU) prepared anaerobic from patients with advanced SLD. Body weight, blood, spleen and liver was sampled every 4 weeks.

Results: Weight gain was attributed to the HFHC diet (Fig1A), with hepatic steatosis and lobular inflammation seen as early as 8 weeks into the diet. After 28 weeks of HFHC diet exposure, the mice had significantly larger spleens ($p<0.01$), livers ($p<0.01$) with higher serum bilirubin and ALT ($p<0.01$) and the perisinusoidal and pericellular hepatic fibrosis was present. At 34 weeks, HFHC-fed mice previously treated with antibiotics had significantly lower intensity and areas of fibrosis, whereas mice post FMT had significantly higher intensity and areas of fibrosis.

Conclusion: HFHC diet propagates liver steatosis. Gut microbiota is required in SLD progression toward steatohepatitis and fibrosis. A humanized mice model of microbial-driven steatohepatitis can be established with a single gavage of fecal microbiota transplant.

Abstract Submission No. 101417
P-0289

Plasma Metabolomic Signatures in Patients with Varying Histological Severity of MAFLD

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Background: MAFLD represents a spectrum of liver disease: steatosis, steatohepatitis, fibrosis and cirrhosis. Patients with MASH and/or fibrosis are at greatest risk of liver and cardiovascular morbidities. With no adequate non-invasive biomarkers, physicians remain reliant on liver biopsies to diagnose MASH. Furthermore, MAFLD in the Asian cohort is understudied. We aim to identify unique circulating lipidomic signatures for MASH and fibrosis in a multi-ethnic cohort of patients from Singapore.

Methods: A targeted approach, using LC-MS/MS on low and high-resolution mass spectrometers, was used to quantify 243 plasma lipids from 164 patients (12 controls, 32 simple steatosis, 41 incomplete MAFL, 36 MASH and 43 advanced fibrosis) paired with liver biopsies. The lipids associated with different stages of MAFLD were identified using multivariate linear regression whilst adjusting for clinical variables such as age and sex.

Results: 7 class of lipids (primary and secondary bile acids, ceramides, cholesterol esters, Hex2Cer, phosphatidylethanolamine, sphingomyelins) were found to be differentially abundant amongst patients with varying severity of MAFLD (Fig1A). Liver histological presence of

steatosis (qval 0.03), lobular inflammation (qval 0.01), ballooning (qval 0.01) and fibrosis (qval 0.02) significantly contributed to the variance of the plasma metabolome (Fig1B). A total of 113 metabolites significantly correlated with liver histology, with enrichment of 22 ceramides associated with lobular inflammation, 10 phosphatidylinositols for ballooning, 8 primary bile acids for fibrosis (Fig1C).

Conclusions: Patients with varying histological severity of MAFLD exhibit unique circulating lipidomic signatures with potential as surrogate markers to determine at risk MAFLD patients with MASH and significant fibrosis.

Abstract Submission No. 101463
P-0290

Gut Microbiome and Body Composition in Patients with Steatotic Liver Diseases

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Objective: Disturbances in gut microbiome have been implicated in the pathophysiology of steatotic liver disease (SLD). This study explores the association between gut microbiome and varying body compositions in patients with SLD.

Methods: We collected stool samples in the National University Hospital, Singapore from 83 patients (mean age 46.9 years-old, 56.2% male) undergoing diagnostic liver biopsy and AMRA body constitutional profiling. Stool samples underwent shotgun sequencing, and subsequent taxonomic and functional profiling using the BioBakery v3 metagenomic pipeline. Using spearman correlation, we identified putative microbial features with SLD-associated body composition indices.

Results: Patients with SLD have significantly elevated liver fat ($p<0.01$), subcutaneous fat ($p=0.03$) and visceral fat ($p<0.01$). Amongst patients with SLD, there is a parabolic relationship with subcutaneous fat and muscle mass; positively associated with mild SLD (i.e. simple steatosis) and negatively associated with fibrotic SLD, whereas visceral fat remains elevated amongst advanced SLD. Twenty-two microbial taxa were significantly correlated with body composition indices. Of note, pro-inflammatory Proteobacteria species (*Escherichia coli*, *Klebsiella* species) and anti-inflammatory Collinsella intestinalis were positively correlated with visceral fat ($q=0.03$) and muscle mass respectively ($q=0.04$).

Conclusion: Our study demonstrated significant differences in microbial taxonomic associated with varying body compositions in patients with SLD, highlighting the potential role of gut microbes in energy regulation, fat storage and muscle mass.

Abstract Submission No. 101469
P-0291

MLKL ATP binding inhibitor attenuated inflammatory response via necroptosis independent pathway.

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Background: The inhibition of the adenosine triphosphate (ATP) pocket in the pseudokinase domain of Mixed Lineage Kinase Domain Like Protein (MLKL) has been observed to have no impact on necroptosis-induced cell death. Recent investigations have highlighted the MLKL independent non-classical MLKL pathway such as NF- κ B-dependent pathway. This study aims to explore the potential anti-inflammatory effects of Compound-4 (CPD-4) in a model of fatty liver disease.

Method: CPD-4, a selective ATP-binding compound, was administered to U937, HT29, and Jurkat T cells, respectively. Necroptosis was induced using SMAC mimetic, zvad-fmk, and TNF- α . Cell viability was assessed using MTT and flow cytometry. The impact of CPD-4 on TNF- α -induced regulation of ICAM-1 and VCAM-1, as well as its inhibitory effects on CXCL1 and CXCL2 expression, were examined through PCR and western blot.

Results: Following the induction of necroptosis, the survival rate of HT29 and U937 cells significantly decreased. In contrast, RAW cells did not undergo cell death after inducing necroptosis. RAW cells exhibited hypermethylation and, unlike U937 cells, evaded cell death in response to necroptosis stimuli. RAW cells did not undergo MLKL phosphorylation but demonstrated activation after necrotic stimulation. Following demethylation, RAW cells induced necrosis-associated cell death. The MLKL ATP pocket-binding inhibitor did not prevent cell death induced by necroptosis but did reduce the expression of CXCL2, ICAM, and VCAM resulting from necroptosis by inhibiting the IKK β and NF κ B pathways.

Conclusion: Although CPD4 cannot inhibit necroptosis, the MLKL ATP-binding inhibitor attenuated the inflammatory response via a necroptosis-independent pathway.

Abstract Submission No. 101559
P-0292

Gemigliptin alleviates succinate induced ER stress and activation of hepatic stellate cells

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Background: Hepatic stellate cells (HSCs) activation is the principal event in the development of liver fibrosis in which succinate-GPR91 signaling has recently been shown to be a contributor. Moreover, endoplasmic reticulum (ER) stress has been reported to involve in HSC activation, but its association with succinate in pathogenesis of fibrosis remains scarce. In this study, we investigated the role of gemigliptin, an antidiabetic dipeptidyl peptidase (DPP)-4 inhibitor, in the succinate-induced ER stress and activation of HSCs.

Methods: LX-2 cells were treated with succinate and gemigliptin. For animal experiments, C57BL/6N mice were divided into 3 groups: control diet, high-fat-high-cholesterol (HFHC) diet, and HFHC diet mixed with gemigliptin.

Results: Succinate significantly induced HSC activation and the increase in the migration of HSCs. The treatment of succinate also caused ER dilation and activated the unfolded protein response (UPR) signaling as PERK, eIF2 α , Bip, suggesting increasing ER stress in HSCs. Moreover, the exposure of HSCs to tunicamycin, an inducer of ER stress, promoted the expression of α -SMA, proliferation of HSCs. In vivo, the level of fibrotic and ER stress markers was increased in

mice fed with HFHC diet and the administration of gemigliptin improved these changes in HFHC-induced mice.

Conclusion: This study showed the involvement of ER stress in the activation of succinate-induced LX-2 HSCs and gemigliptin significantly reduced ER stress in HSC activation. Therefore, gemigliptin may become an anti-fibrotic agent and targeting to succinate and ER stress may be a promising therapeutic in the management of liver fibrosis.

Abstract Submission No. 101603
P-0293

Relation of BMI, hepatic steatosis, and insulin resistance on NAFLD in T2DM

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Introduction: Body mass index (BMI) affects controlled attenuation parameter (CAP) assessment using FibroScan and insulin resistance. The prevalence of NAFLD is increasing with obesity and type 2 diabetes (T2DM). NAFLD or simple steatosis is a liver condition where there is predominant accumulation of triglycerides in the liver without inflammation or hepatocellular damage. Insulin resistance (IR) and homeostatic model assessment of insulin resistance (HOMA-IR), a marker for IR, has been associated with NAFLD.

Objective: This study aimed to determine the relation of body mass index, hepatic steatosis, and insulin resistance of NAFLD in T2DM in Mohammad Hoesin Hospital Palembang.

Method: This is a cross-sectional study involving 52 T2DM patients, done at Mohammad Hoesin Hospital Palembang from January to April 2023. Laboratory, fibroscan, and ultrasonography examination were done on each patient.

Results: 52 T2DM patients consist of 23 male (44.2%) and 29 female (55.8%) with an average age of 58.98 $\pm$ 8.84 years, from which 10 participants were overweight (19.2%) and 21 participants were obese (40.4%). HOMA-IR is a marker to measure insulin resistance and the median of HOMA-IR was 13.447 $\pm$ 16.01 (significant insulin resistance). The prevalence of NAFLD was 55.77% and mean of controlled attenuation parameter (CAP) was 266.25 $\pm$ 77.99 dB/m. The result showed there is a correlation between BMI with CAP ($p = 0.001$, $r = 0.342$) and insulin resistance ($p = 0.024$, $r = 0.237$). There is correlation between insulin resistance and NAFLD in this study ($p < 0.001$).

Conclusion: In this study, BMI is associated with the presence of NAFLD and insulin resistance in T2DM patient.

Abstract Submission No. 101673
P-0294

Role of Hepatic Activin in the glucose metabolism

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Background: We found that Activin, one of TGF β superfamily

proteins, is produced in the liver and has glucose lowering effect in mice. To explore the mechanism whereby Activin improves glucose metabolism, we have performed some experiments in vitro and in vivo. **Methods:** To investigate the effect of Activin in glucose metabolism in cultured hepatocyte, we treated cultured hepatocyte with recombinant protein of Activin and looked up the changes of the expression genes by Q-PCR analysis.

Next, we overexpressed Activin in liver of B6 mice by adenovirus mediated gene transfer, and performed pyruvate tolerance test. We also performed glucose tolerance test using the model mice of type 1 diabetes.

Results: We found that the expression level of G6Pase and PEPCK, key regulators of gluconeogenesis, was dramatically suppressed by treatment with recombinant Activin in primary hepatocyte.

During pyruvate tolerance test, mice overexpressing Activin exhibited significantly lower glucose levels, indicating the suppression of gluconeogenesis by Activin.

Interestingly, suppressive effect of gluconeogenic genes by Activin was also observed in the liver of mice treated by Streptozotocin (model mice of type 1 diabetes). As a consequence, overexpression of Activin resulted in dramatic improvement of glucose tolerance even in the model of type 1 diabetes.

Conclusions: Activin has glucose lowering effect by suppression of hepatic gluconeogenesis. Enhancing the action of Activin in the liver can be a strategy of the treatment for diabetes.

Abstract Submission No. 101728

P-0295

ShenZhu XiaoJi Formula modulates tumor metabolism and immune infiltration in NASH-induced HCC

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With the rapid growth of morbidity, non-alcoholic steatohepatitis (NASH) has become the fastest-growing etiology of hepatocellular carcinoma (HCC). Of note, compared to HCC with other etiology, NASH-induced HCC (NASH-HCC) presents distinct metabolic dysfunction and deteriorative tumour immune escape in response to the immune checkpoint therapy (PD-1/PD-L1). ShenZhu XiaoJi Formula (SZXJF), a herbal prescription of Traditional Chinese Medicine, has been used for treating NASH and NASH-HCC with clinical effectiveness, but the mechanisms are largely unknown. Herein, we aim to investigate the therapeutic effect and mechanism in mouse model of NASH-HCC. As results, SZXJF treatment effectively ameliorated serum lipid and glucose content, hepatic lipid accumulation, lobular inflammation, liver injury and reduced the tumor number in NASH-HCC. Mechanistically, transcriptome analysis revealed that SZXJF might regulate metabolic pathways, cytokine-cytokine receptor interaction and NF- κ B signalling. MMP12 represented a significant change among the DEG, of which the high level was estimated to correlate with increased macrophage infiltration, reduced effector CD8⁺ T cell and increased expression of exhausted CD8⁺ T cell markers in human NASH-HCC. Consistently, we verified that SZXJF treatment down-regulated hepatic MMP12 protein level, inhibited NF- κ B/p65 activation and increased CD8⁺ T cell infiltration compared to the model group of NASH-HCC. Meanwhile, protein expressions of Ki67, PDCD1, TIGIT1, and TREM2 were downregulated in the tumour tissue of mouse liver, showing an immune microenvironment remodeling in NASH-HCC. Collectively, our findings demonstrated that SZXJF intervention could improve NASH-HCC potentially through

regulating metabolic reprogramming and immune microenvironment remodelling via MMP12/NF- κ B signalling, providing a new therapeutic strategy for NASH-HCC treatment.

Abstract Submission No. 101794

P-0296

State of knowledge of type 2 diabetic patients about NAFLD

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Background: Non-alcoholic-fatty-liver-disease(NAFLD) is common in type2 diabetics. The aim of this study is to evaluate the knowledge of type2 diabetics regarding NAFLD and to determine the relationship between their personal characteristics and their level of knowledge.

Patients and Methods: This is a prospective study extending from March 2022 to September 2023.

A questionnaire was completed by 278 type2 diabetics.

Results: The average age was 57.2years with a sex-ratio(M/F) of 2.16. The mean duration of diabetes was 4.2years, with a mean glycated-hemoglobin(HbA1c) of 7.3%.

Average BMI was 26.2.

NAFLD was present in 22%(N=61) of patients, while 16.5%(N=46) had NASH.

40%(N=112) said they'd never heard of NAFLD, and 89.5%(N=249) said they didn't know the difference between NAFLD and NASH.

According to the participants, the main risk factors for NAFLD were: obesity(90%), dyslipidemia(68.3%), diabetes(45%), high blood pressure(21.5%) and certain medications(10.7%).

28% knew that NAFLD corresponds to the accumulation of fats in the hepatocytes, 31.2% that screening was based on abdominal ultrasound and blood tests, 9% that the diagnosis of certainty was made by liver biopsy and 4.3% knew the risk of progression to cirrhosis and hepatocellular carcinoma.

56% reported that NAFLD was reversible, and that treatment was based on physical activity and a change in dietary habits.

Better knowledge of NAFLD was significantly associated with younger age(p=0.03), higher level of education(p=0.002) and history of NAFLD(p<0.001).

Conclusion: It's vital to improve type2 diabetic patients' knowledge of NAFLD, thus enabling better adherence to treatment, a change in dietary habits and the fight against sedentary lifestyles.

Abstract Submission No. 101809

P-0297

Metabolic and pathogenic regulations in hepatocytes with large and small lipid droplet accumulation

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Background and aims: Metabolic-associated fatty liver disease (MAFLD) is characterized by the hepatic accumulation of lipid droplet

(LDs), which were visualized as large and small particles in size. In this study, the pathogenic roles of individual large and small LDs were investigated.

Method: First, the expression patterns of LD markers, perilipins (PLIN2 and 3), were examined with immune-stain in liver tissues of MAFLD patients. Next, the primary human hepatocytes (PHH) with induction of LD accumulation of either large sizes by oleic acid (OA) or of small sizes by TMP-153 were established. The metabolic and pathogenic regulations were examined by transcriptomic analysis, qRT-PCR, western blotting and lipid quantification.

Results: The large LDs displayed PLIN2 decoration on the surface and colocalization with Mallory-Denk bodies in ballooned hepatocytes of the liver tissue, whereas the small LDs were scattered in the cytosol in association with PLIN3. In the PHH with large LDs accumulation, the expressions of PLIN2 and p62 were upregulated, accompanied by the activation of genes involving beta-oxidation and triglyceride synthesis but inhibition of glycolysis. Meanwhile, the PHH with small LDs, the expression of PLIN3 was upregulated, accompanied by the inhibition of triglyceride hydrolysis. The fibroblast-activation protein (FAP) exhibited increases in both groups of PHH but to a greater extent in those induced with small LDs.

Conclusion: The large and small LDs exhibited distinct phenotypes regarding metabolic modelling and might indicate the individual pathogenic role in the progress of MAFLD.

Abstract Submission No. 101901

P-0298

Oxidized HDL is a potential biomarker of hepatic and coronary events in patients with MASLD

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Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common liver diseases. Patients with MASLD are complicated with cardiovascular diseases (CVDs). Although the mortality caused by CVDs differs among studies, CVDs are one of the most common causes of death in patients with MASLD. We have previously reported that oxidized high-density lipoprotein (oxHDL) was associated with liver fibrosis markers. However, the association between oxHDL and CVDs remains unknown. We herein expanded the previous study and investigated the association between oxHDL and CVDs.

Method: A total of 170 patients with MASLD were enrolled. Blood counts and chemistry were examined. Liver fibrosis was assessed by a non-invasive scoring system, including the FIB-4 index and NAFLD fibrosis score (NFS). The characteristic variables were collected based on the clinical records.

Results: Among 170 subjects, the prevalence of MASLD, history of CV events, and hepatic events were 138 (81%), 13 (8%), and 16 (9.4%), respectively. The levels of oxHDL were significantly higher in patients with MASLD. The median of oxHDL in non-MASLD and MASLD groups were 86.5 U/L (35.7-200.6) and 225.3 U/L (37.1-1405.4), respectively. In non-MASLD group, 97% (31/32) were within 200 U/L. The levels of oxHDL were significantly higher in patients with a history of CV events. The medians of oxHDL levels in CV and hepatic events were 273.6 (131.7-591.8) and 370.0 U/L (176.6-840.4), respectively. Treatment agents including anti-HL had little effects on oxHDL levels.

Conclusion: OxHDL is a potential biomarker for CVD in patients with MASLD.

Abstract Submission No. 101971

P-0299

Three Dimensional Structure Like Human Liver, Method Of Hepatotoxicity & Conjugate Like Human Liver

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Background: Genetic analysis an important force in evolution as it allows natural selection to increase or decrease frequency of alleles already in the population. Genetic disease is mostly caused by familiarity in the genetic code. Genes can be used as markers for cell recruitment and activation molecules. This study aims to evaluate the variation and relationship of variation and relationship of three dimensional structure like human liver, evaluation method of hepatotoxicity and conjugate like human liver.

Method: Data obtained from 8 sequences of three dimensional structure like human liver on secondary data form on <https://www.ncbi.nlm.nih.gov/> and selected articles journal evaluated (2015-2023). The genetic analysis constructed by Bootstrap 1000x using MEGA 7.0 software.

Result: the dendogram of 8 sequences were divided into 2 main groups, namely groups A consisting of 7 specimens and groups B consisting of 1 specimens. The optimal tree with the sum of branch length = 7.53041418 is shown. The tree is drawn to scale, with branch lengths (next to the branches) in the same units as those of the evolutionary distances used to infer the phylogenetic tree. This grouping is based on the existence of a similar genetic makeup equation with a high bootstrap value indicating the degree of kinship between specimens and the strength of the phylogenous trees. Grouping was achieved on the basis of differences in expression levels across individual specimens

Conclusion: Information about kinship can be used as an informative source to assembly of superior genes in living of human cells.

Abstract Submission No. 101975

P-0300

Association of MAFLD with Coronary Artery Calcification among Filipino patients in Cebu City

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Background: Non-alcoholic fatty liver disease (NAFLD), now known as Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD), is linked to cardiovascular disease. This renaming emphasizes the role of metabolic problems. Coronary artery calcification (CAC) reflects early coronary artery disease, but data on the MAFLD-CAC link is limited.

Methods: This single-center retrospective study involved adult Filipino patients who underwent CT CAC scoring between January 2021 and January 2023. Clinical and laboratory data were obtained via review of electronic records.

Results: This study involved 147 patients with an average age of 62, primarily females (57.14%), and mostly falling into the Obese-Class I category (31.29%). The most common comorbidities were hypertension (95.24%), dyslipidemia (62.59%), and diabetes mellitus (38.1%). In terms of CAC scores using the CT Agatston method, majority

(30.61%) had low calcium buildup (Stage 2 with scores between 1-99). Approximately 26.53% had higher liver fat content with liver Hounsfield units (HU) below 40, while 73.47% had lower liver fat content with HU equal to or greater than 40. Furthermore, 25.17% of patients with fatty livers were diagnosed with MAFLD, while 74.83% were not. The p-value indicated a significant difference in proportions, suggesting a lower proportion of MAFLD among those who had undergone CT CAC scoring. However, the Pearson Chi-Square statistic (4.051) and the p-value (0.256) indicated no statistically significant association between MAFLD and CT CAC.

Conclusion: The study found a lower proportion of MAFLD diagnoses in patients who underwent CT CAC scoring. Additionally, there was no statistically significant link between MAFLD and CT CAC.

Abstract Submission No. 102094

P-0301

Heat-killed *Lactobacillus brevis* SBL88 improves glucolipid metabolism in MAFLD liver and intestine

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Background: We previously reported that heat-killed *Lactobacillus brevis* SBL88 (SBL88) improves the clinical features of metabolic dysfunction-associated steatotic liver disease (MASLD). We evaluated the further mechanism by which *L. brevis* SBL88 improves the features of MASLD.

Methods: In the MASLD model, mice were induced by feeding a high-fat diet (HFD) (HFD mice) or HFD supplemented with 1% SBL88 (SBL mice). The features of MASLD were evaluated, and RNA sequencing was conducted in the liver. Gene expressions were analyzed using real-time PCR, and protein expression was investigated through western blotting (WB) analysis. Microbiota evaluation was performed using terminal restriction fragment length polymorphism (T-RFLP) in the feces. Additionally, as part of an in vitro study, Huh7 cells and Caco2 bbe cells were cocultured in transwells.

Results: Blood examinations and histopathological findings revealed the improvement of the clinical features of MASLD in SBL mice. RNA sequencing and pathway analysis indicated the impact on the regulation of glucolipid metabolism. Real-time PCR and WB analysis showed significantly higher expressions of IRS-2 or pIRS-2 in the liver of SBL mice. Additionally, the expression of Fiaf was significantly increased, and FoxO1 was significantly decreased in the intestine of SBL mice. However, T-RFLP did not indicate alterations in the microbiota between HFD and SBL mice. In an in vitro study using an intestinal epithelia-hepatocyte transwell model, the expression of IRS-2 and FoxO1 significantly changed when treated with SBL88.

Conclusion: SBL88 could improve MASLD by altering glucolipid metabolism in the liver and intestine without affecting the gut microbiota.

Abstract Submission No. 200036

P-0302

Ganodric acid Nanoparticle ameliorates fatty liver disease via alteration of PI3K/AKT/mTOR pathway

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Background: Nonalcoholic fatty liver disease (NAFLD) is a condition characterized by the accumulation of fat in the liver. In this study, we fabricated the solid lipid nanoparticle (SLN) of ganodric acid (GA) and scrutinized the chemoprotective effect against high fat diet (HFD) and Diethylnitrosamine (DEN) induced NAFLD in rats.

Methods: Double emulsion solvent displacement model was used for the preparation of SLN-GA. Intraperitoneal administration of DEN (100 mg/kg) was used for the induction of HCC in rats for 2 weeks. The rats were divided into 2 groups and received the HFD with or without treatment with SLN-GA for 20 weeks. Body weight, tumor incidence, tumor nodules, hepatic, non-hepatic, apoptosis, antioxidant, pro-inflammatory and inflammatory were estimated. For the determination of gut microbiota, we collected the stools of all rats.

Results: Surface methodology showed the particle size (174.3 nm) and polydispersity index (0.228) for SLN-GA. SLN-GA remarkably suppressed tumor nodules (87.4%), tumor incidence (76.5%) and average size nodules (54.4%). SLN-GA remarkably decreased the level of AFP, ALT, AST, ALP, GGT; non-hepatic parameters viz., bilirubin, total protein, respectively. SLN-GA also suppressed the level of SOD, GSH, GPx, CAT and boosted the level of LPO. SLN-GA significantly ($P < 0.001$) suppressed the level of inflammatory cytokines like TNF- α , IL-1 β , IL-6; inflammatory parameters such as COX-2, PGE2, VEGF, iNOS and NF- κ B, respectively. Moreover, SLN-GA enhanced gut microbial richness and diversity and altered the relative abundance of *firmicutes* and *bacteroides*, respectively.

Conclusion: SLN-GA remarkably suppressed the HFD-induced NAFLD in rats via alteration of gut microbiota and PI3K/AKT/mTOR Signaling pathway.

Abstract Submission No. 200073

P-0303

Screening for NAFLD in general practitioners clinical practice

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Background: Non-alcoholic-fatty-liver disease (NAFLD) is the main cause of chronic liver disease.

The aim of our study is to evaluate the involvement of the general practitioner (GP) in the screening of NAFLD.

Methods: 192 GPs responded to a questionnaire via Google-forms to assess their knowledge and attitude towards NAFLD.

Results: The average age of the participants was 40.3 years with a sex-ratio (F/M) of 1.43.

46.3% worked in the public-sector and 53.7% in the liberal-sector. 33.8% practiced in rural areas.

65.6% reported knowing NAFLD, its association with metabolic-syndrome (84.3%), the risk of progression to cirrhosis (41.1%) and hepatocellular carcinoma (31.2%).

53.6% declared not to screen their patients for NAFLD, 34.9% declared to screen patients with risk factors in particular type 2 diabetes (37.5%), obesity (47.4%), dyslipidemia (26.5%) and taking certain medications (12.5%).

To assess NAFLD, 93.2% requested a blood-count, 70.8% a fasting blood sugar level, 56.7% a lipid profile, 66.6% transaminases and 49.5% an abdominal-ultrasound.

An annual average of 3 new cases of NAFLD are diagnosed by GPs. 41.1% were looking for associated liver fibrosis. 68.2% were aware of the non-invasive screening tests for this fibrosis, notably the

HSI(38.5%), the Fib4(71.3%), the fibrotest(76%), the NAFLD-fibro-sis-score(48.9 %) and fibroscan(73.4%).

37% declared that they didn't refer patients to hepato-gastroenterologists to obtain specialized advice and recommended hygienic and dietary measures (96.8%) and a re-evaluation at 6 months(83.3%).

Conclusion: The diagnosis of NAFLD remains unknown to GP. It's therefore essential to strengthen GP-hepatologist cooperation to optimize the management of this serious pathology whose complications can be disastrous.

Abstract Submission No. 200204

P-0304

Ginsenoside Rg1 counteracts obesity-induced NAFLD by modulating gut microbes and bile acid profile

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Obesity is a global health problem strongly associated with the rising prevalence and severity of nonalcoholic fatty liver disease (NAFLD). There is a close relationship between intestinal micro-organisms and NAFLD. Brown adipose tissue (BAT) is the main non-shivering thermogenic site in mammals. It plays an important role in whole body energy metabolism, which mainly relies on expression of uncoupling protein 1 (UCP1). Ginsenoside Rg1 (Rg1) is the major ginsenoside that can improve metabolic diseases, including cardiovascular diseases and diabetes. Rg1 was gavaged to high-fat diet (HFD)-fed mice and its effect on the gut microbiota were evaluated using 16S rRNA gene amplicon sequencing. Bile acids composition were assessed by targeted metabolomic analysis of fecal samples. In this study, we found that Rg1 reduced lipid droplet size, hepatic triglyceride accumulation and alleviated hepatic steatosis by activating UCP1 expression in BAT, which in turn inhibited HFD-induced weight gain in mice. Furthermore, the intestinal flora of mice was altered, the abundance of *Lachnospirillum*, *Streptococcus*, *Lactococcus*, *Enterococcus* and *Erysipelatoclostridium* was upregulated, and the concentrations of fecal bile acids were altered, with cholic acid and taurocholic acid concentrations being significantly increased. In addition, the beneficial effects of Rg1 were eliminated in mice treated with a combination of antibiotics. In conclusion, these results suggest that Rg1 activates BAT to counteract obesity and hepatic steatosis by regulating gut microbes and bile acid composition in HFD-fed mice.

Abstract Submission No. 200245

P-0305

Studying How Nutrition Advice Affects NonAlcoholic Fatty Liver Disease: Controlled with a Math Model

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The increasing prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) on a global scale raises significant concerns for public health due to its potential to lead to severe liver complications. This investigation explores the effectiveness of individualized nutritional guidance in preventing the progression of NAFLD by evaluating alterations in liver enzymes, fat content, and metabolism. Carried out between 2021 and 2022 at a specialized hepatology clinic, this 12-month study involved 80 participants diagnosed with NAFLD. The cohort

was divided into an intervention group (n=40) receiving personalized nutrition counseling and a control group (n=40) receiving standard care. The counseling interventions comprised customized plans emphasizing caloric reduction, reduced sugar intake, increased fiber consumption, and the inclusion of healthy fats. Baseline, 6-month, and 12-month assessments measured liver enzyme levels (ALT, AST), liver fat content (MRI-PDFF), BMI, and insulin resistance (HOMA-IR). Results indicated a noteworthy 22% reduction in ALT levels ($p < 0.001$) and an 18% decrease in AST levels ($p = 0.002$) in the counseling group at the 12-month compared to baseline. BMI in the counseling group decreased by 2.1 units (95% CI: 1.7–2.5, $p < 0.001$), indicative of improved weight management. Additionally, HOMA-IR values significantly decreased by 32% in the counseling group, enhanced insulin sensitivity. This study underscores the efficacy of personalized nutritional counseling in arresting the progression of NAFLD, evident in reduced liver markers, fat content, BMI, and improved insulin sensitivity. The findings emphasize the role of dietary intervention in NAFLD management, prompting further investigation into sustained effects and underlying mechanisms.

Abstract Submission No. 200262

P-0306

Euiiin-tang ameliorates high-fat diet-induced NAFLD through Nrf2/Sirt1/MAKP pathways in mice

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Nonalcoholic fatty liver disease (NAFLD) is characterized by excessive fat accumulation, inflammation, and cellular injuries in the liver. However, there are no approved treatments for NAFLD. Euiiin-tang (EI) is a traditional polyherb used for attenuating humidity, arthralgia, and obesity in Eastern Asia. Thus, the hepatoprotective effects of EI were examined in high-fat diet (HFD)-induced NAFLD mice model. Mice were fed with HFD or normal fat diet (NFD) for 8 weeks, and orally administered with distilled water, silymarin at 200 mg/kg (SIL), or EI at 250 (EI250) and 500 mg/kg (EI500). The weight gains for 8 weeks were increased in the HFD control compared with the NFD, however, they reduced in treatment groups of the SIL and EI compared with the HFD control. Weight of the liver and fat tissues were increased in the HFD control compared with the NFD, while it significantly reduced in the treatment groups. Serum levels of NAFLD-related parameters (ALT, AST, glucose, HDL-/LDL-cholesterol, and triglyceride) were increased in the HFD control compared with the NFD, however, they were reduced in the treatment groups. Conversely, the serum albumin was reduced in the HFD control compared with the NFD, however, it was increased in the treatment groups compared with the HFD control. The treatments of EI enhanced the hepatic antioxidant and anti-inflammatory activities through Nrf2/Sirt1/MAKP pathways. Histopathological analyses and immunohistochemistry revealed that EI exhibits the antioxidant, anti-inflammatory, and anti-apoptotic effects. These results provide a valuable information for the clinical use of EI in NAFLD.

Abstract Submission No. 100052

P-0307

Prevalence and risk factors of Liver fibrosis in patients with MAFLD undergoing bariatric surgery

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Background: Fibrosis stages affect clinical prognoses of MAFLD. However, prevalence, clinical features of fibrosis in obese Egyptian patients before bariatric surgery are unclear. We aimed to assess fibrosis in MAFLD Patients before bariatric surgery and estimate the utility of non-invasive tests versus liver biopsy.

Methods: A cross-sectional study of obese MAFLD Patients undergoing bariatric surgery at Minia University Hospital, Faculty of Medicine. History, clinical, laboratory, histopathological evaluation, and Non-invasive scores were done.

Results: Of 98 patients, 7 patients were missed, 6 refuse to continue the study. Out of 85 patients, 77% of overweight/obese patients before bariatric surgery showed histopathological fibrosis at liver biopsy. 29% had significant fibrosis and 13% had advanced fibrosis. Fibrosis was significantly higher in the elderly, smokers, diabetics, hypertensives, and chronic HCV infection. Fibrosis was correlated with the increase in BMI, Waist-hip ratio, ALT, AST, triglyceride, cholesterol, uric acid, FBS, HbA1C, and low platelets. Logistic regression showed smoking, higher ages and BMI. Presence of diabetes and hypertension, low platelets, and higher uric acid were independent predictors of significant fibrosis. The non-invasive models, Fibrosis-4 (FIB-4), NAFLD Fibrosis Score (NFS), and AST to Platelet ratio (APRI) provided greater accuracy for predicting significant fibrosis.

Conclusion: significant fibrosis (F_{≥2}) was detected in > 1/3 of patients with MAFLD undergoing bariatric surgery. Presence of smoking, diabetes, hypertension, high WHR, elevated serum uric acid, advanced age, and low platelet level are risk factors for significant fibrosis (F_{≥2}). FIB-4, NFS, and APRI can be used to identify significant liver fibrosis in bariatric surgery patients.

Abstract Submission No. 100076
P-0308

Associations between blood lipids and glucose and ALT strengthen with increasing ALT concentrations

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Objective: Persistent redox state and excessive reactive species involved in carbohydrate and lipids metabolism lead to oxidative damage to liver itself. To learn whether and how fasting plasma levels of lipids and glucose are associated with fasting blood concentrations of ALT, AST and albumin, a total of 198,880 local residents, age range from 18 to 92 years old, without known conditions that impact liver function and metabolism of lipids and glucose, were assembled.

Results: In modeling adjust for confounding factors, the coefficients of the associations between levels of non-HDL-C, HDL-C,

triglycerides and glucose and ALT concentration strengthen from 0.570, -0.867, 0.918 and 0.968 in 1st decile (HDL-C starting from 2nd decile) to 3.185, -6.783, 5.520 and 2.887 in 9th decile in females and from 1.786, -3.433, 1.624 and 0.467 in 1st decile to 4.583, -7.534, 6.388 and 2.019 in 9th decile in males, respectively. The associations between levels of non-HDL-C, triglycerides and glucose and AST concentration also display steep ascents with increasing AST concentration deciles. The associations between albumin concentration and levels of nutrients show relative steady trends across all deciles except triglycerides (associations are only significant in decile 1 to 4 in females).

Conclusions and Relevance: The fasting levels of lipids and glucose are extensively associated with liver function parameters with sex-specific patterns; especially, the higher the concentrations of ALT, the stronger associations with fasting levels of lipids and glucose. Our data suggests excessive carbohydrate and lipids metabolism may cause sub-clinical liver damage.

Abstract Submission No. 100101
P-0309

Constructing a predictive modeling equation using the FLASH in the identification of high-risk MASH

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Objective: This study examined whether the information on the range of Sonazoid TM bubble (SB) destruction is useful for identifying high-risk MASH.

methods: Subjects were 95 patients with MASLD who underwent CEUS and liver biopsy in 4 years. A recommended dose of the contrast agent Sonazoid was infused, and imaging was performed while SB in the liver parenchyma burst using the Flash 10 min after administering Sonazoid. The following measurements were taken from bubble-destruction curves obtained using dedicated analysis software: (1) the range of bubble destruction; (2) bubble destruction rate; and (3) predicted bubble accumulation: they were analyzed together with patient characteristics, blood test results, and pathology results from biopsy.

Results: Among 95 patients with MASLD, 42 had MASH. ROC curve analysis showed the following cutoff values for identifying high-risk MASH: range of bubble destruction, AUROC 0.69; bubble destruction rate, 0.68, and predicted bubble accumulation, 0.69. The range of bubble destruction, bubble destruction rate, predicted bubble accumulation, sex, and AST level were extracted by univariate analysis using logistic regression analysis: sex, AST level, and the range of bubble destruction were extracted by multivariate analysis. The following modeling equation for predicting high-risk MASH was derived: $P = 1 / (1 + e^{-\lambda})$, $\lambda = 0.07 \times \text{range of bubble destruction (mm)} + 0.030 \times \text{AST (U/L)} - 1.468 \times \text{sex (men, 1/woman, 0)}$ -6.151. The AUROC of this equation was 0.847, indicating its diagnostic ability was better than that by the range of bubble destruction alone.

Conclusion: The information on the range of SB destruction, inclusion of sex and AST level, are useful for identifying high-risk MASH.

Abstract Submission No. 100122
P-0310

Useful of laparoscopic sleeve gastrectomy for NAFLD (MASLD)

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Aim: Since 2006 at our hospital, lifestyle modification for obese patients has been provided through a team approach with a physician, dietician, nurse, physical therapist and psychologist. From 2016, a surgeon and anesthesiologist were added to the team for metabolic/bariatric surgery (laparoscopic sleeve gastrectomy: LSG). The aim of this study is to clarify the characteristics of obese patients with NAFLD for whom LSG was effective.

Patients & Methods: Of 40 obese patients who were received LSG between 2017 and 2021 with follow-up period of more than 1 year, 19 were male and 21 were female, 24 were with diabetes, 16 with other complications. The diagnosis of NAFLD was made by liver imaging for fat deposit and stiffness by Fibroscan, and liver biopsy in some cases.

Results: The mean preoperative BMI was 43, the mean Fib-4 index was 0.98, and the postoperative insulin resistance (CPI) of diabetic patients improved significantly, with 15 patients in complete remission and 6 in incomplete remission after surgery. One year after surgery, the mean weight loss was 18.3%, the Fib-4 index did not decrease significantly, but the mean AST (U/L) improved from 38 to 18, ALT (U/L) from 55 to 15, GGT (U/L) from 78 to 40, CAP (dB/m) from 348 to 279, and liver stiffness (kPa) from 12.1 to 7.6, significantly. In patients who underwent follow-up biopsy, there was a trend toward improvement in liver fibrosis.

Conclusion: Since LSG significantly improves hepatic markers in obese patients with NAFLD, metabolic/bariatric surgery should be positively considered.

Abstract Submission No. 100163

P-0311

Impact of Increased or Moderate Alcohol Intake on Metabolic Associated Steatotic Liver Disease

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Background: In 2023, a new disease name, "Steatotic Liver Disease (SLD)" was proposed, along with new diagnostic criteria for metabolic dysfunction. Within this context, metabolic associated steatotic liver disease (MASLD) with increased alcohol intake (MetALD) was first named and a new specific subgroup.

Methods: Participants included in the Taiwan Biobank database were selected. Patients with positive HBsAg, positive anti-HCV, or former drinkers were excluded. MASLD was diagnosed if having hepatic steatosis on ultrasound, plus at least one of cardiometabolic criteria. Increased alcohol intake was defined as weekly alcohol consumption exceeding 210 grams for males and 140 grams for females. The Fib-4 score was used to assess the degree of liver fibrosis, and carotid plaques on duplex ultrasound was employed to diagnose atherosclerosis.

Results: In a total of 18,160 (mean age 55.28±10.41; 33.2 % males) participants, there were 7,316 (40.3%) MASLD patients and 209 (1.2%) MetALD patients. The participants with increased alcohol intake were younger and male predominant. After propensity score matching for age and gender, MetALD patients had higher AST, GGT, FLI, and Fib-4 scores and tended to have a higher proportion of carotid

plaques than MASLD patients. Among MASLD patients, those with moderate alcohol intake had higher values of GGT, FLI, and Fib-4 score and a higher proportion of carotid plaques than those with no/social alcohol intake.

Conclusions: This population-based study indicates that MetALD patients have higher risk of liver disease than those with MASLD. Furthermore, even modest alcohol intake increases the liver and atherosclerotic risks in MASLD patients.

Abstract Submission No. 100189

P-0312

Prevalence of Alcohol Abstinence in Alcohol-Associated Cirrhosis and Its Impact on Survival

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Background: Alcohol-associated cirrhosis is a major public health concern with significant morbidity and mortality. This meta-analysis aims to provide insights into the prevalence of alcohol abstinence among individuals with alcohol-associated cirrhosis and to evaluate its impact on survival outcomes.

Methods: Medline and Embase databases were searched for articles pertaining to alcohol abstinence in people with alcohol-associated cirrhosis. A single-arm analysis regression analysis was conducted to identify Factors associated with alcohol abstinence were identified via regression analysis. Hazard ratios (HR) were calculated via pairwise analysis using the DerSimonian and Laird random effects model.

Results: A total of 18,833 individuals with alcohol-associated cirrhosis were included; 9,745 achieved alcohol abstinence. The prevalence of alcohol abstinence was 53.8% (CI: 44.6% to 62.7%) with sustained abstinence in 52.2% in individuals with alcohol-associated cirrhosis, and 52.7% (CI: 32.7% to 71.8%) in individuals with decompensated cirrhosis. The duration of follow-up significantly influenced abstinence rates; highest rates were observed in studies with less than three years of follow-up (76.1%). Lower levels of ALT, AST, and GGT were also associated with alcohol abstinence. Importantly, alcohol abstinence had a profound positive impact on overall survival regardless of compensation status and study design. Individuals who abstained from alcohol demonstrated significantly higher survival rates (HR: 0.611, 95% CI: 0.506 to 0.738).

Conclusion: Achieving and maintaining abstinence is associated with an improved overall survival, highlighting the critical role of abstinence in the management of alcohol-associated cirrhosis. Further research is warranted to explore its impact on decompensation and hepatocellular carcinoma (HCC) development.

Abstract Submission No. 100190

P-0313

Longitudinal Population Impact of Diabetes on Fatty Liver and Complications. A Nationwide Analysis.

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Introduction: Diabetes remains a leading cause of fatty liver. Thus, we seek to understand how a diabetic or pre-diabetic status in fatty liver patients may correlate with other clinical characteristics and its impact on long term liver health, cardiovascular outcomes, and mortality using data from the US National Health and Nutrition Survey (NHANES) from 1999 to 2018.

Methods: Data from NHANES, utilizing a stratified, multistage, clustered probability sampling design, were analyzed for patients with Fatty Liver. Fatty Liver was defined as hepatic steatosis with at least one of five cardiometabolic risk factors in the absence of other identifiable causes. Demographic and clinical parameters, including diabetes status, were collected. Fibrosis risk was assessed using Fibroscan-based scoring systems. Major Adverse Cardiovascular Events (MACE) included ischemic heart disease, congestive cardiac failure, and cardiovascular mortality.

Results: Among 14,194 Fatty Liver patients, 5,764 were non-diabetic, 4,446 were pre-diabetic, and 3,984 were diabetic. Diabetic patients were older, had a higher prevalence of smoking and hypertension, and exhibited poorer laboratory parameters, with population attributable risk (PAR) of at-risk MASH, advanced fibrosis, MACE, and all cancers at 22.60%, 35.69%, 19.02% and 9.30% respectively. Diabetic patients had a significantly higher overall mortality risk (HR: 1.57) and CVD-related mortality risk (SHR: 1.28) after adjustments for confounders.

Conclusion: Diabetes is associated with an increased risk of at-risk MASH, advanced fibrosis, cardiovascular complications, and overall mortality in individuals with Fatty Liver. Further research is needed to explore the mechanisms underlying these associations and to develop targeted interventions.

Abstract Submission No. 100217
P-0314

SERUM CREATININE-TO-CYSTATIN C RATIO IS ASSOCIATED WITH THE PRESENCE OF OSTEOPENIA IN MAFLD

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Background: Increasing evidence suggests that osteopenia is more prevalent in patients with metabolic associated fatty liver disease (MAFLD) compared to general population.

Methods: This study aimed to evaluate the association between serum creatinine-to-cystatin C ratio (SI) and the presence of osteopenia in MAFLD. Forty MAFLD patients were prospectively included in the study. MAFLD was diagnosed according to the consensus statement on new fatty liver disease nomenclature (2023). Body composition and bone mineral density (BMD) at the spine and hip were assessed using dual x-ray absorptiometry. Osteopenia was diagnosed when T score in either region was between -1.0 and -2.5. Appendicular skeletal muscle mass index (ASMI) was calculated as the sum of the lean muscle mass of the upper and lower extremities adjusted with height. Muscle strength was determined using grip strength (GS) measurement.

Results: Median age was 57.5 years (interquartile range (IQR)=46.75-63); 55% were female. Osteopenia was diagnosed in 17 (42.5%) patients with MAFLD. These patients were older (p=0.003), had lower ASMI values (p=0.003), and lower GS values (p=0.001) compared to those without osteopenia. SI was significantly lower in MAFLD patients with osteopenia (p=0.027). The SI cut-off value of 97.25 allowed

to exclude osteopenia in patients with MAFLD with a specificity of 94.1% (and negative predictive value of 65.3%).

Conclusions: According to our data, SI correlates with the presence of osteopenia in patients with MAFLD and may represent a reliable surrogate marker of decreased BMD in this category of patients.

Abstract Submission No. 100231
P-0315

Comparison of NAFLD and MAFLD liver cancer

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Aim: Recently, MAFLD (metabolic dysfunction-associated fatty liver disease) has been proposed as a disease concept related to fatty liver. We examined and compared the characteristics of hepatocellular carcinoma (HCC) with Non-alcoholic fatty liver disease (NAFLD) and MAFLD.

Methods: The study included patients who underwent radiofrequency ablation (RFA) for first-episode HCC between 2008 and 2022, and whose background liver disease was fatty liver. Data on age, sex, maximum tumor size, number of tumors, Child Pugh classification, and prognosis of patients were collected. HCC cases with NAFLD and MAFLD were compared with respect to these data.

Results: Sixty-two first-episode hepatocellular carcinoma patients treated with RFA during the above period had a fatty liver. The median observation period was 39 months (range 1-134 months). Of these, 19 were diagnosed with NAFLD including duplications, 51 with MAFLD, 3 with NAFLD alone, 35 with MAFLD alone, 16 with duplications of NAFLD and MAFLD, and 8 without both diagnoses. Comparison of the NAFLD group (n=19)/MAFLD group (n=51) including duplications showed that the age was 80 (57-91) years/75 (47-90) years (p=0.019/t test), male-female 6-13/37-14 (p=0.002/χ square test), the maximum tumor diameter was 25 (14-44) mm/24 (12-60)mm, number of tumors 1(1-3)/1(1-7), Child classification: A15/B4/A41/B9/C1, and 33%/32% of deaths were due to causes other than liver disease. Survival analysis showed no difference between two groups.

Conclusion: Comparing NAFLD and MAFLD liver cancers, MAFLD liver cancer was more common in males and at younger ages, but there were no differences in other factors examined, including prognosis.

Abstract Submission No. 100265
P-0316

Correlation of Biopsy-free scoring systems and Fibroscan as screening tools for Liver Fibrosis

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OBJECTIVES: This study aims to determine the correlation of biopsy-free scoring systems and FibroScan as screening tools for liver fibrosis of patients with risk factors of type 2 diabetes mellitus and metabolic associated fatty liver disease (MAFLD).

MATERIALS AND METHODS: This cross-sectional, prospective study was conducted among 130 adult Filipino patients with diabetic-metabolic syndrome for one year. Subjects were asked to answer a clinic-demographic questionnaires and underwent series of laboratory

diagnostic tests. Results were then analyzed using the APRI score, FIB-4 Index and BARD Score comparing it with FibroScan Metavir Scoring to identify liver fibrosis.

RESULTS: The mean APRI score, BARD score, FIB-4 index, and Metavir score of the study population were as follows: 0.56 (SD±1.24), 2.36 (SD±1.06), 1.55 (SD±2.31), and 2.22(SD±0.78) respectively. APRI score was normal in 37%, low in 58%, and high in 5% of the study population. BARD scores demonstrated 58 (45%) patients with low scores (≤ 2) which could be indicative of scarring and likely some cirrhosis. FIB-4 detected 34% of the study population at high risk for liver fibrosis. Apparently, based on Metavir score system, no fibrosis can be detected in 92.3% of patients. There was a statistically significant positive moderate correlation between FibroScan and biopsy-free scoring systems such as APRI ($r=0.481$, $p<0.001$) and FIB-4 ($r=0.557$, $p<0.001$). However, BARD was not significantly correlated with FibroScan ($p=0.624$). APRI carries the highest negative predictive value of 95% compared to BARD (62%) and FIB-4 (77%).

CONCLUSION: Biopsy-free scoring systems such as APRI and FIB-4 are significantly correlated with FibroScan as screening tools for liver fibrosis of patients with risk factors of type 2 diabetes mellitus and MAFLD. Moreover, these tools are capable of ruling out liver fibrosis among patients with at least F2 METAVIR score hence are adequate for use in clinical practice or as a part of referral and follow-up programs wherever this population is treated.

Keywords: diabetes, metabolic syndrome, NAFLD, BARD Score, FIB-4, APRI test

Abstract Submission No. 100268

P-0317

Immune micro-environment reconstruction mediated better antiviral effect in CHB complicated by MAFLD

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Background: The expansion of antiviral indications for CHB has highlighted the significance of studying the antiviral effectiveness in patients with ALT $\leq$ 40 U/L. Research indicated that complicated by MAFLD might affect HBV clearance, but the mechanism is uncertain. This study aims to investigate the impact of complicated by MAFLD on anti-viral treatment in CHB patients with ALT $\leq$ 40 U/L.

Methods: 403 native-treated CHB patients (47.39% MAFLD) who completed at least one year follow-up were finally examined. Further single-cell RNA data analysis of 39929 cells from 21 individuals concluded 6 immune tolerant (IT), 5 immune active (IA), 4 MASH and 6 HBV free Normal Liver (NL).

Results: In the MAFLD group, more patients had significant liver issues (67.54% vs 58.96%) and a higher HBV clearance rate (73.82% vs 59.43%). MAFLD remains an independent factor after adjusting for virals and metabolic factors in multivariate analysis. This association was consistent in all subgroups (P for interaction > 0.05). After quality control, 28232 cells were then grouped into 8 clusters, named according marker genes. The MAFLD group exhibited changes in the immune micro-environment compared to IT group, with an percentage increase in macrophages similar to IA group. TXNIP and EZR had consistent expressions in macrophages of MAFLD and IA groups. Pseudotime analysis revealed key genes during NL to IA, with MAFLD macrophages showing an immune-active profile.

Conclusion: MAFLD had a higher HBV DNA clearance, likely due to its immune micro-environment change resembling IA's active gene expression profile.

Abstract Submission No. 100279

P-0318

Clinical features and real-world treatment patterns of MAFLD patients in China

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Background: Little research to date has investigated the current pharmacological treatment among MAFLD patients in China with a large sample. This study aimed to conduct an observational study based on retrospective real-world data to describe the characteristics and pharmacological treatment patterns of adult patients with MAFLD in China. **Methods:** This is a multicenter, retrospective study. Patients with MAFLD (aged $\geq$ 18) were identified from the tertiary public hospital electronic database between January 1st, 2020 and December 31st, 2022 following APASL 2020 guideline. The electronic records of all subjects were obtained to assess clinical features.

Results: A total of 82,908 patients from 11 hospitals were identified with MAFLD. The mean age of the patients was 53.1 $\pm$ 14.1 years. 64.3% were male, 47.8% had type 2 diabetes (T2DM) and 47.4% had hypertension. The median FIB-4 index was 1.22 (IQR, 0.83–1.85). Among the FIB-4-based fibrosis risk groups, 33.4% (19,840/59,365) were in the intermediate-risk group (1.3–2.67), and 12.3% (7,316/59,365) were in the high-risk group (>2.67). 27.4% of patients received hepatoprotective therapy, and the most frequently prescribed hepatoprotective drug was polyene phosphatidylcholine capsules (7,093/22,705, 31.2%), followed by bicyclol (22.2%). Metformin was the most frequently prescribed medication among MAFLD patients with T2DM (52.4%). Among MAFLD patients with hypertension, the most frequently prescribed drug was metoprolol (24.5%).

Conclusions: Patients with MAFLD are a population with a high burden of comorbidities (mainly diabetes and hypertension), 12.3% of which were high-risk fibrosis based on FIB-4 index. There are significant unmet needs for the management of patients with MAFLD in China currently.

Abstract Submission No. 100290

P-0319

Risk Factors associated to Non-Alcoholic Fatty Liver Disease in patients with type 2 diabetes.

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Background: Type 2 Diabetes Mellitus (T2DM) plays a significant role in the risk of developing Non-Alcoholic Fatty Liver Disease (NAFLD), thus increasing mortality and morbidity. Although the pathogenesis of Non-Alcoholic Fatty Liver Disease is mainly connected to T2DM, risk factors associated with NAFLD in patients with T2DM have not been fully elucidated.

Aim: To explore the risk factors associated with Non-Alcoholic Fatty Liver Disease in T2DM patients

Methods: An analytical cross-sectional study was conducted on T2DM patients at the outpatient clinic of Siloam General Hospital. Patients are grouped into NAFLD and Non-NAFLD, whereby this

diagnosis was done using abdominal ultrasonography. Risk factors assessed in this study include age, gender, BMI, AST, ALT, Albumin, and HbA1c were analysed using Pearson Chi-square and parameter comparison between 2 groups with the Students' T-test.

Result: Of 92 T2DM patients, 73.91% were diagnosed with NAFLD comprised of women at 57.61% with a mean age of 56.14 years old. Asian cut-off for patients' BMI was used, with 76.09% overweight. Majority of the patients also have uncontrolled glycemic levels, 60.87%. In comparison variables between 2 groups, three variables were found to have significant results, including BMI with 26.3294 ± 3.48631 , p-value 0.000, AST with 19.6765 ± 9.9693 , p-value 0.044 and ALT with 22.2353 ± 14.3112 , p-value 0.007. Gender and BMI also significantly correlate with NAFLD, with OR 3.056, 95% CI 1.165-8.016, p-value 0.038 and OR 4.385, 95%CI 1.565-12.284, p-value 0.008, respectively.

Conclusion: BMI, AST, ALT, and gender were significant risk factors associated with NAFLD in T2DM patients.

Abstract Submission No. 100304

P-0320

Neck circumference and the risk of MASLD in non-obese individuals with no visceral obesity

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Background: It is well-known that high body mass index (BMI) and visceral obesity are the risk factors for metabolic dysfunction-associated steatotic liver disease (MASLD). However, it is unclear whether increased neck circumference is associated with MASLD. This study aimed to investigate the impact of neck circumference on MASLD in non-obese individuals with no visceral obesity.

Methods: A cross-sectional study was conducted using nationally representative samples from the Korea National Health and Nutrition Examination Survey 2019–2020. 'Non-obese' was defined as $<25 \text{ kg/m}^2$. Visceral obesity and increased neck circumference were defined as $\geq 90 \text{ cm}$ (male) / $\geq 85 \text{ cm}$ (female) and $\geq 39.4 \text{ cm}$ (male) / $\geq 34.1 \text{ cm}$ (female), respectively. We performed the univariable and multivariable analyses on the risk of MASLD in non-obese individuals with no visceral obesity.

Results: A total of 4065 non-obese adults with no visceral obesity (men, 1521; women, 2544) aged over 40 years were analyzed. The mean levels of neck circumference in men and women were 36.5 cm and 31.9 cm, respectively. The proportion of increased neck circumference in men and women was 4.0 % and 5.9 %, respectively. The proportion of MASLD is 3.5 % (n=144). The prevalence of MASLD in non-obese individuals with no visceral obesity is significantly higher in increased neck circumference than in normal neck circumference (12.3 % vs. 3.1 %, $p<0.001$). The multivariable analysis showed that the risk of MASLD is associated with age ≥ 60 years (odds ratio [OR]: 2.81, confidence interval [CI]: 1.91-4.13), dyslipidemia (OR: 2.86, CI: 1.96-4.18), diabetes mellitus (OR: 6.22, CI: 4.25-9.10), and increased neck circumference (OR: 3.03, CI: 1.88-4.88).

Conclusion: Increased neck circumference is associated with MASLD is high in non-obese individuals with no visceral obesity. Neck circumference can be helpful to evaluate the risk of MASLD in non-obese individuals with no visceral obesity.

Abstract Submission No. 100325

P-0321

Comparative efficacy of pharmacologic therapies in MASH: Systematic review and meta-analysis

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Background: There is an unmet need to understand the efficacy of different pharmacological agents for the treatment of metabolic dysfunction-associated steatohepatitis (MASH), assessed by a decline in magnetic resonance imaging proton density fat fraction (MRI-PDFF). We conducted a network meta-analysis assessing the relative rank-order impact of different pharmacological interventions on a change in MRI-PDFF.

Methods: Medline and EMBASE were searched for randomized controlled trials evaluating pharmacologic therapies in biopsy-proven MASH patients. The primary outcome includes absolute change in MRI-PDFF at week 24 while the secondary outcome was the proportion that achieved MRI-PDFF response (defined as $\geq 30\%$ decline in MRI-PDFF). The analysis was conducted with Bayesian network model and surface under the cumulative ranking curve (SUCRA) analysis.

Results: A total of 14 RCTs with 16 interventions met the eligibility criteria. Aldafermin had the highest probability of being ranked as the most effective intervention for MRI-PDFF decline (SUCRA = 89.59), followed by Pegzofermin (SUCRA = 88.99), and Pioglitazone (SUCRA = 61.41) at week 24. For MRI-PDFF response, Aldafermin (SUCRA = 92.61), Efruxifermin (SUCRA = 81.00) and Resmetirom (SUCRA = 55.54) had the highest probability of being ranked the most effective intervention for achieving MRI-PDFF response at week 12. At week 24, combination of Tropifexor + Cenicriviroc (SUCRA = 72.38), followed by Pegbelfermin (SUCRA = 60.75) and Selonsertib + Simtuzumab (SUCRA = 52.26) was as ranked as the most likely interventions to achieve MRI-PDFF response.

Conclusion: These data provide relative rank-order efficacy of various MASH therapies in terms of improvements in MRI-PDFF.

Abstract Submission No. 100385

P-0322

Characteristics of MASLD compared to NAFLD and MAFLD, and assessment of fibrosis.

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Background: In 2023, a concept known as Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) was introduced at the International Liver Congress of EASL. This concept involves five cardiovascular metabolic risk factors, however its clinical assessment remains undefined. In this study, we conducted a comparison using diagnostic criteria for NAFLD, MAFLD, and MASLD in a general population health examination. Additionally, we assessed liver fibrosis as a risk factor for liver-related mortality.

Method: We analyzed data from 950 adults who participated in a general population health examination. Fatty liver and liver fibrosis were

measured using FibroScan, and individuals with a FibroScan-AST (FAST) score of ≥ 0.35 were categorized as fibrosis-positive.

Results: Among the 310 cases of fatty liver, 222 were classified as MASLD, 273 as MAFLD, and 234 as NAFLD. Additionally, there were also 41 cases of Met-ALD, 23 cases of ALD, 4 cases of DILI, 7 cases of Miscellaneous, and 15 cases of Cryptogenic SLD. There were 36 individuals with fibrosis-positive results. A significant correlation was observed between the FAST score for fibrosis diagnosis and the total number of cardiovascular metabolic risk factors ($r=0.34$, $p < 0.05$). In the multivariate analysis of cardiovascular metabolic risk factors in liver fibrosis, obesity (OR 6.02, 95% CI 1.8-20.3) and high blood pressure (OR 5.45, 95% CI 1.9-16.0) were identified as independent factors with significant differences.

Conclusion: In the new diagnostic criteria of MASLD, obesity and high blood pressure were particularly strongly associated with liver fibrosis.

Abstract Submission No. 100389
P-0323

Reassessing CKD Prevalence in MASLD: A Shift from NAFLD to the MASLD Diagnostic Criteria

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Background: There is a strong association between NAFLD and chronic kidney disease (CKD). However, knowledge is lacking regarding the prevalence of CKD of MASLD and the influence of cardiometabolic risk factors and advanced fibrosis on CKD prevalence within the MASLD.

Methods: The analysis included 6567 participants from NHANES 2017-2020. Steatotic liver disease definitions were based on Fibroscan with controlled attenuation parameters (≥ 248 dB/m), and CKD stages were ascertained using the CKD-EPI equation for estimating glomerular filtration rate.

Results: CKD prevalence displayed no significant discrepancies between the MASLD and NAFLD (17.61% vs. 18.24%, $P = 0.5$), maintaining consistency across all CKD stages. Significant differences in CKD prevalence were found when comparing individuals with MASLD to those without MASLD or NAFLD (17.61% vs. 11.18%, $P < 0.001$), with the largest gap seen in stage 3 (8.22% vs. 4.36%, $P < 0.001$). The prevalence of CKD increases when MASLD is concomitant with a higher risk of advanced fibrosis (LSM ≥ 8 kPa) (31.89% vs. 15.31%, $P < 0.001$). When MASLD was combined with cardiovascular metabolic factors such as type 2 diabetes (T2D) (39.46% vs. 12.69%, $P < 0.001$), hypertension (26.42% vs. 13.93%, $P < 0.001$) and hypertriglyceridemia (22.83% vs. 14.93%, $P = 0.001$), a significant increase in CKD prevalence was noted. In lean MASLD, CKD prevalence differed from that in overweight or obese individuals, but the difference was not statistically significant (17.81% vs. 12.06%, $P = 0.119$).

Conclusions: MASLD and NAFLD demonstrate comparable influences in CKD patient identification. The presence of T2D, hypertension, and hypertriglyceridemia increases the prevalence of CKD among individuals with MASLD.

Abstract Submission No. 100394
P-0324

Evaluating the Diagnostic Efficacy of Several Non-invasive Models for High-risk MASH in MASLD

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Background: MASLD with a score $NAS \geq 4$ and $F \geq 2$ is defined as high-risk MASH. The diagnostic efficacy of non-invasive models like FAST, FIB-4, APRI, Forns, ARR, S Index, and GPR for high-risk MASH remains unexplored in the MASLD population.

Method: Patients diagnosed with NAFLD via liver biopsy at Beijing Ditan Hospital during 2012.1-2020.12 were retrospectively selected to identify the MASLD population. We assessed the diagnostic efficacy for high-risk MASH through sensitivity, specificity, PPV, NPV, and ROC curves.

Results: We identified 309 cases of NAFLD, among which 307 were diagnosed with MASLD, with a concordance rate of 99.35%. 279 MASLD patients were enrolled for analysis, with 117 completing liver transient elastography as a subgroup. In the overall population, significant differences ($P < 0.050$) were noted in FIB-4, APRI, Forns, ARR, S Index, and GPR between the high-risk and non-high-risk MASH groups. FIB-4 exhibited enhanced diagnostic efficacy, AUROC of 0.75 (Figure 1a), S Index and GPR were the weakest. In the subgroup, after incorporating the FAST model, FIB-4, APRI, Forns, ARR and FAST differ between the two groups ($P < 0.050$), whereas S Index and GPR did not show statistical significance ($P = 0.510$, $P = 0.814$). FAST demonstrated the best diagnostic efficacy with higher specificity and PPV, AUROC of 0.82 (Figure 1b), followed by FIB-4.

Conclusion: In our study, 99.35% of NAFLD patients met the MASLD diagnostic criteria. FAST emerged as the most effective diagnostic tool for high-risk MASH within the MASLD population, with FIB-4 being a practical choice amid limited resources. However, the S Index and GPR were not suitable for high-risk MASH diagnosis.

Abstract Submission No. 100405
P-0325

Efficacy of Luseogliflozin in elderly patients with Type 2 Diabetes with MASLD

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Background and Aims: Metabolic dysfunction associated steatotic liver disease (MASLD) is the most common chronic liver disease. Sodium glucose cotransporter-2 inhibitors (SGLT2i) are now widely used to treat diabetes, SGLT2i have been reported to improve MASLD. We aimed to evaluate the effects of SGLT2i, especially Luseogliflozin of MASLD on elderly patients.

Method: A total of 27 consecutive type 2 diabetes patients with MASLD were treated with Luseogliflozin for 24 weeks. We divided into two groups based on age. The first group is over 70 years old with 15 patients, the second group is under 70 years old with 12 patients. We compared laboratory data in two groups, that the change of alanine aminotransferase (ALT) as a liver function and Fibrosis-4 (FIB-4) index as a liver fibrosis in two groups at baseline, 12 weeks and 24 weeks.

Results: All patients were significant decreased in ALT [31.2±18.4 mg/dl at baseline to 23.9±11.6 mg/dl at 12 weeks ($p < 0.01$)]. Both the elderly and non-elderly groups were also significant decreased in ALT [25.3±10.3 mg/dl at baseline to 21.0±6.4 mg/dl at 12 weeks ($p = 0.04$), 38.7±23.5 mg/dl at baseline to 27.6±15.6 mg/dl at 12 weeks ($p < 0.01$), respectively]. No significant change the FIB-4 index was observed period.

Conclusion: Luseogliflozin improved ALT in elderly patients as well as non-elderly patients. Thus, Luseogliflozin may represent a therapeutic choice for elderly type 2 diabetes patients with MASLD.

Abstract Submission No. 100444

P-0326

Alfaamylase prophylactic, therapeutic potential for nonalcoholic steatohepatitis asymptomatic patient

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Nonalcoholic liver disease (NAFLD) is the most common worldwide chronic liver disease. It includes a wide spectrum of histopathological features ranging from simple steatosis, steatohepatitis (ASH), fibrosis and cirrhosis, finally leading to hepatocellular carcinoma (HCC). Due to multifactorial pathophysiological genetic, dietary, environmental, behavioral and metabolic causes, no drug has shown good therapeutic effect. Amylase is expressed on most body organs. It has ant-inflammatory and anti-edematous activity. Multiple clinical studies showed independent associations of low serum amylase copy numbers in NAFLD, metabolic syndrome, diabetes and obesity both type 1 and 2.

Abstract Submission No. 100577

P-0327

Factors influencing liver fibrosis in NAFLD as assessed by magnetic resonance elastography

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Background: Magnetic resonance elastography (MRE) is the most accurate imaging detection for assessing liver fibrosis in nonalcoholic fatty liver disease (NAFLD). However, few studies have investigated the factors influencing liver stiffness measurement (LSM) by MRE. We further investigated the accuracy of MRE in diagnosing liver fibrosis and evaluated the potential clinical factors that may influence LSM.

Methods: This cross-sectional analysis included 124 patients who underwent MRE, MRI-PDFF, and concurrent liver biopsy. The predictive ability of MRE was evaluated by using the receiver operating characteristic (ROC) curve and the area under the ROC curve (AUC). Linear regression models, Spearman's correlation, and subgroup analysis were performed to identify variables affecting LSM.

Results: For the entire cohort, the AUROC (95% CI) of MRE for diagnosing fibrosis stage ≥ 1 , 2, 3, and 4 was 0.80 (0.70-0.90), 0.76 (0.66-0.85), 0.92 (0.86-0.99), and 0.99 (0.99-1.00). In multivariate analyses, clinical variables that only AST had a significant independent correlation with LSMs (coefficient=0.010, $P < 0.001$). In addition, MRE was significantly associated with the grade of lobular inflammation ($r = 0.353$, $p < 0.001$) and hepatocellular ballooning ($r = 0.299$, $p < 0.001$). Subgroup analysis showed LSMs were higher in patients with AST ≥ 2 ULN and inflammation ≥ 2 than in patients with AST < 2 ULN and inflammation < 2 and was statistically significant in early fibrosis.

Conclusion: MRE has a clinically significant diagnostic accuracy for liver fibrosis in NAFLD patients, especially for advanced fibrosis and cirrhosis. Higher AST levels and severity of liver inflammation may influence LSM measured by MRE in early liver fibrosis.

Abstract Submission No. 100625

P-0328

High frequency of metabolic risk factors for MAFLD in the young and adult populations of Mexico.

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Prior research has revealed a high prevalence of metabolic-associated steatohepatitis (MASH) in young Mexican adults. Obesity and metabolic abnormalities are modifiable risk factors when they are detected in a timely manner. This study sought to identify metabolic risk factors (MRF) linked to metabolic-associated fatty liver disease (MAFLD) and liver fibrosis using non-invasive biomarkers in young and adult populations in Mexico.

A cross-sectional study assessing Metabolic Risk Factors (MRF) and non-invasive assessment of the risk of MAFLD: Fatty Liver Index (FLI ≥ 60) and liver fibrosis (APRI ≥ 0.7 -1.0) was performed on 821 participants (265 students aged 15-25 years and 556 adults aged > 26 to 61+). A ROC curve analysis was performed to establish the cut-off values for the appearance of MRF adjusted by age and body mass index (BMI).

A high prevalence of overweight and obesity (60.4%) and MRF, including hyperglycemia (17.6%), hypercholesterolemia (34.9%), hypertriglyceridemia (42.1%), and insulin resistance (30.1%) was detected among the total population. ROC curve analysis determined a cut-off age of 22.5 years and a BMI of 24.3 kg/m^2 as thresholds for the appearance of MRF. The risk of MAFLD was highly prevalent in the student population (15.7%), with a risk for hepatic fibrosis (0.2%) and cirrhosis (0.8%) based on the FLI and APRI markers, respectively.

The study revealed a high prevalence of MRF and early onset of risk of MAFLD among Mexican youth. Future research will be required to explore the genetic susceptibility to obesity, type two diabetes, and MAFLD in the Mexican population and preventive strategies.

Abstract Submission No. 100654

P-0329

The Utility of Non-Invasive Scores of liver Steatosis and Fibrosis in Diabetic NAFLD

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Background: Patients with type 2 diabetes mellitus are known to be at increased risk for NAFLD and advanced fibrosis.

Aim: Assessment of the utility of non-invasive scores of liver steatosis and fibrosis in diabetic and non-diabetic patients with non-alcoholic fatty liver disease (NAFLD).

Methods: This case-control study was conducted on 50 diabetic-NAFLD patients (group I), 40 non-diabetic NAFLD (group II) and a third control group. All subjects were subjected to anthropometric measurements, bioelectrical impedance analysis (BIA), Laboratory tests, along with MRI, and MRE for assessment of liver steatosis and fibrosis.

Results: Female predominance was reported in the three groups (78%, 77.5% & 65%), with mean age (51.46, 48.40, 49.55) years respectively. Liver steatosis was significantly higher ($p=0.007$); in diabetic NAFLD (mean 44.78 ± 23.41 kPa) compared to non-diabetic NAFLD (mean 32.15 ± 20.9 kPa), as well as significant liver fibrosis ($\geq F2$) (mean 2.88 ± 0.81 kPa) compared to non-diabetics (mean 2.46 ± 0.71 kPa) with p value of 0.038. The only non-invasive score of liver steatosis which showed a significant difference ($p=0.005$) between diabetic (mean 89.89 ± 13.47) and non diabetic (mean 82.98 ± 18.53) NAFLD, was the fatty liver index (FLI). Non invasive scores of liver steatosis (lipid accumulation product, fatty liver index and hepatic steatosis index) were positively correlated with the degree of liver steatosis in diabetic NAFLD (p value of 0.007, <0.001 , <0.001 , respectively) and non-diabetic NAFLD (p value of 0.007, <0.001 , <0.001 , respectively). All non invasive scores of liver fibrosis (AST /ALT ratio, NAFLD fibrosis score, FIB 4 and Hepamet fibrosis score) were significantly higher in diabetic NAFLD compared to non-diabetic NAFLD ($p=0.009$, <0.001 , <0.001 , <0.001 respectively) with (mean 1.08 ± 0.42 Vs. 0.87 ± 0.21 , 1.60 ± 2.94 Vs. 0.53 ± 0.96 , 1.21 ± 0.44 Vs. 0.90 ± 0.27 , 0.15 ± 0.11 Vs. 0.03 ± 0.03 ; respectively), while both APRI and kings score had no significant difference between NAFLD subgroups. A positive correlation was found between LSM and FIB-4 score in both NAFLD subgroups (group I and II) with (p value of 0.002 and 0.032, respectively), while APRI was positively correlated with LSM in non-diabetic NAFLD only (p value of 0.030). Sensitivity, specificity, PPV and NPV of FIB-4 score to predict significant liver fibrosis ($\geq F2$) in group I (diabetic NAFLD), were 80%, 73.33%, 66.7% and 84.6% respectively, at cut off level >1.17 , while the values were 50%, 80%, 62.50%, 70.59% and 100%, 0%, 40% using the previously validated cut off levels in viral hepatitis (>1.45) and (>3.25) respectively. Sensitivity, specificity, PPV and NPV of FIB-4 score to predict significant liver fibrosis ($\geq F2$) in group II (non diabetic NAFLD), were 71.43%, 75.76%, 38.5% and 92.6% respectively, at cut off level >0.96 while the values were 14.29%, 96.97%, 50%, 84.21% and 100%, 0%, 17.5%; using the previously validated cut off levels in viral hepatitis (>1.45) and (>3.25) respectively.

Conclusion: All non invasive scores of liver steatosis performed well in all NAFLD patients whether diabetic or non diabetic. The utility of commonly used non invasive scores of liver fibrosis had a poor performance in NAFLD especially in diabetics, except FIB-4 had an accepted performance in these patients.

Abstract Submission No. 100660
P-0330

PDGFR- β as a Non Invasive Biomarker of Liver Fibrosis in Diabetic NAFLD Patients

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Background: Diabetes mellitus is considered one of the most independent predictors of fibrosis progression in patients with NAFLD.

Aim: evaluate the productivity of PDGFR β (Platelet Derived Growth Factor Receptor- β) as a non-invasive biomarker of liver fibrosis in diabetic-NAFLD patients.

Methods: This case-control study was conducted on 50 diabetic-NAFLD patients (group I), 40 non-diabetic-NAFLD (group II), and a third control group. All subjects were subjected to anthropometric measurements, bioelectrical impedance analysis (BIA), Laboratory tests including PDGFR β , along with MRI, and MRE for assessment of liver fibrosis and steatosis.

Results: Female predominance was reported in the three groups (78%, 77.5% & 65%), with mean age of (51.46, 48.40, 49.55) years respectively. Liver steatosis and significant liver fibrosis ($\geq F2$) were higher in diabetic NAFLD when compared to non-diabetics ($p=0.007$, 0.021). Liver stiffness measurement (LSM) was significantly correlated with FIB-4 score in diabetics ($p=0.002$) and non-diabetics ($p=0.032$). PDGFR β was significantly correlated with lipid accumulation product ($p=0.029$), inversely correlated with LDL ($p=0.032$) in diabetics and with LDL in non-diabetics ($p=0.030$). Sensitivity, specificity, PPV and NPV of PDGFR β to predict significant liver fibrosis ($\geq F2$) in diabetic NAFLD patients were 85%, 93.33%, 89.5% and 90.3%, respectively; at cut off >2.5 . While it was 85.71%, 51.52%, 27.3% and 94.4%; at cut off >1.59 in non-diabetics. PDGFR β was the only risk factor for significant liver fibrosis ($\geq F2$) in both diabetic and non-diabetic patients ($p<0.001$).

Conclusion: PDGFR β proved efficacy as a noninvasive biomarker in prediction of significant liver fibrosis ($\geq F2$) in diabetic NAFLD patients.

Abstract Submission No. 100662
P-0331

Fatigue, depression and sleeping disorders are more prevalent in patient with MAFLD.

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Background: Fatigue among MAFLD patients had a negative impact on their health-related quality of life HRQL, morbidity, and mortality. Aim: to determine the prevalence and risk factors of fatigue, depression, and sleeping disorders among patients with MAFLD.

Methods: Two hundreds twenty four Consecutive patients with MAFLD attending the outpatient clinic at the time period from April to October 2023, were subjected to clinical evaluation, laboratory testing including non invasive laboratory markers, fibroscan (measuring

steatosis and fibrosis) and different quantitative and qualitative fatigue score. A control group including 342 patients without MAFLD was taken.

Results: The prevalence of fatigue, depression and sleeping disorders in MAFLD group were 67.8%, 75%, 62.5% vs 21%, 16.4%, 19.5% in the control group respectively ($p < 0.001$, $p < 0.001$ and $p < 0.001$). MAFLD with fatigue was significantly associated with presence and severity of steatosis and fibrosis by fibroscan ($p < 0.0001$). Significant association between MAFLD with fatigue and age ($p < 0.0001$), BMI ($p = 0.01$), waist circumference ($p = 0.002$), T2DM, hypertension, low platelet, high ALT, AST, triglyceride, cholesterol, HbA1C, and Fib-4 (all $p < 0.0001$). The age ($p = 0.000$), BMI ($p = 0.018$, 0.036), waist circumference ($p = 0.002$, 0.009), diabetes ($p = 0.000$), hypertension ($p = 0.000$), steatosis Cap ($p = 0.000$, 0.000), fibrosis ($p = 0.000$), and Fib-4 ($p = 0.000$, 0.027) by univariate and multivariate analysis respectively were considered risk factors for fatigue in MAFLD group. The age ($p = 0.00$), high social level ($p = 0.02$), diabetes ($p = 0.00$), hypertension ($p = 0.00$, 0.008), steatosis cap ($p = 0.00$, 0.000), fibrosis ($p = 0.00$), fib-4 ($p = 0.00$, 0.015) were considered, by univariate and multivariate analysis respectively, independent risk factors for depression in MAFLD group. age ($p = 0.00$), BMI ($p = 0.001$), waist circumference ($p = 0.002$), diabetes ($p = 0.00$), hypertension ($p = 0.00$, 0.003), steatosis cap (0.00 , 0.000), fibrosis (0.00 , 0.000), and fib-4 (0.00 , 0.035) were independent risk factors for sleep disorder in MAFLD.

Conclusion: Fatigue, sleeping disorders and depression are more prevalent in MAFLD patients than in general population.

The lower health utility scores in patients with MAFLD, are associated with more advanced stages of the disease.

Abstract Submission No. 100677
P-0332

Comparing MASLD/MetALD to alcoholic liver disease with metabolic dysfunction in cirrhotic patients

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Introduction: In recent years, cirrhosis and hepatocellular carcinoma (HCC) associated with steatotic liver disease (SLD) have increased. In the new SLD classification published in 2023, SLD with metabolic disorders was classified into metabolic dysfunction associated steatotic liver disease (MASLD) and metabolic dysfunction-associated alcoholic liver disease (MetALD), depending on the amount of alcohol consumed. Alcoholic liver disease (ALD) due to heavy alcohol consumption is also included in steatotic liver disease, and ALD with metabolic dysfunction are not uncommon. Among patients with SLD-related cirrhosis, studies on the differences between MASLD/MetALD

and ALD with metabolic dysfunction are limited, so the present study was designed to compare the two groups.

Methods: Of the 1505 cirrhosis cases that visited our hospital and related facilities between July and September 2021, 636 were SLD-related cirrhosis cases. Of these, 505 cases of SLD-related cirrhosis complicated with metabolic disorders were included. Comparison was made between the MASLD/MetALD group and the ALD with metabolic dysfunction group (ALD group).

Results: 225 were in the MASLD/MetALD group and 280 were in the ALD group. The ALD group was younger (69 yrs., 73 yrs., $P < 0.001$), more male (88.9%, 46.7%, $P < 0.001$), had a lower BMI (24.7, 26.5, $P < 0.001$), and had fewer metabolic dysfunction complications. The complication rate of diabetes (35.5%, 56.0%, $P < 0.001$) and dyslipidemia (16.5%, 24.4%, $P = 0.033$) was lower in ALD group, but there was no significant difference in the complication rate of hypertension (46.2%, 52.9%, $P = 0.152$), cardiovascular events (16.1%, 17.3%, $P = 0.72$), and hepatocellular carcinoma (37.6%, 33.8%, $P = 0.401$) between the two groups. Logistic regression analysis was performed to adjust for covariates. As in the univariate analysis, the ALD group had less BMI (OR 0.876, $P = 0.008$), less diabetes (OR 0.344, $P < 0.001$), more male (OR 9.76, $P < 0.001$) and younger age (OR 0.959, $P < 0.001$). Cardiovascular event complication rates and HCC complication rates did not differ between the two groups on multivariate analysis.

Conclusion: ALD with metabolic dysfunction develops cirrhosis at a younger age than MASLD/MetALD, but the complication rate of cardiovascular events and hepatocellular carcinoma is possibly comparable in both groups.

Abstract Submission No. 100693
P-0333

Does PDFF and MRS always show the same value in the quantification of Hepatic Steatosis?

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Objective: This study aimed to 1) provide a spectrum of values of MRI-PDFF, FFMRS, and FFs measured by two different histopathologic methods [artificial intelligence (AI) and pathologist], 2) to evaluate the correlation among them, and 3) to evaluate the diagnostic performance of MRI-PDFF and MRS for grading hepatic steatosis.

Materials and Methods: Forty-seven patients who underwent liver biopsy and MRI for nonalcoholic steatohepatitis evaluation were included. The agreement between MRI-PDFF and MRS was evaluated through Bland-Altman analysis. Correlations among MRI-PDFF, MRS, and two different histopathologic methods were assessed using Pearson correlation coefficient (r). The diagnostic performance of MRI-PDFF and MRS was assessed using receiver operating characteristic curve analyses and the areas under the curve (AUCs) were obtained.

Results: The means $\pm$ standard deviation of MRI-PDFF, FFMRS, FF measured by pathologist (FFpathologist), and FF measured by AI (FFAI) were 12.04 ± 6.37 , 14.01 ± 6.16 , 34.26 ± 19.69 , and 6.79 ± 4.37 (%), respectively. Bland-Altman bias [mean of MRS - (MRI-PDFF differences)] was 2.06%. MRI-PDFF and MRS had a very strong correlation ($r = 0.983$, $p < 0.001$). The two different histopathologic methods also showed a very strong correlation ($r = 0.872$, $p < 0.001$). Both MRI-PDFF and MRS demonstrated a strong correlation with FFpathologist ($r = 0.701$, $p < 0.001$ and $r = 0.709$, $p < 0.001$, respectively) and with FFAI ($r = 0.700$, $p < 0.001$ and $r = 0.690$, $p < 0.001$, respectively). The AUCs of MRI-PDFF for grading $\geq S2$ and $\geq S3$ were 0.846 and

0.855, respectively. The AUCs of MRS for grading $\geq S2$ and $\geq S3$ were 0.860 and 0.878, respectively.

Conclusion: PDFF and MRS do not always show the same value in the quantification of Hepatic Steatosis. However, MRS and MRI-PDFF can be used as alternative non-invasive reference standards in patients with NAFLD because they have demonstrated strong correlations with each other and with two different histopathological methods.

Abstract Submission No. 100713
P-0334

Comparative Analysis on Clinicopathological Features of MASLD and MAFLD related HCC

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Objective: To analysis the differences of clinicopathological characteristics between MASLD and MAFLD related HCC and correlation with metabolic factors.

Methods: Patients with hepatic malignant tumor hospitalized in Beijing Ditan Hospital from January 2010 to December 2019 were enrolled. Staining of liver tissues with HE, special and immunohistochemical stains were performed. The histological features of the tumour and metabolic characteristics of patients were analyzed.

Results: 5958 patients were diagnosed with hepatic malignant tumor including 273 HCC cases with at least one metabolic risk factor, 40 were underwent liver biopsy. Among them, 25 cases met the diagnostic criteria for MASLD and 20 met the criteria for MAFLD. There were no significant differences between MASLD and MAFLD related HCC in pathological features and laboratory indicators. Among the 40 cases, trabecular type was the most prevalent (17,42.5%), followed by steatohepatitis type (10,25%), scirrhous type (5,12.5%), macrotrabecular type (3,7.5%), solid type (2,5%), pseudoglandular type (2,5%), and clear-cell type (1,2.5%). There were 23 patients (57.5%) without liver cirrhosis. The degree of ballooning of tumor cells ($p=0.002$), proportion positive of Mallory-Denk body ($p=0.004$) and glycogenated nuclei ($p=0.007$), expression of HSP70 ($p=0.011$), and serum TBI level ($p=0.037$) in the liver cirrhosis group were notably higher than those in non-cirrhosis group. The level of serum AKP ($p=0.044$), TCHO ($p=0.016$), TG ($p=0.015$), LDL-C ($p=0.012$), ApoB ($p=0.005$), WBC ($p=0.002$) and PLT ($p<0.001$) were significantly lower than those in non-cirrhosis group.

Conclusion: There was no significant difference in clinicopathological features between MASLD and MAFLD associated HCC. The pathological characteristics of MASLD-associated HCC were correlated with metabolic factors.

Abstract Submission No. 100779
P-0335

Correlation between skeletal muscle mass index and NAFLD and liver fibrosis in patients with T2D

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Objective: To investigate the correlation between muscle mass index and non-alcoholic fatty liver disease (NAFLD) and the degree of liver fibrosis in older patients with type 2 diabetes mellitus (T2DM).

Methods: 1733 patients with T2DM were enrolled and measured the appendicular skeletal muscle mass index (ASMI%), full abdominal

color Doppler ultrasound, biochemistry index, etc. were measured. The patients were divided into NAFLD group and non-NAFLD group, and then NAFLD group were divided into significant liver fibrosis and non-significant liver fibrosis group, the correlation between ASMI% and NAFLD and degree of liver fibrosis was analyzed.

Results: With the decrease of ASMI% quartiles, the detection rate of NAFLD and significant liver fibrosis ($NFS \geq 0.676$) increased ($p<0.001$). After adjusting for confounding factors, the decrease in ASMI% was a risk factor for NAFLD and significant liver fibrosis (logistic regression analysis). As the ASMI% decreased in the male group, the risk of NAFLD increased (Q1: OR=2.529, 95%CI 1.639~3.903, $p<0.001$). In the female group, as the ASMI% decreased, the risk of NAFLD gradually increased (Q1: OR=3.766, 95%CI 2.367~5.992, $p<0.001$). With the decrease of ASMI%, the risk of significant liver fibrosis in both male and female NAFLD populations increased ($p<0.05$). Subgroup analysis showed that regardless of obesity, insulin resistance, disease course more than 10 years, and diabetic peripheral neuropathy, the NFS level of sarcopenia patients was significantly higher than that of the non-sarcoidosis group.

Conclusion: Among patients with T2DM, the incidence of NAFLD and significantly liver fibrosis was higher in people with low ASMI%.

Abstract Submission No. 100808
P-0336

Changes in Prevalence of Steatotic Liver Disease with the New Nomenclature Using MRI-Derived PDFF

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Background: International expert panels proposed new nomenclatures, metabolic dysfunction-associated fatty liver disease (MAFLD) in 2020 and metabolic dysfunction-associated steatotic liver disease (MASLD) in 2023, along with revised diagnostic criteria to replace non-alcoholic fatty liver disease (NAFLD). We aimed to investigate the changes in the prevalence of NAFLD, MAFLD, and MASLD through health check-ups using magnetic resonance imaging-derived proton density fat fraction (MRI-PDFF) to assess hepatic steatosis. We also examined the prevalence of the sub-classifications of steatotic liver disease (SLD) and the differences in characteristics among the sub-categories.

Methods: We included 844 participants who underwent liver MRI-PDFF at our health check-up clinic between January 2020 and November 2022. Hepatic steatosis was defined as MRI-PDFF $\geq 5\%$. Participants were categorized according to NAFLD, MAFLD, MASLD, and sub-classifications of SLD.

Results: The prevalence rates of NAFLD, MAFLD, and MASLD were 25.9%, 29.5%, and 25.2%, respectively. 30.5% of the participants was categorized as SLD. The prevalence rates of the SLD sub-categories were 25.2% for MASLD, 3.7% for MASLD and alcohol-associated liver disease (MetALD), 0.1% for alcohol-associated liver disease, 1.3% for specific etiology SLD, and 0.1% for cryptogenic SLD. Compared with patients in the MASLD group, those in the MetALD group were younger, predominantly male, and exhibited higher levels of serum aspartate aminotransferase, gamma-glutamyl transpeptidase, and triglycerides.

Conclusions: The prevalences of NAFLD and MASLD assessed using MRI-PDFF were similar, with MASLD accounting for 97.3% of the patients with NAFLD. The separate MetALD sub-category may have clinical characteristics that differ from those of MASLD.

Abstract Submission No. 100839
P-0337

VALIDATION OF AGILE 3+ FOR MASLD ADVANCED FIBROSIS IN A CANADIAN COHORT

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Background and Aims: Agile 3+ is a novel non-invasive test (NIT) for advanced fibrosis in patients with metabolic dysfunction-associated steatotic liver disease (MASLD), and includes age, AST/ALT, platelets gender, presence of diabetes and liver stiffness measurement (LSM by VCTE). There are few external validation studies. Our aim was to assess the diagnostic performance of Agile 3+ in comparison with other simple NITs for MASLD F3-4.

Methods: This is a retrospective single-center cohort study including adult patients with biopsy-proven MASLD between 2010 – 2021. Other causes of liver disease were excluded. Diagnostic test performance was assessed using validated thresholds for NIT and Agile 3+ <0.451 and >0.679 to rule-out and rule-in F3-4 using the area under the receiver operating characteristic (AUROC).

Results: Our cohort included 76 patients, with mean age 48 ± 13 years, mostly male (56%), diabetes mellitus in 35%, and F3-4 prevalence 60%. Using validated thresholds, the proportion of patients with indeterminate (test range) scores were: Agile+3 (0.451-0.679) 10.3%, LSM (8-12 kPa) 26%, FIB-4 (1.3-2.67) 32%, NFS (-1.455-0.676) 33%, APRI (0.5-1.5) 42%. For F3-4, all NITs had high specificity (0.89-1.00) but lower sensitivity (0.63-0.82). Corresponding AUROC 0.91 for Agile 3+ was higher than for APRI (0.78, $p=0.02$) and NFS (0.75, $p=0.001$), but similar to VCTE (0.93, $p=0.31$) and FIB-4 (0.87, $p=0.31$).

Conclusions: In our tertiary center cohort Agile3+ had a good diagnostic performance for advanced fibrosis, with relatively lower proportion of patients classified in the indeterminate zone at specified thresholds. Further validation of Agile 3+ in lower prevalence cohorts is required.

Abstract Submission No. 100901
P-0338

The incidence of depression is increasing in individuals with MAFLD/significant fibrosis.

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Background: Growing evidence suggests a link between depression and metabolic dysfunction-associated fatty liver disease (MAFLD) has been proposed. The aim of this study was to determine whether depression scores are associated with MAFLD as well as liver fibrosis in the US general population.

Methods: This cross-sectional study was based on the data from the 2017–March 2020 cycle of the National Health and Nutrition Examination Survey (NHANES) in the US. Depression was defined as Health Questionnaire-9 (PHQ-9) score more than 10. Transient elastography was utilized to evaluate hepatic steatosis and fibrosis with controlled attenuation parameters and liver stiffness measurements, respectively.

Result: Of the 3599 individuals (mean age 49.2 years, 49.9% male), 36.5% had MAFLD. Compared to non-MAFLD controls, depression was more common in MAFLD (10.3% vs 8.3%, $p=0.038$). In individuals with MAFLD with significant fibrosis, prevalence of depression was higher also ($p=0.003$) In MAFLD populations, individuals

with depression were higher proportion of female (64.7% vs 42.9%, $p < 0.001$), divorce/single/ widowed (55.8% vs 34.5%, $p < 0.001$), no more than graduate degree (22.5% vs 14.0%, $p=0.028$), inactive physical exercise (67.6% vs 53.9%, $p < 0.001$), feeling of fatigue (83.8% vs 11.5%, $p < 0.001$), with disease of hypertension (63.9% vs 48.0%, $p=0.001$), sleep disorder (74.2% vs 30.1%, $p < 0.001$), and stroke (10.2% vs 4.4%, $p=0.008$). The prevalence of fatigue (OR 12.14, 95%CI 9.31-22.24), with sleep disorder (OR 3.26, 95%CI 2.05-5.21) was independently with depression in MAFLD patients, and married/living with partner had an inverse association (OR 0.61, 95%CI 0.39-0.95).

Conclusion: In patients with MAFLD, the prevalence of depression increased significantly than those non-MAFLD. Depression was driven by fatigue, sleep disorder. These findings have important clinical implications.

Abstract Submission No. 100905
P-0339

The assessment of serum M2BPGi as a novel fibrosis biomarker in nonalcoholic fatty liver disease.

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Background: Evaluating liver fibrosis is essential for the management of nonalcoholic fatty liver disease (NAFLD). This study was aimed at investigating whether serum mac-2-binding protein glycosylation isomer (M2BPGi) could be a useful circulating biomarker for assessing liver fibrosis in patients with NAFLD.

Methods: In this study, NAFLD was diagnosed by magnetic resonance-based imaging. Serum M2BPGi was quantified by a commercially available immunoassay. The polymorphisms of *PNPLA3* rs738409, *TM6SF2* rs58542926, and *HSD17B13* rs58542926 were determined by allelic discrimination.

Results: Overall, 140 patients with NAFLD were recruited. There were 77 (55%) males and 63 (45%) females, with an average age of 55.7 years. Serum M2BPGi was significantly correlated with magnetic resonance elastography (MRE, $r=0.500$, $p < 0.001$) but was not correlated with proton density fat fraction (PDF). The area under the receiver operator characteristics curves

for M2BPGi in differentiating significant fibrosis ($\geq F2$), advanced fibrosis ($\geq F3$) and cirrhosis (F4) were 0.71 (95% CI: 0.57–0.86, $p=0.002$), 0.79 (0.63–0.95, $p < 0.001$) and 0.91 (0.83–0.99, $p < 0.001$), respectively. At the cut-off value of 0.83 COI, serum M2BPGi displayed sensitivity and specificity of 79% and 77%, respectively, for diagnosing advanced fibrosis. The serum marker level was also correlated with patients' age ($r=0.259$, $p=0.002$), aspartate aminotransferase (AST) ($r=0.431$, $p < 0.001$), presence of type 2 diabetes, and *PNPLA3* genotype, but its correlation with other parameters and polymorphisms was not found. Patients with *PNPLA3* CG and GG genotypes had significantly higher M2BPGi levels than those with CC genotype (0.90 ± 0.69 vs. 0.66 ± 0.39 COI, $p=0.005$). In multivariate analysis, advanced fibrosis was the only independent factor associated with elevated serum M2BPGi.

Conclusion: Our data indicated that serum M2BPGi quantification could be a reliable novel biomarker for the assessment of liver fibrosis staging in patients with NAFLD.

Abstract Submission No. 100908
P-0340

Efficacy of pemafibrate on diet-resistant metabolic dysfunction-associated steatotic liver disease

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a lifestyle-related disease, but there are not a few cases who are resistant to dietary therapy. Pemafibrate is a novel lipid-lowering drug that was developed as a selective peroxisome proliferator activated receptor- α modulator. The aim of the present study was to clarify the efficacy of pemafibrate on diet-resistant MASLD patients with hyperlipidemia.

Methods: Fifty-seven MASLD patients with persistent liver enzyme elevation and hyperlipidemia despite counseling in moderate-carbohydrate restriction (150–200g/day) for more than one year, who received pemafibrate (0.2 mg/day) for 6 months, were analyzed.

Results: There were 29 males and 28 females, median age was 61 years (range 17–71 years), and median body mass index was 25.8 (18.4–41.0). Triglyceride, low-density lipoprotein cholesterol, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and γ -glutamyl transferase (γ -GT) significantly decreased after 6 months ($p < 0.001$), despite body weight, percent body fat, visceral fat area, and percent liver fat did not decrease significantly, and Liver/Spleen ratio significantly decreased ($p = 0.006$). Although no significant decrease was seen in hemoglobin A1c, homeostatic model assessment for insulin resistance significantly decreased ($p = 0.002$). Although shear wave velocity did not decrease significantly, Mac-2 binding protein glycosylation isomer showed a significant decrease ($P < 0.001$). The normalization rates of all liver enzymes, AST, ALT, ALP, and γ -GT were 18% (10/57), 29% (11/38), 42% (22/53), 75% (3/4), and 62% (18/29), respectively.

Conclusions: Pemafibrate for diet-resistant MAFLD patients is effective regardless body weight loss.

Abstract Submission No. 100925
P-0341

AI system for diagnosis of Hepatocellular carcinoma in nonalcoholic steatohepatitis.

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Background: The aim of this study is to develop a novel noninvasive test using an artificial intelligence system (called HCC-Scope) to diagnose an early stage hepatocellular carcinoma (HCC) in nonalcoholic steatohepatitis (NASH).

Methods: 175 NASH patients and 55 patients with NASH-HCC were enrolled for training and validation studies. Of the 55 NASH-HCC, 27 were classified as very early stage HCC (stage 0: single < 2 cm), and 6 were early stage HCC (stage A: single or 3 nodules < 3 cm) based on the Barcelona Clinic Liver Cancer staging system. HCC-Scope determine HCC using 12 parameters of the patients: age, sex, height, weight,

aspartate aminotransferase level, alanine aminotransferase level, gamma-glutamyl transferase level, cholesterol level, triglyceride level, platelet count, diabetes status, and immunoglobulin M-free apoptosis inhibitor of macrophage level. The FMVWG2U47 hardware (Fujitsu Co. Ltd, Tokyo) and the originally developed software were used.

Results: HCC-Scope had 100.0% sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for differential diagnosis between non-HCC and HCC in a training study with and without gray zone analysis. It was also accurately diagnosed in the validation study (95.0% sensitivity, 100.0% specificity, 100.0% PPV, and 97.1% NPV with gray zone analysis and 95.2% sensitivity, 100.0% specificity, 100.0% PPV, and 97.1% NPV without gray zone analysis). HCC-Scope had significantly higher sensitivity (85.3%) and specificity (85.1%) than alpha-fetoprotein (AFP) level, AFP-L3 level, des-gamma-carboxy prothrombin (DCP) level, and the gender-age-AFP-L3-AFP-DCP (GALAD) score.

Conclusion: HCC-Scope can accurately differentially diagnose between non-HCC NASH and NASH-HCC, including very early stage NASH-HCC.

Abstract Submission No. 100950
P-0342

Assessing carotid atherosclerosis risk in metabolic dysfunction-associated steatotic liver disease

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a new term for fatty liver disease and has been recently proposed to replace nonalcoholic fatty liver disease (NAFLD). We analyzed whether the risk of carotid atherosclerosis differed between MASLD and NAFLD status in a large group of asymptomatic adults.

Methods: We performed a cross-sectional study with subjects who underwent health checkup between 2015 and 2020. Hepatic steatosis was diagnosed by sonography and the severity of liver fibrosis was determined using transient elastography and fibrosis-4 (FIB-4) index. Sub-clinical carotid atherosclerosis (SCA) was assessed based on intima-media thickness or plaques on carotid ultrasound.

Results: 65,138 participants were analyzed, including 21,386 MASLD and 15,186 NAFLD. Eighty-seven subjects with NAFLD did not meet the MASLD criteria. Of the total, 9,145 (14.0%) was diagnosed as having SCA. MASLD was significantly associated with SCA with an adjusted odds ratio (aOR) of 1.27 (95% confidence interval [CI], 1.21–1.33), which was similar to NAFLD (1.26 [1.19–1.33]). However, the association lost significance in NAFLD after adjustment of metabolic factors. The association of MASLD with SCA increased with the severity of liver fibrosis, with cases with high FIB-4 levels (≥ 1.3) having an aOR for SCA of 2.14 (95% CI, 2.02–2.27) compared to those without MAFLD, as observed in NAFLD (1.69 [1.56–1.82]). This trend was confirmed using liver stiffness data by a cut-off of 6.5 kPa in both settings.

Conclusions: MASLD newly defined was strongly associated with SCA, especially when accompanied by liver fibrosis. MASLD may predict SCA better than conventional NAFLD.

Abstract Submission No. 100952
P-0343

Marked hepatitis despite minimal steatosis defines genetically-predisposed, hyper-inflammatory NAFLD

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Background: NAFLD patients with severe macrosteatosis yet minimal lobular inflammation, hepatocyte degeneration, and fibrosis—and the extreme opposite of the spectrum i.e. minimal hepatic fat but marked inflammation and hepatocyte ballooning—represent clinico-pathological enigmas. We hypothesized that such “paradoxical” histologic presentations may be driven by inter-individual genetic differences, which could hold clues to new therapeutic targets.

Methods: We analyzed participants who had biopsy for suspected NASH. Histology was graded using CRN NAS. GWAS was analyzed using an IPW methodology to identify variants associated with “paradoxical” histologies. Associations were adjusted for demographics, comorbidities (HLD/HTN/T2DM), medications (including metformin/sulfonylurea/insulin/statins/ACEi/ARB/VitaminE), smoking, caffeine, alcohol consumption, ethnicity and genomic PCs.

Results: n=232 patients were analyzed at time of reporting (M:F=110:122, Chinese/Malay/Indian/Others: 54.4%/27.0%/14.1%/4.4%, BMI median [IQR]32.2[27.2- 38.8]). We identified multiple loci enriched in immune cell-trafficking and innate response (FCGBP [IgG-Fc-mediated immunorecognition], HRG [macrophage activation], LAX1 [B- & T-lymphocyte activation, RAB7B [dendritic cell migration], ARPIN [phagosome formation]); in addition, a variant (rs7636125) in the well-known macrophage trafficking loci CX3CR1 exhibited a pre-adjustment association ($\beta=-0.691$, $p=9.17 \times 10^{-11}$) which was lost after adjustment. We also identified a locus likely implicating sinusoidal endothelial cell dysfunction (APOL3), two redox/antioxidant loci (GSTA1, AKR1B10), and four collagen deposition/ECM remodeling loci (FBN1, FGF14, CTHRC1, LAMC3) associated with severe hepatocyte injury/inflammation despite minimal steatosis.

Conclusions: DNA variants in chemotaxis/immune response, LSEC dysfunction, antioxidant/detoxification, and ECM deposition/ remodeling pathways modulate the severity of hepatitis and hepatocyte ballooning in NAFLD. GWAS of additional n=227 patients (total:n=459) patients is underway, and complete results including fine-mapping will be presented at the meeting.

Abstract Submission No. 101028
P-0344

Fib-4 and Fatty Liver Indices in Low- and High-Risk Prediabetes by Anthropometric Categorization

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Prediabetes, characterized by elevated blood glucose levels not meeting diabetes criteria, requires monitoring to prevent diabetes and its

complications. This population is diverse, with individuals categorized as low or high-risk for cardiovascular issues based on anthropometric indices.

Objective: We aimed to explore if low-risk and high-risk prediabetes patients, as defined by anthropometric indices, also differ in fatty liver index (FLI) and Fib4 scores.

Methods: Our study encompassed various prediabetes subgroups as shown below, totaling 657 patients, analyzed via waist to hip ratio (WHR), body mass index (BMI), visceral adiposity index (VAI), lipid accumulation products (LAP), body shape index (BSI), body roundness index (BRI), conicity index (CI) values. The isolated impaired fasting glucose (IFG) and isolated elevated HbA1c (HbA1c) groups, showcasing consistently lower anthropometric scores, were deemed low-risk, while other subgroups (impaired glucose tolerance (IGT), IFG+IGT, IFG+HbA1c, IGT+HbA1c, IFG+IGT+HbA1c) were labeled high-risk. Beyond numerous parameters, we calculated and tested differences in Fib4 and FLI values between these groups, employing the C statistic for discriminative cut-off values identification.

Results: Fib4 median values were 0.762 (95%CI: 0.683-0.789) and 0.886 (95%CI: 0.826-0.961), FLI were 55.77 (95%CI: 48.79-61.99) and 72.89 (95%CI: 67.12-76.02) in low- and high-risk prediabetes ($p<0.0001$) respectively. Fib4 cut-off was >0.9425 (sensitivity 46.4%, specificity 71.8%; AUC: 0.601; $p<0.0001$), FLI cut-off was 70.20 (sensitivity 53.5%, specificity 67.5%; AUC: 0.622; $p<0.0001$).

Conclusions: Significant differences in FLI and Fib4 values exist between low- and high-risk prediabetics, although their discriminative power is limited. High-risk individuals, according to anthropometric indices, warrant closer monitoring for liver complications.

Abstract Submission No. 101038
P-0345

Triglyceride Level and Liver Disease Evaluated by Liver Stiffness and Attenuation Parameter

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Background and aims: Recently, metabolic dysfunction-associated steatotic liver disease (MASLD) has been proposed as a new concept focusing on concomitant metabolic dysfunction such as diabetes mellitus, hypertension, and dyslipidemia. In the current study, we aimed to study the relationship between liver disease and triglyceride level, focusing on liver stiffness and steatosis evaluated by transient elastography.

Material and Methods: Between January 2022 and December 2022, a total of 2161 patients with successful measurement of liver stiffness and controlled attenuation parameter (CAP) were included. Liver stiffness and CAP were measured by Fibroscan (Echosens, Paris).

Results: The mean age was 60.6 ± 14.8 , with 1109 males and 1052 females. The median values (25th- 75th percentiles) of triglyceride, liver stiffness, and CAP were 103 mg/dL (73-151), 5.1 kPa (3.9-7.2), and 252 dB/m (208-297), respectively. A total of 553 patients had triglyceride levels greater than 150 mg/dL. ALT >30 was more common in patients with hypertriglycemia than those without ($P<0.001$).

Conclusions: Hypertriglycemia is an important parameter in the management of steatotic liver disease. The clinical outcomes after the proper medical intervention should be investigated in future studies.

Abstract Submission No. 101073
P-0347

Evolution of characteristics in NAFLD with and without diabetes: A meta-analysis of the placebo arms

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Background & Aims: The natural course of NAFLD is incompletely understood. We explored the changes in the severity of NAFLD over time by analyzing data from the placebo arms of randomized controlled trials (RCTs), particularly in relation to the presence of diabetes. **Methods:** RCTs of NAFLD that included a placebo treatment arm was identified through systematic search. Primary outcomes were the change in hepatic steatosis and fibrosis. Pooled proportion and mean differences were assessed using generalized linear mix model.

Results: The meta-analysis incorporated 8 RCTs involving 386 patients without diabetes and 24 RCTs involving 637 patients with diabetes, respectively. The median intervention period was 24.0 weeks. The pooled estimate of mean change in steatosis grade by histology was -0.1 (95% CI -0.29 to 0.10) in patients without diabetes, and -0.37 (95% CI -0.52 to 0.23) in patients with diabetes ($P=0.066$). The mean change in fibrosis stage by histology was 0.05 (95% CI -0.08 to 0.18) in patients without diabetes, and -0.03 (95% CI -0.16 to 0.10) in patients with diabetes ($P=0.359$). The mean change in NAFLD activity score was -0.55 (95% CI -0.76 to -0.33) in patients without diabetes, and -1.50 (95% CI -2.14 to -0.87) in patients with diabetes. However, the mean change in ALT (20.22 IU/L, 95% CI -26.42 to -14.03 vs. -4.48 IU/L, 95% CI -8.54 to -0.42) and AST (-10.67, 95% CI -14.86 to -6.49 vs. -2.58, 95% CI -5.02 to -0.14) were significantly larger in patients without diabetes compared to those with diabetes ($P<0.05$).

Conclusion: In the placebo arm, patients with diabetes had a greater improvement in hepatic steatosis than patients without diabetes. The histologic response in patients received placebo treatment according to the diabetes is beneficial in design of further NAFLD trials.

Abstract Submission No. 101081
P-0348

Abnormalities of male sex hormones in patients with MASLD and advanced fibrosis

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Background: The liver and the reproductive system are bidirectionally linked.

Methods: A cross-sectional study was conducted in 82 men with NAFLD. Fibrosis assessment was performed using the Fibroscan. Ordinal logistic regression was used to measure the association of total testosterone and NAFLD progression category.

Results: We found that the associations between the T level and the degree of fibrosis of NAFLD were significant in men aged ≥ 55.8 years ($p<0.05$), with waist circumference ≥ 101.5 cm ($p<0.001$), with dyslipidemia ($P<0.01$) and smoking ($p<0.05$). Patients with low T level have higher degree of fibrosis ($p=0.05$). A significant direct correlation is identified between F3-4 and TT ($p=0.001$).

Conclusions: Abnormal testosterone levels correlate with the degree of liver fibrosis, a direction that could be considered in the management of NAFLD.

Abstract Submission No. 101153
P-0349

Evaluation of NAFLD and MASLD criteria in an Indonesian cohort with liver steatosis

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Background: About 30% of Indonesia urban population have liver steatosis. We aimed to compare the clinical characteristics of patients with liver steatosis based on non-alcoholic fatty liver disease (NAFLD) and the new criteria of metabolic dysfunction-associated steatotic liver disease (MASLD).

Methods: This is a retrospective study of patients with liver steatosis using hospital-based registry. Patients were evaluated for demographics, metabolic risk factors and liver stiffness (LS). Diagnosis of liver steatosis was based on controlled attenuation parameter (CAP) (cutoff value 264 dB/m). LS and CAP were measured using Fibroscan.

Results: We identified 113 patients who fulfilled NAFLD criteria: 61.1% female, mean age 55 ± 10.4 years, median CAP 315 (286-335) dB/m, median liver stiffness 6.05 (4.6-7.9) kPa. Of those with NAFLD, all were classified as having MASLD. The most common risk factors were central obesity (93.8%), BMI ≥ 23 kg/m² (92.9%) and insulin resistance (92.9%).

Conclusion: In our patients with liver steatosis, examined with CAP, we found no differences in clinical characteristics using NAFLD or new MASLD criteria.

Abstract Submission No. 101180
P-0350

Prognostic Index for Predicting 10-year Mortality in MAFLD: A Retrospective Cohort Study

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Background and Aims: Metabolic dysfunction-Associated Fatty Liver Disease (MAFLD) has surpassed chronic viral hepatitis as a leading indication for liver transplantation. Identifying MAFLD patients with a high risk of progression to mortality or transplantation within 10 years is crucial for targeted intervention. This study aimed to develop and validate a prognostic index based on initial clinical and laboratory data.

Methods: We conducted a retrospective analysis of 995 MAFLD patients at our center, randomizing them into a study cohort for index development and a validation cohort for testing its predictive accuracy. Predictor selection was based on demographic, biochemical, ultrasound, and histological data, dichotomized via ROC analysis. Multivariate analysis was employed to construct the prognostic index, which was subsequently validated.

Results: The cohort consisted of 528 females (53.1%), with a mean age of 51.6 ± 12.4 years. Survival without transplantation averaged 21.1 years, with 5- and 10-year survival rates of $92.68 \pm 0.88\%$ and $85.0 \pm 1.46\%$, respectively. Albumin levels, GGT, and platelet count emerged as independent predictors, composing the prognostic index (sensitivity 84.6%, specificity 83.7%, AUC: 0.902). Patients with an index >0.103 had a 38.4% mortality or transplantation rate at 10 years,

compared to 2.3% for those ≤ 0.103 . The validation cohort confirmed the index's predictive reliability ($p=0.09$).

Conclusions: A prognostic index comprising baseline albumin, GGT, and platelet count accurately predicts 10-year mortality and transplantation need in MAFLD patients. This tool can facilitate early identification and enhanced management of patients with aggressive disease trajectories, potentially improving clinical outcomes.

Abstract Submission No. 101193
P-0351

Liver stiffness is associated with liver related morbidity but not cardiovascular events in MAFLD.

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Background: Liver stiffness (LSM), has been demonstrated to predict liver related morbidity (LRM), as well as cardiovascular morbidity in those with diabetes. Our study sought to determine whether elevated LSM predicts cardiovascular events and all cause mortality in all those with MAFLD at an Australian university teaching hospital.

Methods: Patients with MAFLD and received a Fibroscan prior to July 2019 were included in the study. Records up to October 2023 were reviewed. LRM, major adverse cardiovascular events (MACE) or all cause mortality (ACM) were identified.

Results: The analysis included 248 patients (female 154/248, mean age 52.4 yrs SD 13.8). There were 7, 18 and 5 patients with LRM, MACE and ACM respectively. The AUROC was found to be significant for LSM predicting LRM (AUC = 0.795, $p=0.008$, 95% CI 0.569-1.00) but not for MACE (AUC = 0.508, $p=0.908$, 95% CI 0.365-0.651); or ACM (AUC = 0.631, $p=0.317$ 95% CI 0.305-0.957). The optimal LSM cut-off for predicting LRM was found to be > 15.6 kPa. Cox regression analysis revealed there was a significant increase in LRM for LSM > 15.6 kPa (HR 16.95, $p=0.01$), but not for MACE (HR 1.99, $p=0.258$) or ACM (HR 2.2, $p=0.494$).

Conclusions: Our study indicates that LSM correlates with LRM but not MACE or ACM. Limitations include small study size and relative short follow-up period. Further longitudinal data will be useful in confirming these findings.

Abstract Submission No. 101266
P-0352

Study of the Relationship between Vitamin D Levels in Patients with NAFLD

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Non-alcoholic fatty liver disease (NAFLD), over the past few years, has become the most common chronic liver disease, increasingly diagnosed in younger and older individuals.

We aimed to explore the potential link of serum vitamin D concentration with NAFLD and indicators characterizing activity, fibrosis, as

well as lipid and carbohydrate metabolism. A total of 128 participants were identified, 27.3 % ($n=35$) with insufficiency of serum 25-OH-Vitamin D level and 72.7 % ($n=93$) with deficiency, and supplementation of Vitamin D was recommended during 12 weeks. The intake of vitamin D led to an increase in the level of the vitamin D metabolite - 25-OH-D - on average by 20.08 (95% CI: 17.12; 23.18) ng/ml. In 61% of patients, vitamin D levels normalized, with a reduction in deficiency to 15% and insufficiency to 24%.

The intake of vitamin D positively influenced weight reduction, on average by 2 kg ($p < 2.236e-13$), BMI by 0.96 ($p < 2.959e-13$), and a decrease in waist circumference by 4.25 cm ($p < 5.786e-13$). A statistically significant decrease was observed in the concentration of triglycerides by 0.25 mmol/L ($p < 0.001$), glucose by 0.31 mmol/L, and AST (Aspartate Aminotransferase) by 0.78 U/L.

Our cross-sectional study provides evidence that there is a significant correlation between serum vitamin D concentration and NAFLD patients. A minor positive correlation has been observed between vitamin D and FIB-4 (Fibrosis-4) scores and moderate negative correlation with FLI (Fatty Liver Index) scores.

Abstract Submission No. 101289
P-0353

Association of *PNPLA3*, *TM6SF2* and *HSD17B13* variants with NAFLD risk in HIV and non-HIV individuals

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Background: Non-alcoholic fatty liver disease (NAFLD) has multiple risk factors, including genetic factors. People living with human immunodeficiency virus (PLWH) have a higher prevalence of NAFLD compared to those without human immunodeficiency virus (HIV) infection. However, the genetic factors in PLWH with NAFLD are unclear.

Objective: This study aimed to investigate whether *PNPLA3* rs738409, *TM6SF2* rs58542926, and *HSD17B13* rs6834314 were associated with the risk of NAFLD and whether PLWH with NAFLD had similar genetic risk factors as those without HIV.

Methods: These single nucleotide polymorphisms (SNPs) were determined by TaqMan allelic discrimination in blood samples of 142 healthy controls, 136 NAFLD patients, and 253 PLWH with NAFLD.

Results: The genotype distributions of *PNPLA3* (CC vs GG genotypes) were significantly different among the studied groups ($P < 0.05$), while no significant differences were found for the *TM6SF2* and *HSD17B13* genotypes. The NAFLD group showed a higher frequency of *PNPLA3* GG genotype compared to healthy controls (OR 3.8; 95% CI 1.7 - 8.3). Compared to the PLWH with NAFLD group, the NAFLD group had higher frequencies of CG and GG genotypes of *PNPLA3* and a lower frequency of GG genotype of *HSD17B13*. The multivariate analysis revealed factors significantly different between the two groups, including age, controlled attenuated parameter, body mass index, alanine aminotransferase, high-density lipoprotein, gender, *PNPLA3* GG genotype, and *HSD17B13* GG genotype.

Conclusion: *PNPLA3* was associated with NAFLD development while other SNPs were not associated with NAFLD. The genotypes for PLWH with NAFLD were not significantly different from healthy controls.

Abstract Submission No. 101312

P-0354

Prognosis of patients with biopsy-confirmed MASLD - A multicenter study

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Background: AASLD, EASL, and others recently proposed the concept of Steatotic Liver Disease (SLD). We aimed to clarify the prognosis of biopsy-confirmed MASLD.

Methods: We included 1,398 patients with NAFLD who underwent liver biopsy and were centrally pathologically diagnosed. Various clinical and pathological parameters were compared between MASLD and non-MASLD NAFLD patients who did not have any cardiometabolic criteria (CC). 5-, 10-, and 15-year rates of all-cause mortality and liver-related events were calculated.

Results: MASLD was applicable to 1,381 (98.8%) with NAFLD. MASLD vs. non-MASLD NAFLD (n=17): age: (mean) 54.6 vs. 45.6 years (P=0.009), BMI: 28.0 vs. 20.9 kg/m² (P<0.001), diabetes: 36.7% vs. 0% (P<0.001), TG: 159 vs. 107 mg/dL (P=0.029), HDL-C: 49.6 vs. 59.9 mg/dL (P=0.009) and fasting blood glucose: 114 vs. 86.6 mg/dL (P=0.002). Histopathological findings of inflammation, ballooning, fibrosis progression, and percentage of MASH were all significantly higher in MASLD. With a median (range) of 4.6 (0.3-21.6) years of follow up, the prognosis of MASLD was totally good: 47 patients died during the observation period, and one patient underwent orthotopic liver transplantation. The 5-, 10-, and 15-year overall mortality rates for MASLD were 1.9%, 4.9%, and 9.2%, respectively. The incidence rates of liver-related events at 5, 10, and 15 years were 3.3%, 7.2%, and 9.0%, respectively. In contrast, none of the Non-MASLD NAFLD patients died, had liver-related events during observation.

Conclusion: The prognosis of MASLD was similar to that of NAFLD. Non MASLD NAFLD was considered to be a mild disease with a good prognosis.

Abstract Submission No. 101379
P-0355

Effect of ezetimibe on nonalcoholic fatty liver disease: A meta-analysis and systematic review.

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Background and Objectives: Nonalcoholic fatty liver disease (NAFLD) is one of the leading causes of liver cirrhosis. Currently, there are no drugs has been tested for phase III clinical trials or approved by regulatory agencies for the management of NAFLD. Ezetimibe can potentially treat NAFLD by inhibiting lipogenesis, decreasing hepatic free fatty acids, improving insulin sensitivity, and decreasing hepatic inflammation and fibrosis. This study aims to assess the effect of ezetimibe in reducing hepatic fibrosis in patients with NAFLD, including changes in liver imaging, histology, biochemical parameters, insulin resistance, and incidence of liver-related complications.

Methodology: We performed a computerized literature search of PubMed, Cochrane Central Register of Controlled Trials, Science Citation Index Expanded, and Cumulative Index to Nursing and Allied Health Literature, and ClinicalTrials.gov from inception to October 2023. We included meta-analyses, systematic reviews, and randomized controlled trials. Studies with data that met the inclusion criteria were selected. Two authors independently assessed risks for biases and disagreements were resolved by consensus.

Results: This study included five trials involving 243 patients. Three trials compared ezetimibe to placebo, one trial compared ezetimibe and rosuvastatin combination to rosuvastatin monotherapy, and one trial compared ezetimibe to acarbose. Data synthesis showed no significant difference in ezetimibe compared to controls in improving liver fibrosis, liver biochemical parameters, and insulin resistance.

Conclusion: Ezetimibe is not recommended for the treatment of NAFLD due to the lack of evidence of benefit in hepatic fibrosis. Further randomized controlled trials with larger sample sizes and extended observation time is necessary.

Abstract Submission No. 101406
P-0356

Lipid-metabolic induction pro-inflammatory extracellular vesicle in the progression of MAFLD

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Background: Extracellular vesicles (EVs) consisting of DNA, RNA, proteins, and lipids to communicate with neighboring cells are crucial in both physiological and pathological regulations. The lipid-metabolism dysfunction of hepatocytes might affect production, releasing, size distribution and cargo contents of EVs, however, it remains unclear the characteristics of hepatocyte-secreting EVs in the progression of metabolic-associated fatty liver disease (MAFLD).

Method: First, lipid-metabolism dysfunction was induced with two mechanisms in cultivated primary human hepatocytes (PHH), including fatty acid overloads by oleic acid (OA) and impairment of cholesterol-to-cholesteryl ester (CE) by TMP-153, an inhibitor of sterol O-acyltransferase. Next, the hepatic steatosis, cellular senescence and EVs secretion were investigated, including by lipid profiling, filipin and SAβG staining, senescent biomarkers, and nanoparticle tracking analysis. Then, the contents of isolated EVs were examined in the conditional medium and the serum sample of MAFLD patients.

Result: Hepatosteatorosis with prominent triglyceride accumulation was induced in PHH with both groups, with additional CE deposit with OA treatment but without that with TMP-153. The OA-treated PHH secreted smaller size of EVs (≤200 nm), whereas with TMP-153 treatment, the cells exhibited significantly senescent phenotypes and secreting EV in a broad range (0~1000 nm). Furthermore, the cargos in the isolated EVs induced by TMP-153 contained substantially elevation of pro-inflammatory factors at protein and mRNA levels. Finally, the EVs were validated in the serum samples from MAFLD patients stratified by age groups.

Conclusion: Lipid metabolism dysfunction might trigger senescence of hepatocytes to release EVs containing pro-inflammatory factors in the MAFLD progression by aging.

Abstract Submission No. 101414
P-0357

Effects of Body Adipose Composition on Liver Histology of MASLD/MAFLD in an Asian Population

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Obesity is closely related to MASLD/MAFLD, but the relationship of the different adipose components to the severity of the disease is not well understood. The magnetic resonance-based AMRA® body composition measurements were performed in 101 biopsy-proven patients with MAFLD, investigating the correlation of total adipose tissue (TAT), total abdominal adipose tissue (TAAT), abdominal subcutaneous adipose tissue (ASAT) and visceral adipose tissue (VAT) with liver histology. The NASH CRN score was used to divide histological stages. MAFLD patients are older (45.1 ± 12.9 vs. 39.8 ± 11.7) and have higher BMI compared to normal controls (33.8 ± 6.8 vs. 27.1 ± 7.1 , p -val <0.05). On analyzing the subcomponents of AT, the subcutaneous AT was not correlated with HOMA-IR or NASH-CRN components. The VAT index was significantly correlated with all NASH-CRN components (all p -val <0.05), while the VAT volume was significantly related to steatosis, ballooning, and fibrosis (all p -val <0.05) but not lobular inflammation. Additionally, the HOMA-IR was positively correlated to VAT index ($r=0.31$, p -val <0.05) and VAT volume ($r=0.36$, p -val <0.05), while the serum triglyceride (TG) level showed a negative relationship (VAT index: $r=-0.34$, VAT volume: $r=-0.39$; both p -val <0.05). In steatosis, TG levels, VAT index, and VAT volume (mean $r=0.62$ and 0.68 , respectively; all p -val <0.05), but not TAAT, were positively correlated. However, the HOMA-IR in the status of lobular inflammation was only found to correlate to VAT index at mild level and VAT volume at moderate ($r=0.33$ and 0.73 , respectively; both p -values <0.05). The visceral adipose tissue index best correlates with the severity and different components of NASH CRN in Asian patients.

Abstract Submission No. 101433
P-0358

Cryptogenic fibrosis represents genetically-distinct entity in MAFLD spectrum similar to IPF

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Background: Patients with “cryptogenic fibrosis”—ie. marked fibrosis despite minimal hepatic steatosis or low NAFLD Activity Score (NAS)—are increasingly reclassified as MAFLD.

Methods: We analyzed participants from a multi-ancestral Asian cohort who had biopsy for suspected MAFLD. Histology was scored using CRN NAS. To prioritize SNPs associated with paradoxical fibrosis, IPW weights were applied based on inverse-probabilities for each combination of fibrosis stage and NAS steatosis score. Associations were adjusted for demographics, comorbid metabolic disease (HLD/HTN/T2DM), medications (Vitamin E/metformin/sulfonylurea/insulin/statin/ACEi/ARB), smoking, caffeine, alcohol consumption, ethnicity and genomic PCs.

Results: GWAS on $n=232$ patients were analyzed at time of reporting (M:F=110:122, Chinese/Malay/Indian/Others:54.4%/27.0%/14.1%/4.4%, BMI median[IQR] 32.2[27.2-38.8]). We found deleterious alleles involving *NAMPT*, *APOLD1*, *NNMT*, *MTCL1*, *ERN1*, *PTTG1IP*, *FLVCR1-DT* which were prevalent among patients who developed perplexingly-severe (ie. “cryptogenic”) fibrosis despite quiescent NAS scores. Interestingly, except for *PTTG1IP* and *FLVCR1-DT*, these loci have been previously implicated in idiopathic pulmonary fibrosis (IPF). One exception, *PTTG1IP*, has not been linked to fibrotic disorders, but encodes the interaction-partner of PTTG1, which in turn has been strongly-implicated in hepatic fibrosis and portal hypertension; therefore, the association of *PTTG1IP* SNPs with cryptogenic fibrosis could be mediated through its interaction with PTTG1.

Conclusions: Cryptogenic fibrosis represents a genetically-unique entity within MAFLD, with similar genetic architecture to IPF. It is interesting to speculate whether this subgroup may benefit from anti-fibrotic therapies used to treat IPF in view of possible shared biology. GWAS of additional $n=227$ patients (total: $n=459$) patients is underway, and complete results will be presented at the meeting.

Abstract Submission No. 101461
P-0359

Patient awareness of Steatotic liver : Multicenter study

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Background: Patients with steatotic liver (SL) who attend outpatient gastroenterology clinics were the subjects of this study, which sought to assess their awareness and knowledge levels.

Methods: The study included patients aged 18 and above seeking care at gastroenterology outpatient clinics for any reason. Following obtaining consent, participants underwent face-to-face interviews using a structured questionnaire. Questions about hepatic steatosis awareness, understanding of associated diseases and problems, treatment familiarity, preventive strategies, and information sources were all included in the survey.

Results: A total of 1431 patients from nine different centers participated, with 48.5% being male (n: 694) and a mean age of 47.8±15.8 years. Notably, 64.5% were classified as overweight or obese. Surprisingly, 10.9% (n: 156) of patients had never heard of SL. Of those informed, 55.2% (n: 699) received information from healthcare professionals. The majority (85.4%) recognized SL as a serious concern, with obesity (83%) being most commonly associated, while diabetes mellitus (23%) was least associated. Concerningly, 74.6% believed SL could progress to cirrhosis, and 57.3% thought it could lead to liver cancer. While 56.3% considered imaging as the best diagnostic tool, 72.3% emphasized weight loss in treatment, and 31.8% mentioned herbal remedies.

Conclusions: This study underscores the crucial need to educate the public about SL, a leading cause of liver cirrhosis and hepatocellular cancer, which is increasingly prevalent. Efforts should focus on preventive measures through informed public awareness, emphasizing the significance of proper planning and treatment management to curb the progression of this debilitating disease

Abstract Submission No. 101467
P-0360

Low Diagnostic Performance of FIB-4 in Type 2 Diabetes: Impact of Age

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Objectives: The diagnostic performance of fibrosis-4 (FIB-4) in type 2 diabetes mellitus (T2DM) is known to be compromised by spectrum bias. We aimed to investigate the causes of spectrum bias and to determine the most effective approach for implementing FIB-4 in patients with T2DM.

Research Design and Methods: A retrospective biopsy cohort of 1,906 patients with biopsy-proven metabolic associated fatty liver disease (MAFLD) from South Korea, Japan, and Taiwan. Diagnostic performance according to T2DM was again compared after propensity score matching on age, sex, and body mass index (BMI).

Results: The prevalence of advanced fibrosis and cirrhosis was higher in T2DM compared to non-T2DM (26.0% vs 12.2%, $p<0.001$). Patients with T2DM were significantly older than those without (54.9 ± 11.5 vs. 48.9 ± 12.1 years, $p<0.001$). The area under the receiver operating characteristic curve (AUROC) in non-T2DM patients was significantly higher than that of T2DM patients (0.821 vs. 0.761, $p=0.044$). But, AUROCs of FIB-4 according to the same age groups, there was no significant difference of AUROC between patients with T2DM and without (All $p>0.05$), and showed acceptable AUROCs in each group in middle-aged group. After propensity score matching of age, there was no statistically significant difference in the AUROCs of

the T2DM and non-T2DM groups (0.860 vs. 0.761, $p=0.142$) without lowering of sensitivity.

Conclusion: The diagnostic performance of FIB-4 was suboptimal in T2DM patients and could potentially be attributed to the older age distribution among T2DM cohort. FIB-4 remains a valuable tool for excluding advanced fibrosis in middle-aged diabetic patients.

Abstract Submission No. 101569
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Diagnostic value of serum CHI3L1 in a real-world study of nonalcoholic fatty liver disease

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Background: Nonalcoholic fatty liver disease (NAFLD) is linked to liver fibrosis over the long term, however there are currently no non-invasive methods for determining the degree of fibrosis. Here, we look into the relationship between serum Chitinase 3-like 1 (CHI3L1) and liver fibrosis result from NAFLD and assess if it may be used as a predictor for NAFLD.

Methods: A total of 194 patients with biopsy-proven NAFLD were retrospectively enrolled. The demographic characteristics, laboratory variables and pathological features were compared among the subgroups stratified by serum CHI3L1. Correlation analysis between serum CHI3L1 and pathological findings was performed. Serum CHI3L1 alone or in combination with other indices was assessed for its diagnostic efficacy using receiver operating characteristic (ROC) analysis.

Results: Significant differences were seen in the serum CHI3L1 level across patients with varying levels of fibrosis, as well as between non-alcoholic fatty liver and nonalcoholic steatohepatitis (NASH). Serum CHI3L1 was positively correlated with two liver fibrosis biomarkers, namely Fib-4 and NAFLD fibrosis score. With 80.3% sensitivity and 40.6% specificity, a cut-off of 38.7 ng/mL was found to identify people with significant fibrosis (fibrosis grade ≥ 2), and 74.15 ng/mL was found to identify people with advanced fibrosis (fibrosis grade ≥ 3), exhibiting 62.5% sensitivity and 84.3% specificity. Furthermore, the area under the ROC curve for combining serum CHI3L1 and body mass index to identify individuals with NASH activity score > 4 and fibrosis grade ≥ 2 was 0.702.

Conclusions: Serum CHI3L1 exhibits potential as a non-invasive biomarker for patient stratification in NAFLD.

Abstract Submission No. 101594
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A biomarker model of NASH fibrosis progression constructed by lipidomics and metabolomics profiling

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Background: Non-alcoholic steatohepatitis (NASH) is considered the most severe form of non-alcoholic fatty liver disease. It is becoming a major cause of end-stage liver disease such as cirrhosis and hepatocellular carcinoma. However, there are no early biomarkers that can reliably predict which patients are more likely to develop NASH and which NASH patients are more likely to progress to fibrosis. Thus, it is crucial to discover predictive markers of NASH fibrosis.

Methods: We collected serum from 10 healthy individuals, 20 moderate-fibrotic NASH (fibrotic S0-S1) and 20 fibrotic NASH (fibrotic S2-S4) patients. We use mass spectrometry to measure lipids and metabolites. An in-depth analysis of lipids and metabolites was performed in three cohorts to screen for biomarkers. According to VIP>1, the characteristic peaks with significant differences among the three groups were selected through the OLPS-DA model, and the intensity differences between each group were analyzed. Finally, pathway enrichment analysis and diagnostic performance analysis were performed to build a prediction model.

Findings: Compared with healthy people, NASH patients (different grades of fibrosis) have significant differences in the seven lipid metabolism molecules Hex1Cer, Hex1Cer, PE, PE, ST, SHexCer, and LPC. Further analysis found that in moderate-fibrotic NASH vs. healthy people, the molecules with the highest VIP value was ST; while in fibrotic NASH patients vs. moderate-fibrotic NASH patients, the molecule with the highest VIP value was SM. Then we built prediction models based on Lasso or SVM machine learning methods and serum lipid metabolism molecules with VIP>1 (34 or 68) to distinguish NASH patients from healthy people, moderate-fibrotic NASH and fibrotic NASH patients.

Abstract Submission No. 101600
P-0363

Cross-sectional study in general population for prevalence and LSM distribution of MASLD

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Background: The multisociety consensus nomenclature has adopted steatotic liver disease (SLD) with various sub-classifications. We investigated the prevalence of SLD and analyzed the distribution of vibration-controlled transient elastography (VCTE)-derived liver

stiffness measurement (LSM) of metabolic dysfunction associated steatotic liver disease (MASLD).

Methods: A cross-sectional study was conducted in 6530 subjects who received health check-up exams. Conventional B-mode ultrasound was performed in 6530 subjects. Of those subjects with SLD, VCTE was performed.

Results: The prevalence of SLD was 39.5%: MASLD 28.7%, alcohol-related liver disease (ALD) 1.2%, MetALD 8.6%, specific aetiology SLD 0.3%, cryptogenic SLD 0.7%. Liver fibrosis stages classified by VCTE-derived LSM were 89.7/7.5/1.5/0.9/0.4% (fibrosis stage 0/1/2/3/4). We analyzed various cut-off values of FIB-4 for diagnosing VCTE-derived LSM $\geq 8\text{kPa}$. FIB-4 ≥ 1.3 showed that the sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) were 60.6%, 77.0%, 5.3%, and 98.9%, respectively. The referral rate to specialists was 23.8% using FIB-4 ≥ 1.30 . Se of FIB-4 ≥ 1.3 was 55.6% in

Conclusions: A selection bias exists in hepatology centers, then we conducted this general population-based prospective study. FIB-4 showed high NPV but low PPV. FIB-4 might be inadequate as a primary screening for liver fibrosis in the general population. We showed that FLI is useful non-imaging NIT for diagnosing MASLD. UMIN Clinical Trials Registry No. UMIN000035188.

Abstract Submission No. 101760
P-0364

Association of serum total testosterone levels with NAFLD and liver fibrosis in adult Americans

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Background: The association between androgens and NAFLD is complex and not yet fully understood.

Methods: The sample for this study consisted of 3 consecutive cycles of NHANES (cycles 2011-2012, 2013-2014, and 2015-2016) with a total of 29,902 participants. We used USFLI >30 to define NAFLD. The FIB-4 index is a noninvasive method for assessing liver fibrosis in patients with chronic liver disease. Multivariate logistic regression was adopted to explore the relationships.

Results: Our study indicates that higher levels of androgens in the female population are associated with a higher incidence of NAFLD. The highest quartile of testosterone levels compared to the lowest quartile was associated with a 45.4% increased risk of developing NAFLD. In males, we found that the highest quartile of testosterone levels was associated with a 75.2% reduced risk of NAFLD compared to the lowest quartile.

the fibrosis risk in males shows an overall upward trend with increasing testosterone levels. Within the Q3 interval, the fibrosis risk is the highest (adjusted OR=1.557, 95% CI 1.554, 1.560). The effect of testosterone levels on liver fibrosis in females does not show a single trend. Instead, the highest quartile interval exhibits the lowest risk of liver fibrosis (adjusted OR=0.614, 95% CI 0.613, 0.615).

Conclusions: We found that as testosterone levels increased, the risk of NAFLD decreased in males while it increased in females. Additionally, there was a significant association between high testosterone levels in males and the risk of liver fibrosis, which persisted even after adjusting for known confounding factors. These relationships remained independent.

Abstract Submission No. 101763
P-0365

Non Invasive Parameters compared to FibroScan for the assessment of liver stiffness in Fatty Liver

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Background: Given the Invasive nature, cost, and complications, Liver biopsy has been replaced by non-invasive evaluation of liver stiffness using Fibroscan technology. MAFLD (Metabolic dysfunction-associated fatty liver disease) includes imaging and blood markers and doesn't keep liver biopsy as a mandatory diagnostic criterion. To reduce the cost of follow-up fibroscan assessments and ensure applicability at the primary care level, It is desirable to have a blood-based marker that would tally with liver stiffness.

Methods: Noninvasive blood tests namely FIB-4, APRI, NPAR (neutrophil percentage-albumin ratio), PLR (Platelet-to-lymphocyte ratio), and NLR along with fibro scan were performed on MAFLD patients. Patients were grouped into two - Less fibro progressed (F0, F1, F2) and Fibro Progressed group (F3 and F4) Sensitivity, Specificity, Positive Predictive Value, and Negative predictive value were obtained.

Results: Of the blood markers FIB-4 (Sensitivity-0.692, Specificity-0.804, Positive predictive value (PPV)-72.97 Negative Predictive Value (NPV) -77.36, Diagnostic Accuracy (DA) - 75.63) and APRI (Sensitivity -0.820, Specificity - 0.627, PPV -62.75, NPV -82.05, DA - 71.21) correlated better with fibroscan values. PLR has a very high specificity (Specificity -0.980 and PPV-66.6) well above FIB-4 and APRI and comparable PPV as that of FIB-4 and APRI. Regarding CAP NPAR showed a negative correlation (Correlation coefficient of 0.329 and p-value of 0.002); no other parameters correlated with CAP

Conclusions: Based on these results, FIB-4 and APRI may be used for follow-up assessment and may substitute fibroscan evaluation. The role of PLR as a specific marker of liver stiffness and NPAR correlating with CAP needs further exploration.

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Abstract Submission No. 101771

P-0366

MAFLD increases the incidence of HCC in SVR patients with HCV infection

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Background: Liver carcinogenesis is suppressed when sustained virologic response (SVR) achieved by antiviral therapy. However, the risk of liver carcinogenesis does not completely disappear after SVR. Therefore the identification of risk factors for carcinogenesis in the SVR patients is important. This study was to assess the incidence of hepatocellular carcinoma (HCC) in patients who achieved SVR by direct antiviral agents (DAA) with and without Metabolic dysfunction associated fatty liver disease (MAFLD).

Methods: We enrolled patients who achieved SVR by oral DAA treatment (n=257). We examined the incidence of HCC, extrahepatic disease and all and liver related mortality, retrospectively.

In this study, liver steatosis was diagnosed in patients with an average CT value of liver parenchymal less than 50 HU on non-contrast-enhanced CT before DAA treatment.

Results: During a median follow-up period of 6.0 years, 7 patients (2.9%) developed HCC. The 3- and 5-year cumulative HCC development rates were 3.6% and 6.0%, respectively, in all patients. In patients

with the MAFLD, the 3- and 5-year HCC development rates were 10.0% and 18.9%, whereas those were 2.2 % and 3.1 %, in the patients without MAFLD, respectively. (P<0.001).

Compared with non-MAFLD group, MAFLD group had significantly increased overall mortality (8.3 vs 1.9, HR=4.36), incidence of HCC (12.5 vs 1.9, HR=6.57), cardiovascular disease (4.2 vs 0.95, HR=4.42) and decompensated cirrhosis (2.08 vs 0.95, HR=2.12).

Conclusion: Our data indicate that MAFLD were associated with significantly increased overall mortality, and incidence of HCC. Based on these results, the strategy for follow-up of SVR patients with chronic liver disease C should be reconsidered.

Abstract Submission No. 101774

P-0367

Serum CK18f predicts 'MASH resolution' and 'at risk MASH' in patients with MASLD

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Background: The objective of this study was to determine whether the apoptotic marker serum Cytokeratin18f (CK18f) could aid in predicting MASH resolution and treatment response, as well as identifying 'at risk MASH' in patients with MASLD.

Methods: A cohort of 565 MASLD patients underwent a liver biopsy. The study explored liver fibrosis markers and CK18f to predict 'at-risk MASH' patients. Additionally, 110 MASLD patients underwent repeated liver biopsies over a mean 4-year period, comparing serum CK18f changes (Δ CK18f) with liver histological changes (stage, grade, steatosis, and NAS). The study evaluated whether CK18f predicts MASH resolution without worsening liver fibrosis or improvement in liver fibrosis stage without worsening MASH.

Results: Among patients with FIB-4 index ≥ 1.3 , 64% demonstrated CK18f ≥ 260 and possible 'at-risk MASLD,' recommended treatment (Sen 80%, Spe 36%, PPV 64%, NPV 56%). Conversely, FIB-4 index < 1.3 cases with CK18f < 260 were rule out 'at-risk MASLD' (Sen 85%, Spe 34%, PPV 43%, NPV 80%). In the 110 repeated liver biopsy cases, lobular inflammation, hepatocellular ballooning, and NAS changes strongly correlated with Δ CK18f changes. Δ CK18f significantly decreased (P<0.0001) in patients with 'no worsening fibrosis and improved NAS'. Multiple regression analysis associated with Δ CK18f levels. The Δ CK18f decreased (p<0.05) in patients with 'improving fibrosis and no worsening NAS', and associated with Δ type IV collagen 7S levels.

Conclusion: Serum CK18f is a useful non-invasive diagnostic marker for 'at risk MASLD' and can determine treatment efficacy without liver biopsy.

Abstract Submission No. 101786
P-0368

Pharmacodynamics of multiple oral doses of ALG-055009, a THR β agonist, in hyperlipidemic subjects

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Background: ALG-055009 is a nanomolar potent thyroid hormone receptor beta (THR β) agonist being developed for the treatment of metabolic dysfunction-associated steatohepatitis (MASH).

Method: ALG-055009-301 is a completed first-in-human Phase 1 study (NCT05090111) combining evaluation of single-ascending doses (SAD) in healthy volunteers (Part 1), multiple-ascending doses (MAD) in subjects with mild hyperlipidemia (Part 2), and the relative bioavailability/food effect (Part 3) of a softgel formulation in healthy volunteers. Across Parts 1-3, single (≤ 4.0 mg) and multiple (≤ 1.0 mg x 14 days) once daily oral solution doses of ALG-055009 were well tolerated in healthy volunteers and subjects with mild hyperlipidemia (HL; LDL-C >110 mg/dL, respectively (Charfi et al., APASL 2023). In Part 2, HL subjects (N=10/cohort) were randomized 4:1 to receive ALG-055009:placebo. Reported here are pharmacodynamic data from Part 2.

Results: In Part 2, 50 HL subjects (94% male, mean age 41 years, mean BMI 26.5 kg/m²) were enrolled across 5 cohorts. Daily dosing with ALG-055009 for 14 days resulted in generally dose-dependent decreases in LDL-C, apolipoprotein-B, VLDL, and triglycerides with maximum decreases of 26.8%, 27.6%, 35.7%, and 35.7%, respectively, relative to baseline at 1.0 mg. For other lipids evaluated (e.g., total cholesterol and non-HDL cholesterol), levels were either unaffected or the effect was modest. A dose-dependent increase in sex hormone binding globulin (SHBG), a marker of target engagement in the liver, up to 95% relative to baseline was also observed.

Conclusion: Favorable, dose-dependent pharmacodynamic effects on atherogenic lipids and SHBG were observed with multiple dosing of ALG-055009 in HL subjects.

Abstract Submission No. 101854
P-0369

Saroglitazar improves steatosis and fibrosis in metabolic-associated fatty liver disease

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Background: Saroglitazar, a dual peroxisome proliferator-activated receptor α/γ agonist, is a potential therapeutic option for metabolic-associated fatty liver disease (MAFLD). This prospective, observational, real-world study aimed to determine the efficacy and safety of Saroglitazar in patients with MAFLD.

Methods: We included patients with MAFLD who received Saroglitazar 4 mg once daily for 48 weeks. Blood investigations, liver stiffness measurement (LSM), and controlled attenuation parameter (CAP) (FibroScan) were done at baseline, 24 weeks, and 48 weeks. Data was analyzed by ITT.

Results: Of 241 patients screened, 162 were included, and 131 completed 48 weeks of treatment (mean age 51.8 $\pm$ 11.6 years, 70.2% males, mean body mass index 29.2 $\pm$ 5.1). Of the 131 patients, 87 had

diabetes, 52 had hypertension, and all had dyslipidemia. After 48 weeks, alanine transaminase (ALT) reduced significantly from 91 (46–142) to 35 (29–51) ($p < 0.0001$) and aspartate aminotransferase (AST) (U/L) from 84 (44–116) to 33 (28–47) ($p < 0.0001$) and LSM (kPa) from 9.5 (7.1–11.9) to 6.8 (5.9–8.6) ($p = 0.018$). CAP, glycated hemoglobin, and lipid parameters also improved significantly. On linear regression, there was a significant association between percent change in ALT and AST with TG reduction after treatment ($p = 0.013$ and 0.032 respectively).

Conclusion: We conclude that Saroglitazar leads to significant improvement in transaminases, LSM, and CAP in MAFLD patients.

Abstract Submission No. 101986
P-0370

Metabolic-Associated Fatty Liver Disease and hyperferritinemia

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Background: Metabolic-Associated Fatty Liver Disease (MAFLD) is the commonest chronic liver disease worldwide and one of the leading causes of liver cirrhosis and hepatocellular carcinoma. New definition of MAFLD refers to hepatic steatosis in addition to one of the following criterias: overweight/obesity, presence of type 2 diabetes mellitus (T2DM), or evidence of metabolic dysregulation. Cardiometabolic criteria in adults at least 1 of 5 are following:

1. BMI ≥ 25 kg/m² or Waist circumference $\geq 94/\geq 80$ cm for Europid men/women
2. Fasting glucose (GLUC) ≥ 5.6 mmol/L or 2-h post-load glucose levels ≥ 7.8 mmol/L or HbA1c $\geq 5.7\%$ or treated for T2DM
3. Arterial pressure $\geq 130/85$ mmHg or specific antihypertensive drug
4. Serum triacylglycerols (TG) >1.7 mmol/L or lipid lowering treatment
5. high density lipoprotein (HDL) cholesterol $<1.0/<1.3$ mmol/L men/women or lipid lowering treatment.

The aim of the study is evaluation of correlation BMI, liver function tests, and lipid profile with MAFLD in small Armenian cohort.

Methods: 72 patients with ultrasound-diagnosed hepatic steatosis were involved in the study (62.5% male), 23–76 years old (51.0 $\pm$ 12.3), BMI 31.7 $\pm$ 5.0 kg/m². We evaluated following biochemical and lipids profile parameters: AST, ALT, GGT, GLUC, TG, cholesterol (CHOL), HDL, low density lipoprotein (LDL), ferritin (FERR).

Results: 41% had diabetes, 70% with BMI ≥ 30 kg/m², FERR elevated in 47%, F4 had 14% of patients. Range and mean $\pm$ SD/SE: FERR 24–1947 ng/mL (396.7 $\pm$ 61.4); TG 0.8–57 (3.3 $\pm$ 0.8), CHOL 2.8–19.5 (5.9 $\pm$ 2.3), HDL 0.4–1.8 (1.0 $\pm$ 0.3), LDL 0.6–9.1 mmol/L (3.8 $\pm$ 1.5), GGT 18–960 U/L (83.4 $\pm$ 14.8), ALT 8–339 (62.9 $\pm$ 6.1), AST 12–192 (41.3 $\pm$ 3.9), GLUC 4.4–24.6 mmol/L (6.8 $\pm$ 2.9).

Conclusions: In ultrasound-diagnosed hepatic steatosis average level of enzymes and ferritin is high. Presence of Cardiometabolic criteria and high risk of atherosclerosis is revealed in more than third of patients with MAFLD.

Abstract Submission No. 101988
P-0371

Comparison of liver fibrosis among patients with NAFLD with or without viral marker

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INTRODUCTION: Hepatitis B, C, and D virus infection and fatty liver disease are major causes of liver cirrhosis and have become one of the major public health problems worldwide. We aimed to assess fibrosis stage of NAFLD patients with or without hepatitis virus markers

MATERIALS AND METHODS: The research involved 11,696 participants, utilizing the elastography device (Fibrotouch) to assess fatty liver and cirrhosis from 2015 to 2023 at Happy Veritas Hospital. Subsequently, a focused statistical analysis was conducted on data from 4,508 participants with fatty liver, applying specified exclusion criteria.

RESULT: Among participants with fatty liver, the prevalence of liver cirrhosis was relatively low in age groups without detected viruses, than those with HBV alone, combined HBV and HDV, and HCV detected. However, in the 45-49-year-old group with HBV alone, the occurrence of liver cirrhosis (mean=27.34±8.36, p=0.005) was notably higher compared to other groups. Conversely, within the combined HBV and HCV group, the average age was 26.9, whereas in the control group, it was 23.3.

Correlation analysis showed that liver stiffness was positively correlated with the degree of obesity (r=2.741, p=0.001), while a negative correlation was observed with age. A positive correlation was observed between HBV positive participants with steatosis and liver stiffness (r=1.924, p=0.001), suggesting that HBV infection may be expected to exacerbate cirrhosis.

CONCLUSION: The risk of cirrhosis may escalate in association with fatty liver, hepatitis B virus infection, high BMI, and the presence of comorbid diabetes, exhibiting age-specific patterns.

Abstract Submission No. 102024
P-0372

Familial NAFLD Cirrhosis Case Series

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Nonalcoholic fatty liver disease (NAFLD) is a prevalent global cause of chronic liver disease with a multifactorial origin involving genetic and environmental factors. This case report discusses a 66-year-old male with NAFLD cirrhosis, his two siblings also diagnosed with undiagnosed NAFLD cirrhosis, indicating familial aggregation. The patient had various comorbidities, including diabetes, hypertension, and chronic kidney disease, with a history of cirrhosis for seven years. Despite medical efforts, the disease progressed to decompensated cirrhosis, leading to the patient's death in 2020.

The patient's sister, also diagnosed with liver test elevation and diabetes, and another deceased brother with cirrhosis underscored the familial predisposition to NAFLD. It was only known that he was also an obese and diabetic patient. Despite interventions such as diet and exercise, their conditions mirrored each other on imaging and clinical parameters.

This case report emphasizes the increased risk of NAFLD among relatives of affected individuals and the presence of shared genetic and environmental factors. It highlights the importance of screening family members for early detection of undiagnosed NAFLD and metabolic disorders. Implementing lifestyle modifications and, if necessary, pharmacotherapy at an early stage could potentially prevent NAFLD progression in these individuals.

Abstract Submission No. 102090
P-0373

Predictive Factors for Major Adverse Cardiovascular Events Among Patients with Biopsy-Proven MASLD

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is closely associated with metabolic syndrome and significantly increases long-term risk of cardiovascular disease. We aimed to study the predictive factors associated with major adverse cardiovascular events (MACE).

Methods: A retrospective cohort study was conducted on adults with biopsy-proven MASLD, enrolled between January 2007 and May 2019 with follow-up until November 2023. The primary outcome was MACE occurrence, defined by coronary artery disease (CAD), and cerebrovascular disease (CVD). Secondary outcomes included factors associated with MACE.

Results: Among 276 patients with biopsy-proven cases, 152 (55.1%) were female, mean age 42.2±13.9 years. The mean BMI was 39.0±13.4 kg/m², and 174 (63.0%) were classified as obese. Diabetes was present in 120 (43.5%), dyslipidemia in 161 (58.3%), and hypertension in 154 (55.8%). Advanced fibrosis was 29 (10.5%) patients, and steatohepatitis (MASH) from biopsy was 85 (30.8%) patients.

Over a median 7.8-year follow-up (7.2, 11.4), MACE occurred in 30 (10.9%) patients, including 19 (6.9%) with CAD and 12 (4.3%) with CVD. Univariate analysis identified age, sex, BMI, diabetes, hypertension, MASH from biopsy, advanced fibrosis, FIB-4, APRI, and NFS score as factors associated with MACE. Multivariate analysis revealed age (aOR 1.23(1.14-1.33), p<0.001), presence of diabetes (aOR 1.89(1.12-4.98), p=0.026), and FIB-4 score (aOR 1.95(1.13-3.34), p=0.016) as independent predictors of MACE (**Table**).

Conclusion: In this real-world longitudinal study, MASLD and MASH significantly increased risk of cardiovascular disease. Age and diabetes were established as key risk factors for MACE, with FIB-4 score identified as an independent and significant predictor for MACE occurrence.

Abstract Submission No. 200021
P-0374

Study on Prothombin Time and Liver Dysfunction in Metabolic Syndrome Patients in Rajshahi, Bangladesh

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Background: Metabolic syndrome (MetS) is an important public health concern with a cluster of non-communicable diseases (NCD) related health problems.

Objective: To strengthen the understanding of the association between liver enzymes and the risk of metabolic syndrome this study was designed to investigate the relationship between metabolic syndrome and other factors such as body mass index (BMI) with liver function tests, that is, aspartate aminotransferase (AST), ALT and γ -glutamyl transferase (GGT) and prothrombin time in Bangladeshi adults.

Subjects: We screened patients for metabolic syndrome and 634 Bangladeshi adults (age range: 18–88 years) were enrolled and the factors related to metabolic syndrome were investigated.

Results: The prevalence rate of metabolic syndrome in Bangladeshi adults 31.9% using the modified ATP III criteria. Males had a slightly higher prevalence rate than females ($P < 0.01$), and prevalence of metabolic syndrome increases with age and had significantly higher BMI values and AST, ALT levels and INR ($p < 0.001$). According to the logistic regression analysis, elevated levels of ALT and INR were significantly associated with the prevalence of MetS ($p < 0.01$ and $p < 0.001$, respectively).

Conclusion: Abnormal liver functions of different extents and magnitudes have been found in metabolic syndrome patients, ALT and INR should be considered during the management of metabolic syndrome patients and also to assess their long-term follow-up prognosis.

Abstract Submission No. 200022
P-0375

Relationship between colorectal polyp and non-alcoholic fatty liver disease: A cross-sectional study

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Background: Both non-alcoholic fatty liver disease (NAFLD) and colorectal neoplasms are prevalent and on the rise worldwide. Recent research has linked NAFLD to a higher incidence of colorectal polyps, and it is speculated that insulin resistance and chronic inflammation in NAFLD patients may facilitate the development of colorectal polyps and cancer.

Methods: This cross-sectional analytic study was conducted among 280 participants who underwent screening colonoscopy at Rajavithi Hospital, Bangkok, Thailand, between 2018 and 2021. Patients with a history of significant alcohol consumption and a family history of colorectal cancer were excluded. The aims of the study were to evaluate the prevalence and relationship between colonic polyps and the presence of NAFLD. NAFLD was defined by the presence of steatosis on ultrasonography with feature(s) of metabolic dysfunction.

Results: Of the 280 participants, 66.5% were female, with a mean age of 57.5 ± 11 years and a mean BMI of 23.3 ± 3.9 kg/m². Diabetes mellitus and hypertension were noted in 29.2% and 70.8%, respectively. Upon colonoscopy, colorectal polyps were found in 15.4% of cases (65% tubular adenoma, 28% hyperplastic, and 7% inflammatory polyps). In the multivariate analysis, age (adjusted OR 1.04; 95% CI: 1.01–1.08, $p = 0.025$) and presence of NAFLD (adjusted OR 2.70; 95% CI: 1.35–5.45, $p = 0.005$) were associated with the presence of colorectal polyps.

Conclusion: NAFLD is associated with an increased prevalence of colorectal polyps in asymptomatic, average-risk individuals. Therefore, early screening colonoscopy may be considered before the age of 45–50 if the person has NAFLD.

Abstract Submission No. 200030
P-0376

Dapagliflozin in the management of diabetic patients with Non-alcoholic fatty liver disease

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Background: SGLT2 inhibitors increase urinary glucose excretion via inhibiting glucose reabsorption in the proximal renal tubules. They are associated with increase in fatty acid (FA) mobilization from adipose tissues and FA uptake and beta-oxidation in the liver. They also have the potential to reduce various multiple risk factors for arteriosclerosis, such as obesity, dyslipidaemia and hypertension, as well as diabetes.

Overview: In this observational study, our objective was to see the reduction in liver fat content, hepatic steatosis, inflammation and/or fibrosis in diabetic patients with the addition of the SGLT2 inhibitor dapagliflozin in comparison to standard anti-diabetic therapy without SGLT-2 inhibitors or GLP-1 receptor agonists.

Primary objective: To study the improvement of hepatic steatosis in diabetic patients with NAFLD.

Secondary objectives: To see improvement in the following parameters:

1. Hepatic transaminases
2. Hepatic fibrosis in patients who are followed up for more than six months
3. Insulin Resistance
4. Weight and body fat.

A total of 70 subjects were selected. Two groups of patients were selected for observational comparative study.

● Group 1: Diabetic patients suffering from NAFLD, who were taking SGLT2 inhibitor Dapagliflozin 10 mg OD along with other anti-diabetic treatment excluding GLP1 receptor agonists.

● Group 2: Diabetic patients suffering from NAFLD, who were on anti-diabetic treatment without SGLT2 inhibitors or GLP1 receptor agonists.

Fibroscan, Liver function tests, Fasting lipid profile and other parameters were done every 12 weeks.

Results: We found significant reduction in liver fat content, based on fibroscan follow up.

Abstract Submission No. 200063
P-0377

Comparison of the efficacy of UDCA versus vitamin E+C in patients with NASH

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Background and aim: Nonalcoholic steatohepatitis is a frequent liver disease that can progress to cirrhosis and for which effective therapy is still lacking. Despite an important role of oxidative stress in the pathogenesis of NASH, antioxidant approaches have not been investigated sufficiently.

The aim of the study was to compare ursodeoxycholic acid versus vitamin E plus vitamin C in patients with nonalcoholic steatohepatitis.

Methods: Patients with diagnosis of NASH were randomly assigned to receive either UDCA 15 mg/per kg/day (group A) or vitamin E 800 mg/day plus vitamin C 500 mg/day (group B) for 12 months and control group, which did not receive any medical treatment. Lifestyle modification was advised to all groups. The primary study end point was improvement in alanine transaminase levels, secondary end points were improvement in steatosis score and improvement in fibrosis score.

Results: 107 patients were included 35 in the group A, 52 in the group B and 20 in control group, 11 patients dropped out, non because of side effects. Baseline characteristics were not significantly different between groups. After 12 months treatment with vitamin E plus C, as compared with UDCA, was associated with a significant reduction of mean alanine aminotransferase levels. Similarly, there was significant reduction of both mean steatosis score and fibrosis score.

Conclusion: Vitamin E plus C combination is an effective, safe and inexpensive treatment option in patients with NASH and may be useful to reduce damage from oxidative stress and slow the process leading to cirrhosis.

Abstract Submission No. 200107
P-0378

Efficacy Of Flaxseed In Non-Alcoholic Fatty Liver Disease: A Systematic Review and Meta-Analysis

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Non-alcoholic fatty liver disease (NAFLD) is prevalent worldwide and can lead to cirrhosis. Recently, there is growing interest in using foods rich in antioxidants to treat metabolic disorders such as NAFLD. Flaxseed (*Linum usitatissimum*) is rich in omega-3 and fiber. Therefore, this study aims to review evidence regarding efficacy of flaxseed in NAFLD. Literature search was conducted on four databases: PubMed, Embase, Cochrane, and Scopus using keywords flaxseed, non-alcoholic fatty liver disease and related terms. At the start of search, 111 studies were identified and using appropriate eligibility criteria, four clinical trials were selected and assessed for methodological quality using Cochrane RoB 2.0. Random effects meta-analysis was done in two studies, comparing flaxseed and lifestyle changes. The other two studies used different forms of flaxseed and additional intervention for control group. Results were expressed in mean difference (MD) of change from baseline. After 12 weeks, flaxseed group show significant improvement in liver enzymes (pooled MD -6.35, 95% CI: -9.21 to -3.49, $p < 0.0001$), lipid profile (pooled MD -16.08, 95% CI: -25.35 to -

6.81, $p = 0.0007$), liver fibrosis (pooled MD -0.57, 95% CI: -1.09 to -0.04, $p = 0.04$), and steatosis (pooled MD -26.93, 95% CI: -38.94 to -14.92, $p < 0.0001$) when compared to lifestyle group. However, there is no significant difference in inflammatory biomarkers. In NAFLD patients, flaxseed demonstrated significant improvement in liver enzymes, steatosis, fibrosis, and metabolic profile, but not inflammatory biomarkers, when compared to lifestyle changes only. More robust clinical trials with standardized regimen and development of placebo for flaxseed should be conducted.

Abstract Submission No. 200108
P-0379

Insilico -interactions between Saroglitazar, Ferulic acid, and keto-hexokinase for MASLD.

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Background and Aims: Non-Alcoholic Fatty Liver Disease renamed as metabolic dysfunction-associated liver disease (MASLD), is a global health issue that causes excessive liver fat deposition without alcohol usage. Basic fatty liver to non-alcoholic steatohepatitis can lead to liver fibrosis, cirrhosis, and hepatocellular carcinoma. Research is essential because to multidimensionality, complex pathophysiology, and rising prevalence from sedentary lifestyles and unhealthy diets. Computational study analyses Saroglitazar and Ferulic acid interactions with human Ketohexokinase using docking, simulations, and network pharmacology to propose potential MASLD treatments.

Method: Utilized computational methodologies to examine binding interactions of Saroglitazar (CID: 60151560) and Ferulic acid (CID: 445858) with human Ketohexokinase (KHK: P50053, PDB ID: 6W0W). Active site analysis was performed using CDD server and BIOVIA Studio 2019. Best complex was used for molecular dynamics simulation and trajectory analysis along with functional associations based on biological process and molecular function done by using STITCH server.

Results: Human ketohexokinase protein (Uniprot ID: P50053) was obtained. Additional KHK PDB Structure (6W0W) was retrieved for docking. Ferulic Acid (CID: 445858) and Saroglitazar (CID: 60151560) were PubChem Database SDF files. Active site analysis used CDD server and BIOVIA Discovery Studio 2019. Docking analysis identified Arg108, Trp225, Glu227, Gly229, Ala230 Pro246, Pro247, Val250, Thr253, Gly257, Cys282, Gly286 and Cys289 as potential active site residue DESMOND molecular dynamics simulation and trajectory analysis equilibrated after 40ns using the best complex Saroglitazar (CID: 60151560) and KHK.

Conclusion: Study shows that Saroglitazar and Ferulic acid are strong KHK inhibitors for metabolic diseases, including MASLD, suggesting multi-target treatments.

Abstract Submission No. 200131
P-0380

The Role of Short-Term Resistance Training in Changing Hepatic Fat Content: A Pilot Study

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BACKGROUND: Previous research confirms exercise and diet reduce hepatic fat content (HFC) in individuals with non-alcoholic fatty liver disease (NAFLD). Impact of short-term resistance training combined with controlled diet not thoroughly investigated. This study examines effect of four-week resistance training on HFC and related markers while maintaining consistent diet.

METHODS: 18 sedentary men participated in daily resistance training, with an intensity set at 60-70% of their one-repetition maximum. Additionally, they followed a customized diet. HFC, the presence of fatty liver, and various blood markers were assessed before and after the intervention.

RESULTS: The intervention significantly reduced by approximately 10% in HFC ($p=.006$). Additionally, significant improvements were observed in BMI, body fat percentage, albumin, total cholesterol, and LDL cholesterol after the intervention ($p=.001$, $p=.001$, $p=.015$, $p<.001$, $p<.001$ respectively). However, variables such as muscle mass, AST, ALT, PLT, glucose, insulin, TG, and HDL cholesterol showed no significant changes. Interestingly, changes in AST and ALT demonstrated a positive correlation with changes in BMI ($r=0.667$, $p=.004$; $r=0.780$, $p<.001$ respectively) and body fat percentage ($r=0.560$, $p=.016$; $r=0.727$, $p=.001$ respectively). Changes in ALT also showed a positive correlation with changes in muscle mass ($r=0.470$, $p=0.049$). Changes in the CAP demonstrated a positive correlation with changes in insulin ($r=0.523$; $p=.031$).

CONCLUSIONS: Results suggest four-week resistance training combined with controlled diet effectively reduces HFC in sedentary men. Correlations highlight complex relationship between physical activity, diet, body composition, and liver health. Further research is needed to comprehend underlying mechanisms and optimize resistance training for NAFLD management.

Abstract Submission No. 200165
P-0381

A Descriptive study of Metabolic associated steatotic liver disease (MASLD) in Myanmar

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Background: Metabolic-associated steatotic liver disease (MASLD), formerly known as nonalcoholic fatty liver disease, is increasing globally. However, most of the research data are from the western world and lack data from Asian countries where people's bodies, dietary habits, and lifestyles are different. In Myanmar, there is scant data available for MASLD or its complications. In this study, we describe the registry data of the Yangon GI-Liver centre, which received mixed patients from urban and rural areas.

Methods: Data from 817 patients were available for analysis ($n=817$) between May 2017 and April 2022. SPSS (version 21.0; IBM, Inc., New York) was used to analyse the data.

Results: Of the 817 patients, 427 (52 %) were male and 390 (48 %) were female. The age groups ranging from 15-83 years. The mean BMI of male and female patients was 22 (Standard Deviation 2.4) and 25 (standard deviation 3.5), respectively. Overall, 458 patients (56%) had steatosis of varying grades, of which 37% had severe steatosis. Among them, 1% of the patients had clinically significant fibrosis F2-F4 detected by fibroscan. A total of 23 patients (2.8 %) had metabolic-associated steatohepatitis (MASH). 14% of patients with HbA1C >5.7 mmol/L.

Conclusion: This study provides a glimpse of MASLD in Myanmar and its potential associated risks and complications. We can utilise these data to implement the prevention and management strategies of MASLD in the country with the need for increased efforts and urgency.

Abstract Submission No. 200166
P-0382

Role of primary care physicians in combating metabolic associated steatotic liver disease in Myanmar

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Background: We acknowledge from the global literature that obesity, type 2 diabetes mellitus (DM), and dyslipidaemia are the major predictors or complications of metabolic-associated steatotic liver disease (MASLD). According to 2014 data, the prevalence of diabetes is 10.8% and pre-diabetes is 19.7% in Myanmar, but we have scanty of data with regards to MASLD in the country.

Methods: We analysed the registry data of 817 patients ($n=817$) from the Yangon GI-Liver Centre (YGLC) from May 2017 to April 2022. SPSS (version 21.0; IBM, Inc., New York, USA) was used to analyse the data. Pearson Chi square test and Pearson correlation was done to determine association between steatosis grading with HbA1C, BMI and waist circumference. significance level was set at $p<0.05$.

Results: There was a positive association between steatosis grading and HbA1C: 15% ($p<0.001$), BMI: 29% ($p<0.001$), and waist circumference: 37.7% ($p<0.001$).

Conclusion: As we found a positive association between steatosis grading and HbA1C, BMI, and waist circumference highlighted the importance of the role of primary care physicians' collaboration in the early detection and management of MASLD. Primary care physicians are the centres of patient care pathways. By using simple laboratory tests to predict the risk and complications of MASLD, such as FIB-4 and APRI, treating its associated risk factors, such as providing statins and anti-diabetes, encourages patients to adopt a healthy lifestyle, and activates referral pathways to hepatologists. The combined efforts will be more effective in tackling the global epidemic wave of MASL or its complications.

Abstract Submission No. 200277
P-0383

Efficacy and safety of incretin-based therapy in MASLD patients with type 2 diabetes mellitus

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Background and Aim: The aim of this study was to evaluate the efficacy and safety of oral semaglutide (Sema), a GLP-1 receptor agonist, and tirzepatide (TZP), a dual GIP/GLP-1 receptor agonist, in patients with metabolic dysfunction-associated steatotic liver disease (MASLD) complicated by type 2 diabetes mellitus (T2DM).

Methods: Verification 1; multi-institutional prospective study. Eighty-three patients with MASLD who received Sema for T2DM were included. Sema was initiated at a dose of 3 mg once daily, and the dose was gradually increased. Verification 2; single-center prospective pilot study. Thirteen patients with MASLD who received TZP for T2DM were included. TZP was initiated at a dose of 2.5 mg once weekly and was increased to a maintenance dose of 5.0 mg once weekly at week 4.

Results: Verification 1; Sema treatment resulted in significant improvements in glycemic control, liver transaminases, and lipid profiles with weight loss throughout the 24 weeks. In 43 patients after 48 weeks of treatment, CAP and each non-invasive test for liver fibrosis decreased significantly from baseline. A number of gastrointestinal disorders, including grade 1-2 nausea, were observed during the observation period. Verification 2; TZP treatment resulted in a decrease in body weight at week 12, together with improvements in glycemic control, liver transaminases, and TG. Gastrointestinal disorders such as grade 1-2 nausea and constipation were frequently observed. The subsequent course of treatment is being followed.

Conclusion: Sema and TZP treatments offered a favorable effect on MASLD as well as improving diabetic status and reducing body weight.

Abstract Submission No. 100868
P-0384

Combination method of fusion imaging and CEUS in ablation with artificial pleural effusion/ascites

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Purpose: To investigate the usefulness of combining fusion imaging (ultrasound-computed tomography or ultrasound-magnetic resonance imaging) and contrast-enhanced ultrasound (CEUS) before and during ablation with artificial pleural effusion/ascites for hepatocellular carcinoma that is difficult to visualize with ultrasonography. Materials and methods: Percutaneous radiofrequency ablation with artificial pleural effusion/ascites was performed in 53 patients with 82 HCCs. Even if the lesion was not visualized by conventional ultrasonography, we performed a preliminary inspection using fusion imaging before ablation to predict where the lesion would be visualized when pleural effusion/ascites were created. After creating artificial pleural effusion/ascites, the expected area was searched using ultrasonography, and the visualized lesion was confirmed using CEUS and ablated. The usefulness of this method was examined based on imaging findings immediately after treatment, 3 months later, and 6 months or more later.

Results: Immediately after treatment, the complete ablation rate was 96% (79 lesions), the local recurrence rate was 7% (6 lesions), and the major complication was 2% (one case of hemothorax).

Conclusion: By combining fusion imaging and CEUS before and during ablation with artificial pleural effusion/ascites, lesions can be detected quickly and accurately, allowing safe and reliable treatment.

Abstract Submission No. 101146
P-0385

Long-Term Outcomes of Combined RFA and Multipronged Ethanol Ablation for Unfavourable HCC

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PURPOSE: To evaluate the local efficacy, safety and long-term outcomes of combined radiofrequency ablation (RFA) and multipronged ethanol ablation (EA) in the treatment of unfavourable hepatocellular carcinoma (HCC) and to determine the prognostic factors for survival. **METHODS:** Between August 2009 and December 2017, 98 patients with 110 unfavourable HCC nodules who underwent combined RFA and multipronged EA were retrospectively enrolled in the study. Unfavourable HCC was defined as a medium (3.1-5.0 cm) or large (5.1-7.0 cm) HCC nodule, a tumor located at a high-risk site or a perivascular tumor. The treatment response, overall survival (OS) and recurrence-free survival (RFS) were analysed. The Kaplan-Meier method and Cox proportional hazards regression model were used to evaluate the prognostic factors.

RESULTS: Complete ablation was obtained in 80.9% (89/110) of the tumors after initial treatment. Major complications were observed in 3(3.1%) patients. The cumulative incidence of local tumor progression (LTP) was 23.5% at 5 years, and no variable was found to be an independent predictive factor for LTP. The five-year OS and RFS rates were 41.9% and 34.0%, respectively. Multivariate analysis showed that serum AFP level, tumor size, residual tumor after ablation and extrahepatic metastases were significant prognostic factors for OS ($p=0.023$, $p=0.030$, $p=0.001$, and $p=0.010$, respectively). Tumor type and number of tumors were predictive factors for RFS ($p=0.029$ and $p=0.001$, respectively). Perivascular tumor was not an independent predictive factor for OS or RFS.

CONCLUSION: Combined RFA and multipronged EA is a safe and effective treatment for unfavourable HCC, especially for perivascular tumors.

Abstract Submission No. 101274
P-0386

Radiofrequency ablation for the treatment of hepatocellular carcinoma just below the hepatic capsule

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Aim: When performing radiofrequency ablation (RFA) for the treatment of hepatocellular carcinoma (HCC), it is necessary that the insertion of electrodes into the center of the tumor through the hepatic

parenchyma under ultrasound guidance. However, tumors located just below the hepatic capsule require special puncture techniques. This retrospective study aimed to analyze the efficacy and outcomes of RFA for HCC located just below the hepatic capsule.

Methods: Eighty-one patients with HCC located just below the hepatic capsule underwent RFA from January 2008 to October 2022 in our institute. Data on the patients' baseline characteristics, treatment results, and adverse events were investigated. Factors associated with local tumor recurrence were also examined.

Results: The patients' baseline characteristics were as follows: 59 were male, median age of 74 years, and 68 were classified as Child-Pugh class A. The majority of the patients' population had tumors that measured <2.0 cm (n=56), and most were located on the right liver lobe (n=53). Monopolar RFA was used in 56 patients, while no-touch ablation using bipolar RFA was used in 25. The treatment success rate was 92.5%, with only six lesions of inadequate ablative margins. Five of the six cases (83.3%) with inadequate ablative margins underwent monopolar RFA, but the difference was not significant (P=0.368). Local tumor recurrence was observed in 19 patients, the local tumor recurrence rate was shown 13% at 1 year, 29% at 3 years, 33% at five years, and 33% at ten years after initial RFA treatment, respectively. The multivariate analysis of factors associated with local tumor recurrence using the COX proportional hazards model showed "insufficient ablative margin" (HR 8.16, 95% C. I. (1.93-34.5), P=0.004). Adverse events occurred in 17 patients, but all patients were recovered by the conservative therapy.

Conclusion: In the present study, obtaining a sufficient ablative marginal area using either monopolar or bipolar RFA systems are able to be reduced local tumor recurrence for the treatment with HCC located just below the hepatic capsule.

Abstract Submission No. 101419

P-0387

Sonazoid Enhanced Ultrasound for Image-Guided Procedures and Ablation

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Teaching Points: Sonazoid-enhanced ultrasound (SEUS) is a recently introduced contrast-enhanced ultrasound using Sonazoid (GE Healthcare) offering the vascular phase and the unique post-vascular Kupffer phase for helping diagnose hepatic tumors. Its role has been primarily focused on differentiating benign and malignant hepatic tumors. However SEUS can be used not only for diagnosis but also image-guided procedures including biopsy and tumor ablation of the liver. In this exhibit, we demonstrate diverse clinical settings in which SEUS plays important roles for the interventional procedures as an excellent guiding tool.

Table of Contents: 1) Physics of SEUS, 2) Diagnostic roles of SEUS, 3) Introduction of SEUS during liver biopsy, 4) SEUS as a guidance tool for tumor ablation, 5) Tips for using SEUS.

Abstract Submission No. 101432

P-0388

RFA with laparoscopic support is useful for difficult cases to treat Hepatocellular Carcinoma

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Back ground: HCC of S4 surface at back of right rim or severe obesity cases are difficult to visualize and puncture by abdominal US. We performed RFA under general anesthesia with laparoscopic observation (L-RFA).

Case1: 67y.o.M. ALD-LC treated for multifocal HCCs. CT revealed 1.1cm, 0.8cm HCCs. TACE and P-RFA was performed, but insufficient cauterization. Laparoscope found on the surface of liver and confirmed by US. Cool-tip 3cm needle was punctured. Histology was poorly differentiated HCC, but there was no local recurrence. For recurrence at other sites, MWA and immune checkpoint inhibitors were administered, the patient is currently alive for 5 years.

Case2: 62y.o.M. HCV-LC treated P-RFA and myocardial infarction. TACE was performed second times, but insufficient. Laparoscopic US confirmed a mosaic-like 2.0 cm HCC with the portal vein on the dorsal side, and puncture from the caudal side of the tumor.

Case3: 90y.o.F. HCV-LC, initial HCC appears in S4 caudal surface beside duodenum. Laparoscopic US showed an irregular shaped 2.0 cm HCC. 2 cm needle was punctured. Caudal surface, dorsal side, and part of falciform membrane were cauterized.

Case4: 63y.o.F. BMI 39.3kg/m² with HCV natural cure and MASH-LC, who have a history of operation and P-RFA. HCC appears in S3 surface and in contact with stomach. Treatment with TACE was insufficient. Laparoscope revealed a protruding tumor on liver surface, 2 cm needle is punctured and cauterized. **Result:** All tumors were treated with cool-tip needle, and was punctured through normal liver tissue, sufficiently cauterized and confirmed by CECT

Conclusion: If HCC exists at S4 surface or severe obese cases at liver surface in other areas, L-RFA is useful to treat safely and effectively.

Abstract Submission No. 101959

P-0389

Percutaneous Microwave Ablation and Lenvatinib on Intermediate-Stage Hepatocellular Carcinoma

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Background: Systemic therapy has been used as a first-line treatment for intermediate-stage HCC, especially for larger (≥5 cm) or multiple lesions. Based on the REFLECT trial, lenvatinib has been approved as a first-line treatment for unresectable HCC in different parts of the world. Lenvatinib has exhibited favorable results in inhibiting tumor angiogenesis and tumor growth. The present study aimed to evaluate efficacy of combined percutaneous microwave ablation therapy and lenvatinib in patients with intermediate hepatocellular carcinoma.

Methods: Thirteen patients with Child Pugh B-HCC were included in the study. The patients had no prior history of systemic treatment. Of them, 4 received both PMAT and Lenvatinib, while 9 of them received PMAT monotherapy. The clinical outcomes used to evaluate treatment included tumor size, MELD Na, and Child Pugh Class.

Results: The 2 treatment arms were followed up on a monthly basis for 6 months, there were no significant difference on MELD Na scores (p-value = 0.068) and tumor size progression on both treatment arms (p-value = 0.271). For the first 5 months of the study, there was no significant difference on Child Pugh Classes, however on the 6th month, based on the repeat measures ANOVA there was significant increase on the CPC of monotherapy arm in comparison with combination therapy, PMAT + Lenvatinib (p value < 0.05) which has stable CPC.

Conclusion: Our proposed combination therapy may potentially be effective in patients with Child Pugh B- HCC. A larger scale, multicenter, prospective study is warranted to confirm the findings.

Abstract Submission No. 102036
P-0390

Considerations for Part-time Doctors Performing Ablation

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Background: In areas with a small number of physicians, even large hospitals do not have full-time physicians specializing in ablation, so part-time physicians may perform ablation.

Patients: As a part-time physician, I performed more than 160 cases of radiofrequency ablation for liver cancer at a large hospital with more than 800 beds in Chiba Prefecture from 2015 to 2022. On working days, I perform contrast-enhanced ultrasound in the morning and ablation in the afternoon. Patients who are considered for ablation must come to the hospital for contrast-enhanced ultrasonography, and I will decide whether it is indicated or not (treatment will be performed at a later date). Since this examination also serves as a planning echo, the need for artificial pleural effusions and ascites, appropriate body positioning and ultrasound imaging methods should also be noted. CT is taken the day after treatment to determine the effectiveness of treatment and to check for any complications. The full-time physician is asked to manage the perioperative period. Patients whose antithrombotic therapy cannot be interrupted and hemodialysis patients are at high risk of bleeding, so avoid ablation at part-time setting. Other high-risk lesions may also be referred to other facilities or considered for alternative treatment.

Results: One case of intrahepatic hemorrhage was observed, but the bleeding was cured with conservative treatment. There were no other major complications, and we continue to provide safe treatment.

Conclusion: What to consider when performing ablation on a part-time setting.

Abstract Submission No. 102056
P-0391

Contrast-Enhanced Low-MI THI: A useful imaging support for the locoregional therapy for liver tumor

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Background: Contrast-Enhanced Low-MI THI (Low-Mechanical Index of Tissue Harmonic Imaging) is a useful imaging support technique for the locoregional treatment for liver tumors; it provides B-mode (THI)-like images overlaid with CHI (contrast harmonic imaging) contrast information. We show the characteristics of this method based on our experience at our hospital.

Method: ARIETTA 750LE or ARIETTA 850 (Fujifilm Medical) was used as an ultrasound machine, with a contrast agent Sonazoid. The basic condition settings for low-MI THI were as follows: the MI value was set around 0.20 using a wideband probe (1-6MHz), with

maximized screen gain in conjunction with appropriate focus, that was sufficiently deeper than the lesions.

Results: Low-MI THI allowed superior resolution to that of CHI, which was commonly used for contrast imaging; the ability to set higher frame rates and the improved visualization of deep lesions were advantages. In addition, using as a reference for fusion imaging, low-MI THI enabled treatment for the lesions that were difficult to visualize in B mode. It was also useful for the evaluation of treatment efficacy.

Conclusion: Low-MI THI is superior to the ordinary contrast mode. Combination of Low-MI THI with Fusion is an efficient imaging support for the treatment, as well as post-treatment evaluation of liver tumors.

Abstract Submission No. 200127
P-0392

Temperature Profile and Safety of Grounding Pads during Radiofrequency Ablation

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Background: Radiofrequency ablation (RFA) systems deliver larger amount of electric current than standard electrical surgical units whose intended use is dissection and hemostasis. Due to this nature, many of the RFA systems require application of multiple grounding pads to prevent skin burn. However, risk cannot be fully eliminated just by using designated number of grounding pads. We monitored temperature distribution on grounding pads during current deposition to obtain better understanding of heat profile on the grounding pads during RFA.

Methods: Thermographic monitoring of temperature of grounding pads placed on healthy volunteers was conducted using arfa RF ABLATION SYSTEM under various conditions relating to energy delivery and grounding pad configurations.

Results: Temperature correlated positively and negatively with the amount of energy delivered and surface area of grounding pad(s), respectively. However, an extreme condition of 10-minute continuous delivery of 120W resulted in tolerable temperature rise up to 40.2°C. When two pads were placed in uneven distances from the active pole, the closely located one generated more heat. Comparison of two each of pads placed on the thigh and the back demonstrated higher temperature spots at the former suggesting more even current distribution over entire surface on the pads placed on the back.

Conclusions: arfa RF ABLATION SYSTEM can be used safely when the instructions from the manufacturer are followed. Application of the grounding pads on the back may mitigate hot spots caused by concentration of electric current at the leading edge of a grounding pad.

Abstract Submission No. 200136
P-0393

Usefulness of the dual thermometers and non-slip needle processing of arfa RF Ablation System.

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Background: arfa RF ABLATION SYSTEM (arfa) is equipped with two temperature sensors (Dual Temperature Sensors) at the tip of the

needle electrode. One thermometer monitors the cooling water temperature in the needle (TM1), while the other can monitor tissue temperature (TM2).

The insulating sheath has a polyurethane (PU) non-slip surface to reduce the motion of electrode position after puncture.

Methods: The temperatures of TM1 and TM2 were monitored in a clinical case during ablation to see the functional differences between the two.

In a bench-top setting, an electrode with insulated sheaths without and with the non-slip coating were punctured, and the resistance at each extraction was measured and compared.

Results: During ablation, TM1 maintained a temperature of around 14°C. TM2 showed 32 °C before ablation and reached 70 °C at 11 seconds, then over 99°C just before a break. Both TMs 1 and 2 repeated similar behavior between a total of 3 breaks obtained.

The average extraction resistance without PU was 0.68N, and that with PU was 1.05N. The extraction resistance with PU was significantly higher ($p=0.003$).

Conclusions: The tissue thermometer enabled monitoring of the tissue temperature during ablation, suggesting that it is a reliable parameter to judge whether the tumor site is ablated.

The presence of a non-slip device increased the extraction resistance. This suggests that the needle electrode is stable in a static state after puncture. These features which are unique to arfa among the RFA system commercially available in Japan provide clinical usefulness.

Abstract Submission No. 200155

P-0394

Cox model risk score to predict survival of intrahepatic cholangiocarcinoma after thermal ablation

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Purpose: To explore factors associated with overall survival (OS) and progression-free survival (PFS) of intrahepatic cholangiocarcinoma (iCCA) after ultrasound-guided ablation and establish a model for risk evaluation.

Methods: Data from 54 patients with 86 iCCAs between August 2008 and October 2022 were retrospectively analyzed. Cox regression were used to analyze the effects of clinical features on OS and PFS. Based on the variables screened by multivariable analysis, a model was established to obtain the risk score. The model was further verified by bootstrap validation. The clinical usefulness of the model was evaluated by the decision curve analysis (DCA).

Results: During follow up, 39 patients died and 49 patients developed recurrence. Pre-ablation CA199 level > 140 U/ml was the only independent predictor of poor PFS. Age > 70 years, early recurrence, maximal diameter of tumor size > 1.5 cm and pre-ablation CA199 level > 140 U/ml were significantly associated with poor OS. Then a model was established based on the above four variables to predict the survival outcomes of the patients after thermal ablation. The performance of this model was good [area under the curve (AUC) for 1-year, 2-year, 3-year, 5-year was 0.767, 0.854, 0.791 and 0.848]. After bootstrapping for 1000 repetitions, the AUC were similar to the initial model. DCA also demonstrated the model had good positive net benefits.

Conclusion: The established model in this study could predict the survival outcomes of the patients with iCCA after thermal ablation, but further research was needed to validate the results.

Abstract Submission No. 200177

P-0395

Electromagnetic Interference Test between a Radiofrequency Ablation System and a Cardiac Pacemaker

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Background: Application of radiofrequency ablation (RFA) for the patients implanted with Cardiac Implantable Electronic Devices (CIEDs) is generally contraindicated. Nevertheless, there are cases in the clinical practice that RFA is performed in these patients after careful risk-benefit assessment. This in-vitro experiment aimed to reveal the electromagnetic interference (EMI) between an RFA system and a cardiac pacemaker (PM) implanted in the patients.

Methods: A PM, an active RFA electrode and a grounding pad of arfa RF ABLATION SYSTEM were placed in a saline filled plastic tub, furthermore, changes in state of the PM were observed under various conditions including the relative position of the two devices, the RF output power level, and the programming of the PM.

Results: Higher risk of oversensing was associated with RF output power level, distance and relative position of the two devices as well as the pacemaker-related factors including use of DDD mode and unipolar configuration. Joule heating occurred at the tip of the leads when the pacemaker and the RFA electrode came into direct contact.

Conclusions: Many of the risks demonstrated in our experiment seemed uncommon to be encountered in the standard liver RFA procedure. The risk of EMI during liver RFA perform in the patients implanted with PM could be minimized by acquiring sufficient knowledge and conducting appropriate preventive measures.

Abstract Submission No. 200219

P-0396

Predicting Severe Infection after Ablation of Liver Malignancies Based on Inflammatory Indicators

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Background: The prognosis of patients with severe infectious complications after percutaneous thermal ablation is significantly worse than that of non-severe patients, but no effective predictors have been published.

Purpose: To explore the preoperative and postoperative predictors for severe infection after thermal ablation of liver malignancies, and to construct prediction models based on peripheral inflammatory indicators.

Materials and methods: 8655 ultrasound-guided percutaneous thermal ablation procedures of liver malignancies at a tertiary referral hospital from January 2012 to November 2023 were respectively reviewed. Patients with infectious complications after ablation were included and divided into severe and non-severe groups based on whether they developed sepsis and/or septic shock. Prediction models were established by stepwise logistic regression.

Results: A total of 85 patients were enrolled in this study, including 69 (81.2%) patients with primary tumors and 16 (18.8%) with metastatic tumors. 18 (21.2%) patients were severe and 69 (78.8%) were non-severe. In the pre- and post-ablation model, preoperative monocytes ratio (OR=0.71; 95%CI: 0.55-0.96; $P=0.026$) and procalcitonin (PCT) first examined after fever (OR=1.23; 95%CI: 1.09-1.39;

$P=0.001$) were independent predictors of severe infection. In the pre-ablation model, tumor type (metastatic vs. primary, $OR=5.35$; 95%CI: 1.53-18.75; $P=0.009$) and preoperative monocytes ratio ($OR=0.77$; 95%CI: 0.61-0.98; $P=0.035$) were independent predictors. The AUCs of the two models were 0.869 and 0.777, respectively.

Conclusion: Peripheral blood cells and inflammatory indicators combined with other clinical characteristics are helpful to predict severe infection after thermal ablation of liver malignant tumors, including tumor type, preoperative monocytes ratio and PCT first examined after fever.

Abstract Submission No. 100269
P-0397

Ninvamix: Multimodal Deep Learning model for Detection of Liver Fibrosis in normal ALT CHB Patients

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Background: Researches have indicated disease progression in hepatitis B patients with normal ALT levels. While liver biopsy offer assessment, it is invasive. Existing predictive tools lack integration of CT images and clinical metrics, leading to poor accuracy for patients with normal ALT levels. In this study, we formulate a multimodal deep learning model that combines CT images with clinical metrics for precise advanced fibrosis detection.

Methods: A multimodal deep learning model was developed based on ResNet18 and SVM to diagnose advanced liver fibrosis. It combined CT images and 20 clinical indicators. Data was collected and split into training and validation sets (7:3) from 784 hepatitis B patients with normal serum ALT who underwent abdominal CT and liver biopsy. Multimodal model was compared with existing noninvasive scores.

Results: Our model performed well in diagnosing advanced liver fibrosis. The AUCs were 0.85 and 0.88 on the training and test sets, respectively. The AUCs of the five existing noninvasive scores, GPR, FIB4, RPR, APRI, and Sindex, were 0.79, 0.76, 0.72, 0.79, and 0.78 on the training set, and 0.80, 0.71, 0.74, 0.81, and 0.80 on the test set, respectively.

Conclusions: Our model can integrate CT images and clinical metrics to diagnose advanced liver fibrosis in hepatitis B patients before liver enzyme changes. It outperforms existing noninvasive scores. It may provide a new noninvasive tool for liver fibrosis screening and monitoring in hepatitis B patients.

Abstract Submission No. 101393
P-0398

Competence of the ChatGPT for the Japanese Hepatologist Examination: Initial Experience

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Background: ChatGPT is an AI developed by OpenAI and is called a large language model. In this study, we evaluated the ability of the ChatGPT; GPT-4 using questions that require knowledge equivalent to that of a medical specialist examination.

Material and Methods: The target examination was the Japanese Society of Hepatology's Liver Specialist Certification Examination Question-and-Answer and Explanation Vol. 6, and the AI was OpenAI's ChatGPT; GPT-4. The knowledge data is currently available until April 2023. This AI can handle text and images, but has not been trained to interpret medical images at this time. There are 102 questions in total, excluding those that require images to be answered. The language used for the prompts was Japanese, the same as the question text.

Results: Of the 102 questions, 22 contained images. Of the 102 questions, 22 contained images, but 20 of these images were directly related to the answer. Excluding these, we examined the ChatGPT answers to 82 of the 102 questions. Of the 82 questions, 67 (81.7%) gave the correct answer. 15 incorrect answers were found to be due to lack of knowledge (10), logical inconsistency (1), fictitious evidence (3), and difficulty in interpreting the question itself (1).

Conclusion: ChatGPT showed a high ability to answer the Japanese hepatologist examination questions. It is expected that ChatGPT will become a powerful assistant for medical practitioners in the future by improving the performance of AI itself, learning high-quality professional evidence, and further medical-specific tuning.

Abstract Submission No. 101973
P-0399

Machine Learning for Stratifying Autoimmune Hepatitis Phenotypes: Precision Therapeutic Insights

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Background/Aim: Autoimmune Hepatitis (AIH) exhibits a spectrum of immunological phenotypes, demanding precise characterization for tailored therapeutic approaches. This study aims to dissect distinct immune signatures associated with varied clinical presentations using machine learning, enhancing stratification for personalized treatment interventions.

Methods: Peripheral blood samples from 50 AIH patients were subjected to flow cytometry, cytokine assays, and RNA sequencing. Leveraging k-Nearest Neighbors and XGBoost algorithms, we integrated multi-omics data to train models correlating immune signatures with clinical phenotypes and treatment responses.

Results: Machine learning models demonstrated notable accuracy, achieving an 87% accuracy in predicting treatment response (k-Nearest Neighbors) and a 90% accuracy in classifying patients into immunological subtypes (XGBoost). Feature importance analysis unveiled specific immune cell populations, cytokine profiles, and gene expression patterns linked to treatment outcomes.

Conclusions: This study emphasizes machine learning's potential in understanding AIH's complex immunological landscape, enabling precise classification and guiding tailored therapies. Integrating machine learning into AIH management represents a transformative, personalized approach to autoimmune liver disease, addressing the imperative need for individualized strategies.

Abstract Submission No. 200061
P-0400

Hepatocellular Carcinoma Detection based on Deep Learning using Multi-sequence Data

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Background and Objectives: Diagnosis of hepatocellular carcinoma (HCC) on liver MRI needs analysis of multi-sequence images. However, developing computer-aided detection (CAD) for every single sequence requires considerable time and labor for image segmentation. Therefore, we developed CAD for HCC on the hepatobiliary phase (HBP) of gadoteric acid-enhanced magnetic resonance imaging (MRI) using a convolutional neural network (CNN) and evaluated its feasibility on multi-sequence, multi-unit, and multi-center data.

Methods: Patients who underwent gadoteric acid-enhanced MRI and surgery for HCC in Korea University Anam Hospital (KUAH) and Korea University Guro Hospital (KUGH) were reviewed. Finally, 170 nodules from 155 consecutive patients from KUAH and 28 nodules from 28 patients randomly selected from KUGH were included. Regions of interests were drawn on the whole HCC volume on HBP, T1-weighted (T1WI), T2-weighted (T2WI), and portal venous phase (PVP) images. The CAD was developed from the HBP images of KUAH using customized-nnUNet and post-processed for false-positive reduction. Internal and external validation of the CAD was performed with HBP, T1WI, T2WI, and PVP.

Results: The performance of the CAD for HBP, T1WI, T2WI, and PVP at false-positive rate 0.5 were (0.87 and 87.0), (0.73 and 73.3), (0.13 and 13.3), and (0.67 and 66.7) in KUAH and (0.86 and 86.0), (0.61 and 53.6), (0.07 and 0.07), and (0.57 and 53.6) in KUGH, respectively.

Conclusions: This result implies that the CAD developed using a single MRI sequence may be applied to other similar sequences and this will reduce labor and time for CAD in multi-sequence MRI.

Abstract Submission No. 200172
P-0401

Comparison of Machine Learning Algorithm in Predicting Living Status of Hepatitis Patients

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Hepatitis is an inflammation of the liver caused by various infectious viruses and noninfectious agents, resulting in a range of health issues, some of which can be fatal. In this study, we will use artificial intelligence approaches to classify patients based on the possibility of living or dying.

This study will compare several algorithms such as Artificial Neural Network (ANN), K Nearest Neighbor (KNN), and Support Vector Machine (SVM). The data obtained from Kaggle with a total of 142 data with 19 attributes.

The model will be evaluated using three test metrics. Accuracy shows how optimally the algorithm works in general, sensitivity shows the algorithm's performance in classifying the 'die' class, while specificity shows how well the algorithm is in classifying the 'life' class. Based on the results, ANN provides the most optimal results with the highest accuracy of 93%, sensitivity of 80% and specificity of 95%. In the SVM algorithm, although the resulting accuracy and specificity are quite good, it cannot predict which patients will die according to sensitivity value equal to zero. The results obtained also show that among the three algorithms used, the KNN algorithm has the worst

performance. The results influenced by an unbalanced amount of data where there were 26 data in the 'die' class and 116 data in the 'life' class.

Based on the results of the comparison carried out on the ANN, SVM, and KNN methods, the results showed that the most optimal algorithm was the ANN algorithm with an accuracy of 93%.

Abstract Submission No. 100167
P-0402

Inhibitory effect of GLP-1RA on liver cirrhosis-induced skeletal muscle atrophy in diabetic mice

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Background: Recent studies have demonstrated the molecular role of the glucagon-like peptide-1 receptor agonist (GLP-1RA) in skeletal muscle homeostasis; however, the therapeutic efficacy of semaglutide, a GLP-1RA, on skeletal muscle atrophy in chronic liver disease (CLD) under the diabetic condition remains unclear.

Methods: We used *in vivo* diabetic CLD-related sarcopenic models in KK-A^y mice and *in vitro* atrophy models C2C12 myocytes to investigate therapeutic efficacy of semaglutide.

Result: Semaglutide inhibited psoas muscle atrophy and suppressed declines in grip strength in mice. Moreover, semaglutide inhibited ubiquitin-proteasome-mediated skeletal muscle proteolysis and promoted myogenesis in C2C12 myocytes. Mechanistically, this effect of semaglutide on skeletal muscle atrophy was mediated by multiple functional pathways. First, semaglutide protected against hepatic injury in mice accompanied by increased production of insulin-like growth factor 1 and reduced accumulation of reactive oxygen species (ROS). These effects were associated with decreased proinflammatory cytokines and ROS accumulation, leading to suppression of ubiquitin-proteasome degradation in the skeletal muscle tissue. Moreover, semaglutide inhibited the amino acid starvation-related stress signaling which was activated under chronic liver injury, resulting in the recovery of mammalian target of rapamycin activity in the skeletal muscle of mice. Second, semaglutide improved skeletal muscle atrophy by directly stimulating GLP-1R in myocytes. Treatment with semaglutide induced cAMP-mediated activation of PKA and AKT, enhanced mitochondrial biogenesis, and reduced ROS accumulation, thereby resulting in inhibition of NF- κ B/myostatin-mediated ubiquitin-proteasome degradation and the augmentation of heat-shock factor-1-mediated myogenesis.

Conclusion: Semaglutide may have potential as a new therapeutic strategy for CLD-related skeletal muscle wasting.

Abstract Submission No. 100251
P-0403

Vitamin D deficiency exacerbates alcohol-related liver injury via gut barrier disruption

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Background: Endogenous lipopolysaccharide (LPS) that translocates via the disrupted intestinal barrier plays an essential role in the progression of alcohol-related liver disease (ALD). Vitamin D deficiency is observed in ALD, and it participates in regulating gut barrier function. Therefore, we investigated that the effect of vitamin D deficiency on ethanol (EtOH)- and carbon tetrachloride (CCl₄)-induced liver injury relevant to gut barrier disruption in mice.

Methods: To investigate the hypothesis, we fed female C57BL/6J mice a liquid diet containing 2.5% EtOH and intraperitoneal injections of CCl₄ twice weekly for 8 weeks. The mice were divided into vitamin D-deficient (vitamin D: 1.6 IU/kg) and vitamin D-sufficient (vitamin D: 54.4 IU/kg) groups. In addition, we cultured CaCo2 cells to examine the direct effects of vitamin D on intestinal cells.

Results: The EtOH/CCl₄-treated mice developed hepatic steatosis, inflammation, and fibrosis, which were significantly enhanced by vitamin D-deficient diet. Vitamin D deficiency enhanced gut hyperpermeability by inhibiting the intestinal expressions of tight junction proteins including ZO-1, occludin, and claudin-2/5/12/15 in the EtOH/CCl₄-treated mice. Consequently, it induced Kupffer cell infiltration and LPS/toll-like receptor 4 signaling-mediated proinflammatory response. Based on the in vitro assay, vitamin D-mediated vitamin D receptor activation inhibited EtOH-stimulated paracellular permeability and the downregulation of tight junction proteins in Caco-2 cells.

Conclusion: Vitamin D deficiency exacerbates alcohol-related liver injury via gut barrier disruption and hepatic overload of endotoxin.

Abstract Submission No. 100994

P-0404

Digital image analysis reveals different fibrosis patterns in congestive hepatopathy versus MASH

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Background: Congestive heart failure can cause congestive hepatopathy (CH) featured by liver congestion, sinusoidal dilatation, centrilobular necrosis and fibrosis, so called cardiac sclerosis. Similar to metabolic dysfunction-associated steatohepatitis (MASH), the fibrosis starts from centrilobular area and progression to bridging fibrosis and cirrhosis. We aim to explore the feasibility of using SHG/TPEF microscopy in assessing liver fibrosis in CH and compare the fibrotic patterns between CH and MASH.

Method: Unstained sections from 24 CH cases with Dai scheme stages 0, 1, 2 and 3 were imaged using SHG/TPEF microscopy. Quantified collagen parameters in the liver lobule regions (portal, peri-portal, zone 2, peri-central and central vein) were obtained from qFibrosis measurements and represented as radar plots. The results were compared to 156 untreated MASH cases across NASH-CRN F0 to F4.

Results: For every stage, the overall fibrosis measured by SHG was lower in CH cases than NASH cases, with significant difference for F0 ($p < 0.01$). This is also observed with the smaller radar plot area representing CH compared with MASH cases. The periportal fibrosis and perisinusoidal fibrosis were consistently and significantly lower in CH cases than NASH cases across all stages (Figure).

Conclusion: SHG/TPEF microscopy reveals different fibrosis patterns between CH and NASH which may reflect different damage and repair mechanism between these two entities. Further validation with an additional larger number of CH cohort with clinical outcome correlation will provide insight for future use of SHG/TPEF microscopy in evaluating disease severity that aid clinical management.

Abstract Submission No. 101019

P-0405

Structural Distortion and Prothrombotic Phenotypes of Lymphatic Vessels in Cirrhotic Livers

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Background: Dysfunctional lymphatic vessels (LVs) can exacerbate cirrhosis progression. However, their structural changes and functional implications in cirrhosis remain to be characterized. This study aims to elucidate histological alterations in LVs in cirrhotic livers, and integrate transcriptomic profiles of hepatic lymphatic endothelial cells (LECs) in both human patients and a murine model of liver fibrosis/cirrhosis.

Methods: Liver samples from primary sclerosing cholangitis (PSC) patients and bile duct ligation (BDL) induced cholestatic/cirrhotic mice were used. Transcriptomic analysis was conducted on human liver LECs (gene dataset: GSE77627) from 9 cirrhotic patients and 6 healthy individuals. Additionally, mouse liver LECs were isolated from cholestatic mice representing fibrotic and decompensated cirrhosis stages. Podoplanin and Lyve-1 were used as LV markers.

Results: In cirrhotic livers of PSC patients, there was a significant increase in distorted and narrowed LVs ($p < 0.001$, $n = 13$) compared to controls ($n = 8$). This distortion positively correlated with the fibrotic area ($p < 0.001$, $R^2 = 0.43$, $n = 21$). Notably, blood-filled LVs were present in cirrhotic PSC patients (45.1% of total cirrhotic patients, $p = 0.0191$) compared to controls. These blood-filled LVs were associated with the accumulation of fibrin(ogen), a coagulation factor, on the LV endothelial surface in both cirrhotic patients ($p < 0.001$, $n = 13$) and decompensated cirrhotic mice ($p < 0.001$, $n = 3$) compared to control groups. Our transcriptomic analysis further revealed the upregulation of coagulant, thrombotic, and platelet-related signaling pathways in LECs from cirrhotic patients and mice, aligning with the prothrombotic phenotype we observed.

Conclusion: The structural distortion and prothrombotic phenotypes observed in cirrhotic livers might contribute to decompensation of cirrhosis. The disrupted LVs in cirrhotic livers are considered to promote the development of ascites.

Abstract Submission No. 101022

P-0406

Macrophage Fibronectin-1 Promotes Liver I/R Injury Resolution Through Lymphangiogenesis

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Background: Lymphatic vessel(LV) numbers increase in the liver after I/R injury. Fibronectin-1, a matrix protein, facilitates lymphatic endothelial cells(LECs) proliferation. Increased fibronectin-1 expression in liver macrophages during liver lymphangiogenesis, the formation of new LVs. We **hypothesized** that macrophage fibronectin-1 facilitates lymphangiogenesis and subsequently promotes the liver recovery after I/R injury.

Method: Hepatic I/R injury was induced in macrophage-specific fibronectin knockout(FN M

Abstract Submission No. 200041

P-0407

Myoblast cells harboring the capacity of liver regeneration do not promote proliferation of HCC

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Background: We previously reported utility of myoblast cell (MC) sheet transplantation for liver regeneration for liver cirrhosis. However, considering that patients with liver cirrhosis are potentially at risk for development of hepatocellular carcinoma (HCC), influence of MC on HCC growth should be investigated prior to clinical application of the MC sheet transplantation for cirrhotic patients. Thus, to confirm the safety of the sheet transplantation for liver failure in terms of tumor progression, we examined the effect of MC on the HCC proliferation including the tumor microenvironment *in vitro* and *in vivo* model.

Methods: *In vitro*, we assessed the effect of adding supernatant obtained from MC on the proliferation of Hepa1-6, an HCC cell line, and tumor endothelial cell (TEC) obtained from in the cell line-derived tumor tissue. *In vivo*, we examined the effect of MC on cancer for C57/BL/6 mice.

Results: *In vitro*, adding the supernatant of MC did not exhibit significant effect on the proliferation of Hepa1-6. On the other hand, the proliferation of TEC was significantly suppressed by adding supernatant of MC for 48 hours. *In vivo*, subcutaneous tumor size after two weeks of the Hepa1-6 injection with MC injection was smaller than in that without MC injection ($127.4 \pm 29.8 \text{ mm}^2$ vs. $235.6 \pm 78.0 \text{ mm}^2$).

Conclusions: These results suggested that MC does not promote the HCC progression. MC sheet transplantation could be an effective treatment for the liver failure, even in the presence of potential HCC.

Abstract Submission No. 200241

P-0408

Establishment of a new extraction method for extracellular vesicles derived from mouse liver tissues

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Background: Extracellular vesicles (EVs) are vesicles composed of a lipid bilayer membrane that are secreted from almost all cells in the body, and are a heterogeneous group that plays an important role in intercellular communication. Researches focusing on EVs in liver diseases have reported the use of EVs isolated from cell culture media or body fluids. However, very few studies have focused directly on EVs derived from liver tissue. Therefore, we researched and developed a protocol to isolate EVs from mouse liver tissue.

Methods: To isolate EVs from liver tissue, liver tissue was gently dissociated into small pieces and incubated with culture medium. Cells and debris were removed by filtration and centrifugation. After these steps, EVs were collected by ultracentrifugation. To evaluate the extraction of EVs, Nanoparticle tracking analysis (NTA) was performed to evaluate the concentration and size distribution. Furthermore, EVs markers CD63, CD81, and CD9 were evaluated by Western blotting.

Results: NTA revealed that most of the EVs isolated from liver tissues were in the range of 40 to 300 nm, consistent with the size of common EVs. Furthermore, the expression of EVs markers CD63, CD81, and CD9 was confirmed by Western blotting.

Conclusions: We have established and optimized an effective method to isolate high-quality EVs from mouse liver tissue. This protocol will help advance mechanistic studies of liver-derived EVs.

Abstract Submission No. 100164

P-0409

Combination Assay of Methylated *HOXA1* with Tumor Markers Shows High Sensitivity for Early-Stage HCC.

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Background: Although patients with non-viral-related hepatocellular carcinoma (non-viral HCC) have been increasing in Japan, there is no established surveillance system for them. To address this issue, we performed this study. In this study, we developed a novel index consisting of conventional tumor markers and methylated *HOXA1*(m-*HOXA1*), which we reported as a useful biomarker for HCC, and assessed the diagnostic performance for HCC.

Methods: We collected serum samples from 516 participants including 154 healthy subjects, 93 chronic liver disease (CLD) patients without HCC, and 269 HCC patients. Participants were divided into a control group comprising healthy subjects and patients with CLD and a HCC group. We measured serum m-*HOXA1* copy numbers using "combined restriction digital PCR assay" which was developed by us to measure CpG methylation levels. Alpha-fetoprotein (AFP) and des-gamma-carboxy prothrombin (DCP) were also evaluated.

Results: Performing multivariate logistic regression analysis, we developed a novel index named as ASDAm-H1 (Age, Sex, DCP, AFP and *m-HOXAI*) for detecting HCC. Area under the curve was 0.96 with a sensitivity of 86.2% and a specificity of 93.9%. Furthermore, ASDAm-H1 index showed an identical sensitivity for both viral and non-viral HCCs even at early stage: a sensitivity for overall early-stage HCC, non-viral early-stage HCC, and viral early-stage HCC was 76.3%, 78.0%, and 75.0%, respectively.

Conclusions: We showed distinguished performance of the ASDAm-H1 index to detect viral and non-viral HCC even at an early stage. This index may be applicable to a non-viral HCC surveillance system.

Abstract Submission No. 100334
P-0410

Estimating the Measurement Uncertainties of the PIVKA-II assay through Monte Carlo Simulation

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Background: Measurement uncertainty (MU) estimation has become an important process in clinical laboratories; however, calculating the MUs of protein induced by vitamin K absence or antagonist II (PIVKA-II) is difficult because of the complex mathematical calculations required in calibration. We aimed to quantify the measurement uncertainty (MU) for PIVKA-II (Abbott, IL, USA) using the Monte Carlo simulation (MCS), which is a computational algorithm that simulates statistical sampling to obtain numerical results through complex mathematical calculations.

Methods: Using the internal quality control results, we performed precision profiling of instrumental reading (relative light units; RLU), and the coefficient of variances were used as the relative uncertainties of RLU. Using these precision profiles, we simulated the y-weighted 4 parameters logistic calibration curves using MCS trials. Then, the MUs of PIVKA-II corresponding to each RLU were estimated through MCS.

Results: At 7.6 mAU/mL, the lower limit of the analytical measurement range (AMR), the MU was calculated to be the maximum of 25.0%. As the PIVKA-II result increased, the MU gradually decreased and was calculated to be the lowest value of 8.6% at 393.1 mAU/mL. After that, the MUs of PIVKA-II tended to gradually increase, showing a MU of 11.8% at 30,000 mAU/mL, the upper limit of the AMR. At the clinical decision point (40.0 mAU/mL), the MU of PIVKA-II was 12.0%.

Conclusions: MCS is adequate to estimate the MUs of hs-cTnI for entire measurement range, and these results would be clinically useful for estimating the MUs of the PIVKA-II in clinical laboratories.

Abstract Submission No. 100673
P-0411

ITGA6 as a Promising Biomarker for Early Detection and Prognosis of Hepatocellular Carcinoma

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Background: HCC remains a lethal cancer type, with early detection being pivotal for improved patient outcomes. The ITGA6 gene has been explored as a potential blood marker for early HCC detection.

Methods: We employed a comprehensive methodological approach, starting with the analysis of the GSE114564 dataset, which encompasses various stages of liver disease. This initial analysis identified 972 differentially expressed genes in HCC, with a refined analysis highlighting 59 genes specifically differentially expressed in early HCC. Subsequent validation was conducted in multiple datasets.

Results: ITGA6 was consistently upregulated in HCC. Analysis of progression-free survival (PFS) and overall survival (OS) for tumor grade G1 patients revealed that those with high ITGA6 expression had an elevated risk ratio. ITGA6 was predominantly expressed in Tumor Endothelial Cells (TECs) and was enriched in angiogenesis-related pathways. A positive correlation was observed between ITGA6 expression and pro-tumorigenic immune cells, but not with anti-tumorigenic immune cells.

Conclusions: Our findings underscore the potential of ITGA6 as a blood-based marker for early HCC detection. Its interaction with the tumor microenvironment suggests avenues for further research, potentially leading to novel HCC management strategies.

Abstract Submission No. 100681
P-0412

Fibrinogen Family as a Novel Diagnostic Marker in Hepatocellular Carcinoma

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Background: Hepatocellular carcinoma (HCC) is a lethal cancer, emphasizing the critical need for early detection. Fibrinogen, comprising FGA, FGB, and FGG, has been explored as a potential biomarker.

Methods: We analyzed Fibrinogen expression in the liver using data from GTEx Portal and TCGA. A cohort of 90 patients from Ajou University Hospital was evaluated using qRT-PCR. Additionally, the serum of 244 patients (Normal 30, Chronic Hepatitis 32, Cirrhosis 32, HCC 150) was assessed using ELISA to determine Fibrinogen protein concentration.

Results: Fibrinogen showed high liver expression but decreased expression in HCC tissues. Over 70% of HCC tissues in our cohort showed down-regulation of all three genes. ELISA results indicated a consistent decrease in FGA, FGB, and FGG levels from normal to HCC.

Conclusions: Our findings suggest the potential of the Fibrinogen family, either alone or in combination, as a promising diagnostic marker for HCC.

Abstract Submission No. 100733
P-0413

Non-invasive tests as continuous measures of hepatic fibrosis in NAFLD

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Fibrosis in NASH is the only histological finding that correlates with liver related outcomes, and its improvement is a key outcome measure in assessing therapeutics. Fibrosis is currently scored categorically, which lacks sensitivity in detecting smaller differences in fibrosis. We aimed to evaluate performance of NITs in correlating with a validated continuous histological fibrosis score (qFibrosis).

Patients with biopsy-proven NAFLD and no other liver disease were enrolled. Biopsies were quantitatively analysed for fibrosis with an artificial intelligence-based tool (qFIBS by HistoIndex). FIB-4, APRI, NFS, VCTE, AGILE 3+ and FAST were measured. The relationship between histological scoring for fibrosis and qFib, as well as between NITs and qFib was evaluated by linear regression analysis.

248 patients were recruited from 2014 to 2021.

qFibrosis and fibrosis score had a linear relationship (R^2 0.39, $p < 0.001$).

qFibrosis correlated with all NITs (all $p < 0.001$), with R^2 of 0.12, 0.12, 0.14, 0.44, 0.27 and 0.18 for FIB-4, APRI, NFS, VCTE, AGILE 3+ and FAST.

On scatterplots, confidence intervals for regression lines are narrowest at qFibrosis 1-3.

qFibrosis correlates well with fibrosis scores. NITs may have a role as continuous measures of fibrosis in NAFLD. Given narrow CIs, NITs may perform well at mild-moderate fibrosis where early intervention has greatest yield. VCTE is moderately correlated and greatest dynamic range, and may be the most useful NIT for evaluating fibrosis as a continuous variable.

Abstract Submission No. 100873

P-0414

Tumor marker elevation during post-operative surveillance in patient with hepatocellular carcinoma

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Purpose: aimed to evaluate factors influencing tumor marker elevation and their performance in detecting recurrent hepatocellular carcinoma (HCC) during post-operative surveillance.

Methods: We retrospectively analyzed 705 patients who underwent curative resection for HCC between January 2018 and March 2020. Post-operative surveillance included alpha-fetoprotein (AFP) and prothrombin-induced by vitamin K absence or antagonist-II (PIVKA-II) along with imaging exams. The cutoff values for AFP elevation were 20 ng/mL, and for PIVKA-II, 40 mAU/mL. Tumor marker normalization was defined as AFP < 20 ng/mL and PIVKA-II < 40 mAU/mL. Multivariable analysis was conducted to identify factors associated with tumor marker elevation. The positive predictive value (PPV) and negative predictive value (NPV) for HCC recurrence detection were calculated.

Results: Recurrence occurred in 34.6% (244/705). Independent factors linked to AFP elevation included recurrence (OR:21.89; 95% CI:7.46–64.18), preoperative AFP elevation (OR:3.63; 95% CI:1.73–7.63), log AFP at normalization (OR:12.68; 95% CI:3.52–45.70), and cirrhosis (OR:2.15; 95% CI:1.03–4.49). PIVKA-II elevation was independently associated with recurrence (OR:3.96; 95% CI:2.48–6.33), preoperative PIVKA-II elevation (OR:2.17; 95% CI:1.21–3.87), log PIVKA-II at normalization (OR:33.35; 95% CI:4.85–229.53), and

vascular invasion (OR:2.37; 95% CI:1.07–5.26). Using AFP elevation, the PPV and NPV for recurrence were 82.5% (95% CI:38.9%–97.2%) and 81.4% (95% CI:78.5%–84.1%), while PIVKA-II elevation showed PPV and NPV of 88.8% (95% CI:69.6%–96.5%) and 81.3% (95% CI:78.3%–83.9%).

Conclusion: Tumor marker elevation during post-operative surveillance was associated tumor marker levels at preoperative and normalized state as well as recurrence. AFP and PIVKA-II demonstrated significant PPV and NPV in detecting recurrence.

Abstract Submission No. 101368

P-0415

HBV surface antigen glycan isomer (HBsAgGi), correlates with HBV-DNA and HBV-RNA virions

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Background: In HBV patients' sera, infectious particles containing HBV-DNA (Dane particles) or HBV-RNA particles are enveloped with hepatitis B virus surface antigen (HBsAg). Infectious particles contain L-, M-, and S-HBsAg, while non-infectious sub-viral particles (SVPs) mainly contain S-HBsAg. Because SVPs present much more than infectious particles, S-HBsAg is the most abundant in all HBV particles. Thus, general HBsAg test using S-HBsAg antibodies cannot distinguish infectious and non-infectious particles. Previously, we found that O-glycosylated M-HBsAg was enriched in HBV-DNA particles. In this study, we developed and examined a new antibody to detect infectious particles, which should contain O-glycosylated M-HBsAg, called as HBsAg glycan isomer (HBsAgGi).

Methods and Results: Western analysis indicated that HBsAgGi antibody recognized M-HBs modified with O-glycan but not L-HBs without O-glycan on the PreS2 of genotype C. Immunoprecipitation (IP) experiments confirmed that both HBV-DNA and HBV-RNA-containing particles were immunoprecipitated by HBsAgGi antibody. HBsAgGi localized in ER to Golgi in MHBs-expressing cells. In treatment naïve chronic hepatitis B patients, serum HBsAgGi level was significantly correlated with the HBV-DNA level ($p=0.002$, $n=32$). However, HBsAgGi level was not associated with HBV-DNA level after NA treatment, which is consistent with the IP results.

Conclusions: O-glycosylated M-HBsAg is unique to genotype C infectious virions. New HBsAgGi antibody recognizes infectious HBV virions containing HBV-DNA or HBV-RNA, indicating that the infectious particles with HBsAgGi are generated through glycosylation pathway. Furthermore, NA treatment altered HBV-DNA and HBV-RNA status but not much HBsAgGi, suggesting that HBsAgGi is an useful monitor of infectious HBV particles during therapy.

Abstract Submission No. 101563

P-0416

Tumor stiffness as imaging biomarker for prediction of survival after curative resection for HCC

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Background: Tumor stiffness measurement (TSM) using magnetic resonance elastography (MRE) could assess tumor mechanical properties and predict hepatocellular carcinoma (HCC) recurrence. The aim of this retrospective study was to investigate whether preoperative TSM by MRE can predict survival after curative resection for HCC.

Methods: One hundred-one patients with HCC who underwent pre-operative MRE and curative resection were retrospectively analyzed. Potential associations of tumor stiffness and other clinicopathological variables with OS and RFS were analyzed in both univariate and multivariate Cox proportional hazards analyses. The optimal tumor stiffness cutoff value was determined using the minimal *P*-value approach.

Results: In the multivariate analysis, TSM (hazard ratio [HR], 1.20; 95 % confidence interval [CI], 1.02–1.41; *P* = 0.034), multiple tumors (HR, 2.17; 95 % CI, 1.05–4.35; *P* = 0.037), and tumor capsule (HR, 0.51; 95 % CI, 0.29–0.93; *P* = 0.029) were selected as independent risk factors of recurrence. On the other hand, TSM (HR, 1.36; 95 % CI, 1.07–1.75; *P* = 0.012) was selected as only an independent prognostic factor of overall survival in the same model. When the optimal cutoff point was set at 5.81 kPa, patients with TSM value $\geq$ 5.81 kPa were at a significantly greater prognostic factor of survival (HR, 5.47; 95% CI, 1.98–15.04; *P* < 0.001) than those with TSM value <5.81 kPa.

Conclusion: Higher tumor stiffness was associated with higher risk of recurrence and death. Therefore, TSM using MRE is a useful imaging biomarker for prediction of survival prognosis after curative resection for HCC.

Abstract Submission No. 101664
P-0417

EFFECT OF PESTICIDE CONTAMINATION ON PROTEIN LEVELS AND ANTIOXIDANT ACTIVITY IN RICE

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Rice, the world's second-most important crop, is often subjected to harmful practices like excessive pesticide use to combat pest infestations. Studies have shown that consuming pesticide-contaminated food can lead to serious health problems, including an increased risk of liver cancer. Since rice is a staple food consumed daily for extended periods, it's crucial to investigate how these pesticides affect the rice. This study aims to shed light on the effects of high pesticide concentrations on the total protein content and antioxidant activities of rice. For this study, the *Oryza sativa* variety MR263 was chosen and grown in a mixture of three parts soil, two parts sand, one-half part organic fertilizer, and one-half part peat moss. The rice was then exposed to pesticide concentrations four and six times higher than usual. The total protein and antioxidant activity of the rice were then measured using the Bradford and SOD tests on a UV-Vis Spectrophotometer. Our study revealed significant changes (*p* < 0.05) in total protein and antioxidant activity when rice was contaminated with six times the typical pesticide concentration. The accumulation of heavy metals in rice plants due to excessive pesticide application may induce oxidative stress, potentially leading to adverse health effects for rice consumers, including an increased risk of liver cancer and other liver-related ailments. Therefore, accurate identification of antioxidant proteins in rice plants is crucial for developing biosensors that can detect food contaminated with high levels of pesticides.

Keywords: superoxide dismutase, ANOVA-analysis of variance.

Abstract Submission No. 101904
P-0418

Bile acids- A new Biomarkers for assessment of drug induced liver injury (DILI) in patients on ATT

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Aim: Total bile acids (TBA) and other liver enzymes have been biomarkers of liver injury for decades. To identify novel serum biomarkers with greater specificity for liver injury is current need. The objective of this study was to assess the individual bile acids (IBA) as a new biomarker in ATT-DILI patients.

Methods: In this study, TB patients were divided into two groups (Control and DILI). Control group include the adults who were exposed to ATT but did not develop DILI. DILI patients were included based on the following threshold criteria: (1) Exposure within 3 months of ATT, (2) Aspartate transaminase (AST) and/or Alanine transaminase (ALT) > 2 x upper limit of normal (ULN) or Rise in Alkaline phosphatase (ALP) > 2 x ULN or Rise in Bilirubin > 2 x ULN with any rise in AST and ALT elevation. LC-MS/MS method used to measure three IBA; deoxycholic acid (DCA), glycocholic acid (GCA), and taurocholic acid (TCA).

Results: 78 patients (36 in control and 42 in DILI group) recruited who were on ATT. LC-MS/MS method used to analyse the plasma samples for the IBA estimation. The baseline characteristics and LC-MS/MS data are given in Figure. The LFTs value were significantly higher in DILI group. 40.48% patients show cholestatic type injury followed by hepatocellular (38.09%) and mixed type (21.43%). Out of 42, 14 patients (33.33%) had jaundice while 2 patients (4.76%) died during the treatment. The mean concentration of the GCA and TCA were 7644 ng/mL (*p* < 0.0001) and 4607 ng/mL (*p* < 0.0002) respectively for DILI patient. The DCA level (28.9 ng/mL) was significantly (*p* < 0.02) lesser in the control group.

Conclusion: Overall, our results indicate that DCA, GCA and TCA are promising biomarkers for ATT induced liver injury. It may be useful for diagnosis in DILI.

Abstract Submission No. 101974
P-0419

Association of high iron and ferritin levels to chronic hepatitis in Mongolia

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Introduction: Elevated ferritin and iron levels are common in patients with chronic hepatitis of non-viral origin. Excess iron and ferritin can

cause liver damage and increase the risk of fibrosis, cirrhosis, and hepatocellular carcinoma.

Methods: This study aims to investigate the level of liver inflammation in people with elevated iron and ferritin levels. The study included 170 people with maximum elevated iron levels 26.9-55.9 mg/dl and 132 people with 250-2326.8 ng/mL and the percentage of those people with hepatitis were investigated.

Results: Our study determined the percentage of hepatitis in people with elevated ferritin and iron levels. In the control group with normal ferritin, the incidence of elevated ALT was 38%, compared to 86.4% in the elevated ferritin group. However, elevated AST was detected 42% in the normal ferritin control group and 87.9% in the elevated ferritin group. In the control group with normal iron, the incidence of elevated ALT was detected in 43.2% of patients, while in the group with high iron, it was 74.3%. In the iron-normal control group, AST elevation was 32.7 percent, compared to 60.9% in high serum iron group. Prevalence of high iron serum load was 3.97% among total outpatient test takers, which is much higher than other countries.

Conclusion: High ferritin was more associated to elevated ALT levels 86.4%, whereas high iron level group had slightly lower (74.3%) than that of ferritin's. In this study we could not confirm etiology of high ALT levels within normal control groups.

Abstract Submission No. 102086

P-0420

HALP score is a useful predictor of prognosis after hepatectomy for hepatocellular carcinoma

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Background: The haemoglobin, albumin, lymphocyte, and platelet (HALP) score is an immune-nutritional assessment score that is a prognostic indicator for several malignant tumours. This study aimed to investigate its prognostic value in patients who underwent hepatectomy for hepatocellular carcinoma.

Methods: The data of 685 patients with hepatocellular carcinoma who underwent hepatectomy at Kurume University between 2006 and 2021 were retrospectively analysed. The patients were classified into high and low HALP score groups based on a cut-off HALP score determined using a receiver operating characteristic curve. To minimise bias, 1:1 propensity score matching was performed. Kaplan-Meier curves were used to estimate survival time, and data were evaluated using the log-rank test. Univariate and multivariate analyses were performed using Cox hazard or logistic regression models for assessing survival time and postoperative outcomes, respectively.

Results: Low HALP scores were significantly associated with poor overall survival ($P = 0.0066$). Univariate and multivariate analyses revealed that HALP score independently predicted overall survival ($P = 0.005$). However, the HALP score was not significantly related to recurrence-free survival or postoperative outcomes.

Conclusions: The HALP score is a simple, inexpensive tool for predicting prognosis after hepatectomy for hepatocellular carcinoma.

Abstract Submission No. 102092

P-0421

A Novel, Highly Sensitive Diagnostic Method Using Glycosylated Ferritin for Early-stage HCC

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Background: As hepatocellular carcinoma (HCC) is one of the most intractable cancers, early detection is important in improving the prognosis of patients. Because we found that glycosylated ferritin is a possible biomarker of HCC, we performed this study to investigate the diagnostic performance of a combination of markers for early-stage HCC.

Methods: We used serum samples from 138 patients with HCC including 47 patients with Barcelona Clinic Liver Cancer stages 0 and A, categorized as early-stage HCC, and 197 patients with chronic liver disease including 96 patients with liver cirrhosis (LC). First, we measured alpha-fetoprotein (AFP) and des-gamma-carboxy prothrombin (DCP) levels. Second, after glycosylated ferritin was separated using concanavalin A, non-glycosylated and total ferritin levels were measured. Finally glycosylated ferritin was calculated by subtracting the non-glycosylated ferritin level from the total ferritin level. Using multivariate logistic regression analysis, we developed a new index for the detection of HCC, which we named GFAD (age, glycosylated ferritin, total ferritin, AFP, DCP).

Results: The area under the receiver operating characteristic curve (ROC-AUC) of GFAD was 0.94, with a sensitivity of 89.9% and specificity of 86.4% at a cut-off value of 0.397 as designated by the Youden index. When restricted to LC and early-stage HCC, the sensitivity was 76.6% with a ROC-AUC of 0.87, which showed excellent performance in discriminating between LC and early-stage HCC.

Conclusions: GFAD appears to be a highly sensitive diagnostic tool for early-stage HCC that may be useful for the early detection of HCC in patients with LC.

Abstract Submission No. 200106

P-0422

GPX4 mediates glucose metabolism via Akt-mTOR axis in ICC

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INTRODUCTION: The oncological role of glutathione peroxidase 4 (GPX4) has been extensively investigated. However, the clinical implications of GPX4 and its oncological mechanism regulating the tumorigenesis in patients with intrahepatic cholangiocarcinoma (ICC) remain unknown. This study aimed to evaluate the prognostic impact of GPX4 and its underlying molecular mechanisms in patients with ICC.

METHODS: The study consisted of clinical and experimental studies. In clinical study, 57 patients who underwent hepatectomy for ICC between 2010 and 2017 were analyzed. Based on the immunohistochemistry, patients were divided into GPX4 high (n=15) and low (n=42) groups, and clinical outcomes were assessed. In experimental study,

the roles of GPX4 in tumor activity and gene or protein expressions associated with glucose metabolism and Akt-mTOR axis were analyzed in ICC cell lines.

RESULTS: The clinical study revealed that GPX4 high group showed significant associations with high SUVmax (≥ 8.0 , $p=0.017$), multiple tumors ($p=0.004$), and showed GLUT1 high expression with a trend towards significance ($p=0.053$). Overall and recurrence-free survival in GPX4 high expression were significantly worse than those in the GPX4 low expression ($p=0.038$ and $p<0.001$). In the experimental study, inhibition of GPX4 using GPX4 inhibitor attenuated cell proliferation and migration in ICC cell lines. Inhibition of GPX4 also decreased the expression of glucose metabolism-related genes, such as *GLUT1* or *HIF1 α* . In mechanically, GPX4-mediated glucose metabolism was regulated in Akt-mTOR axis.

CONCLUSIONS: GPX4 is a significant prognostic marker in patients with ICC. Furthermore, GPX4 can mediate glucose metabolism of ICC.

Abstract Submission No. 200160
P-0423

Smart diagnostic strategy for SARS-CoV-2 viruses in real 166 patients samples.

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Background: Various studies including ours have reported weaknesses of the current COVID-19 diagnostics including limited sensitivity, and even the gold-standard polymerase chain reaction (PCR) is advised to be repeated to avoid misdiagnosis. ⁽¹⁻³⁾ This clinical study was conducted to evaluate the diagnostic performance of our previously designed Smart-CoV (Patents: JP2022-161370 と WO2022-219967) as a thermo-responsive preanalytical strategy in COVID-19 diagnosis compared to PCR.

Methods: A prospective study included 166 subjects was conducted. Nasopharyngeal swabs from all participants were collected and tested for SARS-CoV-2 virus with and without Smart-CoV. SARS-CoV-2 detection sensitivity was estimated depending on PCR analysis results with and without Smart-CoV, and the patient's full clinical evaluation.

Results and conclusions: Smart-CoV enabled the purification and enrichment of only virus's native forms without cross-reactivity to remnant viral RNA; hence, it avoids false positive results. Moreover, samples that tested as false negative due to low viral load, were confirmed to be positive using Smart-CoV and even in samples that tested positive with and without Smart-CoV, viral load was significantly increased with Smart-CoV. As shown in figure 1, Smart-CoV improved PCR diagnostic specificity, sensitivity, and accuracy up to 100% instead of 89.4%, 53.3%, and 69.8% respectively.

Abstract Submission No. 200162
P-0424

NUPR1: a potential targeted immunotherapy in pan-cancer

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Objectives: NUPR1 is a stress-induced chromatin-related factor, which is consistently over-expressed in cancer tissues, especially in tumors with poor prognosis and significant drug resistance to anti-tumor therapy. We used The Cancer Genome Atlas (TCGA) pan-cancer data to assess the role of NUPR1.

Methods: We used TCGA (The Cancer Genome Atlas), GEO (Gene Expression Omnibus) data sets and many bioinformatics tools to explore the role of NUPR1 in pan-cancer. We used R package "clusterProfiler" to carry out NUPR1 enrichment analysis. Then we analyzed the association between NUPR1 expression and the level of immune cell infiltration. Furthermore, we evaluated the relationship between NUPR1 and immune activation genes, immune checkpoint, immune suppression genes, chemokines and chemokine receptors.

Results: Based on TCGA, NUPR1 is differently expressed in different tumor types, and it is related to the survival status. In addition, NUPR1 was significantly associated with immune-related and metabolism-related pathways, closely related to T-cell infiltration, immune checkpoints, immune activation genes, immune suppressive genes, chemokines, and chemokine receptors.

Conclusions: Our findings suggest that NUPR1 is a potential biomarker for cancer. NUPR1 may coordinate with other immune checkpoints to modulate the immune microenvironment and could be used to develop new targeted immunotherapy drugs.

Abstract Submission No. 100143
P-0425

ACUTE SEVERE HEPATITIS IN CHILDREN ACROSS THE PRE-PANDEMIC AND CORONAVIRUS ERA IN SINGAPORE

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Background: This study aims to describe acute severe hepatitis (ASH) in Singaporean children before coronavirus-2019 (COVID-19) pandemic and during the outbreak of COVID-19.

Methods: This was a single-centre retrospective study of children aged 0-16 years presenting with ASH, defined by serum alanine transaminase and/or aspartate transaminase >500 U/L based on WHO definition. Cases were analysed: 2018-2019 (pre-pandemic) and 2020-2022 (coronavirus pandemic). AUHC was defined as ASH in which viral hepatitis A-E, other infective agents, immunologic, metabolic, drug/toxic and structural causes were excluded.

Results: Total of 112 cases of ASH were included with average of 27 cases/year and 19 cases/year in the pre-pandemic and COVID-19 pandemic periods respectively. Although numbers were limited, an increase in AUHC was observed in the pandemic period (Image 1). Out of the 8 cases of AUHC in the pandemic period, Adenovirus and SARS-CoV-2 were detected in 1 and 2 patients respectively. All 5 cases of AUHC in the pandemic period were associated with severe aplastic anaemia (AA) requiring bone marrow transplant, whereas no cases of severe AA was seen in the pre-pandemic period. In addition, there was an increase in systemic inflammatory/autoimmune disorders resulting in ASH during the pandemic period. Overall, none of the patients died and only one patient had liver transplant.

Conclusion: AUHC and severe hepatitis associated AA were higher in the pandemic years although the overall numbers remained low. The corresponding increase in systemic inflammatory disorders in the pandemic period may lend support to possible auto-inflammatory process in the pathogenesis of AUHC.

Abstract Submission No. 100247
P-0426

PROFILE OF ADULT FILIPINO PATIENTS WITH HEPATOLITHIASIS IN A TERTIARY HOSPITAL

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Background: Hepatolithiasis is endemic to East Asia with a prevalence of 30-50%. However, the etiology of the disease is not yet fully studied and various extensive and expensive procedures are proposed for the management of the disease.

Objective: The study aims to describe the clinical characteristics among adult hepatolithiasis patients at Rizal Medical Center from January 2016 to December 2021.

Methods: The study is a single-center, retrospective descriptive study chart review of patients with imaging diagnosed with hepatolithiasis.

Results: A total of 46 patients were included in the study. Nineteen (41%) were male and twenty-seven (59%) were female with mean age of 49.13±11.99 years (Table 1). Age distribution shows the highest among the 31 to 40-year-old age group. Majority presented with cholangitis (52.17%) (Table 2).

All underwent ultrasonography. Forty-three (93%) underwent Abdominal CT scan and three (7%) underwent Magnetic resonance imaging with majority of stones found in the left intrahepatic duct (Table 3).

Many underwent Endoscopic retrograde cholangiopancreatography with stone extraction (50%). Of those who underwent the procedures, five (10.87%) had morbidities and 3 (6.52%) were mortality cases (Table 4,5).

Conclusion: In our study, the majority of the patients are female within the 31 – 40-year-old age group. Most are from the Metro Manila. On presentation, patients are usually in cholangitis, and diagnosis is done initially by ultrasonography and CT scan.

Major treatment measures such as endoscopic procedures and hepatectomy are rendered but most patients undergo ERCP followed by hepatectomy with morbidity and mortality rates of 10.87% and 6.52%, respectively.

Abstract Submission No. 100339
P-0427

Mediation of radiation-associated hepatocellular carcinoma risk by HBV and HCV infections

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Background: Previous cohort studies of atomic bomb survivors have shown that radiation exposure is an independent risk factor for hepatocellular carcinoma (HCC) and is associated with an increased prevalence of chronic hepatitis B virus (HBV) infection. To investigate to what extent HBV and hepatitis C virus (HCV) infections might

mediate the risk through indirect pathways between radiation exposure and HCC, we estimated mediation proportions for HBV and HCV infection on risk of HCC in a prospective clinical cohort study.

Methods: Among 4,345 atomic bomb survivors who underwent hepatitis screening tests between 1993 and 1995, 111 HCC cases were identified from 1993 to 2011 through local cancer registries in Hiroshima and Nagasaki, Japan. We used three statistical methods: traditional risk analysis with proportional hazards regression, mediation analysis with logistic regression to estimate mediation proportions, and sensitivity analysis employing the E-value to evaluate the impact of unadjusted confounding.

Results: Adjusted for age, sex, city, proximal-distal location at the time of exposure, and hepatitis virus infection status, the hazard ratio (HR) of HCC for 1 Gy radiation was 1.22 (95% confidence interval [CI]: 0.91-1.64). HRs for HBV and HCV infection directly were 8.3 (3.2-21) and 34 (23-51), respectively. The estimated mediation proportions were 11% for HBV infection and 33% for HCV infection.

Conclusions: This study suggested that a meaningful fraction of the radiation-related risk of HCC is mediated through viral infection. However, because of few cases and potential confounding of the estimated associations between viral infection rates and radiation, further study is required.

Abstract Submission No. 100352
P-0433

Epidemiology of Biliary Tract Cancer in the Young Adults: Global Descend and Regional Expansion

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Backgrounds: The escalating incidence of early-onset gastrointestinal cancers is becoming a primary global health concern. Biliary tract cancer has been relatively understudied in this regard.

Methods: We utilized data from the Global Burden of Disease Study 2019 to investigate the temporal trends in EOBTC, encompassing the estimation of frequencies and age-standardized rates (ASRs) of EOBTC incidence and mortality from 2010 to 2019.

Results: EOBTC constituted nearly 7 percent of all BTC cases worldwide. The incidence rates of EOBTC decreased significantly in most regions, except in the Eastern Mediterranean (annual percentage change +1.04%), where the incidence is rising. The ASR of EOBTC-related mortality from obesity increased in most regions, with the highest increase in Southeast Asia and low, middle SDI strata.

Conclusions: There was a reduction in the burden of EOBTC globally, except for Eastern Mediterranean countries and low-middle SDI countries. Study regarding this distinct form of BTC need to be conducted to understand the rising burden in these regions.

Abstract Submission No. 100596
P-0434

Determinants of Changes in Serum HBV DNA Levels: A Community-based Follow-up Study

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Background: The REVEAL-HBV study demonstrated long-term changes in serum HBV DNA levels as an important predictive factor for HCC development. However, the factors determining the long-term changes in serum HBV DNA levels remain unclear.

Methods: Participants (n=275) with baseline HBV DNA levels $>10^7$ copies/mL in the REVEAL-HBV study were enrolled. We used a group-based trajectory model to identify distinctive groups of long-term changes of HBV DNA levels during 11 years of follow-up. Multivariate-adjusted hazard ratios and 95% confidence intervals of possible determinants were estimated using logistic regression.

Results: Four distinctive trajectory groups of long-term changes in HBV DNA levels were identified. Group 1 (n=107, 38.9%) had persistently high levels of HBV DNA ($>10^7$ copies/mL). Group 2 (n=50, 18.2%) had mildly decreased but $>10^6$ copies/mL HBV DNA levels at the end of the follow-up period. Group 3 (n=64, 23.3%) had significantly decreased but $>10^4$ copies/mL HBV DNA levels at the end of the follow-up period. Group 4 (n=54, 19.6%) had rapidly decreasing and $<10^4$ copies/mL HBV DNA levels at the end of follow-up. Multivariate logistic regression analyses demonstrated that sex, baseline ALT level, HBeAg status, HBV genotype, and quantitative HBsAg level were significant determining factors for long-term changes in HBV DNA levels. Female participants with normal ALT levels, positive HBeAg status, HBV genotype C, and higher baseline HBsAg levels were more likely to have persistently high HBV DNA levels.

Conclusions: Our study identified important factors determining long-term changes in HBV DNA levels and provided insights to inform management decisions for chronic HBV patients.

Abstract Submission No. 100652
P-0435

Association between HLA Zygosity and Long-term Changes in Serum qHBsAg Levels: The REVEAL-HBV Study

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Background: Quantitative HBsAg (qHBsAg) levels are important biomarkers of chronic hepatitis B in predicting disease activity and monitoring treatment response. However, the determinants of the long-term changes in serum qHBsAg levels are unclear. Human leukocyte antigen (HLA) complex diversity plays an important role in immunosurveillance. Thus, our study aimed to explore the role of HLA complex diversity in the long-term changes in serum qHBsAg levels.

Methods: The participants (N=2300) were recruited from the REVEAL-HBV study with repeat measurements of qHBsAg levels during an 11-year follow-up period. A group-based trajectory model was used to determine distinctive groups of long-term changes in serum qHBsAg levels. We used genotyping data to represent the 4-digit HLA alleles at six loci, including the classical HLA class I genes (HLA-A, HLA-B, and HLA-C) and classical HLA class II genes (HLA-DRB1, HLA-DQB1, and HLA-DPB1). Multinomial logistic regression was used to analyze the associations between HLA zygosity and the long-term changes in qHBsAg levels.

Results: Long-term changes in qHBsAg levels varied highly among chronic HBV. Nine distinct trajectory groups with different long-term changes in qHBsAg levels were identified using the group-based trajectory model. After adjusting for the age, sex, ALT level, HBV DNA level, and HBV genotype, homozygosity at HLA class II loci, particularly HLA-DQB1, significantly correlated with the long-term changes in qHBsAg levels.

Conclusions: HLA zygosity is significantly associated with long-term changes in serum qHBsAg levels. Our results imply an important role of individual immune status on the management of HBV infection.

Abstract Submission No. 100711
P-0436

Impact of Clinical Characteristics & Treatment on Cholangiocarcinoma Prognosis in Southern Thailand

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Background: Cholangiocarcinoma (CCA) is most common in North-eastern Thailand and other parts of Asia where liver flukes are prevalent. However, it is unknown whether CCA patients in low and high liver fluke prevalence areas are similar. We aimed to analyze clinical characteristics and outcomes of CCA patients in Southern Thailand.

Methods: We retrospectively reviewed 223 patients diagnosed with CCA between 2018-2021 in a tertiary-care center in Southern Thailand. Clinicopathologic data were reviewed and compared between intrahepatic, perihilar, and distal CCA (iCCA, pCCA, and dCCA, respectively). Overall survivals (OS) were determined and analyzed by Kaplan-Meier method and multivariable Cox regressions.

Results: The mean age was 63.9 years; 50.7% were men. The most common subtype was iCCA (49.3%), followed by pCCA (36.3%) and dCCA (14.3%). Most patients were diagnosed at a later stage: 59.4% TMN stage IV and 23.3% stage III. Cirrhosis was presented in 6.3%, while the presence of liver fluke was not detected. Only 15.1% of the cohort were deemed resectable. The median OS for iCCA, pCCA, and dCCA patients, were 27.3, 22.0, and 19.3 weeks, respectively (p=0.9). One-year survival rate differed significantly between resectable and

unresectable patients (85.2% vs 21.2%, $p<0.0001$). TMN stage (aHR 1.88), palliative biliary drainage (aHR 0.31), and systemic chemotherapy (aHR 0.19) were independent predictors for mortality in unresectable pCCA and dCCA patients. In unresectable iCCA patients, only systemic chemotherapy was significant (aHR 0.30).

Conclusions: Most patients were diagnosed late, and the median OS was only 5–6 months. Unresectable CCA patients with systemic chemotherapy and palliative biliary drainage had better survival rates.

Abstract Submission No. 100941

P-0437

Granulomatous Liver Disease in the Current Decade: A Clinico-Radio-Pathological Study in Thailand.

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Background: Granulomatous liver disease (GLD) is a rare condition characterized by the formation of hepatic granulomas attributed to various etiologies. A comprehensive evaluation of GLD from a multi-aspect perspective is currently lacking. We aimed to investigate etiologies, and clinico-radio-pathological characteristics of patients with GLD in recent years.

Methods: We conducted a retrospective study at a tertiary-care center in Thailand, all patients underwent liver biopsy between 2011-2021 were reviewed. Patients with the histopathological report of granulomas in their liver specimens were included. Clinical presentations, radiological, and laboratory data closest to the procedure date were collected.

Results: Of 1377 liver biopsy specimens, 41 patients had GLD (2.98%). Of those, 63.4% were male, the etiologies of GLD were as follows: 26(63.4%) infectious, 7(17.1%) non-infectious, and 8(19.5%) undetermined. Common presentations included abnormal liver tests (87.5%) and weight loss (61.9%). Among infectious granulomas, mycobacterium infections (tuberculosis [TB], 13/ non-tuberculous [NTM], 3) were predominant. Compared with other causes, the final diagnosis of mycobacterium was found to be associated with a significantly lower BMI, more extra-gastrointestinal involvement, and lower serum albumin levels. Caseating-type granulomas were observed in 16% of non-tuberculosis cases. One-third of GLD patients demonstrated no focal lesion on liver imaging whereas multi-focal lesions were the most common radiological finding (43.9%).

Conclusions: In this modern era, infectious cause, especially mycobacterium infections, remains the primary etiology of GLD. It is important to note that granuloma types are not pathognomonic for specific diseases, emphasizing the need for extensive evaluation beyond liver biopsy to determine the underlying etiology.

Abstract Submission No. 101016

P-0438

Sex Disparities in Liver Cancer in Asia-Pacific : Insights from the Global Burden of Disease 2019

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Background: Liver cancer is emerging as a significant global health concern, particularly in the Asia-Pacific region but the sex difference remains elusive. This study aims to examine the sex differences in liver cancer incidence over a 10-year period in Asia.

Methods: Employing data from Global Burden of Disease Study 2019, our analysis delves into temporal trends in liver cancer across Asia-Pacific. We calculate age-standardized rates (ASRs) for liver cancer, along with associated death and disability-adjusted life-years (DALYs), stratified by sex. To assess changes in age-standardized rates over time, we computed the annual percent change (APC).

Results: Our findings reveal a persistent sex disparity in liver cancer burden from 2010 to 2019 in Asia-Pacific region, despite a decline in incidence for both sexes. Specifically, the male age-standardized incidence rate (ASIR) was twice as high in Southeast Asia and three times higher in the Western Pacific region compared to females. While liver cancer incidence decreased in females in both regions, it increased in males in Western Pacific region. Southeast Asian males exhibited a decreasing trend, albeit less pronounced than in females. Similar patterns were observed in age-standardized death rates (ASDR) and age-standardized DALYs rates.

Conclusion: Our study underscores a substantial sex difference in liver cancer across the Asia-Pacific region, emphasizing the urgent need for effective interventions. These findings underscore the importance of implementing sex-sensitive health policies to address the burden of liver cancer through screening and treatment. Further exploration of genetic and behavioural factors is crucial for understanding and addressing this issue.

Abstract Submission No. 101205

P-0439

Characteristics of quality of life in elderly patients with chronic liver disease

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Objective: In Japan, as the elderly population increases, there are more opportunities to treat elderly patients with chronic liver disease (CLD). Elderly patients often have physical, mental, financial, and social difficulties that can reduce their quality of life (QOL). We aimed to clarify the characteristics of QOL in elderly patients with CLD.

Methods: A total of 931 patients with CLD who visited our hospital between February 2020 and March 2021 were included. Among them, 616 patients were analyzed after excluding patients with liver cancer. We divided them into 3 groups; the non-elderly group (254 cases), the young-old group (205 cases), aged 65 to 74 years, and the old-old group (157 cases), aged 75 years or older. Health-related QOL was assessed using the SF-36v2® standard version, and scoring was based on the 2017 National Standard Values.

Results: Physical component summary (PCS) in the analyzed cases was lower than the national standard. Mental component summary (MCS) and role component summary (RCS) were higher than the national standard. PCS was significantly lower in both the young-old and old-old than in the non-elderly. MCS was higher in both the young-old and old-old than in the non-elderly. RCS was not significantly different among three groups. Grip strength was lower in the elderly than in the

non-elderly group. The age-related decline in PCS in patients with cirrhosis is more remarkable than in patients with chronic hepatitis.

Conclusion: When treating elderly patients with CLD, it is important to pay attention to the decline in physical QOL.

Abstract Submission No. 101580

P-0440

Gamma-glutamyl transferase and the risk of disease-specific mortality in patients with diabetes

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Background/Aims: There exist a paucity of data regarding whether gamma-glutamyl transferase is associated with disease-specific mortality in patients with type 2 diabetes mellitus. This study aimed to investigate the association of serum gamma-glutamyl transferase levels with all-cause and disease-specific mortality in patients with diabetes mellitus using a Korean nationwide health-screening database.

Methods: A total of 9,687,066 patients without viral hepatitis or liver cirrhosis who underwent health examination in 2009 were included. These patients were divided into four groups according to sex-specific quartiles of serum gamma-glutamyl transferase levels.

Results: During a median follow-up period of 8.1 years, 222,242 deaths were identified. The all-cause mortality rate increased as the serum gamma-glutamyl transferase levels became higher (highest quartile vs. lowest quartile: hazard ratio [HR], 1.57; 95% confidence interval [CI], 1.55–1.59; *p* for trend <0.001). Similar trends were observed for cardiovascular disease (HR, 1.57; 95% CI, 1.53–1.62), ischemic heart disease (HR, 1.40; 95% CI, 1.33–1.48), and stroke (HR, 1.72; 95% CI, 1.60–1.85) in the highest quartile, as compared with the lowest quartile (*p* for trend <0.001). As the gamma-glutamyl transferase quartiles became higher, mortality rates related to cancer (HR, 1.56; 95% CI, 1.52–1.60), liver disease (HR, 9.42; 95% CI, 8.81–10.07), respiratory disease (HR, 1.55; 95% CI, 1.49–1.62), and infectious disease (HR, 1.73; 95% CI, 1.59–1.87) also increased in the highest quartile, as compared with the quartile (*p* for trend <0.001).

Conclusion: Serum gamma-glutamyl transferase levels may be useful for the risk assessment of all-cause and disease-specific mortality among patients with type 2 diabetes mellitus.

Abstract Submission No. 101670

P-0441

Predicting outcome in portal & splanchnic vein thrombosis: A 12-year retrospective study in Thailand

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Background: Splanchnic vein thrombosis including portal vein, mesenteric vein and splenic vein thrombosis is increasingly recognized in clinical practice and associated to mortality. However, the studies of splanchnic vein thrombosis are limited in Thai population. This study

aims to describe the prevalence, clinical features, treatment, outcome and factor associated outcome in Thai populations.

Methods: We conducted a retrospective study including patient diagnosed with portal, mesenteric and splenic vein thrombosis in the past 12 years, collected data from medical record and analyze the patient characteristic and factor associated with favorable or unfavorable outcome which include death associated or not associated with thrombosis.

Results: During the study period in 2011 - 2023, A total of 86 patient diagnosed with splanchnic vein thrombosis in in HRH Princess Maha Chakri Sirindhorn Medical Center. The period prevalence of splanchnic vein thrombosis was 0.024%. Portal vein involvement was 89.53%, Mesenteric vein involvement was 31.19% and Splenic vein involvement was 19.16%. Major risk factor is cirrhosis (62.79%). Clinical manifestation often leads to diagnosis is abdominal pain (79.07%). The patient received treatment with anti-coagulant was 31.4%. Factor associated with unfavorable outcome were age (*p*=0.0336), Child-Pugh score (*p*=0.044), Serum albumin (*p*=0.0081) and Ascites (*p*=0.047).

Conclusion: Prevalence of Splanchnic vein thrombosis in this hospital is 0.024%. The most involving part is Portal vein thrombosis. Major risk factor is cirrhosis. Clinical manifestation often leads to diagnosis is abdominal pain. Majority of patient got favorable outcome after diagnosis. Risk factor associated with unfavorable outcome are age, Child-Pugh score, serum albumin and Ascites.

Abstract Submission No. 101699

P-0442

Seropositivity and risk factors of HBV and HCV in transgender population in an urban area of BD

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Background: The burden of HBV and HCV infections in the transgender population remains an underestimated issue. Determining the prevalence of these infections in transgender people could be important for health policymakers and health workers to develop a screening programs and hepatitis B vaccination program for this high-risk group.

Objectives: The study aimed to determine the prevalence of HBV and HCV infection and the risk factors for HBV and HCV infections among the transgender populations of Chattogram, Bangladesh.

Methods: A conveniently selected 231 transgender individuals from health awareness campaign programs, private chambers, and different health facilities of Chattogram, Bangladesh, were included. Self-reported risk factors data were collected, and blood samples were obtained from the subjects and sent for hepatitis B surface antigen (HBsAg) and antibody to HCV (anti-HCV) tests.

Results: The prevalence of HBsAg (+) and anti-HCV (+) was respectively 4.8% (11/231) and 0.4% (1/231), and 12.6% had a positive family history of HBV. Seventy-one (30.6%) had received dental treatment, 21 (9.1%) received blood transfusion, 75 (32.5%) were sharing nail cutter, 13 (5.2%) were shaving in the saloon, 5 (2.2%) had history of substance abuse, 221 (95.7%) pierced nose/ear, 55 (23.8%) painted tattoo on their body, and 72 (31.2%) were homosexual. Only 3.5% of the participants reported being vaccinated against HBV, and 121 (52.4%) used condoms during intercourse.

Conclusions: The serological prevalence of HBV and HCV was low. Nevertheless, vaccination program needs to be strengthened in transgender populations.

Keywords: Transgender, Hepatitis B, Hepatitis C.

Abstract Submission No. 101826
P-0443

Prevalence of MAFLD-Related Hepatocellular carcinoma; A systematic review and meta-analysis

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BACKGROUND: Metabolic dysfunction-associated fatty liver disease (MAFLD) is an important cause of hepatocellular carcinoma (HCC) globally, however the proportion attributable to MAFLD is unclear. The novel MAFLD diagnostic criteria allows objective diagnosis in the presence of steatosis plus defined markers of metabolic dysfunction, irrespective of concurrent liver disease. We aimed to determine the global prevalence of MAFLD in HCC cohorts, including estimation of the proportion of “mixed-aetiology” HCC.

METHODS: A systematic review and meta-analysis was performed, searching for studies systematically ascertaining MAFLD in HCC cohorts, defined using international expert panel criteria including ethnicity specific BMI cut-offs. A comparison of clinical and tumour characteristics was performed between patients with MAFLD as the sole aetiology of HCC, non-MAFLD aetiology, and mixed-aetiology HCC.

RESULTS: 22 studies comprising 56,565 individuals with HCC were included. Total pooled prevalence of MAFLD was 48.7% (95% CI; 34.5% – 63.0%). MAFLD as the sole cause of liver disease accounted for 12.4% (95% CI; 8.3% – 17.3%). In individuals with HCC due to hepatitis B virus (HBV), hepatitis C virus (HCV) and alcohol related liver disease (ARLD), the prevalence of MAFLD was 40.0% (95% CI; 30.2% – 50.3%), 54.1% (95% CI; 40.4% – 67.6%) and 64.3% (95% CI; 52.7% – 75.0%) respectively. Mixed-aetiology HCC was phenotypically distinct from “pure” MAFLD HCC and non-MAFLD HCC.

CONCLUSION: MAFLD is common as a sole HCC aetiology, but more so as a co-factor in mixed-aetiology HCC. Studies should accurately diagnose and report MAFLD to better understand the interaction between concurrent liver diseases.

Abstract Submission No. 101833
P-0444

Disease burden of viral hepatitis B and C in 2020, Japan: with a view to elimination.

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Objective: To estimate the number of chronic hepatitis virus infected persons (carriers) in 2020 using the National Data Base (NDB) and epidemiological data from the Hepatitis Epidemiology Study Group, and national statistics.

Methods: Hepatitis virus carriers were divided into 20 HBV states and 26 HCV states according to liver disease states (asymptomatic carriers, chronic hepatitis, compensated cirrhosis, non-compensated cirrhosis, liver cancer), social presence (undiagnosed carriers, patients) and treatment type (non-nucleic acid analog, nucleic acid analog, IFN, DAA, other treatments).

The number of carriers of each state in 2020 was estimated by sex, age, and liver disease states using NDB analysis and the estimated number of carriers as of 2011 reported in JVH2018. Data cleansing was performed according to the flowchart, and the number of patients by treatment type in 2020 was estimated based on the NDB analysis, excluding subjects considered to be for testing purposes or Fake HBV, etc.

Results and Conclusion: Although the results are tentative, the number of potential carriers in 2020 was (1) 240,000–260,000 for HBV and 190,000–320,000 for HCV, and (2) 210,000 for HBV and 240,000 for HCV among the number of patients who are receiving treatment excluding those undergoing observation. Other research results will be reported in detail on the same day.

Abstract Submission No. 100083
P-0445

CD8+ T cell exhaustion signatures in HBV-HCC: Prognosis & Immunotherapy

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Background: Hepatocellular carcinoma (HCC) is the fourth leading cause of cancer-associated mortality. Some clinical studies of HCC therapies have indicated a more effective response to immune checkpoint inhibitors (ICIs) therapy in patients with HBV-positive HCC (HBV+ HCC) than in those with HBV-negative HCC (HBV-HCC).

Method: We integrated scRNA-seq (GSE149614) and bulk RNA-seq (TCGA-LIHC and ICGC-JP) data. Then CD8+ T cell exhaustion-related genes (TERGs) were identified through pseudotime analysis. Differential analysis and LASSO-Cox regression were applied to construct CD8+ T cell exhaustion index (TEI) based on the expression of TERGs. Simultaneously, we systematically evaluated the predictive value of TEI in terms of prognosis and immunotherapeutic efficacy. Gene set enrichment analysis and RT-qPCR explored mechanisms underlying HBV-mediated CD8+ T cell exhaustion in HCC.

Results: The study unveiled that, compared to HBV- HCC, HBV+ HCC exhibited higher proportion of exhausted CD8+ T cells (Tex). We identified 3,172 TERGs that play a crucial role in CD8+ T cell exhausted progression. The TEI constructed based on TERGs demonstrated substantial predictive value for prognosis and immunotherapeutic efficacy. Moreover, TEI also serves as an independent prognostic factor for HCC, and the nomogram incorporating TEI, TNM staging, and vascular invasion exhibited excellent predictive value for prognosis in HCC. Subsequent mechanistic exploration revealed that HBV infection may promote CD8+ T cell exhaustion in HCC by inhibiting tyrosine catabolism in hepatocytes.

Conclusion: We established a novel TEI model by comprehensively analyzing CD8+ T cell exhausted progression which can accurately predict clinical prognosis and immunotherapeutic efficacy of HBV-related HCC.

Abstract Submission No. 100155
P-0446

Lenvatinib modifies the tumor microenvironment in HCC and assembles GZMK⁺CD8 T cells

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Background: Lenvatinib is a multiple kinase inhibitor and showed clinical efficacy in patients with hepatocellular carcinoma (HCC). Lenvatinib was expected to enhance the effect of immune checkpoint inhibitors (ICIs), but their combination therapy could not prove synergistic effect in a Phase III trial.

Methods: Our study aimed to elucidate the effects of lenvatinib on tumor immune microenvironment and clarify the mechanism that prevents the synergistic effect with ICIs. HCC specimens from five patients treated with neoadjuvant lenvatinib and ten controls were analyzed using RNA-sequencing and digital spatial profiling to explore the molecular effects of lenvatinib.

Results: Lenvatinib not only has direct antitumor effects but also recruits cytotoxic GZMK⁺CD8 T cells into the intratumoral stroma, a process facilitated by CXCL9 from tumor-associated macrophages. The majority of these cytotoxic CD8 T cells appeared to be trapped in the intratumor stroma.

Conclusions: Lenvatinib modifies the tumor immune microenvironment by recruiting GZMK⁺CD8 T cells, turning immunologically “cold” tumors “hot”. This transformation is significant, yet lenvatinib-treated HCC might still be “altered-excluded” due to the physical barriers created by extracellular matrix (ECM). Combining treatments for ECM may enhance the effectiveness of immune cells recruited by lenvatinib, especially when used in combination with ICI.”

Abstract Submission No. 100224
P-0447

Treatment with a new barbituric acid derivative induces apoptosis in hepatocellular carcinoma cells

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Hepatocellular carcinoma (HCC) is the primary type of liver cancer, and it is the sixth common cancer in the world with a higher mortality. Sorafenib, the first-line drug for advanced HCC, can effectively increase the median survival time. However, long-term received sorafenib usually acquired resistance, therefore, developing novel agents is urgently needed to treat HCC. Previously, we identified a series of barbituric acid derivatives and found that one of the compounds exhibited the best ability to ameliorate TGF- β 1-induced hepatic stellate cell activation and liver fibrosis. In this study, we extend this barbituric acid derivative (named 2g) and analyze the anti-HCC effect and its underlying mechanisms. The results demonstrated that 2g has a cytotoxic effect to inhibit HCC cell viability in both dose- and time-dependent manner. Flow cytometry analysis showed that the early and latent stages of apoptosis rate were significantly increased in 2g-treated cells. Western blot data revealed that compound 2g treatment increased caspase 8 and cleaved caspase 3 expression. In addition, the mRNA expression of anti-apoptosis genes Bcl-2 and survivin were decreased in 2g-treated cells. In conclusion, compound 2g may facilitate the apoptosis signal by increasing the expression of apoptosis-related

proteins and downregulating the anti-apoptosis genes in HCC cells, which suggests its use as a new strategy for HCC treatment.

Abstract Submission No. 100230
P-0448

Long-term di(2-ethylhexyl) phthalate exposure reduces sorafenib sensitivity in liver cancer cells

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Di(2-ethylhexyl) phthalate (DEHP) is worldwide common plasticizer. Nevertheless, DEHP is easily leached out to the environment due to lack of covalent bond with plastic. High dose of DEHP exposure is often observed in hemodialysis patients because of continual usage of plastic medical devices. DEHP exposure also promotes liver damage and further leads to liver cancer. So far, the impact of DEHP exposure on sorafenib treatment sensitivity is still unclear. Accordingly, we established long-term DEHP exposed HCC cells and NOD/SCID mouse model to investigate the effects and the mechanisms of long-term DEHP exposure on sorafenib sensitivity. The results showed that long-term DEHP exposure increased epithelial-mesenchymal transition potential and decreased sorafenib sensitivity in HCC cells. Next generation sequencing showed that long-term DEHP exposure triggered migratory related genes expressions and blunted sorafenib treatment induced genes alterations. In NOD/SCID mouse model, we showed that long-term DEHP exposure accelerated subcutaneous HuH7 cells growth. Regarding the anti-HCC effects of sorafenib in-vivo, subcutaneous HuH7 tumor grew slowly in sorafenib-treated mice. Nonetheless, the anti-tumor growth effect of sorafenib was not observed in long-term DEHP-exposed mice. Higher mesenchymal markers and proliferating cell nuclear antigen (PCNA) expression were found in sorafenib-treated long-term DEHP-exposed mice. In conclusion, long-term DEHP exposure promoted migratory activity in HCC cells and decreased sorafenib sensitivity in tumor-bearing mice.

Abstract Submission No. 100285
P-0449

MTA1 contribute to HCC progression through regulation of diverse metastatic signatures

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Background: Metastatic tumor antigen 1 (MTA1) and its major isoform, MTA1dE4, have been implicated in the developing and early recurrence of hepatitis B virus-related hepatocellular carcinoma. However, the specific involvement of MTA1 and MTA1dE4 in regulating cancer-promoting gene expression remains unexplored.

Methods: We established the stable MTA1 knockdown cells using SK-HEP1 and HepG2 hepatoma cells (designated as KDSK and KDG2). Subsequently, we conducted in vitro soft agar and tumorsphere formation assays to assess tumorigenicity. We employed promoter assay to evaluate the transcriptional regulatory activities of both MTA1 and MTA1dE4. Transcriptomic analysis was applied to

elucidate RNA expression profiles, and the expression levels of differential expression genes (DEGs) were quantified using quantitative real-time PCR.

Results: MTA1dE4 demonstrated a tumorigenicity-promoting ability similar to MTA1, with even greater efficiency. Notably, MTA1dE4 displayed an increased capacity to suppress the promoter activity of E-cadherin. Transcriptomic analysis revealed significant changes in the transcriptional expression of 1280 genes in parental cells, of which 1049 genes (81.96%) were upregulated and 231 genes (18.04%) were downregulated compared to MTA1-knockdown cells. Specifically, 792 genes (81.56% upregulated and 18.4% downregulated) and 625 genes (73.92% upregulated and 26.08% downregulated) displayed significant changes, respectively. Gene set enrichment analysis (GSEA) demonstrated that the majority of DEGs in MTA1/KDSK cells were associated with a “multicancer invasiveness signature,” while those in KDSK/MTA1dE4 were related to “APC targets.”

Conclusions: MTA1 and MTA1dE4 play distinct roles in regulating various subsets of target genes. Some are associated with inhibiting cell migration, while others are involved in promoting cancer metastasis.

Abstract Submission No. 100340
P-0450

Targeting DYRK1A synergise with OXPHOS inhibition through activating TGFβ signaling

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Mitochondria are not only essential for cellular energy metabolism, but they also play a critical role as modulators of cellular responses to microenvironmental stress. Numerous studies have demonstrated that interventions targeting mitochondria function may hold promise as potential approaches for the treatment of various types of cancer. Our findings suggest that the combination of a DYRK1A inhibitor and OXPHOS inhibitors could represent a promising therapeutic strategy for targeting mitochondria. Furthermore, our data has uncovered the crucial role of the TGFβ signaling pathway in determining the sensitivity of oxidative phosphorylation inhibitors.

Abstract Submission No. 100514
P-0451

IL-6 is a useful biomarker for selection of systemic therapies in hepatocellular carcinoma

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Background and Aim: This study aims to identify biomarkers for treatment response of atezolizumab plus bevacizumab (Atezo+Bev) I patients with hepatocellular carcinoma (HCC).

Methods: Among patients who received Atezo+Bev or Lenvatinib (Len) as a first-line systemic therapy at our hospital, 96 patients were enrolled in the HCC group after propensity score matching, while 20

tumor-free patients were enrolled as a control group. Seventeen serum cytokines were measured by Luminex multiplex assay at the start of treatment. The Cox proportional hazards regression model was used to assess the prognostic effects of clinical factors and cytokine levels.

Results: Angiopoietin-2, CEACAM-1, IL-6, and IL-8 levels were significantly higher in the HCC group than in the control group. Optimal cutoff values for these cytokines were determined using receiver operating characteristic (ROC) analysis. In the Atezo+Bev group, univariate analysis revealed that high levels of serum IL-6 (≥ 9.2 pg/mL, $p < 0.01$) and IL-8 (≥ 102.3 pg/mL, $p < 0.05$) were associated with shorter PFS. Among them, only elevated IL-6 (HR 5.80; $p < 0.01$) was identified by multivariate analysis as an independent risk factor. In the Len group, no significant differences in PFS were observed for any item. Although there was no overall difference in PFS between the Atezo+Bev group and the Len group, subset analysis of low IL-6 patients revealed longer PFS in the Atezo+Bev group than in the Len group (Log-rank, $p = 0.02$).

Conclusions:

Serum IL-6 level is a useful predictor of therapeutic benefit from Atezo+Bev treatment.

Abstract Submission No. 100581
P-0453

Circulating exoPD-L1 predicts the outcome of patients with HCC who received atezolizumab-bevacizumab

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Background: Hepatocellular carcinoma (HCC) is a highly aggressive disease that is usually diagnosed at an advanced stage. Advanced HCC has limited treatment options and often has a poor prognosis. Atezolizumab-bevacizumab significantly improved survival rates as a first-line treatment and became the new standard of care. The interaction between the programmed cell death receptor 1 (PD-1) and its ligand (PD-L1) contributes to immune evasion and exosomal PD-L1 is a marker of poor outcome after surgery or chemotherapy in patients with various types of cancers. However, the role of PD-L1-containing exosomes in patients with advanced HCC receiving atezolizumab-bevacizumab is remains to be elucidated. We therefore determined the prognostic significance of circulating exosomal PD-L1 in advanced HCC patients receiving atezolizumab-bevacizumab.

Methods: This study enrolled 28 HCC patients receiving atezolizumab-bevacizumab between Dec 2020 and Jan 2023. Exosomes were extracted from serum samples using the ExoQuick Exosome Precipitation Solution. Exosomal PD-L1 was detected by Exocounter.

Results: The total number of exosomes and PD-L1 positive exosomes increased significantly as the mUICC stage of HCC progressed ($P < 0.05$). Comparing between the early and advanced stage, the number of Exosomal PD-L1 significantly increased in the advanced stage. The overall survival and progression-free survival were significantly lower in patients with lower circulating levels of exosomal PD-L1 (log-rank test: $P = 0.015$ and 0.007 , respectively).

Discussion: In conclusion, this study has provided strong evidence that circulating exosomal PD-L1 are novel prognostic markers and therapeutic targets for advanced HCC who received atezolizumab-bevacizumab.

Abstract Submission No. 100613
P-0454

Hesperidin Dextrin nanoformulation attenuates diethylnitrosamine-induced hepatic cancer in animal

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Introduction: Hepatocellular carcinoma (HCC) is the most prevalent type of liver cancer and one of the leading causes of cancer-related deaths worldwide. The present investigation aimed to synthesize the hesperidin-Dextrin nano-formulation (HPSLNL) against diethylnitrosamine (DEN)-induced liver cancer, and its underlying mechanism.

Method: HP-SLNL has been developed by solvent evaporation method and characterized by various instrument such as FTIR, X-ray diffraction, and field emission scanning electron microscopy. Rats were utilized to induce HCC by intraperitoneal injection of DEN and treated with HPSLNL for a period of 22 weeks. The rats were assessed macroscopically to estimate the hepatic nodules and the body weight, food, and water intake. Serum and tissue were separated so that biochemical characteristics could be estimated.

Result: XRD also indicates the drug peak, but FTIR demonstrated that there is no compound-polymer interaction. Rats given HP-SLNL treatment showed suppression of the tumor nodules, both in terms of number and average size of the nodules. Lowering the amount of alpha fetoprotein and improving body weight, HP-SLNL also had an effect on non-hepatic measures including total protein, bilirubin, creatinine, and urea, as well as hepatic markers like AST, ALT, and ALP. It also changed cytokines levels, (TNF- α , IL-1 β , IL-6, IL-4, IL-10, and IL-17) and inflammatory markers, such as COX-x, iNOS, PGE2, and NF- κ B. Bcl-2 was significantly decreased and Bax, PDCD5, and p53 levels were increased by HP-SLNL therapy.

Conclusion: Based on the findings, we may conclude that HP-SLNL changed oxidative stress and inflammation to have a chemoprotective impact on hepatic cancer.

Abstract Submission No. 100707
P-0455

An MTA1 Major Variant, MTA1dE4, with Enhanced Metastatic and Tumorigenic Potential in HCC

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Background: Alternative splicing generates MTA1dE4, an exon 4-deleted form of metastatic tumor antigen 1 (MTA1), with a less understood role in hepatocarcinogenesis than extensively studied MTA1. Here, we characterize the structural, molecular, and functional attributes of MTA1 and MTA1dE4, elucidating their contributions to tumor metastasis.

Methods: We established stable MTA1 knockdown cells using human HepG2 and murine Hepa1-6 hepatoma cells, designated as KDG2 and KD1-6, respectively. Next, we conducted in vitro and in vivo tumorigenicity assays. To further investigate the metastatic potential, we utilized an intra-splenic injection mice model. Additionally, structural analyses and modeling were employed to predict the molecular and biological functions of MTA1 and MTA1dE4. To explore the interacting partners of MTA1/MTA1dE4 and facilitate the investigation of

unknown mechanisms in tumor metastasis, co-immunoprecipitation (co-IP)-coupled with mass spectrometry (MS) strategy was employed. **Results:** MTA1dE4 exhibited tumorigenic and metastatic potential comparable to that of MTA1 but with greater efficiency, consistent with a positive correlation between MTA1dE4 overexpression and early recurrence in clinical observation. The two isoforms differ in the bromo-adjacent homology (BAH) domain, leading to structural alterations that enhance the structural stability and molecular functionality of MTA1dE4 compared to MTA1. Co-IP/MS data revealed largely identical interactors but also with isoform-specific interactors for MTA1 and MTA1dE4. Notably, MTA1dE4 broadly interacts and co-expresses with migration-associated proteins, potentially contributing to the tumorigenic and metastatic capacities of cancer cells.

Conclusion: The conformational changes in MTA1's BAH domain confer greater resilience and a modified activity profile, allowing precise adaptation to the specific requirements of cancer cells.

Abstract Submission No. 100884
P-0456

Isolation, culture and characterization of patient derived CD34+ liver cancer stem cells

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Background: Liver cancer stem cells can be a possible cause of chemo-resistance of hepatocellular carcinoma (HCC). CD34+ stem cells play an important role during liver development and regeneration. Previously we isolated and cultured CD34+ cells from conventional hepatoma cell line (PLC/PRF/5 cells). This study was undertaken to optimize the methods for the isolation and culture of the patients derived liver cancer stem cells and to evaluate its characteristics.

Methods: The HCC specimens and data used in this study were provided by the Radiation Tissue Resources Bank of Korea Cancer Center Hospital. Patient derived CD 34+ cancer stem cells were isolated from human HCC tissues using fluorescence-activated cell sorting. Purified CD34+ cells have been cultured in vitro on mouse embryonic fibroblast feeder cells. Then we explored the expression of CD34 and stem cell markers. Also we compared the expression of stem cell markers between CD34+ cells and CD34- cells.

Results: The expressions of CD34, CD44 and CD133 were 9.8%, 4.8%, and 0.16% respectively. The HCC cells and fibroblasts were isolated and cultured, however the growth of cells was not maintained. We can observe that Nanog, Oct4, Sox2, CD44 and CD133, the stem cell markers were highly expressed in CD 34+ cells than CD34- cells.

Conclusion: We could isolate and characterize the CD34+ cancer stem cells from human HCC tissues. Thus CD34+ liver cancer stem cells can be used for the studies of chemo-resistant HCC. Further studies for the optimal culture methods with the patient derived cancer stem cells are needed.

Abstract Submission No. 100978
P-0457

Analysis of Clinical Characteristics between AFP Levels in Hepatocellular Carcinoma Patients

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Background: Hepatocellular carcinoma (HCC) is a common malignancy in Asia. Around 5.4% of Indonesians developed HCC, but in Makassar, about 13.8% of HBV patients advanced to HCC. Although alpha-fetoprotein (AFP) is a biomarker utilized in the clinical diagnosis of HCC, roughly about 40% of HCC patients do not have high serum AFP levels. Therefore, we aim to investigate the clinical and tumor characteristics between AFP positive and negative in HCC patients.

Methods: Between 2017 and 2022, this retrospective cohort study was carried out at a tertiary care facility in Makassar, Indonesia. Baseline patient characteristics, virological status, AFP level, CT Abdomen, Barcelona-Clinical Liver Cancer (BCLC) staging, size of the tumor, and child-pugh were drafted from the medical record.

Results: There were 408 HCC subjects in all, with 308(75.4%) male and an average age of 54,1 years. HBV infection 284 (69.6%), HCV infection 43 (10.5%), and non-viral reasons 81 (18.8%) were the underlying liver causes. 186 patients (or 45.5% of the total) had BCLC Stage B, while 129 patients (or 31.6%) had BCLC Stage C. Only 53 patients (12.9%) had tumors less than 3 cm, while 284 (69.6%) had tumors larger than 5 cm. HCC patients with larger tumor sizes, liver cancer with portal vein thrombosis, and the high BCLC stage had significantly higher serum AFP levels ($p < 0.005$).

Conclusions: This study showed that there are significant differences in clinical pathologic characteristics between AFP-positive and negative HCC patients which may be helpful for the management and prognostication of the disease.

Abstract Submission No. 101044
P-0458

Hepatocellular Carcinoma Subclassification Using Comprehensive microRNA Expressions of TCGA data

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Background: The involvement of microRNAs in liver carcinogenesis has been reported, but comprehensive classifications based on microRNA expression data have been limited. In this study, we performed subclassification of hepatocellular carcinoma (HCC) using microRNAs based on data from The Cancer Genome Atlas (TCGA).

Methods: We downloaded pre-processed genetic mutations, mRNA, and microRNA expression data of 360 cases of HCC from the GDAC Firehose browser (<https://gdac.broadinstitute.org>). Utilizing the expression levels of 540 microRNAs, hierarchical clustering was performed using the Ward method, classifying the 360 HCC cases into 5 clusters. For each cluster, we calculated p-values using Fisher's exact test and t-test for the genetic mutations and mRNA expression levels, respectively.

Results: In clusters 1, 2, 3, 4, and 5, there were 44, 153, 82, 56, and 25 cases, respectively. Regarding genetic mutations, cluster 3 showed a higher prevalence of BAP1 mutations and a lower frequency of CTNNB1 mutations, whereas cluster 4 exhibited a higher occurrence of CTNNB1 mutations. In cluster 1, the expression of genes located on the X chromosome, such as SSX and MAGE families known as cancer-testis antigens, was upregulated. Additionally, microRNA expression from the chromosome 19 cluster (C19MC) was significantly

elevated. Cluster 5 displayed increased expression of imprinted genes located on the chromosome 14, including DLK1, MEG8, and MEG3, along with elevated expression of AFP and SALL4. The microRNA clusters C14MC and C19MC are known to undergo imprinting and have been implicated in placental development.

Conclusion: We conducted a comprehensive subtyping of HCC based on microRNAs.

Abstract Submission No. 101077
P-0459

The hepatocyte nuclear factor 1 homeobox A (HNF1A) Gene Polymorphism & AFP in HCC Egyptian Patients

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Hepatocyte nuclear factors (HNFs) were first identified as liver-enriched transcription factors that might participate in a variety of activities related to the transcription of genes unique to the liver. Aim of study: revealing the impact of HNF1A gene variations on disease progression in HCC patients complicating HCV infection and its relation to serum AFP level. Patients and method: Participants in the study were classified as Group I: Includes 32 HCC patient with low and high AFP; Group II: Includes 36 CHC patients, and Group III: Included 26 apparently healthy volunteers as a control group. HNF1A gene polymorphisms (rs 2464196 and rs 1169310) were genotyped by real-time PCR using rotor gene PCR system.

Results: The highest frequency of AA and GA genotypes of HNF1A (rs2464196) polymorphism in both HCC and chronic HCV patients compared to controls ($P=0.002$ and $P=0.004$, respectively). Regarding rs1169310 gene polymorphism, no significant difference was found among different genotypes between the studied groups and controls. Additionally, HCC the patients harbor AA genotype for rs2464196 had significantly increased AFP ≥ 200 ng/ml level (those patients are older age and child score class B), whereas, HCC patients with rs1169310 SNPs for HNF1A had no significant association with AFP level in HCC patients.

Conclusion: The rs2464196 polymorphism of HNF1 is associated with increased AFP level and HCC disease progression which may implicated as a genetic marker for diagnosis and prognosis of HCC patients.

Abstract Submission No. 101147
P-0460

Role of plasma EV-miR-19-3p as a novel diagnostic and prognostic biomarker for non-viral-related HCC

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Background: Extracellular vesicle-derived microRNAs (EV-miRNAs) are promising circulating biomarkers for chronic liver disease, including hepatocellular carcinoma. This study explored the potential significance of plasma EV-miRNAs in non-hepatitis B-, non-hepatitis C-related HCC (NBNC-HCC).

Methods: We compared plasma EV-miRNA profiles between NBNC-HCC and control groups, which included non-alcoholic fatty liver disease (NAFLD) and healthy controls by using the NanoString method. The differentially expressed EV-miRNAs were validated in another set of plasma samples by qRT-PCR. Additionally, the diagnostic and prognostic roles of potential biomarkers were further analyzed.

Results: In the discovery set, a total of 66 significantly differentially expressed EV-miRNAs between the NBNC-HCC and control groups were identified. In the validation set, plasma-derived EV-miRNAs, including miR-19-3p, miR-16-5p, miR-223-3p, miR-30d-5p, and miR-451a were significantly elevated in NBNC-HCC compared with the control groups. Based on bioinformatics analysis, these miRNAs were found to contribute to biological processes, including protein targeting, nuclear transport, and cell cycle. Moreover, enriched Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways revealed that these miRNAs participated in several cancer-related signaling pathways. Among them, EV-miR-19-3p exhibited the best diagnostic performance with the area under the curve (AUC) of 0.82 (95 % CI; 0.75-0.88, $P < 0.001$), and displayed high sensitivity for detecting alpha-fetoprotein-negative HCC and early-stage HCC (76.9% and 80.0%, respectively). In multivariate analysis, an elevated level of EV-miR-19-3p was an independently unfavorable predictor of overall survival in patients with NBNC-HCC.

Conclusion: Our data indicated that EV-miR-19-3p could serve as a novel circulating biomarker for the diagnosis and prognosis of patients with NBNC-HCC.

Abstract Submission No. 101279
P-0461

Functional evaluation and mechanism study of hnRNP-F in hepatocellular carcinoma development

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Background: Heterogeneous nuclear ribonucleoprotein (hnRNP-F) is a member of the hnRNP family proteins that has been implicated in multiple cancers, suggesting its role in tumorigenesis; however, it is unclear whether hnRNP-F could affect the hepatocellular carcinoma (HCC) or antitumor immunity against HCC.

Methods: A correlation of hnRNP-F expression with prognosis was analyzed in the TCGA database. Then we applied in vivo and in vitro methods by Cre-LoxP animal models, flow cytometry and cell proliferation assay to reveal the behaviors of hnRNP-F in HCC tumorigenesis. The specific regulatory mechanism of hnRNP-F on the development of HCC was analyzed by RNA sequencing.

Results: hnRNP-F is significantly upregulated in HCC tissue, and its increased expression is associated with a poor prognosis in HCC patients. In animal models, we observed that hepatocyte-specific knock-out of hnRNP-F inhibited hepatocarcinogenesis. In human liver cancer cells, hnRNP-F promoted tumor proliferation, migration and invasion. We also observed that hnRNP-F knock-out in animal models could significantly affect the number of CD8⁺ T cells which consequently reprogrammed the tumor microenvironment (TME).

Conclusions: These findings suggest that hnRNP-F could promote cell proliferation in HCC and reprogram tumor microenvironment, which may serve as a potential target for the treatment of HCC patients.

Keywords: Hepatocellular Carcinoma (HCC), Heterogeneous nuclear ribonucleoprotein F (HnRNP-F), Cell proliferation, Tumor microenvironment (TME)

Abstract Submission No. 101282
P-0462

Abnormal alternative splicing of MELK regulated by USP39 promote HCC progression

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Background: Abnormal alternative splicing regulated by spliceosome-associated factors contributes to various solid tumors. Increasing studies have focused on the feasibility and effectiveness of spliceosome-targeted therapies (STTs) which target cancer-related isoforms and various splicing regulators. Ubiquitin-specific protease 39 (USP39), a spliceosome component of the U4/U6.U5 tri-snRNP complex, has been reported to promote carcinogenesis through splicing regulation in hepatocellular carcinoma (HCC). Nevertheless, the targets and mechanism underlying USP39 regulating RNA splicing remain unclear in HCC progression.

Methods and Results: Hepatocellular specifically overexpression of USP39 have been proved to promote chemically-induced HCC process, verifying the pro-tumor function of USP39. Bioinformatic analysis based on our previously published RNA-seq data showed that USP39 selectively regulated hundreds of alternative splicing events, of which exon skip events took the majority. Among these events, USP39 mediated Maternal embryonic leucine zipper kinase (MELK) splicing switch from long-term (MELK-L) to short-term (MELK-S) increased tumorigenesis potential of HCC cells. QRT-PCR detection using our in-house clinical samples showed a positive relation between USP39 expression and MELK-S proportion. The expression of MELK-S was relatively high in HCC tumor tissues. Patients with high MELK-S proportion had poorer prognosis. Moreover, in-vitro experiments showed that MELK-S promoted cell proliferation and cell cycle.

Conclusion: These findings demonstrate the role of USP39 as a splicing regulator in HCC biology and highlight the potential of USP39 and MELK as a therapeutic target in HCC.

Key words: HCC, USP39, MELK, alternative splicing, spliceosome

Abstract Submission No. 101283
P-0463

ASH1L promotes HCC progression by regulating HSC activation

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Background: Activated hepatic stellate cells (HSCs) are the main sources of myofibroblasts, which are the central driver of liver fibrosis. Many researchers have suggested that activated HSCs can promote hepatocellular carcinoma (HCC) development. However, the precise mechanisms remain largely unknown.

Methods: To mimic the stimulation of HSCs in the tumor microenvironment, human HSCs were cultured in the conditional medium from human HCC cells supernatant. RT-PCR and western blot were used to identify the key methyltransferases associated with HSC activation. We generated HSC-specific deficient mice GFAP-Cre + flox/flox (SK), parenchymal hepatic cells specific deficient mice Alb-Cre + flox/flox (HK), and double deficient mice GFAP-cre + Alb-Cre + flox/flox (DK). Fibrosis-associated mouse hepatocarcinogenesis was induced by DEN-CCL4 to explore the function of the regulator in HSCs and hepatic cells. A transwell non-contact co-culture system was used to investigate the interaction between HCC cells and HSCs.

Results: We found the conditional medium of HCC cells could promote HSC activation. ASH1L was one of the most greatly increased in advanced tumor tissues compared with other H3K4me3 methyltransferases. In vitro, knocking down ASH1L in HSCs inhibits HCC cell proliferation, but did not affect HCC cell proliferation. In the DEN-CCL4-induced HCC mouse model, the knockdown of ASH1L in liver hepatocytes and HSCs could decrease the tumor number. These results suggested that ASH1L could regulate HCC progress by regulating HSC activation.

Conclusions: We propose that in the tumor microenvironment, ASH1L promotes the proliferation of tumor cells by regulating the activation of stellate cells, thereby regulating the development of liver cancer.

Abstract Submission No. 101294

P-0464

Disorder liver circadian reffect diseasis prognosis of liver cancer

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Background: The liver is the largest circadian organ in the human body. Epidemiological findings indicate that circadian dysfunction increases the risk of hepatocellular carcinoma (HCC). However, the molecular evidence of circadian dysregulation in the role of HCC prognosis remains unclear.

Methods: A total of 378 circadian genes were collected from CircaDB. Multi-omics data and relevant clinical information were obtained from TCGA, GEO, and CNGB. Integrated bioinformatics analyses and experimental validation were performed in this study.

Results: The multiomics landscape of circadian genes reveals extensive disruption in HCC. Through integrated bioinformatics approach, the key features of disorder in the tumor microenvironment were further uncovered. Further analysis reveals that the tumor microenvironment in HCC also exhibits disordered circadian rhythms. Inhibition of IL18RAP in T cells within the tumour microenvironment are associated with immune function suppression, whilst overexpression of GNL2 in tumour vascular endothelial cells is associated with angiogenesis. Additionally, elevated of RBM17 and ZDHHC18 in tumour cells are related to tumour stem cells. In vivo and in vitro experiments reveal that RBM17 promotes cell cycle transition. Knockdown of RBM17 inhibits the cancer stem cell phenotype by regulating CD133 and promotes chemosensitivity of HCC. Prognostic models based on circadian dysregulation effectively predict HCC prognosis and treatment responses (TACE, Sorafenib, immunotherapy).

Conclusions: The circadian rhythm of HCC is extensively disordered in multi-omics dimensions and in the tumor microenvironment. Dysregulation of circadian rhythms can effectively predict the prognosis and treatment response of HCC. Knockdown of RBM17 inhibits malignancy, highlighting therapeutic potential.

Abstract Submission No. 101303

P-0465

Upregulation of ISYNA1 in hepatocellular carcinoma is correlates to patient prognosis

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Background: The gene of ISYNA1 has been little researched in hepatocellular carcinoma (HCC). Here, we aimed to explore its expression and function in HCC.

Methods: Data of ISYNA1 was downloaded from public databases including Human Protein Atlas (HPA) and The Cancer Genome Atlas. The rat HCC model was constructed by intraperitoneal injection of diethylnitrosamine. HE staining, MASSON staining, PAS staining, and KI67 immunohistochemistry of liver tissues were performed. The real-time quantitative PCR (qRT-PCR) and Western blot (WB) approaches were used to detect the expression of ISYNA1.

Results: The results of public databases showed that the expression of ISYNA1 mRNA and protein was upregulated in HCC tissues compared with normal tissues. And compared with ISYNA1 higher expression group, the HCC patients with lower ISYNA1 expression had better prognosis in overall survival and disease-specific survival. In the rat HCC model, qRT-PCR and WB results also showed that ISYNA1 expression was significantly elevated in the HCC compared with the control. By immune cell infiltration (ICI) analysis, the results showed that ISYNA1 expression was significantly correlated to the enrichment scores of B cells, T cells, macrophages, neutrophils, and dendritic cells in HCC. In addition, we identified two drugs that associated with ISYNA1 including DB01840 and DB04516.

Conclusion: Our study demonstrated that ISYNA1 was upregulated in HCC tissues and its upregulation was associated with poor prognosis in HCC patients. Furthermore, ISYNA1 may be a potential biomarker and therapeutic target for assessing prognostic value and modulating ICI levels in HCC.

Abstract Submission No. 101328

P-0466

Importin α 4 was accumulated in nucleus of liver cancer cells with p62/SQSTM1-positive aggregates.

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Background: Aggregation of autophagic substrate p62/SQSTM1 which accelerates cellular proliferation via Nrf2 pathway was observed in human hepatocellular cancer tissue. We identified Importin α 4 and 14-3-3 ζ ; as an insoluble nucleoprotein increased by autophagic dysfunction. We evaluated the relationship between these autophagy-related proteins expression in hepatic cancer cells.

Methods: Tissue sections were prepared from 20 surgically resected liver cancer tissues, and immunohistochemical staining of p62/SQSTM1, Importin α 4, and 14-3-3 ζ ; was performed. The correlation of these proteins expression and laboratory data (platelet count, serum AST, ALT, gGTP, FIB4 Index) or histological score of hepatic fibrosis and inflammation in non-cancer area was evaluated by Spearman's rank correlation coefficient analysis.

Results: Aggregation of p62/SQSTM1 was observed in cytoplasm of cancer cells from 18 resected liver cancer samples and the rate of cancer cells with p62/SQSTM1-positive aggregates was $57.9 \pm 10.4\%$ of all hepatocellular carcinoma cells. Nuclear expression of 14-3-3 ζ ; and Importin α 4 was observed in all resected samples. The rate of cancer cells with nuclear expression of 14-3-3 ζ ; was $42.9 \pm 6.4\%$ and Importin α 4 was $79.0 \pm 4.7\%$. The rate of cells with p62/SQSTM1-

positive aggregates was correlated with nuclear expression of Importin $\alpha 4$ but not 14-3-3 ζ .

Conclusion: It was suggested that nuclear accumulation of Importin $\alpha 4$ is associated with abnormality of proteostasis in human hepatocellular carcinoma cells similarly to aggregation of p62/SQSTM1. Therefore, p62/SQSTM1 and Importin $\alpha 4$ might be useful as a diagnostic and prognostic marker in liver cancer.

Abstract Submission No. 101336
P-0467

Potential of combined therapy between sorafenib and SRC1 inhibitors in overcoming HCC heterogeneity

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Background and Aims: The efficacy of Sorafenib (SOR) in hepatocellular carcinoma (HCC) is limited, due to cellular heterogeneity. Thus, new or combined therapy strategies are warranted. This study aims to analyze the potential of combined therapies using SRC1 inhibitors in HCC.

Method: SRC1 as molecular target was defined from in-silico analysis. SRC1 expressions was assessed in HBV-transgenic mouse C57BL/6J-TG(ALB1HBV)44BRI/J and different hepatic cell lines: S1/TGF β -Wnt subtype (HLE), S2/progenitor (HepG2) and immortalized hepatocyte (IHH), together with protein expression by Western blot. Cells were treated with monotherapies of SOR and two SRC1 inhibitors saracatinib (SAR) and dasatinib (DAS) and in combined therapies of SOR+SAR and SOR+DAS, with concentrations ranging from 0.02 to 10 μ M. Lethal concentrations 50 (LC50) of all combinations were calculated by cytotoxicity test. Migration capacities were assessed by wound healing and transwell migration assay.

Results: The mRNA expression of Src1/pp60c-src in transgenic mice was increased along with hepatocarcinogenesis ($p < 0.0001$), while in HCC cells SRC1 expression was 10-fold higher compared to hepatocytes ($p < 0.05$). Following treatments, SOR, SAR, and DAS monotherapy alone were not significantly toxic. However, combined therapies of SOR+SAR and SOR+DAS resulted in a dose-dependent cytotoxicity in both HCC cells, with lower LC50 values was noticed in HepG2. In contrast for IHH where SOR+SAR combination was not toxic. Functional analysis using wound healing and transwell assay also showed that combined therapies highly inhibited cells migration compared to monotherapies alone ($p < 0.05$).

Conclusion: Combined therapies between SOR and SRC1 inhibitors can be potential treatment to encompass cellular heterogeneity in HCC.

Abstract Submission No. 101367
P-0468

Hepatocellular Carcinoma Cells Avoid Apoptosis by Interacting with T Cells via CD40-CD40L Linkage

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Background: Hepatocellular carcinoma (HCC), a leading cause of global cancer-related deaths, is associated with elevated soluble CD40 levels in HCV-SVR patients. We aimed to investigate CD40's role in HCC progression.

Methods: We examined CD40 levels in HCC patient tissues and cell lines, studying their interaction with CD4⁺T cells. RNA sequencing analysis was performed to explore the mechanisms of CD40 induction.

Results: Poorly differentiated HCC tumour tissues exhibited high membrane-bound CD40 (mCD40) expression, in contrast to non-tumour areas. Poorly differentiated HCC cells (SNU387, HLE, and HLF) showed high expression of mCD40 compared with well-differentiated HCC cells (Huh7, HepG2) which exhibited minimal CD40 expression with high promoter methylation. Co-culturing activated CD40L-expressed CD4⁺ T cells with HLFs led to a modest 3.2% increase in cell death. However, pre-neutralizing CD40 significantly induced HLFs apoptosis (10.9%), while pre-neutralizing integrin $\alpha 5\beta 1$ reduced this to 1.7%. Moreover, pre-blocking both CD40 and integrin $\alpha 5\beta 1$ caused only 1.9% of cell death. Furthermore, co-cultivation of activated CD4⁺ T cells with HLFs resulted in elevated CD40 levels, in a cell ratio- and time-dependent manner. RNA sequencing of HLFs co-cultured with activated CD4⁺ T cells revealed the upregulation of interferon (IFN) and immune response pathways. Elevated IFN-gamma levels in the activated T cell media stimulated the JAK1/STAT3 pathway, resulting in increased HLF CD40 expression. Inhibiting JAK1 and STAT3 effectively reduced CD40 expression in HLFs following IFN-gamma stimulation.

Conclusion: CD40 expression in poorly differentiated HCC cells prevents cell death by interacting with CD40L⁺ T cells. Targeting CD40 may represent a promising anticancer therapy.

Abstract Submission No. 101373
P-0469

Antitumor effect of biofabricated silver nanoparticles of caffeic acid against hepatocarcinogenesis

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Background: Over recent years, metal nanoparticles, especially silver (Ag) nanoparticles have been accepted as promising therapeutic tools for cancer diagnosis as well as treatment. Caffeic acid (CFA) is a natural phenolic acid that possesses antitumor activity. The current study was designed to explore the in vitro and in vivo antitumor effect of CFA-mediated biofabricated silver nanoparticles (CFA-AgNPs) against hepatocellular carcinoma (HCC).

Methods: CFA-AgNPs were synthesized by co-precipitation method and characterized by various techniques such as ultraviolet-visible spectroscopy, fourier-transform infrared spectroscopy (FTIR), energy dispersive X-ray analysis (EDX) and field emission scanning electron microscopy (FESEM). Cytotoxic potential of CFA-AgNPs was investigated by MTT assay on HepG2 cells by in vitro method. Subsequently, apoptosis and associated gene expression were determined by using flow cytometry assay and quantitative real-time polymerase chain reaction (qPCR), respectively. In vivo study was performed in male Sprague Dawley rats by inducing diethylnitrosamine (DEN, 200mg/kg) administration and the CFA-AgNPs were given by oral gavages at two different dose levels (10 and 20mg/kg for 16 weeks). On the last day of the study, various antiproliferative parameters were determined including hematological profile, serum biomarkers and inflammatory cytokine levels for each group.

Result: Characterization techniques confirmed the formation of spherical crystalline CFA-AgNPs with a size range of 50-80 nm and having a strong peak of Ag. FTIR results showed the existence of possible bioactive functional groups of phytoconstituents in the synthesized CFA-AgNPs. Further, CFA-AgNPs exhibited significant ($p < 0.05$) cytotoxic effects and flow cytometry results revealed stimulation of apoptosis. An increase in p53 and Bax expressions and a reduction in Bcl-2 expression along with upregulation of accompanied Bax/Bcl-2 ratio were observed in qPCR results. In vivo results demonstrated that the CFA-AgNPs administered group significantly downregulated ($p < 0.01$) the serum marker hepatic and non-hepatic enzymes and pro-inflammatory markers such as tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6) and interleukin-1 β (IL-1 β) as compared to DEN alone group.

Conclusion: Results of the current investigation recommended the inhibition potential of CFA-AgNPs against DEN-induced damaging effects on the liver via an antioxidant defense system and modulation of Bax/Bcl2 as well as proinflammatory cytokines. CFA-AgNPs can be utilized as a superior approach to improve the clinical results against HCC.

Abstract Submission No. 101387
P-0470

HCC are exacerbated by IL-1R1 deficiency and Myeloid-derived Suppressor Cell in Tumor Immunotherapy

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Background: Malignant solid tumors exhibit fast proliferation of immature and myeloid-derived suppressor cells (MDSC). Hepatocellular carcinoma (HCC) patients with high IL-1 expression had a worse prognosis, survival, and treatment response. Gemcitabine, a popular anticancer drug, may extend life by affecting tumor microenvironment MDSC and IL-1 signaling. However, the precise mechanism by which IL1R1 recruits MDSCs associated with HCC remains unknown.

Methods and Results: A hydrodynamic injection (HDI) mouse model of HCC was developed for this research to mimic human disease. In addition to tumor-intrinsic oncogenicity, we have shown that IL1 β is elevated in the serum of patients with HCC. Furthermore, we have demonstrated that both serum and hepatic IL-1 β levels are increased in HCC-HDI mice. In comparison to wide-type (WT) mice, IL1R1^{-/-} mice exhibited an elevated liver-to-body weight ratio, a higher percentage of Ki-67 expression in hepatocytes indicating suboptimal histopathological differentiation of HCC, and increased population of hepatic MDSCs, CD4⁺PD1⁺ cells, and conventional T cells (Tregs), and

the accelerated progression of HCC. Using gemcitabine reduced tumor growth and quantity, reversing those effects. Gemcitabine inhibited tumorigenicity in HCC by decreasing the number of hepatic MDSCs and increasing the number of tumor-infiltrating CD8⁺ T cells.

Conclusions: The pro-tumorigenic effects of IL-1 were balanced by its effects on monocytic MDSCs, which exacerbated inflammation and HCC development. IL-1 signaling causes cell-type-specific responses in HCC-HDI mice, which determine the hepatic tumor microenvironment's inflammatory tone and disease progression. These findings provide light on IL-1R1 and MDSCs in HCC, suggesting a therapeutic target.

Abstract Submission No. 101389
P-0471

UGDH promotes process of hepatocellular carcinoma by regulating metabolism of tumor cells

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Background: The gene of Udp-glucose 6-dehydrogenase (UGDH) plays an important role in exogenous metabolism and acts as a key mediator in several cancer developmental signaling pathways. However, its expression and function in hepatocellular carcinoma (HCC) is still unclear.

Methods: The expression and related clinicopathological information of UGDH were downloaded from The Cancer Genome Atlas and Gene Expression Omnibus databases. A rat HCC model was established using intraperitoneal injection of diethylnitrosamine. HE staining, MAS-SON staining, PAS staining, and KI67 immunohistochemistry of liver tissues were performed. The real-time quantitative PCR (qRT-PCR) and western blotting (WB) were used to detect the expression of UGDH.

Results: The results of public databases showed that the mRNA expression of UGDH was significantly upregulated in HCC tissues compared with normal tissues. And the HCC patients with lower UGDH expression had better prognosis in overall survival and relapse-free survival. In the rat HCC model, qRT-PCR and WB results also showed that UGDH expression was significantly increased in the HCC compared with the control. Furthermore, by analyzing the differentially expressed genes between high-UGDH and low-UGDH samples, we obtained the 228 key targets of UGDH. The Gene Ontology and Kyoto Encyclopedia of Genes and Genomes enrichment analyses showed that these UGDH-related genes were correlated to Cell division, Cell cycle, and Metabolic pathways.

Conclusions: Our study showed that UGDH was upregulated in HCC and its upregulation was associated with poor prognosis in HCC patients. UGDH might exert its carcinogenic effects by regulate metabolism to promote HCC cell proliferation.

Abstract Submission No. 101518
P-0472

Obesity is associated with normal FIB-4 in nonalcoholic fatty liver disease related HCC

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Background: The fibrosis-4 (FIB-4) index has been incorporated in major guidelines to risk stratify patients with nonalcoholic fatty liver disease (NAFLD), and patients with FIB-4 <1.3 are considered to be at low risk of advanced fibrosis. We aimed to evaluate the factors associated with falsely low FIB-4 scores in patients with nonalcoholic steatohepatitis (NASH)-HCC.

Methods: We included adult patients diagnosed with NASH-HCC from 2008-2021 at five academic centers in Japan, South Korea, Singapore, and the United States. Predictors associated with FIB-4 <1.3 were investigated with multivariate logistic regression models. P-values <0.05 were considered statistically significant. All analyses were conducted in RStudio 2021.09.0.

Results: We included 472 patients with NASH-HCC, of which 33 patients (7%) had FIB-4 <1.3. In multivariate analysis, diabetes (OR 0.47, 95%CI 0.22–0.99, p=0.048) and cirrhosis (OR 0.21, 95%CI 0.08–0.50, p=0.001) were associated with decreased likelihood of FIB-4 <1.3. Obesity (defined as >27.5 kg/m² in Asians, and >30.0 kg/m² in non-Asians) was associated with increased likelihood of FIB-4 <1.3 (OR 2.33, 95%CI 1.07–5.01, p=0.030) (Figure 1). In subgroup analysis of 213 patients without cirrhosis, 25 patients (12%) had FIB-4 <1.3. In patients without cirrhosis, obesity continued to be associated with increased likelihood of FIB-4 <1.3 (OR 2.84, 95%CI 1.16–6.87, p=0.020).

Conclusion: In patients with NASH-HCC, obesity was associated with increased likelihood of FIB-4 <1.3 regardless of the presence of cirrhosis. Further studies are required to evaluate the effectiveness of FIB-4 as a risk stratification tool in the general population for patients with obesity but without diabetes

Abstract Submission No. 101523
P-0473

Exosomal ncRNAs: a significant contributor to the immunosuppressive tumor microenvironment of HCC

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Hepatocellular carcinoma (HCC) is a primary malignant neoplasm originating in the liver. In the past few years, there seems to be an increasing emphasis on the invention of pharmaceuticals that specifically target immunological checkpoints and immune cells. In truth, the efficacy of immunotherapy is heavily contingent upon the tumor microenvironment (TME). TME is a multifaceted communication system comprising diverse elements. Recent studies have indicated that exosomes serve as a developed means of communication among bioactive molecular cells while also additionally executing an essential part in the microenvironment of tumor immune suppression. Moreover, exosomal non-coding RNAs (ncRNAs) can induce activation in tumor cells and immune cells with immunosuppressive properties, such as CAFs, TAMs, TANs, CD⁸ T cells, Tregs, and Bregs. Activation of this pathway promotes the growth of tumor vascular, the transfer of gene changes in metabolism, and the transformation of malignant phenotypes. This helps the immune system avoid detection and the growth of tumors. Hence, comprehending the mechanisms by which exosomal ncRNAs modulate tumor cells or immune cells inside the TME is crucial for the development of more comprehensive and efficacious immunotherapy protocols. This article offers a complete overview of the characteristics of exosomal ncRNAs in relation to the advancement of HCC. It elucidates the mechanisms by which exosomal ncRNAs influence tumor cells and immune cells, leading to the reconstruction of the tumor immunosuppressive microenvironment. Additionally, the article explores the therapeutic potential of exosomal ncRNAs as a promising biological target or carrier in HCC treatment.

Abstract Submission No. 101678
P-0474

Galactose Conjugated PPI Dendrimers for Liver Targeting

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Cancer therapy needs site-specific drug delivery to affected cells and should avoid affecting healthy cells. Liver is prominent organ of body and has Asialoglycoprotein receptor expression. The research aimed to develop dendrimer based drug delivery providing enhanced therapeutic potential of anti-cancer agent (doxorubicin) by effective targeting to liver cells.

5.0G Dendrimers were synthesized by divergent method. Ethylene diamine was core material and Acrylonitrile branching unit. Synthesis was performed on basis of two steps i.e Double Michael addition and Catalytic hydrogenation. Dendrimers were confirmed by FTIR, NMR and Mass spectroscopy and then conjugated with galactose. Shape and size were characterized by Transmission Electron Microscopy (TEM), drug loading efficiency, In-vitro drug release and stability studies. Ex-vivo studies constituted Hemolytic toxicity study. In-vivo studies, Pharmacokinetic parameters and Biodistribution Studies were performed.

Thus Galactosylated PPI dendrimers showed high doxorubicin loading, sustained release and excellent biocompatibility as evident by low hemolytic toxicity. Presence of ligand on dendrimer molecule, elevated receptor mediated binding thereby targeting higher concentration of doxorubicin to lung. Higher concentration of GPPI-DOX was found to be significant compared to PPI-DOX and DOX. Possibly galactose having more affinity towards asialoglycoprotein receptors of liver parenchymal cells, more amount of drug had accumulated in liver. Finally, it can be concluded that galactose-coated PPI dendrimers found to be most suitable for delivery of Doxorubicin HCl. Galactose conjugation can be utilized to not only target asialoglycoprotein receptors of liver, but also to reduce hemolytic toxicity. Furthermore, this

delivery system could reduce drug associated toxic effects by selective targeting hepatoma cells.

Abstract Submission No. 101679
P-0475

Liquid Crystalline Nanoparticles (LCNPs) based delivery of an Anticancer bioactive, Methotrexate

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Liver cancer is a disease of uncontrolled cell growth, which may invade adjacent tissue and cause infiltration beyond the liver. Most of potent and effective anticancer drugs used in liver cancer therapy shows poor bioavailability at desired site as well as toxic in nature. The aim of the study was to investigate mannose modified Liquid Crystalline Nanoparticle (LCNPs) carrier for efficient and site specific delivery of potent anticancer drug (Methotrexate) used in hepatic carcinoma therapy.

MTX loaded LCNPs were prepared by lipid cast film method and sonication method. Nanoparticles were characterized *in-vitro* for their shape, size, percent drug entrapment and stability by Optical Microscopy, Cross Polarized Light Microscopy (CPLM), Transmission Electron Microscopy (TEM), X-ray diffraction (XRD) and Atomic Force Microscopy (AFM).

In-vitro stability studies reveal that LCNPs formulations are stable for 120 days at room temperature. *Ex-vivo* cell cytotoxicity was performed on Human hepatoma cell line. *In-vivo* studies included fluorescence microscopy and organ distribution studies which show the Mannose modified LCNPs exhibit better accumulation in liver as compared to unmodified system. The results of the present study indicate this system is more stable as compared to other system.

Eventually it may be concluded that incorporation of MTX in mannose modified LCNPs increases residing time of drug in the body by altering of pharmacokinetics and biodistribution pattern, and the drug primarily concentrates in the liver. This system showed excellent cytotoxicity towards cancer cells. From the present investigation it is evident that this system may be used for liver cancer and other liver disease.

Abstract Submission No. 101686
P-0476

Long-term Antiviral Therapy Improving ER Stress, Mitochondrial, and Metabolic Functions Reduces HCC

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Background and Aims: The need of antiviral therapy in hepatitis B virus (HBV) carriers with normal or minimally elevated ALT levels is controversial. Animal models of HBV-associated hepatocellular carcinoma (HCC) are needed for translational research and as platforms for testing novel therapies.

Methods and Results: We established a novel mouse model of HBV-associated HCC (strain D14-122; HCC incidence 89% in the absence of ALT elevation) by crossing HBV transgenic mice with *Mir-122* tumor suppressor knockout mice. Early-onset hepatic steatosis, progressive liver fibrosis, and reduced lysosome degradation in late phase of autophagy were observed during tumorigenesis in D14-122. NMR non-targeted metabolomics analyses and microarray showed steatosis, inflammation, and ROS-induced genomic instability as early as age 4-8 mo. Antiviral therapy reduced HCC incidence 30-35% in these mice, through amelioration of endoplasmic reticulum stress, promotion of autophagy, and inhibition of C/EBP-homologous protein (CHOP)-mediated apoptosis. Decreases of lipid deposit and hyperglycemia, ER stress markers were observed one month after antiviral therapy and reductions of p62 (Mallory-Deng body, known to be carcinogenic) and ER stress markers were found in NUC-treated mice without HCC at late phase. Strong deposits of p62 in HBV-related human HCC support the findings in this novel mouse model.

Conclusion: This study reveals a novel mechanism of liver injury that HBV hijacks autophagy and down-regulates miR-122, leading to endoplasmic reticulum stress, mitochondrial dysfunction, and metabolic reprogramming. These findings explain the mechanism of antiviral treatment in reducing the incidence of HCC in HBV carriers in the grey zone of treatment guidelines.

Abstract Submission No. 101692
P-0477

Serum miRNA biomarker for predicting Hepatocellular Carcinoma risk after HCV eradication

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Background and purpose: Hepatocellular carcinoma (HCC), a prevalent global cancer, often arises from persistent viral infections, particularly Hepatitis C virus (HCV). MicroRNAs (miRNAs) are small, noncoding RNAs that direct posttranscriptional regulation of gene expression. Although HCV eradication with direct-acting antivirals reduces HCC risk, ongoing surveillance is crucial for cirrhotic patients even after achieving sustained virologic response (SVR). We aim to identify miRNAs that can predict HCC onset after HCV elimination and analysis of their functions.

Methods: A retrospective study compared two groups: one immediately post-SVR and another at 5 years post-SVR, further divided into HCC and non-HCC subgroups. Serum miRNA expression was analyzed using microarray and small RNA-seq. Candidate miRNAs were identified through differential expression and LASSO regression analyses, validated using two independent sample sets. *In-vitro* studies using HepG2 cells transfected with mimics of the candidate miRNAs produced western blot and RNA-seq data.

Results: MiRNA-x3 was significantly up-regulated in HCC-HCV-SVR compared to no-HCC-HCV-SVR, confirmed by two independent

validations. In-vitro studies suggested miRNA-x3's involvement in cell cycle G1/S phase transition and DNA damage.

Conclusion: MiRNA-x3 may predict hepatocarcinogenesis risk in HCV-SVR patients; ongoing work aims to confirm these findings.

Abstract Submission No. 200044

P-0478

Investigating Hypoxia, EMT, and CD8+ T Cells in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) metastasis and invasion are key factors contributing to treatment failure and poor prognosis. Epithelial-mesenchymal transition (EMT), a cellular process, plays a critical role in this progression. Hypoxia, a common feature of solid tumors, induces EMT in tumor cells. CD8+ cytotoxic T cells, although possessing anti-tumor effects, exhibit contradictory functions. Hypoxia in the tumor microenvironment inhibits CD8+ T cell activity and function via tumor cell signaling molecules, promoting EMT and impairing CD8+ T cell quantity and function, facilitating immune escape. Additionally, the hypoxic microenvironment reduces mitochondrial function, impeding mitochondrial transfer, affecting tumor cell metabolism and immune cell function. The fundamental pathogenesis of the tumor's hypoxic microenvironment in Traditional Chinese Medicine involves qi deficiency, blood stasis, and Qi stagnation. Blood stasis hinders blood vessel flow, obstructing Qi and blood circulation. This causes local microcirculatory disturbances, obstructed tissue fluid drainage, and the development of a hypoxic microenvironment. Thus, interventions targeting the hypoxic microenvironment, such as traditional Chinese medicine formulas like QizhuKangai decoction, have potential in inhibiting HCC growth and metastasis by addressing EMT, angiogenesis, and improving blood circulation. Understanding the mechanisms underlying these effects may provide novel approaches for tumor treatment.

Abstract Submission No. 200051

P-0479

Knowledge mapping of MIRNA in hepatocellular carcinoma from 2012-2022:a bibliometric analysis

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Background: This study aims to reveal the research hotspots, scientific preface and future trends in this field by conducting a metrological analysis of the literature related to miRNA research in hepatocellular carcinoma.

Methods: Articles related to miRNA research in hepatocellular carcinoma in the Web of Science Core Collection (WoSCC) were searched. The annual distribution, countries, institutions, authors, journals, citations and keywords of published articles from 2012-2022 were visualized and analyzed by CiteSpace and VOSviewer software.

Results: A total of 7065 English-language articles published between 2012 and 2022 were collected, with the majority of publications coming from China (n=2419), followed by the United States and Egypt, with Sun Yat-sen University having the highest number of publications

of all institutions (n=153). The top published and co-cited authors were Chen, Gang, and Bartel DP, respectively. articles were mainly published in Oncotarget (n=119). Initially, the hotspots were "hmv", "mir-21", "akt3" and "beta-catenin", while in recent years the focus has shifted to "sorafenib resistance", "exosome", "stem cell" and "pi3k".

Conclusion: miRNAs are of great research importance in elucidating HCC occurrence, progression, treatment and prognosis prediction, and have become prospective biomarkers and therapeutic targets for HCC. Therefore, actively exploring the detailed mechanisms of miRNA-mediated HCC onset and progression may offer promising prospects for future improvements in clinical outcomes of HCC patients.

Abstract Submission No. 200087

P-0480

Identifying Therapeutic Targets in Hepatocellular Carcinoma: An Integrated Bioinformatics Analysis

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Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide, with a high incidence rate and poor prognosis. In this study, we performed an integrated bioinformatics analysis to identify potential therapeutic targets for HCC. We first analyzed the gene expression profiles of HCC samples from The Cancer Genome Atlas (TCGA) database and identified differentially expressed genes (DEGs). Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses were then conducted to explore the biological functions and pathways associated with these DEGs. Furthermore, protein-protein interaction (PPI) network construction and module analysis were performed to identify key proteins and their interactions in HCC. Finally, we validated the potential therapeutic targets by examining their expression levels in HCC tissues and cell lines. Our results revealed that several key genes and pathways, including TP53, CTNNB1, and PI3K-Akt signaling pathway, may play crucial roles in HCC development and progression. These findings provide new insights into the molecular mechanisms underlying HCC and may help guide the development of novel therapeutic strategies for this disease.

Abstract Submission No. 200151

P-0481

Deciphering HCC Development Linked to lncRNA02313 and Building a Predictive Model

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Mitochondrial permeability transition (MPT) has recently garnered attention in its association with various tumor types, including hepatocellular carcinoma (HCC). In the context of HCC, our study focuses on the exploration of the involvement of MPT in driving necrosis and its correlation with the long non-coding RNA LINC02313. Limited research has been conducted on MPT-driven necrosis-related lncRNAs in the context of liver cancer. To investigate the potential role of MPTDRlncRNAs, we obtained RNA-sequencing data and corresponding clinical information from HCC patients through the TCGA database. MPT-driven necrosis-related genes were extracted from the Gene Set Enrichment Analysis (GSEA) database. Through comprehensive analyses, we identified LINC02313 as a significant

MPTDNRlncRNA associated with differential expression in HCC. Utilizing univariate Cox regression analysis, we further determined the prognostic significance of LINC02313 in the context of MPT-driven necrosis in HCC. A novel prognostic signature comprising MPTDNRlncRNAs, including LINC02313, was constructed using LASSO-COX. The predictive accuracy and utility of this signature were rigorously evaluated through diverse statistical methodologies. In addition to bioinformatics analyses, we performed RT-qPCR experiments on HCC cell lines to validate the expression levels of MPTDNRlncRNAs, particularly emphasizing the role of LINC02313. Our findings revealed a distinctive 5 MPTDNRlncRNAs signature specific to HCC, where LINC02313 played a pivotal role. This study pinpoints LINC02313 as a crucial factor in MPT-driven necrosis linked to hepatocellular carcinoma development. Additionally, it introduces a promising prognostic signature that could advance our understanding of the disease and potentially influence personalized therapeutic approaches in liver cancer.

Abstract Submission No. 200176
P-0482

GOLGI PROTEIN 73(GP73) IN DIAGNOSIS OF PRIMARY HEPATOCELLULAR CARCINOMA

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Background: The incidence of hepatocellular carcinoma (HCC) is increasing worldwide as well as in Myanmar. Since incidence and mortality rates of HCC are roughly equivalent, early detection of HCC is important. Serum Golgi Protein 73 (GP73) is considered as a potential tumor biomarker for the detection of HCC. However, the diagnostic accuracy of GP73 for HCC is still conflicting. This research was designed to assess the diagnostic efficacy of GP73 in HCC.

Methods: This was a hospital based cross sectional descriptive study carried out from July 2020 to October 2021. Eighty patients were allocated into two groups (43 patients with HCC and 37 patients without HCC). Serum alpha fetoprotein (AFP) and GP73 were tested for all the participants. Detection of focal hepatic lesions were based on imaging by triphasic computed tomography.

Results: The mean value of GP73 was 9.3ng/ml in HCC group and 8.5ng/ml in those without HCC group (p=0.904). AUROC curve for GP73 was 0.51 with an optimal cutoff point of 3ng/ml. Therefore, the diagnostic accuracy of GP73 was 56% (sensitivity-67% and specificity-43% at a cutoff point 3ng/ml), whereas AFP had the diagnostic accuracy was 68% (sensitivity-72% and specificity-62% at a cutoff point 20ng/ml).

Conclusion: This study revealed that GP73 does not appear to be an accurate and new biomarker in diagnosis of HCC. The results of this study are not conclusive but it will provide the stimulus and enthusiasm for further research.

Abstract Submission No. 200220
P-0483

Polyploidy determines a distinct subset of hepatocellular carcinoma exhibiting aggressive features

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Genome duplication, or polyploidization, is prevalent phenomenon in cancer, however its significance in hepatocellular carcinoma (HCC) remains largely unknown. We aimed to evaluate polyploidy status in HCC using clinical specimens and to elucidate its clinicopathological significance. We performed multi-colored fluorescence in situ hybridization using pathological specimens from 56 human HCCs. Markers indicative of polyploidy were explored by transcriptome analysis of cultured hepatoma cells. Polyploidy was identified in 36% of HCCs, distinguishing an aggressive subset of HCC characterized by elevated serum alpha fetoprotein, distinctive histology, and poor prognosis compared to near-diploid HCCs. We detected novel indicators of polyploidy in HCCs, which were overexpression of ubiquitin-conjugating enzymes 2C and the abundance for polyploid giant cancer cells with distinct appearance. These markers served as indicators of polyploidy in HCC and predicted poor prognosis. Diagnosis of polyploidy by artificial intelligence-based image analysis also revealed aggressive features of polyploid HCC in a large cohort. Polyploidy in HCC is associated with increased aggressiveness, through enhanced chromosomal instability.

Abstract Submission No. 200227
P-0484

MDK is a prognostic biomarker associated with tumor metastasis

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Hepatocellular carcinoma is a malignant type of carcinoma with complicated pathogenesis. Intermediate factor (MDK) is a heparin-binding growth factor that is strongly expressed during embryogenesis, and its expression is weak or undetectable in normal adult tissues. Studies have shown that serum MDK is elevated in most HCC and may have a diagnostic role for early tumors. By detecting the level of MDK in the cancer tissues and adjacent tissues of hcc patients, this study explored its expression level and clinical significance in the disease, in order to provide references for clinical diagnosis and treatment of HCC. The clinicopathological significance and molecular function of MDK were analyzed and evaluated by comprehensive bioinformatics. The expression of MDK in HCC was verified in TCGA, GEO and Oncomine databases, and the survival of MDK was analyzed based on TCGA database. The MDK co-expression genes and their regulatory factors were classified using LinkedOmics.

Abstract Submission No. 200234
P-0485

Microwave ablation of primary liver and lung tumor

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Primary lung cancer is the third most common cancer in the worldwide and the leading cause of cancer-related deaths. In Mongolia, an estimated 6702 people were diagnosed new cancer, and liver cancer is the

first rank or 32% of all cancer in 2021. Non-small cell lung cancer (NSCLC) is the most common, accounting for 80 to 85 percent of lung cancer cases. They are often linked to a history of smoking and tend to be found in the central part of the lungs, near a main airway. In the case of primary double tumors, according to the International Classification of Tumors, it belongs to the 4th stage of malignant tumors, so supportive treatment is necessary. We present a clinical case of primary double tumors of the liver and lung were treated by microwave ablation. Patient M, 69-year-old man, had been suffering from abdominal and chest pains for 2 months and coughing up green sputum. He was diagnosed with combined primary liver and lung cancer in November 2022. He has smoked for 50 years and has HCV related liver cirrhosis. Liver biopsy was hepatocellular carcinoma /clear cell carcinoma/ and lung biopsy was poorly differentiated squamous cell lung carcinoma. Diagnosis: HCC in segment SVII of liver T2NxMx non-small cell carcinoma in lower lobe of left lung T3N1Mx Stage IV. In our clinical case, the combined treatment of TACE+MWA for liver cancer and MWA for lung cancer were effective and quality of life improved after 6 months.

Abstract Submission No. 101742
P-0486

CDKN2A promotes hepatocellular carcinoma by inhibiting the Cuproptosis pathway

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Background: The global prevalence and clinical features of hepatocellular carcinoma (HCC) render it a significant malignancy. A novel mode of cellular demise, known as cuproptosis, is the subject of this investigation, intending to determine its potential involvement in HCC. **Methods:** The expression of cuproptosis-related genes and their relationship to the prognosis of HCC were determined using various databases including the Cancer Genome Atlas, Gene Expression Omnibus, Human Protein Atlas, and GEPIA. Co-expressed genes were investigated using CBioPortal, followed by GO, and KEGG analysis, to elucidate the potential mechanisms of CDKN2A co-expressed genes. The protein-protein interaction network and hub genes of these co-expressed genes were identified using Cytoscape.

Results: The protein and mRNA levels of CDKN2A were found to be up-regulated in HCC, and this up-regulation was negatively correlated with prognosis in HCC. On the other hand, FDX1 was positively associated with prognosis, although their mRNA levels did not show significant changes between HCC and control groups. The GO and KEGG analyses revealed that the co-expressed genes of CDKN2A were mainly enriched in processes related to chromosome segregation, catalytic activity (acting on DNA), chromosomal region, cell cycle, and DNA replication. Additionally, the hub genes of CDKN2A were found to be increased in HCC and were negatively associated with prognosis.

Conclusion: The involvement of cuproptosis in the pathogenesis and progression of HCC warrants consideration, while CDKN2A holds

promise as a prospective therapeutic target and prognostic indicator for HCC.

Abstract Submission No. 101758
P-0487

Hepatoma-derived growth factor as a possible target gene for the treatment of HCC

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Background/Aims: We identified a novel growth factor, hepatoma-derived growth factor (HDGF). HDGF is highly expressed in the HCC tissues, and the expression level of HDGF is an independent prognostic factor for the disease-free and overall survival in patients with HCC. The purpose of this study is to examine whether HDGF can be a potential target molecule for the treatment of HCC.

Methods: (1) We generated the stably HDGF-overexpressed or HDGF-silenced hepatoma cell lines by the introduction of HDGF cDNA or sh-RNA, and examined the effects of the increased or reduced HDGF expression on the proliferation of hepatoma cells. (2) We investigated the effects of the exogenous and endogenous overexpression of HDGF on the proliferation and tubular formation of HUVEC (human umbilical vein endothelial cells) *in vitro*. (3) We examined whether the introduction of HDGF cDNA can induce the VEGF expression.

Results: (1) Introduction of HDGF DNA stimulated the proliferation of hepatoma cells, whereas reduction of HDGF by sh-RNA suppressed the growth of the hepatoma cells. (2) Administration of recombinant HDGF significantly increased the cellular number of HUVEC *in vitro*, and HDGF-treated HUVEC formed longer vessel-like tubes *in vitro* than those formed by PBS-treated control cells. (3) HDGF induced VEGF expression through the activation of the VEGF promoter.

Conclusions: HDGF is a unique molecule which has dual characteristics; one as a growth stimulating factor on hepatoma cells and the other as an angiogenic factor. HDGF is therefore considered to be a potential target molecule for the treatment of HCC.

Abstract Submission No. 101803
P-0488

Screening program for early stage of liver cancer in Ulaanbaatar: Single Center Study

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Objective: Screening and diagnosis in early stage of liver cancer in high-risk population group

Materials and Methods: These patients are controlled in screening in early stage of liver cancer in Happy Veritas Clinic and Diagnostic Center. The total number of patients included for screening was 10682 patients such as *abdominal ultrasound* and to identify serum AFP *every 3 months*. 181 patients were included in the study, who had complete

set of data, and *are regularly controlled for screening* in early stage of liver cancer.

Results: 181 patients with an average age of 54 ± 11 (range: 23 - 89 years old) were included in the study. In the result, causes of *liver fibrosis* were HCV 59.1% (107), HBV 24.9% (45), HBV/HDV 13.3% (24), HCV/HBV 2% (3), HCV/HBV/HDV 0.6% (1) and without hepatitis viruses 0.6% (1). According to the study, F2 was 64.6% (117), F3 27.1% (49) and F4 8.3% (15). We studied the changes in laboratory tests and depending on the patient's fibrosis stage. Increasing fibrosis stage or liver cirrhosis has decreased platelets, albumin and total protein level ($p \leq 0.001$). However, we observed ALT level, which increased in F3 and decreased F4. Liver cancer nodule is detected in 4 patients, they had fibrosis stage F4 in Fibroscan analysis and average level of AFP was 86.

Conclusion: We conclude that patients in F4 stage in Fibroscan analysis have higher risk of developing liver cancer. Therefore, health care providers need regularly screening and testing in early stage of liver cancer in high-risk population.

Abstract Submission No. 101820

P-0489

Phenotypic Linkage Between m⁶A Methylation and Immune Microenvironment in Hepatocellular Carcinoma

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Purpose: The crucial role of N⁶-methyladenosine (m⁶A) methylation in anti-tumor immunity and immunotherapy has been broadly depicted. However, the molecular phenotypic linkages between m⁶A modification pattern and immunological ecosystem are expected to be disentangled in hepatocellular carcinoma (HCC), for immunotherapeutic unresponsiveness circumvention and combination with promising drug agents.

Methods: Modification patterns of m⁶A methylation were qualitatively dissected according to large-scale HCC samples profiling. The immune phenotypic linkages were determined by systematically evaluating their tumor microenvironment composition, immune/stromal-relevant signature, immune checkpoints correlation and prognostic value. Individual quantification was achieved by m⁶Ascore construction, intensified by longitudinal single-cell analysis of immunotherapy cohorts and validated in our in-hospital cohort. Candidate therapeutic agents were also screened out.

Results: Three distinct m⁶A methylation patterns were determined in high accordance with inflamed-, excluded- and desert- immunophenotype, robustly validated in our in-hospital cohort. To be precise, Immune-inflamed high-m⁶Ascore group was characterized by activated immunity with favorable prognosis. Stromal activation and absence of immune cell infiltration were observed in low-m⁶Ascore phenotype, linked to impaired outcome. Patients with low-m⁶Ascore demonstrated diminished responses and clinical benefits for cohorts receiving immunotherapy. Single-cell dynamic change of m⁶A methylation level in exhausted CD8 T cell and fibroblast was depicted in immunotherapy cohort fore and art. Derived from m⁶A methylation pattern, seven potential frontline drug agents were recognized as promising choice.

Conclusion: Our work bridged the credible linkage between epigenetics and anti-tumor immunity in HCC, unraveling m⁶A modification pattern as immunological indicator and predictor for immunotherapy. Individualized m⁶Ascore facilitated strategic choices to maximize therapy-responsive possibility.

Abstract Submission No. 101983

P-0490

Knockdown of NPLOC4 induces cuprotoxicity to promote HCC progression

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Background: Hepatocellular carcinoma (HCC), with high incidence and mortality, is the result of many malignant liver diseases. Nuclear protein localization protein 4 (NPLOC4) primarily participates in the ubiquitin-mediated degradation of ER proteins. The role of NPLOC4 in HCC and its prognostic significance remains unknown.

Methods: The expression level of NPLOC4 was predicted by bioinformatics and detected in HCC cell lines and tissues by quantitative reverse transcription PCR (qPCR). The effects of NPLOC4 on cancer cell proliferation, apoptosis, and migration were evaluated by colony formation, cell counting kit 8 (CCK8), and transwell. The levels of Cu and cuprotoxic-associated proteins were predicted by Western blotting, immunofluorescence, and Cu detection kit. Gain- or-loss-of-function assays were used to identify the function and underlying mechanisms of NPLOC4 in HCC.

Results: We found that NPLOC4 was significantly upregulated and predicted a poorer prognosis in HCC tissues. NPLOC4 significantly promoted HCC cell proliferation and inhibited apoptosis in vitro and in vivo. Mechanistically, depletion of NPLOC4 increased intracellular copper ions and cuprotoxic-related proteins, resulted in HCC cells apoptosis increased. While inhibition of cuprotoxicity by Tetrathiomolybdate (TM) would abolish these effects.

Conclusions: In summary, knockdown of NPLOC4 promoted the cuprotoxicity, eventually increasing apoptosis and decreasing HCC cell proliferation. This study provides a promising diagnostic marker and therapeutic target for HCC patients.

Abstract Submission No. 200016

P-0491

Investigating the mechanisms of QZACP in inhibiting HCC via network pharmacology

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Purpose: Qizhu Anti-cancer Prescription (QZACP) can inhibit the progression of Hepatocellular carcinoma (HCC), reduce its recurrence rate and prolong survival, but its exact mode of action is still unclear. This study aims to investigate the mechanism of QZACP in treating HCC.

Methods: Components in QZACP decoction were analysed using mass spectrometry. A subcutaneous tumor formation model of nude mice was constructed to further analyse the active components of QZACP that had entered tumour tissues through oral administration. Potential targets of QZACP in inhibiting HCC were identified and confirmed via network pharmacology and molecular docking.

Results: QZACP decoction contained deacetyl asperulosidic acid methyl ester (DAAME), paeoniflorin, calycosin-7-glucoside, liquiritin, glycyrrhizic acid, astragaloside IV, saikosaponin A, curdione, and actylenolide II. Moreover, DAAME, paeoniflorin, liquiritin, and glycyrrhizic acid in QZACP could enter HCC tissues after oral administration. Among these, DAAME was the most highly expressed in tissues. Through network pharmacological analysis and Western blotting verification, STAT3, VEGFA, JUN, FGF2, BCL2L1, AR, TERT, MMP7, MMP1, ABCB1, CA9 and ESR2 were the targets of QZACP inhibiting HCC. Molecular docking showed that the binding site of DAAME and CA9 had good stereocomplementarity, and the docking score was -8.1 kcal/mol. Western blotting and immunohistochemical results also confirmed that DAAME reduced the expression of CA9 protein in HCC.

Conclusions: QZACP inhibits HCC by reducing the expression of STAT3, VEGFA, JUN, FGF2, BCL2L1, AR, TERT, MMP7, MMP1, ABCB1, CA9, and ESR2. DAAME is an important active component of QZACP for treating HCC, and may inhibits HCC by targeting the expression of CA9.

Abstract Submission No. 200020
P-0492

Qizhu formula alters the profile of SASP to enhance immunosurveillance in hepatocellular carcinoma

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Background: Induction of a senescence-associated secretory phenotype (SASP) with immunostimulatory properties is an effective method to enhance the immunosurveillance ability of hepatocellular carcinoma (HCC). The Qizhu formula (QZ), based on the principles of strengthening the body's resistance and removing toxins for detumescence, can improve the survival rate of HCC patients, but its pharmacological mechanism is still unclear.

Methods: A diethylnitrosamine (DEN)-induced primary liver cancer model of C57B/L6 mice was constructed to evaluate the tumor-inhibitory effect of QZ. QZ-regulated infiltrating immune cells in liver nodule tissue were assessed. QZ-induced HCC cell senescence was examined by β -galactosidase staining. RNA sequencing data from senescent cells were used to identify SASP factors involved in HCC immunomodulation.

Results: QZ induced senescence and inhibited HCC cell proliferation. In HCC model mice, QZ treatment inhibited tumor growth and promoted NK cell and CD8⁺ T-cell infiltration. The protein expression levels of SASP factors HGF, DCN, and CxCL14 were increased and that of APLN was reduced in the hepatic nodules of mice in the QZ group compared with those in the model group. Further, conditioned media from QZ-medicated serum-treated HCC cells enhanced the migration and antitumor effects of splenic immune cells.

Conclusion: Our results suggest that QZ inhibits disease progression in HCC model mice. Mechanistically, QZ could have anti-HCC properties by inducing HCC cell senescence, modulating HGF, DCN, CxCL14, and APLN protein expression in senescent HCC cells, and promoting NK cell and CD8⁺ T cell infiltration, which could in turn enhance immunosurveillance in HCC.

Abstract Submission No. 200025
P-0493

MMP9 as a downstream of CTNNB1^{GOF} promotes immune escape and resistance to anti-PD-1 therapy in HCC

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CTNNB1 mutations have been observed in approximately 20–39% of hepatocellular carcinoma (HCC) and these mutations result in significantly higher levels of immune escape and resistance to anti-PD-1. However, what acts as a downstream target gene of *CTNNB1* mutations to determine this primary function is not well understood. We showed that MMP9 is frequently upregulated in gain of function (GOF) *CTNNB1* mutant HCC. Elevated MMP9 drives suppressive immune microenvironment and anti-PD-1 resistance by reducing infiltration and cytotoxic function of CD8⁺ T cells in tumors. Mechanistically, we primarily demonstrate that MMP9 secreted by HCC cells mediated slingshot protein phosphatase 1 (SSH1) shedding from CD8⁺ T cells, resulting in inhibited C-X-C motif chemokine receptor 3 (CXCR3)-mediated intracellular signaling of G protein-coupled receptors (GPCRs) and suppressed activation of cofilin in CD8⁺ T cells. Finally, we designed MMP9 rabbit monoclonal antibody to treat *CTNNB1* mutant patient-derived xenograft (PDX) models, which greatly enhanced the anti-tumor efficacy of PD-1 antibodies. MMP9 presents itself as a promising target for CTNNB1^{GOF} to improve immune activation and anti-PD-1 efficacy, raising an effective combination strategy for precision immunotherapy.

Abstract Submission No. 200034
P-0494

Chemoprotective effect of crocetin against hepatocellular carcinoma via alteration of gut microbiota

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Background: Crocetin is a plant derived natural apocarotenoid dicarboxylic acid that showed the pharmacological activity against the various diseases. Previous report focused on the colorectal cancer effect, still chemoprotective effect against hepatic cancer still unexplored. In this study, we scrutinized the chemoprotective effect of crocetin against the diethylnitrosamine (DEN) induced hepatocellular carcinoma (HCC) in rats and explore the underlying mechanism.

Methods: Single intraperitoneal injection of DEN (200 mg/kg) was used for the induction of HCC in rats. The rats were divided into different groups and received the oral administration of crocetin till 22 weeks. The rats hepatic nodules were macroscopically and microscopically evaluated. The hepatic, antioxidant, non-hepatic, inflammatory parameters and cytokines were estimated. The faecal microbiota was used to investigate the chemoprotective effect of intestinal microbiota.

Result: Crocetin effectively suppressed the incidence of tumor nodules, incidence and weight of hepatic tissue. Crocetin significantly ($P < 0.001$) suppressed the hepatic parameters like alpha feto protein (AFP), aspartate transaminase (AST), alkaline phosphatase (ALP), alanine transaminase (ALT), acid phosphatase (ACP); non-hepatic parameters viz., total protein, blood urea nitrogen, creatinine; antioxidant parameters include catalase (CAT), glutathione (GSH), glutathione peroxidase (GPx), glutathione-S-transferase (GST), superoxide

dismutase (SOD), malondialdehyde (MDA) and protein carbonyl. Crocetin considerably suppressed the level of inflammatory cytokines and inflammatory mediators. Crocetin also altered the relative abundance of *Bacteroides*, *Mucispirillum*, *Brevundimonas*, *Lactobacillus*, *Clostridium* and *Alloprevotella*.

Conclusion: We can say that crocetin remarkably exhibited the chemoprotective effect against the DEN induced HCC in rats via alteration of oxidative stress, inflammation and gut microbiota.

Abstract Submission No. 100066

P-0495

Multidisciplinary Management of Hepatobiliary Tumours at a tertiary hospital in Singapore

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BACKGROUND: Asia carries the heaviest burden of hepatocellular carcinoma (HCC), the third leading cause of cancer-related mortality worldwide. There is evolving data supporting a multidisciplinary approach in HCC management to optimise individualized treatment and improve clinical outcomes. Here, we share our experience of the weekly MTB meetings at Singapore General Hospital (SGH) and National Cancer Centre (NCC) (SGH-NCC HCC MTB).

METHODS: A retrospective review of cases submitted to the SGH-NCC HCC MTB from March 2021 to March 2023 was conducted. The attendees included specialists from eight departments/divisions from our institution, and it is open to physicians/patients from other hospitals in Singapore. Descriptive statistics were performed using Microsoft Excel.

RESULTS: There were 805 case discussions in 97 MTB meetings during the study period. The majority of the cases were listed by gastroenterologists/hepatologists (n = 359, 44.6%), followed by surgeons (n = 307, 38.1%), medical oncologists (n = 125, 15.5%), radiation oncologists (n = 6), and interventional radiologists (n = 2). Of all the discussions, 613 (76.1%) were unique patient cases, and an average of 3.1 discussions were held for cases with repeated MTB discussions (n = 192). Twenty-eight cases required histology review by the gastrointestinal (GI) pathologists during the meetings. Twenty-four patients had a transition of care after the MTB discussion.

CONCLUSION: A large number of cases were discussed at our weekly SGH-NCC HCC MTB in the past 2 years. Most of the cases were raised by gastroenterologists and hepatologists. Many required a transition of care after the MTB discussion.

Abstract Submission No. 100128

P-0496

The relative contribution of estradiol to hepatocellular carcinoma: A mendelian randomization

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Abstract

Objective: Estradiol and multiple sclerosis (MS) have been linked to cancer risks in observational studies. The causal nature of the association between the two and hepatocellular carcinoma (HCC) is unclear. We aim to test whether estradiol and MS are casually associated with the risk of HCC by using Mendelian randomization (MR) analysis.

Methods: Estradiol, MS and HCC genome-wide association study (GWAS) data were obtained from a public database. An inverse-variance-weighted (IVW) method was used as the primary MR analysis. Sensitivity analyses were examined. Multivariate MR (MVMR) was utilized to correct the confounders, and mediation analysis was used. Finally, we used HCC risk to infer the reverse causality with estradiol. **Results:** Random effects IVW results were (Estradiol-HCC: odds ratio (OR)=0.703, 95% confidence interval (CI)= [0.508, 0.973], P=0.034; MS-HCC: OR=0.722, 95% CI= [0.645, 0.808], P=1.50×10⁻⁸; Estradiol-MS: OR=2.103, 95% CI= [1.862, 2.376], P=5.65×10⁻³), demonstrating a causal link between estradiol levels and a lower risk of HCC. Through MVMR, the causal effect of estradiol and MS on HCC remained significant (P<0.05). Mediation analysis proved that MS mediated the causative connection between estradiol and HCC, and mediating effect on HCC was 58.52%. Reverse MR showed HCC could affect estradiol levels negatively.

Conclusions: This MR study confirmed the causal effect between estradiol levels and HCC risk, with MS playing a mediating role. It may provide a new view on HCC occurrence and development mechanisms.

Keywords: Estradiol, Multiple sclerosis, Mendelian randomization, Hepatocellular carcinoma, Causal relationship

Abstract Submission No. 100130

P-0497

Clinical outcomes of next-generation microwave thermosphere ablation for hepatocellular carcinoma

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Background and aim: We investigated the clinical outcomes of patients with hepatocellular carcinoma (HCC) who underwent next-generation microwave thermosphere ablation (MTA).

Methods: A total of 429 patients with 607 HCCs (maximum tumor diameter ≤40 mm) were included.

Results: The primary etiologies of HCC were hepatitis-related: 259 (60.4%) cases of HCV, 31 (7.3%) cases of HBV, and two instances of both. The median maximum tumor diameter was 15.0 (interquartile range, 10.0–21.0) mm. There were 86 tumors in areas of the liver where MTA is difficult. The most common location was near the primary and secondary branches of the intrahepatic portal vein (26 nodules). The cumulative local tumor recurrence rates at 1, 2, and 3 years were 4.4%, 8.0%, and 8.5%, respectively. The cumulative local tumor recurrence rate differed significantly by tumor size group: ≤20 mm group (n=483), 20–30 mm group (n=107), and ≥30 mm group (n=17) (p<0.001). The cumulative local tumor recurrence rate was similar by difficult-to-treat status (p=0.169). In the multivariable analysis, tumor

size (per 1 mm) (hazard ratio [HR], 1.07; 95% confidence interval [CI], 1.03–1.11; $p < 0.001$) and ablative margin (per 1 mm) (HR, 0.81; 95% CI, 0.70–0.92; $p = 0.002$) were significantly associated with local tumor recurrence. Only tumor size (per 1 mm) (odds ratio, 1.08; 95% CI, 1.02–1.15; $p = 0.015$) was significantly associated with complications.

Conclusions: MTA is a safe and effective local ablation therapy for HCC, even for tumors in areas of the liver where local ablation therapy is difficult.

Abstract Submission No. 100187

P-0498

Hepatocellular carcinoma treatment using Smart Fusion in dialysis patients

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Introduction: Approximately 700 maintenance dialysis patients are seen at our hospital, including the main hospital and branch hospitals. Among them are patients with HCC that develops from viral hepatitis. Advances in ultrasound equipment have improved the accuracy of HCC treatment and diagnosis.

This time, we had the opportunity to use microwaves for maintenance dialysis patients using Smart Fusion and needle navigation installed in Toshiba APLIOi800, so we will report it. Informed consent was obtained from all patients and the treatment was performed.

Subjects and Methods: Ten maintenance dialysis patients treated from January 2018 to February 2022. An EMPRINT antenna was used for treatment.

Method: Toshiba APLIOi800 was used. Conventional convex probes and microconvex probes were used as probes. The built-in function is Smart Fusion. This method can display ultrasound images and volume data from other modalities such as CT and MRI in association with positional information using a magnetic sensor. Enforceable.

Needle navigation has a function that can confirm the position of the needle. It is possible to treat even when the tumor is overprinted and the visualization is poor due to bubbles.

RESULTS: It was possible to visualize all tumors. In this study, CT images were used in 9 cases, and MRI was used in 1 case. No serious side effects occurred after treatment.

Conclusion: By using this method, it was thought that maintenance dialysis patients could be safely and accurately treated.

Abstract Submission No. 100193

P-0499

LASSO-Based Machine Learning model for Prediction of Liver Failure in HCC Patients Undergoing TACE

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PURPOSE: Transcatheter arterial chemoembolization (TACE) is a commonly used method for the nonsurgical treatment of hepatocellular carcinoma (HCC); however, it can cause liver failure with rapid progression and high mortality.

METHODS: We organized and analyzed the data of patients with HCC undergoing TACE at our hospital. Screening indicators related to

liver failure were analyzed using least absolute shrinkage and selection operator (LASSO) regression to establish a predictive model.

RESULTS: Prothrombin activity (odds ratio [OR] [95% confidence interval (CI)], 0.965 [0.931-0.997]; $p = 0.040$), tumor number (OR [95% CI], 2.328 [1.044-5.394]; $p = 0.042$), and vascular invasion (OR [95% CI], 2.778 [1.006-7.164]; $p = 0.039$) are independent risk factors for liver failure after TACE. The prediction model established based on these results had areas under the curve of 0.821 and 0.813 for the training and validation groups, respectively.

CONCLUSION: The prediction model established using LASSO regression can predict the risk of liver failure after TACE and confirm whether patients with advanced HCC can benefit from TACE.

Abstract Submission No. 100216

P-0500

A comparative study between radiation therapy and RFA for HCC in difficult-to-RFA area

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Purpose: Percutaneous radiofrequency ablation (RFA) is the mainstay of radical local therapy for hepatocellular carcinoma (HCC), but it is often difficult to treat HCC located close to the liver surface, vessels, or other organs. For such difficult-to-replace HCC, we sometimes perform RFA using techniques such as artificial pleural effusion, CT/MRI fusion, and Multipolar RFA system, in addition to IVR-CT room combination, and sometimes choose radiation therapy (RT), but the usefulness of the two has not been compared. In this retrospective comparative study, we compared the usefulness of RT and RFA in the past for HCC patients with difficult RFA sites.

Methods: Among HCC patients who underwent RT or RFA for curative purposes between January 2013 and December 2021, 22 and 71 patients were selected from each group, respectively, with tumor diameter less than 3 cm, single tumor, and difficult-to-RFA area, and local recurrence rate, and complications were compared between the two groups.

Results: Between the groups that received RT or RFA (hereafter RT group vs. RFA group), median age, ALBI score, and median tumor diameter did not differ significantly. The cumulative local recurrence rate within the observation period was not significantly different between the two groups (log rank test, $p = 0.031$), and Cox proportional hazards analysis (multivariate analysis) showed that AFP alone was a significant independent factor for local recurrence (HR: 1.0, $p = 0.045$).

Conclusion: Radiotherapy and RFA were equally effective in treating HCC in RFA-difficult areas, and radiotherapy could be a substitute for RFA in RFA-difficult areas.

Abstract Submission No. 100223

P-0501

Severe colitis after tremelimumab plus durvalumab in a patient with hepatocellular carcinoma

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Introduction: Tremelimumab plus durvalumab (Tre+Dur) improve prognosis in patients with unresectable hepatocellular carcinoma (HCC). Treatment with Tre+Dur is accompanied by immune-mediated adverse event (imAE).

Case Presentation: A 56-year-old woman presented right hypochondrium pain. Computed tomography (CT) images showed massive liver tumor with right portal vein invasion (maximal diameter of tumor: 14cm) and left adrenal metastasis. Her Child-Pugh score was 5. The patient was diagnosed as HCC with BCLC stage C, and underwent treatment with Tre+Dur. Two weeks after first administration of Tre+Dur, the patient developed fever and diarrhea 20 times a day. CT images revealed bowel wall thickening. Colonoscopy showed erosion and indistinct vascular pattern. Biopsy from transverse colon and rectum revealed apoptotic bodies and lymphocyte infiltration. We diagnosed her as imAE colitis. After admission, we initiated prednisolone therapy (1mg/kg/day) and her symptom was improved. However, she developed recurrent diarrhea and fever when we tapered off prednisolone. Colonoscopy revealed multiple punched-out ulcers in the ileum and colon. We initiated infliximab therapy, and symptoms improved after 2 courses of infliximab therapy. She was discharged 68 days after admission. Four courses of treatment have been completed without complication. There were no findings suggesting recurrence at a month follow-up visit.

Conclusions: We experienced a case of steroid-refractory colitis that developed after treatment with Tre+Dur. In our case, infliximab therapy was a safe and effective treatment option for patients with steroid-refractory imAE after Tre+Dur.

Abstract Submission No. 100252

P-0502

Clinical Outcome of Sorafenib versus Lenvatinib for Unresectable HCC in Taiwanese Elderly Population

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Background: Sorafenib and lenvatinib are two tyrosine kinase inhibitors (TKIs) approved as first-line treatments for unresectable hepatocellular carcinoma (HCC). However, few studies discussed the efficacy of sorafenib or lenvatinib on elderly patients.

Methods: This retrospective study analyzed the medical records of patients with unresectable HCC receiving sorafenib or lenvatinib as the first-line therapy from July 2020 to December 2022 at MacKay Memorial Hospital in Taiwan. The elderly group was defined as patients who were 65 years of age or older at the time they began using TKIs. We analyzed patients' baseline general data, radiological best overall response, progression-free survival (PFS) and overall survival (OS) between sorafenib and lenvatinib groups.

Results: 53 elderly patients with sorafenib and 29 elderly patients with lenvatinib were enrolled. The characteristics of all elderly patients in two groups were shown in Table 1. The characteristics of patients between the two groups were not significantly different. The radiological best overall response was shown in Table 2. There was no significant

difference in PFS and OS survival curves between sorafenib and lenvatinib groups (Figure 1, 2).

Conclusions: Sorafenib, compared to lenvatinib, had a trend of longer OS but shorter PFS, and lower disease control rate and objective response rate in elderly patients with unresectable HCC. However, no significant difference was achieved. Therefore, sorafenib and lenvatinib may be selected as reasonable therapy for unresectable HCC in elderly patients. More prospective studies are needed to draw a firm conclusion.

Abstract Submission No. 100272

P-0503

Liver cancer is the fastest rising cancer related to obesity

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Background: High body mass index (BMI) is a major risk factor for cancer development, but its impact on the global burden of cancer remains unclear.

Methods: We estimated global and regional temporal trends in the burden of cancer attributable to high BMI, and the contributions of various cancer types using the framework of the Global Burden of Disease Study.

Results: From 2010 to 2019, there was a 35% increase in deaths and a 34% increase in disability-adjusted life-years from cancers attributable to high BMI. Globally, the age-standardized death rates for cancer attributable to high BMI increased over the study period (annual percentage change [APC] +0.48%, 95% CI 0.22 to 0.74%). From 2010 to 2019, the greatest number of deaths from cancer attributable to high BMI occurred in Europe, but the fastest-growing age-standardized death rates and disability-adjusted life-years occurred in Southeast Asia. In stratified analysis by cancer types, liver cancer was the fastest-growing cause of cancer mortality (APC: 1.37%, 95% CI 1.25 to 1.49%) attributable to high BMI.

Conclusion: The global burden of cancer-related deaths attributable to high BMI has increased substantially from 2010 to 2019. The greatest increase in age-standardized death rates occurred in Southeast Asia, and liver cancer is the fastest-growing cause of cancer mortality attributable to high BMI. Urgent and sustained measures are required at a global and regional level to reverse these trends and slow the growing burden of cancer attributed to high BMI.

Abstract Submission No. 100286

P-0504

Advanced HCC Treated with Atezolizumab: Complete Response but Immune Colitis, Pancreatitis

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Objective: The optimal use of immune checkpoint inhibitors (ICIs) remains uncertain, particularly concerning treatment duration and

maintaining tumor immunity after achieving antitumor effects. We present a case where Atezolizumab and Bevacizumab (ATZ/Bv) led to a complete response in advanced HCC but also induced severe immune-related adverse events.

Case: An 84-year-old male was diagnosed with hepatocellular carcinoma in April 2022. After using ATZ/Bv post-transarterial chemoembolization (TACE), complete tumor remission was achieved by January 2023. However, the patient exhibited symptoms of immune-related colitis and pancreatitis, attributed to ATZ/Bv. Treatment with prednisolone, infliximab, and granulocyte removal therapy proved effective.

Discussion: ICIs, which inhibit co-stimulation like PD-1/PDL-1 in T cell receptors, can boost tumor immunity but may also trigger autoimmunity. This can lead to clinical manifestations resembling known autoimmune diseases. The challenge lies in determining when to halt treatment to prevent sudden adverse effects and whether intermittent ICI administration is necessary to sustain antitumor immunity. Once immune-related adverse events (irAEs) manifest, treatments akin to those for corresponding autoimmune diseases have shown effectiveness, as in the presented case.

Conclusion: Treatments paralleling those for established autoimmune diseases are effective against ICI-related adverse events. Further studies are essential to delineate the ideal utilization of ICIs.

Abstract Submission No. 100305

P-0505

Risk of acute kidney injury by chemotherapeutic agents in patients with HCC undergoing TACE

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Background: Acute kidney injury (AKI) is a crucial factor for the prognosis of liver cirrhosis and it can develop in patients with hepatocellular carcinoma (HCC). This study aimed to evaluate the effect of chemotherapeutic agents on the risk of AKI in patients with HCC undergoing transarterial chemoembolization (TACE).

Methods: A total of 370 HCC patients with baseline serum creatinine (SCr) ≤ 1.5 mg/dL undergoing TACE as an initial therapy were included. We compared the differences in the development of AKI between the use of doxorubicin and cisplatin in patients undergoing TACE for HCC. Also, the risk factors for the development of AKI were investigated during TACE. The AKI was defined based on the International Club of Ascites (ICA)-AKI criteria.

Results: The mean age was 60.8 years. The mean SCr levels at baseline, one day, two months, and four months after TACE were 0.9, 0.9, 0.9, and 1.1 mg/dL, respectively. The AKI within four months after TACE developed in 43 patients (12%). The AKI stages were non-AKI in 327 (88%), stage 1 in 13 (4%), stage 2 in 12 (3%), and stage 3 in 18 patients (5%). The proportion of the use of cisplatin and doxorubicin was 18% (n=65) and 82% (n=305), respectively. There was no difference in baseline sCr levels between cisplatin group and doxorubicin group (0.9 ± 0.2 mg/dL vs. 0.9 ± 0.3 mg/dL, $p=0.490$). However, the risk of AKI in cisplatin group was significantly higher than in doxorubicin group (29% vs. 8%, $p<0.001$). Multivariable analysis indicated that the risk factors for AKI were serum albumin ≤ 3.5 g/dL (hazard ratio [HR] 3.44 with 95% confidence interval [CI] 1.51-7.82, $p=0.003$), BCLC stage C (HR 6.48 with 95% CI 2.65-15.87, $p<0.001$), presence of ascites (HR 9.43 with 95% CI 4.21-21.10, $p<0.001$), and use of cisplatin (HR 3.02 with 95% CI 1.24-7.32, $p=0.015$).

Conclusion: The risk of AKI development is high in HCC patients treated with cisplatin-based TACE. The chemotherapeutic agent in patients receiving TACE for HCC should be chosen considering its nephrotoxicity in patients with hypoalbuminemia, advanced stage, and the presence of ascites, in particular.

Abstract Submission No. 100328

P-0506

Impact of elevated indirect bilirubin in systemic treatment for hepatocellular carcinoma

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Background: Despite inclusion of bilirubin in prognostic indicators for hepatocellular carcinoma (HCC), the impact of benign hyperbilirubinemia (BH) on outcomes in HCC has not been studied.

Objective: To evaluate outcomes of unresectable HCC patients with or without BH.

Methods: We retrospectively reviewed patients with elevated total bilirubin (1.3 mg/dL or higher) who received first-line systemic therapy for unresectable HCC at our institution with either atezolizumab and bevacizumab combination therapy or lenvatinib between April 2018 and September 2022. Patients were considered to have BH if indirect bilirubin accounted for over 50% of total bilirubin.

Results: Seventeen patients were included. Nine cases had BH. Although there were no significant differences in baseline characteristics between the BH and non-BH groups, more patients in the BH group had Barcelona Clinic Liver Cancer staging B (67% vs. 25%), received Lenvatinib (89% vs. 63%), and achieved overall response (33% vs. 0%) or disease control (89% vs. 75%). Modified albumin-bilirubin grade and Child-Pugh score were also similar, but median PIVKA-II was significantly lower in the BH group (48 vs 2,196 mAU/mL, $P=0.003$). Median overall survival (943 vs. 141 days, $P=0.032$) was significantly longer in the BH group, although the difference in median progression-free survival was not significant (209 vs. 110 days, $P=0.169$).

Conclusion: Prognoses in BH patients receiving systemic therapy for HCC may be better than their non-BH counterparts. Larger, multicenter studies are desirable to elucidate the impact of BH on outcomes in HCC.

Abstract Submission No. 100332

P-0507

Lenvatinib as 2nd line in post-immunotherapy for hepatocellular carcinoma

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Background: Atezolizumab plus bevacizumab (AteBev) are first-line therapy for unresectable hepatocellular carcinoma (uHCC), but no second-line therapy has been established for PD patients. This study aims to evaluate the efficacy of lenvatinib (LEN) in patients with HCC by

evaluating of serum cytokine in patients who failed to respond to AteBev treatment.

Methods: 60 uHCC patients who received AteBev. Dynamic computed tomography was performed after 6, 9, and 12 weeks treatment and blood samples were collected at baseline and after 3 weeks.

Results: After 6 weeks of AteBev treatment, 19 patients had PR, 12 patients had SD, and 29 patients had PD. ORR showed 31.7%. 20 patients were treated with LEN as second-line therapy due to irAE or PD. 9 patients had CR or PR and 11 patients had SD or PD. ORR showed 45.0%. Tumor stage II/III/IVA/IVB = 0/4/4/1, and BCLC stage B1/B2/B3/C = 0/4/0/5 in the CR+PR group, while in the SD+PD group, 1/5/14, 0/7/4. Serum levels of FGF-19 increased significantly after treatment in the CR+PR group ($p = 0.0414$) and the SD group ($p = 0.0431$), although there was no significant difference in the PD group. There was no significant difference in serum levels of soluble FGF-R4 in the PR group and the SD group, although those levels increased after treatment in the PD group.

Conclusion: LEN was useful as second-line therapy for HCC patients who did not respond to AteBev treatment. Patients whose FGF pathway is activated by AteBev treatment are expected to respond to LEN.

Abstract Submission No. 100341

P-0508

Therapeutic efficacy and safety of atezolizumab plus bevacizumab therapy by liver function

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Background and aims: Atezolizumab plus bevacizumab (ATZ/BEV) therapy for unresectable hepatocellular carcinoma (HCC) may also be used in patients with impaired liver function in real practice. The aim of this study was to examine the efficacy and safety of ATZ/BEV therapy by liver function.

Methods: A total of 348 HCC patients who received ATZ/BEV therapy as first-line chemotherapy were studied. We investigated treatment efficacy, safety, and survival by liver function.

Results: Two hundreds and eight patients had a Child-Pugh score (CPS) 5, 109 patients had a CPS 6 and 31 patients had a CPS 7 or higher. The object response rate was not significantly different among the three groups (39.4%, 36.3% and 40.7%, respectively: $P = 0.84$). No significant differences were observed in the disease control rate (78.8%, 75.5% and 74.1%, respectively: $P = 0.73$). Though there was also no significant difference in the progression free survival ($P = 0.17$), overall survival decreased with worse liver function ($P < 0.01$). After treatment initiation, liver function declined in all groups, and the incidence of Grade 3 or higher adverse events (AEs) was significantly higher in patients with CPS 7 or higher ($P = 0.018$). The rate of treatment discontinuation due to worsening liver function or AEs was highest in patients with CP 7 or higher.

Conclusion: Although there was no difference in treatment response based on liver function, particular attention should be paid to the management of AEs associated with ATZ/BEV therapy in cases of impaired liver function.

Abstract Submission No. 100351

P-0509

Hydroxychloroquine reduced the risk of hepatocellular carcinoma in hepatitis C virus patients.

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Background: Chronic hepatitis C virus(HCV) infection is one of the leading causes of hepatocellular carcinoma(HCC) worldwide. Hydroxychloroquine(HCQ) is a medication used to treat malaria and autoimmune disorders and recent studies have suggested that it may also have anti-cancer properties based on autophagy and non-autophagy mechanisms. This study investigates the correlation between HCQ use and the risk of hepatocellular carcinoma in patients with chronic HCV infection.

Method: HCV infected patients were enrolled from Taiwan's National Health Insurance Research Database(covering January 1, 2006, to December 31, 2016). The association between HCQ use and HCC risk was evaluated using the Kaplan-Meier method and Cox proportional hazards regression.

Results: 139,263 HCV patients were enrolled and individual matching with 1:10. Among 1,598 patients using HCQ(defined as ≥ 28 cumulative defined daily doses[cDDDs]), 62 developed HCC. Comparatively, among 15,980 patients not using HCQ(≤ 28 cDDDs), 975 were diagnosed with HCC. HCQ use by HCV patients showed a significantly reduced HCC risk with an adjusted hazard ratio(aHR) of 0.68(95% CI,0.51-0.92).

Conclusion: HCQ use appears to lower the risk of HCC among patients with HCV infection, suggesting potential benefits in preventing HCC in this population. Further research is necessary to confirm these findings and underlying mechanisms.

Abstract Submission No. 100365

P-0510

Treatment outcomes of transarterial chemoembolization for early hepatocellular carcinoma

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Aims: The treatments of choice in patients with early-stage hepatocellular carcinoma (HCC) are surgical resection, local ablation therapy, and liver transplantation, but transarterial chemoembolization (TACE) is commonly performed due to variations in patients and liver diseases. This study aimed to assess the efficacy of TACE in patients with early-stage HCC.

Methods: A retrospective analysis was performed of all TACE procedures performed at Kyung Hee University Hospital at Gangdong during a 15-year period (July 2006 to November 2021). Patients with solitary tumors ≤ 5 cm were included.

Results: The study included a total of 97 eligible patients with early HCC ≤ 5 cm initially treated with TACE. The mean participant age was 63.47 ± 11.02 years, and of whom, 69 were males (71.1%). A complete response was achieved in 84 (86.6%) patients after the first TACE

procedures, with 1-, 2-, and 3-year survival rates of 91.8%, 87.3%, and 75.4%, respectively. In a multivariate analysis, the patients with an initial alpha-fetoprotein (AFP) ≤ 20 ng/mL ($p = 0.02$) and complete response after the first TACE ($p = 0.03$) were associated with overall survival.

Conclusions: TACE can treat patients with early-stage HCC who are unsuitable for ablation or surgery resulted comparable survival benefit to standard treatment.

Abstract Submission No. 100372

P-0511

Liver injury in patients with HBV-related HCC undergoing TACE combined with TKIs plus ICIs

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Objective: To explore the liver injury and its effect on overall survival (OS) in patients with HBV-related hepatocellular carcinoma (HCC) treated by transarterial chemoembolization (TACE) combined with tyrosine kinase inhibitors (TKIs) plus immune checkpoint inhibitors (ICIs).

Methods: Patients with HBV-related HCC who received TACE-TKIs-ICIs combination therapy from 1 January 2020 to 31 December 2021 were enrolled. Liver injury and OS were the main endpoints.

Results: As of 31 March 2022, 52 (43.7%) of the 119 patients developed hepatic adverse events: 15 with grade 1 liver injury, 19 with grade 2, 16 with grade 3, and 2 with grade 4. The median time of liver injury was 2.5 months (0.1-23 months) after the patients received ICI for the first time. Both univariate and multivariate analysis indicated that lack of antiviral preventive was a risk factor for liver injury (OR=0.149; 95%CI: 0.050-0.442; $P=0.001$). A total of 45 patients died during the follow-up period, and the median survival time (MST) was 22.4 months for all patients. Our findings suggested that baseline high Child-pugh grade (HR=2.612; 95%CI: 1.234-5.530; $P=0.012$), high alpha-fetoprotein level (HR=2.766; 95%CI: 1.454-5.259; $P=0.002$), liver injury events (HR=1.887; 95%CI: 1.019-3.495; $P=0.044$) were associated with death. The MST of patients without liver injury, grade 1-2 and grade 3-4 liver injury were undefined, 13.7 months and 11.1 months, respectively (log-rank $P=0.034$).

Conclusion: Nearly half of HBV-related HCC patients treated with TACE-TKIs-ICIs encountered liver injury. Lack of preventive antiviral therapy was a risk factor for liver injury. Patients who developed liver injury had a poor prognosis.

Keywords: HBV-related HCC; TACE; TKI; ICI; liver injury

Abstract Submission No. 100373

P-0512

Secondary Cholestasis in Patients with HBV-related Advanced HCC Treated with TACE plus ICIs and TKIs

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Objective: To investigate the clinical characteristics and prognosis of secondary cholestasis in patients with HBV-related advanced hepatocellular carcinoma treated with a combination of transarterial chemoembolization (TACE), immune checkpoint inhibitors (ICIs) and tyrosine kinase inhibitor (TKIs).

Methods: This study enrolled patients with HBV-related advanced hepatocellular carcinoma who visited at the Affiliated Hospital of Xuzhou Medical University from January 1, 2020 to December 31, 2022. All patients were treated with a combination therapy of TACE plus TKIs and ICIs. The secondary occurrence and influencing factors of cholestasis after combination therapy were analyzed, and its impact on prognosis was further analyzed.

Results: A total of 106 patients with HBV-related advanced hepatocellular carcinoma were enrolled. The probability of secondary cholestasis within 3 months, 6 months, 1 year, 2 years and 3 years after TACE+ICIs+TKIs combination therapy was 9.4%, 12.3%, 15.1%, 24.5% and 24.5%, respectively. Most patients with secondary cholestasis are persistent and progressing rapidly. The median survival time (26.9 months) was significantly longer in patients without secondary cholestasis than in patients with cholestasis (13.7 months) ($P < 0.05$). Cholestasis occurs, baseline AST and PTA level are independent risk factors for overall survival (OS). There was no significant difference in adverse reaction between patients with and without secondary cholestasis during the treatment process ($P=0.810$).

Conclusion: Secondary cholestasis is common in patients with HBV-related advanced hepatocellular carcinoma who adopt a combination therapy of TACE plus TKIs and ICIs, and the disease progresses rapidly and has a poor prognosis.

Key words: Hepatocellular carcinoma; Cholestasis; Transcatheter arterial chemoembolization; Tyrosine kinase inhibitor; Immune checkpoint inhibitors

Abstract Submission No. 100386

P-0513

The efficacy and safety of atezolizumab & bevacizumab with unresectable hepatocellular carcinoma

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Introduction: Treatment responses of unresectable hepatocellular carcinoma (HCC) remain unacceptably low and treatment modalities are limited. After the IMbrave 150 trial was announced, there are still few published data on the atezolizumab and bevacizumab in South Korea. We analyzed the efficacy and safety of atezolizumab & bevacizumab based on real world data.

Method: In retrospective cohort study, data on 28 patients with unresectable HCC, with Child-Pugh (CP) scores of 5-8, were collected from a university hospital between September 2020 and October 2022. All patients were treated with 1200mg of atezolizumab plus 15mg per kilogram of body weight of bevacizumab intravenously every 3 weeks.

Method: In retrospective cohort study, data on 28 patients with unresectable HCC, with Child-Pugh (CP) scores of 5-8, were collected from a university hospital between September 2020 and October 2022. All patients were treated with 1200mg of atezolizumab plus 15mg per kilogram of body weight of bevacizumab intravenously every 3 weeks.

Conclusion: For managing unresectable HCC, atezolizumab & bevacizumab may be a valuable and safe treatment modality, but long-term follow-up and large scale studies are needed in the future.

Abstract Submission No. 100436

P-0514

Retreatment of Immune Checkpoint Inhibitors after Immune-related Adverse Events in unresectable HCC

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Background: Immune checkpoints inhibitors (ICIs) are recommended as the first-line and second-line systemic treatment for unresectable hepatocellular carcinoma (uHCC). Previous report suggests that the development of immune-related adverse events (irAE) correlates favorable clinical outcomes. However, it is not clear about the impact of different types of irAE on tumor response and the safety of rechallenge. **Methods:** From May, 2017 to Oct. 2022, 215 consecutive uHCC patients who received ICIs monotherapy or in combination with tyrosine kinase inhibitors (TKIs) as the first-line (n=133) or second-line systemic therapy (n=82) in Taipei Veteran General Hospital were retrospectively reviewed. The tumor responses were assessed according to RECIST 1.1 criteria. The grades of irAE were evaluated according to CTCAE v5.0.

Results: Of them, 40 (18.6%) developed at least grade 2 irAE (graded ≥ 2 , irAE2), including 19 (8.8%) dermatitis, 9 (4.2%) hepatitis, 7 (3.3%) pneumonitis, and 5 (2.3%) miscellaneous. The irAE2 more frequently occurred during cycle 2 to cycle 4 of ICI treatment. Development of irAE2 was associated with higher disease control rate and better progression free survival (PFS). Among the 40 patients with irAE2, the median duration of steroid treatment was 6.36 weeks (0.14-25.57 weeks). Interestingly, 32 (80%) received ICI rechallenge after irAE subsided, and recurrence of irAE occurred in 9 (4 by dermatitis, 3 by hepatitis, and 2 by miscellaneous)

Conclusions: irAE2 is not uncommon for uHCC under ICIs therapy, which is associated with better DCR and PFS. Rechallenge of ICI may be safe for two thirds of the cases under closely surveillance.

Abstract Submission No. 100437
P-0515

Spontaneous regression of hepatocellular carcinoma after abstinence from alcohol: A case report

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63-year-old male

He fell and fractured his right olecranon. He was referred to our orthopedic department for surgery. In preoperative screening, abnormal liver function test was pointed out. He had a history of heavy alcohol consumption and was diagnosed with alcoholic cirrhosis. Ultrasonography showed a 6 cm hypoechoic lesion in the right lobe of the liver. The level of alpha-fetoprotein (AFP) was 3098 ng/mL and des-gamma-carboxy prothrombin (DCP) was 2083 mAU/mL. Hepatocellular carcinoma (HCC) was suspected. He was instructed to abstain from alcohol and first underwent surgery for bone fracture under

general anesthesia prior to further evaluation of the liver lesion. Dynamic computed tomography (CT) after discharge showed, in the equilibrium phase, a 6 cm low-density area in the segment 5 of the liver and other similar small lesions. Although tumor stain in the early phase of dynamic CT was not evident, the diagnosis of HCC was made, taking into account the elevated tumor markers. Atezolizumab plus bevacizumab therapy was considered, but tumor markers measured just prior to the start of therapy were markedly reduced to AFP 361 ng/mL and DCP 47 mAU/mL. Although CT showed no significant changes, the start of the treatment was postponed due to the possibility of spontaneous regression of the tumors. During the follow-up, tumor markers decreased further and CT showed shrinkage of the tumor. Abstinence from alcohol may have been the cause of spontaneous regression.

Abstract Submission No. 100464
P-0516

Cutaneous Metastasis from Hepatocellular Carcinoma: A Rare Cause of Periumbilical Bulging Tumor

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A 64-year-old man presented with a slow-growing, firm, non-painful, bulging mass adjacent to the umbilicus. The mass measured up to 3 cm in diameter and was dark purplish in color. The patient has a history of hepatitis C viral-related cirrhosis, Child-Pugh score B7, complicated by esophageal varices. He had been diagnosed with Hepatocellular carcinoma (HCC) four years ago, initially at Barcelona Clinic Liver Cancer stage B. He received several rounds of trans-arterial chemo-embolization and radiofrequency ablation (RFA). However, recurrent HCC occurred a few months later, and he subsequently underwent laparoscopic partial hepatectomy. The patient was otherwise well until the appearance of the periumbilical protruding mass. Abdominal computed tomography revealed portal venous thrombosis and a periumbilical tumor with hypervascularity and subcutaneous extension. The patient underwent en-bloc resection of the tumor. The excisional biopsy specimen confirmed metastatic HCC with free section margins. After the surgical removal of the subcutaneous metastatic tumor, the patient received radiotherapy for portal venous thrombosis.

Cutaneous metastases of HCC are exceedingly rare. Some of them were reported to be caused by tumor seeding during diagnostic or therapeutic procedures, such as liver biopsy, percutaneous ethanol injection and RFA. This case, however, is among a small minority of reported cases of cutaneous metastatic HCC associated with abdominal surgical intervention and is considered a consequence of port-site metastasis (PSM). PSM is characterized by direct malignant cells implantation at a trocar insertion site after a laparoscopic resection of an intra-abdominal tumor. Possible pathogenesis includes two leading factors: pneumoperitoneum and direct tumor contamination.

Abstract Submission No. 100473
P-0517

Clinical Course and Prognosis of Long-Term Survivors of Hepatocellular Carcinoma

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Background and Aims: This study investigated the long-term prognosis and clinical course of patients who survived for more than 5 years after HCC diagnosis.

Method: This retrospective cohort study used data from the Korean National Health Insurance Service database. A total of 35,348 subjects newly diagnosed with HCC between January 2008 and December 2010 were followed up until December 2018.

Results: A total of 11,514 (32.6%) survived for 5 years after diagnosis of HCC among 35,348 patients diagnosed with HCC. Five-year survivors had a higher proportion of females, younger age, more frequent etiology of HBV, less frequent liver cirrhosis, diabetes mellitus, and hypertension, and received curative treatment more frequently than non-survivors. The additional 1-, 3-, and 5-year survival rates were 90.7%, 77.6%, and 68.4%, respectively. Patients who underwent curative treatment as the first treatment for HCC showed a higher additional 5-year survival rate than those treated with non-curative therapy (74.5% vs. 64.2%). Among the HCC survivors, 44.4% underwent HCC retreatment 5 years after HCC diagnosis. The additional 5-year survival rate was 54.9% in the HCC retreatment group. The overall 5- and 10-year cumulative probabilities of secondary primary malignancies in HCC survivors were 15.36% and 27.54%, respectively. The most frequent second primary malignancy was prostate cancer, followed by colorectal and pancreatic cancers.

Conclusion: Our study highlights that a significant proportion of patients with HCC achieve long-term survival beyond 5 years, with favorable outcomes associated with curative treatments.

Abstract Submission No. 100488
P-0518

Gut microbiota-associated cytokine response and immunotherapy outcomes in hepatocellular carcinoma

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Despite the introduction of immune checkpoint inhibitor (ICI)-based therapies for advanced hepatocellular carcinoma (HCC), patient prognosis remains unfavourable due to poor response rate. While the impact of the gut microbiota on the efficacy of ICI is well demonstrated, its role in combined anti-PD-L1/anti-VEGF-A therapy against HCC remains unexplored. This study aims to elucidate the links between the gut microbiota and response to immunotherapy in HCC.

HCC patients eligible for immunotherapy consented to have stool and blood samples collected before and 12 weeks after anti-PD-L1/anti-VEGF-A immunotherapy. DNA was eluted from stool samples and 16S rRNA sequencing was performed to identify the gut microbiota composition. We extracted the serum and analysed for cytokines using LUMINEX MagPix[®]. Results were compared using two-way ANOVA with Tukey's multiple comparison test, Chi-square test, one-way ANOVA or Pearson's test. Comparisons where $p < 0.05$ were statistically significant.

At 12 weeks post-ICI-based therapy, responders displayed enrichment of *Parabacteroides*, *Butyrivibrio*, and *Ruminococcus*. In parallel, a surge in peripheral VEGF-A, RANTES, and LIF levels at 12 weeks was observed in responders relative to baseline. The enriched bacterial strains found in responders correlated with an immune milieu rich in anti-tumoral cytokines. Conversely, non-responders exhibited increased *Roseburia*, the presence of which was associated with a shift towards a pro-tumoral cytokine response.

Our findings suggest that gut microbiota-associated changes in the peripheral immune environment may influence ICI-based therapy efficacy against HCC. This raises the potential of manipulating the gut microbiota to increase responsiveness to ICI-based therapy in HCC patients.

Abstract Submission No. 100521
P-0519

Diagnostic Dilemma: Large Well Differentiated Non-AFP Producing HCC with Atypical Imaging Features

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BACKGROUND: Due to the complexity of hepatocarcinogenesis, Hepatocellular Carcinoma can present with varying characteristics leading to atypical imaging findings. The classical feature of arterial phase enhancement and washout on the portal/delayed phase may not be appreciated, posing diagnostic challenges. Establishing a definitive diagnosis is crucial for decision-making on management and treatment options.

CASE PRESENTATION: A 66-year-old male presenting with three months history of progressive right upper quadrant pain, easy fatigability and weight loss. Initial workups revealed elevated liver enzymes, prolonged INR, previous hepatitis B infection, and normal CEA, C19-9, AFP. Ultrasound and CT Scan showed cirrhosis, and multiple liver masses with malignant characteristics. PET-Scan was negative for metastasis. Percutaneous liver biopsy was equivocal showing atypical malignant cells (CK7+, CK20-, HepPar-).

DISCUSSION: Diagnostic imaging tests were conducted, including Liver Elastography (F4) to stage fibrosis in chronic liver disease and Four-phase Dynamic CT Scan to describe lesions. LI-RADS interpretation showed several arterially enhancing lesions with no washout, suggesting Atypical HCC or Combined HCC-Cholangiocarcinoma. MRI of the Liver was also performed, showing early enhancing foci without demonstrable washout. Both CT and MRI results were inconclusive, leading to a Laparoscopic-Guided Biopsy, which revealed well-differentiated hepatocellular carcinoma (CD34+, CAM5.2+, Glypican3-). The patient was classified as Advanced Stage by BCLC criteria. Systemic therapy with Lenvatinib 12mg/tab once daily was initiated.

CONCLUSION: Hepatocellular carcinoma (HCC) is diagnosed non-invasively with CT and MRI, resorting to biopsy for inconclusive cases, emphasizing the need for understanding HCC complexities and imaging variations for accurate treatment planning.

Abstract Submission No. 100551
P-0520

Thrombocytopenia did not increase RFA related bleeding risk in patients with HHC and Cirrhosis

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Abstract

Objective: This study aimed to assess the bleeding risk during the perioperative period of radiofrequency ablation (RFA) in patients with hepatocellular carcinoma (HCC) and moderate thrombocytopenia.

Methods: A retrospective analysis was conducted on 184 patients with cirrhosis and HCC who underwent RFA at the Department of Gastroenterology and Hepatology, West China Hospital, between June 2020 and February 2023. The patients were divided into two groups: group A (platelet count $<50 \times 10^9/L$) and group B (platelet count $\geq 50 \times 10^9/L$). The study compared the differences in postoperative complications and mortality within 90 days between the two groups. Additionally, regression analysis was performed to investigate the relationship between platelet count and postoperative complications.

Results: Group A comprised 58 patients with a median platelet count of $35 \times 10^9/L$, while Group B comprised patients with a median platelet count of $81 \times 10^9/L$. Group A had higher median INR values and incidence of ascites compared to Group B (1.3 vs. 1.2, $P < 0.01$; 46.5% vs. 30.1%, $P = 0.04$). There were no significant differences in terms of BCLC stage, Child-Pugh grade, or prior decompensation events of cirrhosis between the two groups. Out of the total patients, 18 (9.8%) experienced postoperative complications, with 4 patients (2.2%) suffering from major perioperative bleeding. The incidence of major perioperative bleeding and postoperative complications did not significantly differ between group A and group B (0% vs. 3.2%, $P = 0.31$; 10.3% vs. 9.5%, $P = 0.86$). Regression analysis indicated that thrombocytopenia does not increase the risk of postoperative bleeding, while mild ascites was identified as an independent risk factor for postoperative complications. Within 90 days after the operation, three patients (1.6%) died, with only one patient's death attributed to operation-related causes.

Conclusion: This study suggests that RFA can be safely performed in patients with liver cirrhosis complicated by moderate thrombocytopenia. A preoperative platelet count of less than $50 \times 10^9/L$ should not be considered a contraindication for RFA.

Abstract Submission No. 100575
P-0521

Short-Term Clinical Outcomes and Safety of Microwave Ablation for Hepatocellular Carcinoma Treatment

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Purpose: This study aims to assess the short-term clinical outcomes and safety profile of microwave ablation therapy in the management of hepatocellular carcinoma (HCC).

Materials and Methods: A retrospective analysis, approved by the institutional review board, was conducted. The study cohort comprised 255 patients (185 males, 70 females; mean age $\pm$ standard deviation: 66 ± 10 years) with 237 cases of HCC. These patients underwent microwave ablation (MWA) treatment between May 2021 and June 2023.

Tumor characteristics, including size and location, were evaluated. One-year rates of local tumor progression (LTP), intrahepatic distant recurrence (IDR), and extrahepatic recurrence (ER) were examined. Safety was assessed through an analysis of complications.

Results: The median follow-up period was 11.6 months (range: 0 to 26 months). MWA was the initial treatment for 29% (29/255) of patients, while the others had undergone prior treatments. The average tumor size was 1.5 cm (range: 0.6 to 4 cm). Among the tumors, 16.8% (40/237) were located perivascularly, and 10.5% (25/237) were subcapsular. The 1-year rates of LTP, IDR, and ER were 4.5%, 40%, and 4.5%, respectively. Complications occurred in 3% (7/255) of cases, including instances of bleeding, biloma, and perihepatic abscess.

Conclusion: Microwave ablation can be an effective and secure therapeutic approach for hepatocellular carcinoma

Abstract Submission No. 100597
P-0522

Comparison of regorafenib for unresectable hepatocellular carcinoma in young and elderly patients

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Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality worldwide. Regorafenib, after sorafenib, has been a standard of care for unresectable HCC; however, its efficacy in different age groups, specifically young and elderly patients, is under-explored.

Methods: We conducted a retrospective analysis of patients diagnosed with unresectable HCC who received sorafenib followed by regorafenib upon disease progression or intolerance between 2017 and 2022. Patients were categorized into two groups: young (<65 years) and elderly (≥ 65 years) at the time of diagnosis of HCC. We compared baseline characteristics, treatment response, and overall survival (OS) between the two groups.

Results: A total of 55 patients were included in the analysis with 28 patients (51%) in the young group (<65 years) and 27 patients (49%) in the elderly group (≥ 65 years). No statistically significant differences were noted when comparing the patient characteristics between the young and elderly groups (Table 1). The median OS following regorafenib treatment was 18 months for the young group and 16 months for the elderly group, although this difference was not statistically significant ($p = 0.534$). A significant difference was found in OS after regorafenib treatment between the elderly group receiving concurrent treatment and those not receiving it ($p = 0.008$) (Figure 1).

Conclusions: In our real-world data, compared to the clinical trial study, regorafenib demonstrates a better survival benefit in young and elderly patients with unresectable HCC after sorafenib. Intriguingly, within the elderly, concurrent treatment significantly influenced OS. Further prospective studies are necessary to draw a definitive conclusion.

Abstract Submission No. 100600
P-0523

Impact of grip strength in hepatocellular carcinoma treated with atezolizumab plus bevacizumab.

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Background & Aims: This study evaluated the impact of sarcopenia-related factors (muscle strength and skeletal muscle mass) on the survival of unresectable hepatocellular carcinoma (u-HCC) patients treated with atezolizumab bevacizumab (ATZ+BEV).

Methods: This observational study enrolled patients with u-HCC who received ATZ+BEV from October 2020 to September 2023 (n=89). A low muscle mass was defined as skeletal muscle index (SMI) <42 and <38 cm²/m², and low muscle strength was defined as a grip strength (GS) <28 and <18 kg in men and women, respectively.

Results: A decreased GS and decreased SMI were found in 38 and 33 patients, respectively. The median observation period was 9.7 months, with an objective response rate of 39.3%, disease control rate of 80.9%. The OS of the normal GS group was significantly higher than that of the decreased GS group (P<0.01), while that of the normal and decreased SMI groups did not differ markedly (P=0.87). There were no significant differences in the PFS between the normal GS and decreased GS groups (P=0.28) or the normal SMI and decreased SMI groups (P=0.32). A multivariate cox proportional hazards model showed that modified albumin-bilirubin-grade (mALBI) 2b (hazard ratio [HR] 2.34), AFP > 100mAU/ml (HR 2.39) and a decreased GS (HR 3.11) were independently associated with an increased risk of poor prognosis.

Conclusions: In addition to the hepatic functional reserve and tumor marker, a decreased GS was a poor prognostic factor in patients with u-HCC treated with ATZ+BEV.

Abstract Submission No. 100623

P-0524

Difficulty in adjusting the dose modification of cabozantinib in hepatocellular carcinoma

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Background: The aim of this study was to investigate clinical outcomes for cabozantinib in patients with unresectable hepatocellular carcinoma, with focus on the dose modification.

Methods: Thirty-two patients were analyzed. The tumor response was assessed based on RECISTv1.1. Serum aldolase (ALD) value and each trough concentration of cabozantinib (Ctrough) weekly for 6 weeks after starting treatment were measured.

Results: Regarding the initial dose of cabozantinib, 18 patients (56%) received 20 mg (LD group) and 14 patients (44%) received ≥40mg (HD group). The rate of dose reduction, interruption, and dose up rate at 6week was 84%, 47%, and 19%, respectively. Malaise and protein urea were often occurred. There is a significant positive relationship between cumulative Ctrough during 6 weeks and relative dose intensity (RDI) (r = 0.848, p < 0.001). Although there was no significant difference in progression free survival (PFS) between LD group and HD group, group with high RDI during 6 weeks (≥34%) tended to have a longer PFS in low RDI group (5.9M .vs 3.5M, p=0.072). Protein urea,

AST/ALT elevation, and decrease in platelets were more frequently occurred in HD group compared with LD group (p=0.093, 0.049, 0.099). ALD values during 6 weeks significantly correlated with each Ctrough (r=0.664, p<0.001). ROC curve analysis showed that ALD ≥ 9.05 mg/dl accurately predicted the onset of dose reduction and/or interruption, with an area under the 0.804.

Conclusion: Low initial dose of cabozantinib could be feasible. Serum ALD value could be helpful in case of considering the dose up of cabozantinib.

Abstract Submission No. 100627

P-0525

Atezolizumab and Bevacizumab Combined with Radiotherapy for HCC with Macroscopic Vascular Invasion

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Background: Hepatocellular carcinoma (HCC) with macroscopic vascular invasion presents a significant clinical challenge. This retrospective study aimed to evaluate the treatment outcomes of atezolizumab and bevacizumab in combination with radiotherapy for this advanced HCC stage.

Methods: Ten patients diagnosed with HCC accompanied by macroscopic vascular invasion, treated at Asan Medical Center between October 2021 and February 2023, were included. Four patients received atezolizumab and bevacizumab first, followed by radiotherapy after a minimum of six months, while six patients received concurrent therapy. Atezolizumab (1200 mg) and bevacizumab (15 mg/kg) were administered intravenously. The median radiation dose was 35 Gy, delivered in 2.5- to 3-Gy daily fractions, adjusted based on tumor extent and location. Radiologic responses were assessed according to the modified Response Evaluation Criteria in Solid Tumors.

Results: Radiologic responses were observed in 3 (30%) patients, with 30% achieving partial response, 50% stable disease, and 20% progressive disease. Median overall survival and progression-free survival were 17.3 and 8.3 months, respectively. The treatment regimen exhibited manageable toxicity, with grade 1 acute toxicities observed in three patients during combined radiotherapy. Additionally, one patient experienced Child-Pugh score deterioration by ≥ 2 within 3 months post-radiotherapy, and another reported grade 2 pneumonitis and dermatitis following atezolizumab and bevacizumab treatment.

Conclusion: This retrospective study suggests that the combination of atezolizumab and bevacizumab with radiotherapy holds promise as a treatment option for HCC with macroscopic vascular invasion. Nevertheless, further investigations are essential to confirm these findings and establish an optimal management approach for advanced-stage HCC patients.

Abstract Submission No. 100695

P-0526

Prognostic role of diabetes in HCC patients on best supportive care: An Indonesian experience

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Background & Aim: Type 2 diabetes mellitus (T2DM) is a risk factor for hepatocellular carcinoma (HCC). However, the prognostic data related to T2DM and survival in HCC patients treated with best supportive care (BSC) is limited. We evaluated the median overall survival (OS) of HCC patients treated only with BSC, stratified by T2DM.

Methods: This is a single-centre, observational cohort study at Dr Cipto Mangunkusumo Hospital Jakarta Indonesia, a tertiary referral hospital. Survival analysis was performed using Kaplan-Meier method and the log-rank test.

Results: From 2015 to 2021, there were total 417 HCC patients treated only with BSC, with a mean age of 54 years (SD:12.18), 80.1% were male. 48 (11.5%) patients had T2DM. The median OS was 11 months (95% CI: 0.64-21.36) for patients with T2DM, and 8 months for patients without T2DM (95% CI: 4.7-11.3). There was no statistical difference in OS, stratified by T2DM ($p=0.879$).

Conclusion: In our cohort, fewer HCC patients on BSC had T2DM. T2DM did not appear to affect survival in HCC patients on BSC.

Abstract Submission No. 100727

P-0527

Preoperative weight loss program for HCC patients with high body mass index in hepatectomy.

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Background: This study aimed to investigate the usefulness of a weight-loss program (WLP) in patients with a high body mass index (BMI) prior to liver resection (Hx) for hepatocellular carcinoma (HCC).

Methods: Among 445 patients with HCC who underwent initial Hx between 2000 and 2020, 19 with a high BMI (≥ 25.0) were enrolled in our WLP since 2014. For calorie restriction, the amount of energy consumed was calculated as the standard body weight (SBW) $\text{kg} \times 20\text{--}25$ kcal/day. Protein mass was calculated as $\text{SBW kg} \times 1.0\text{--}1.2$ g/day to maintain skeletal muscle mass. Patients also performed both aerobic and resistance exercises. The before-and-after changes were compared, and the effect of WLP on the short- and long-term results was investigated.

Results: The average length of WLP was 21 days, and weight loss was successfully achieved in all patients. Body fat mass was reduced during the program, while skeletal muscle mass was maintained. WLP led to improvements in liver function and fibrotic markers, without tumor progression. There were no postoperative complications ($\geq$ Clavien-Dindo [CD] III). A retrospective comparison of postoperative outcomes revealed that those in the WLP group showed a significantly shorter operation time and improved postoperative morbidity rate ($\geq$ CD III) with decreased postoperative hospital stay. There were no significant differences in long-term prognosis based on participation in the WLP.

Conclusions: WLP with multidisciplinary intervention improved short-term outcomes after Hx in patients with HCC and a high BMI.

Abstract Submission No. 100770

P-0528

rhTPO and platelet transfusion in HCC patients with severe thrombocytopenia undergoing ablation

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Background: Liver cancer with severe thrombocytopenia (sTCP) usually require prophylactic platelet transfusion before ablation procedures to reduce bleeding risk. Identifying effective medicament has important significance and recombinant human thrombopoietin (rhTPO) maybe a reliable choice.

Methods: Retrospective collection 1487 cases with HCC undergoing percutaneous thermal ablation at Tianjin Third Central Hospital between January 2020 and June 2023. Excluding rhTPO treatment period < 5 days, 105 patients with sTCP ($\text{PLT} < 50 \times 10^9/\text{L}$) were finally enrolled and divided into four groups: control group (no platelet elevation therapy, $n=20$), rhTPO group ($n=12$), combined treatment group (rhTPO and platelet transfusion, $n=25$), and PLT group (platelet transfusion, $n=48$). Evaluation indicators include response rate ($\text{PLT} \geq 50 \times 10^9/\text{L}$ within 48 hours after ablation), complete blood count, liver function, and adverse events.

Results: No difference in baseline characteristics among the treatment groups. In control group, PLT decreased from $46.20 \pm 2.57 \times 10^9/\text{L}$ to $40.20 \pm 8.67 \times 10^9/\text{L}$ after ablation. The treatment response rates were respectively 15.0%, 91.7%, 76.0%, and 47.9% ($P < 0.05$). The postoperative PLT in rhTPO group was higher ($76.92 \pm 26.57 \times 10^9/\text{L}$) than the other groups ($P < 0.05$). It is worth noting that the ALT levels in the rhTPO group (61.42 ± 36.49 U/L) was significantly lower than the other groups, which was partly due to the liver protective effect of rhTPO. No significant adverse events was observed related to rhTPO.

Conclusions: In HCC patients with sTCP undergoing thermal ablation, standard dose and course (5 days and more) rhTPO treatment can effectively increase platelet count, reducing platelet transfusion rate and improving perioperative safety.

Abstract Submission No. 100789

P-0529

Prediction of survival and analysis of prognostic factors for patients with ANHC

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Purpose: Hepatocellular carcinoma (HCC) has a poor prognosis, and alpha-fetoprotein (AFP) is widely used to evaluate HCC. However, the proportion of AFP-negative individuals cannot be disregarded. This study aimed to establish a nomogram of risk factors affecting the prognosis of patients with AFP-negative HCC and to evaluate its diagnostic efficiency.

Patients and methods: Data from patients with AFP-negative initial diagnosis of HCC (ANHC) between 2004 and 2015 were collected from the Surveillance, Epidemiology, and End Results database for model establishment and validation. We randomly divided overall cohort into the training or validation cohort (7:3). Univariate and multivariate Cox regression analysis were used to identify the risk factors. We constructed nomograms with overall survival (OS) and cancer-specific survival (CSS) as clinical endpoint events and constructed

survival analysis by using Kaplan-Meier curve. Also, we conducted internal validation with Receiver Operating Characteristic (ROC) analysis and Decision curve analysis (DCA) to validate the clinical value of the model.

Results: This study included 1811 patients (1409 men; 64.7% were Caucasian; the average age was 64 years; 60.7% were married). The nomogram-based model related C-indexes were 0.762 (95% confidence interval (CI): 0.752-0.772) and 0.752 (0.740-0.769) for predicting OS, and 0.785 (0.774-0.795) and 0.779 (0.762-0.795) for predicting CSS.

Conclusion: The age, ethnicity, tumor diameter, tumor grade, surgery, chemotherapy, and radiotherapy were independent prognostic factors for patients with ANHC. We developed a nomogram model for predicting the OS and CSS of patients with ANHC, with a good predictive performance.

Abstract Submission No. 100803
P-0530

Single-cell sequencing reveals the immune landscape in tumors and PBMCs under immunotherapy

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By single-cell sequencing of hepatocellular carcinoma tissues and PBMCs from six patients, we found in the hepatocellular carcinoma tissues that the single-cell sequencing ended up dividing a total of 18 subpopulations, including 11 hepatocellular carcinoma cell subpopulations, which suggests that there is already a significant heterogeneity among tumor cells within the hepatocellular carcinoma itself. Second, we found that within the group with poorer immunotherapy efficacy, macrophages were significantly suppressed in hepatocellular carcinoma tissues, with their numbers and proportions significantly decreased. Differential gene function enrichment of macrophages also revealed that their functions such as antigen-presenting function and T-cell activation were suppressed, and in terms of other immune cells, T-cells and NK-cells did not differ significantly between groups. This suggests that the diminished antigen-presenting function may have contributed to the diminished killer T-cell function and thus the efficacy of immunotherapy. In PBMC, we also found reduced proportions of B cells and macrophages within the less efficacious group, and functionally found a significant reduction in the classical macrophage lineage in the macrophage subset of the less efficacious patients. This suggests that interactions between immune cells may be one of the key influences on the efficacy of immunotherapy.

Abstract Submission No. 100867
P-0531

One case of hepatitis B cirrhosis complicated with liver cancer was cured

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One case of hepatitis B cirrhosis complicated

with liver cancer was cured

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He is a 56-years-old male patient. The patient had an abnormal hepatitis B series in 1998. In August 2008 the patient was diagnosed with liver cancer in the General Hospital of the Chinese People's Liberation Army, he underwent right hepatocellular carcinoma resection, the right liver was moderately differentiated hepatocellular carcinoma and cirrhosis. In 2010, Tenofovir was started. In 2020, due to drug resistance, "Tenofovir" will be replaced with "Tenofovir dipifurate fumarate". 2021.2 Return visit to our clinic. we carried out various examinations: hepatitis B series quantitative: HBsAg 213.35 IU/ml HBsAb < 0.5 mIU/ml HBcAb 0.03 (S/CO) HBcAb 15.3 (S/CO); HsHBV DNA was Not detected (IU/ml); ALT 22 (U/L), AST 19 (U/L); abdominal B-ultrasonography: liver parenchyma echo slightly coarse; Child-Pugh Grade A. After the contraindication of interferon was ruled out for evaluation, Peg-IFN-α2b 135 μg subcutaneous injection was started once a week. HBsAg decreased to 19.85 IU/ml at 20 weeks, but abnormal thyroid function was found at that time, and T4 was slightly elevated. The patient's thyroid function returned to normal after 1 month of disuse. HBsAg 7.76 IU/ml at 24 weeks, in order to avoid the side effects caused by interferon, Peg-IFN-α2b 90 μg was used for further treatment from 24 weeks, HBsAg 0.06 IU/ml at 72 weeks and HBsAg 0.05 IU/ml at 84 weeks. At the 96th week, HBsAg of the patient was 0 IU/ml, HBsAb was greater than 10 mIU/ml for the first time, and was 37.98 mIU/ml, achieving clinical cure.

Abstract Submission No. 100872
P-0532

Citrullinated Glial Fibrillary Acidic Protein Is Related with Prognosis of Hepatocellular Carcinoma

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Citrullination is a posttranslational modification via peptidylarginine deiminases (PAD), leading to significant alterations in protein structure and function. Glial fibrillary acidic protein (GFAP), highly susceptible to the attack of PAD, was increased in activated hepatic stellate cells and myofibroblasts accumulated in hepatic fibrosis. Recently, although the expression of citrullinated GFAP (cit-GFAP) is increased in hepatic fibrosis, its expression and role of cit-GFAP in hepatocellular carcinoma (HCC) is unknown. This study investigated whether the expression of cit-GFAP affects recurrence and survival in HCC patients who underwent hepatic resection. A total of 168 HCC patients were enrolled (median follow-up: 39 months). Eighty-one cases of HCC demonstrated a higher expression of cit-GFAP. The expression of cit-GFAP was correlated with male sex, hepatitis B virus positivity, and higher Edmonson-Steiner grade. There was no association between cit-GFAP expression and age, diabetes mellitus, hypertension, liver cirrhosis, Child-Pugh class, major portal vein invasion, white blood cell counts, platelet counts, serum alanine transferase, total bilirubin, albumin, alpha-fetoprotein, HCC size or number. The mortality

rates in HCC patients with higher cit-GFAP expression were worse than those with lower cit-GFAP expression. After multivariate cox analysis, larger tumors and higher cit-GFAP expression were independent risk factors for postoperative survival. The recurrence rates of patients with higher cit-GFAP expression were slightly higher than those of patients with lower cit-GFAP expression, but it was not statistically significant. We report the abnormal accumulation of cit-GFAP in patients with HCC. Also, cit-GFAP expression is closely associated with survival of HCC patients.

Abstract Submission No. 100894

P-0533

Higher platelet count can be a biomarker to suspect HCC in patients with CLD.

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BACKGROUND: Hepatocellular carcinoma (HCC) is the third most common cause of cancer deaths worldwide. Several clinical studies have indicated correlation between high platelets (PLT) and increased risk of distant metastasis & post-transplant recurrence of HCC. However, the correlation of PLT with occurrence of HCC & BCLC staging and etiology & severity of underlying CLD are not well studied.

AIM: To assess the role of platelet counts in predicting occurrence of HCC in patients with chronic liver disease (CLD) of various etiologies.

METHODS: 100 CLD patients were divided equally in group A (HCC) and group B (Non HCC). PLT counts were compared between two groups using statistical methods. PLT counts were also compared in HCC group for different stages of BCLC & underlying severity and etiology of CLD.

RESULTS: PLT counts were significantly higher in group A compared to group B ($p < 0.0001$). Statistical significance observed in subgroup of MASLD ($p < 0.0012$) between group A and B. Statistical significance ($p < 0.02853$) observed between different CTP stages in group A with respect to PLT count using one way ANNOVA test. There was no statistical significance observed when PLT counts were compared in group A with respect to different stages of BCLC.

CONCLUSION: Higher PLT counts were observed in patients with HCC compared to those without it. PLT counts correlates with severity of underlying CLD and MASLD etiology in HCC patient. PLT counts did not correlate with BCLC staging of HCC. So, high PLT counts can be used to suspect HCC in patients with CLD.

Abstract Submission No. 100913

P-0534

Machine-learning based prediction of microvascular invasion and early recurrence in HCC under 5cm

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Background/Aim: Tumor size is known to be a major risk factor for microvascular invasion (MVI) which is highly correlated with postoperative recurrence in patients with hepatocellular carcinoma (HCC). However, it is difficult to predict MVI before surgery in patients with HCC less than 5 cm. Recently, radiomics-based machine learning has emerged as a powerful tool to determine the characteristics of tumors. This study aimed to develop a machine-learning based radiomics model to predict MVI and early recurrence (<2 years) in patients with HCC less than 5 cm.

Method: We retrospectively enrolled 280 patients from four institutions who underwent surgical resection for HCC less than 5cm between March 2011 and August 2018. Radiomics features were extracted from abdominal CT images of HCC. We used four machine learning-based algorithms including Logistic Regression (LR), Support Vector Machine (SVM), Random Forests (RF) and Extreme Gradient Boosting (XGB). Each dataset was tested with 5-fold cross-validation.

Result: The average age of all patients was 59.0 years, and they were predominantly male (78.6%). In 78 patients (27.9%), MVI was confirmed, and 56 patients (20.0%) had early recurrence. The area under the curve (AUC) to predict MVI were 0.749 for LR, 0.733 for MLP, 0.727 for RF, 0.789 for XGB. AUC to predict early recurrence were 0.693 for LR, 0.577 for MLP, 0.659 for RF, 0.607 for XGB.

Conclusion: We confirmed that the machine-learning based radiomics model can predict MVI and early recurrence in patients with HCC less than 5 cm. Further validation is needed.

Abstract Submission No. 100917

P-0535

Update on HBV versus non-HBV related Hepatocellular Cancer in the Philippines

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Background: Hepatocellular carcinoma (HCC) is the 2nd leading cause of cancer death in the Philippines. Previous reviews place Hepatitis B as the most common cause of HCC in Filipinos. Globally, metabolic syndrome is an emerging risk factor for HCC. This study reviews clinical features of HBsAg + vs HBsAg- HCC in a Filipino cohort.

Methods: Clinical data of 89 Filipino patients with HCC enrolled in the CANDLE Study were analyzed. Differences between HBV-related and non-HBV-related HCC patients were analyzed.

Results: Non-HBV HCC were more likely cirrhotic (86.05% vs 56.52%). Additionally, over half (53.5%) of patients in the non-HBV group were anti-HBc reactive. HBsAg negative HCC patients were more likely to have components of metabolic syndrome: diabetes (48.84% vs 17.39%), dyslipidemia (41.86% vs 8.70%), and obesity (66.67% vs 26.92%). However, HBV-related HCC were older (66 vs 55), had higher body mass index (BMI) (26.5 kg/m² vs 23.6 kg/m²)

and fasting blood sugar (FBS) levels. Both HBsAg+ and the HBsAg-HCC had a significant number of patients with normal AFP (16.7% and 22.5%) and PIVKA II (16.7% and 10.0%).

Conclusion: Hepatitis B persists as an important risk factor for HCC in the Philippines. Comorbid diseases like diabetes, dyslipidemia, and obesity should be considered as important risk factors that potentiate HCC risk in HBsAg reactive and negative populations. A reconsideration of current screening guidelines based on these findings may increase sensitivity for HCC detection.

Abstract Submission No. 100944

P-0536

Delphi consensus statement on the etiology of first-episode hepatocellular carcinoma in our hospital

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Purpose: Hepatitis B can be controlled with nucleic acid analogs, and hepatitis C can be eliminated with direct-acting antiviral agents. On the other hand, hepatocellular carcinoma (HCC) of non-B nonC (non-B nonC), which is non-viral in nature, is becoming more prominent.

Subjects: We included 88 cases of first-episode hepatocellular carcinoma (HCC) diagnosed at our hospital between January 2018 and September 2023.

Methods: We investigated the etiology of first-episode hepatocellular carcinoma patients at our hospital assigned since 2018, following the nomenclature according to the Delphi consensus statement published in the Journal of Hepatology.

Results: There were 5 cases of hepatitis B (6%), 21 cases of hepatitis C (24%), and 62 cases of non-B non-C hepatitis (70%).

Fifty-three percent of 21 hepatitis C cases and 70% of 62 non-B non-C hepatocellular carcinomas were MAFLD, MASH, or MetALD associated with metabolic syndrome.

Conception and Conclusion: It is important to strengthen collaboration with regional cardiology, neurology, nephrology, and diabetes and metabolic medicine departments with metabolic syndrome-related diseases to provide consultation for cases with ALT >30U/L, which is the criterion for Steatotic liver disease.

Abstract Submission No. 100965

P-0537

The efficacy and safety of atezolizumab/bevacizumab versus lenvatinib for hepatocellular carcinoma

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Background: The success of the multinational phase III REFLECT and IMbrave 150 trial demonstrated the efficacy of lenvatinib (LENV) and atezolizumab/bevacizumab (ATE/BEV) in advanced hepatocellular carcinoma (HCC) patients with preserved liver function. We aimed to compare the efficacy of and safety of the two regimens in the setting of first-line treatment for unresectable HCC patients.

Methods: We conducted a single-center, retrospective study of HCC patients who received either ATE/BEV (n=80) or LENV (n = 50), between February 2019 and March 2023 from CHA Bundang Medical

Center. We analyzed progression-free survival (PFS) and overall survival (OS) in relation to the baseline patient characteristics.

Results: Median age was 62 years, with male predominance (87.4%). Mean OS time was significantly longer in ATE/BEV group (23.6 vs 21.7months; $p<0.001$). The OS time in ATE/BEV group has not yet reached the median. Patients with Child-Pugh A had better OS than those with Child-Pugh B (32.6 ± 1.8 , 17.2 ± 21.9 months, $p<0.001$). Also, patients with ALBI grade I had better OS than those with ALBI grade 2 and 3 (32.0 ± 2.1 vs 25.2 ± 2.7 , $p=0.11$). Meanwhile, lower baseline AFP (<200) or PIVKAI (<100) were associated with longer OS. In multivariate analysis by Cox regression hazards model, treatment regimen was the only independent prognostic factor associated with OS. Also, the patients with viral hepatitis did not show better outcome when compared with those without viral hepatitis in both groups. Lastly, the proportion of the patients with worsening liver function, whose ALBI or MELD scores increased 3 months after treatment, was not different in both groups.

Conclusion: In this real-world study, ATE/BEV showed significantly superior efficacy in terms of survival time when compared with LENV in unresectable HCC patients regardless of the cause of hepatitis. The safety in terms of liver function preservation was not different between the both treatment groups.

Abstract Submission No. 101020

P-0538

LASSO-Based Machine Learning model for Prediction of Liver Failure in HCC Patients Undergoing TACE

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PURPOSE: Transcatheter arterial chemoembolization (TACE) is a commonly used method for the nonsurgical treatment of hepatocellular carcinoma (HCC); however, it can cause liver failure with rapid progression and high mortality.

METHODS: We organized and analyzed the data of patients with HCC undergoing TACE at our hospital. Screening indicators related to liver failure were analyzed using least absolute shrinkage and selection operator (LASSO) regression to establish a predictive model (Fig A).

RESULTS: Prothrombin activity (odds ratio [OR] [95% confidence interval (CI)], 0.965 [0.931-0.997]; $p=0.040$), tumor number (OR [95% CI], 2.328 [1.044-5.394]; $p=0.042$), and vascular invasion (OR [95% CI], 2.778 [1.006-7.164]; $p=0.039$) are independent risk factors for liver failure after TACE, and a nomogram was developed for clinical applications (Fig B). The prediction model established based on these results had areas under the curve of 0.821 and 0.813 for the training (Fig C) and validation groups, respectively. Additionally, decision curve analysis curves were obtained, demonstrating that the predictive model yielded more net benefits (Fig D).

CONCLUSION: The prediction model established using LASSO regression can predict the risk of liver failure after TACE and confirm whether patients with advanced HCC can benefit from TACE.

Abstract Submission No. 101047

P-0539

The Utility of PIVKA-II as a Biomarker For Treatment Response In Hepatocellular Carcinoma

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Background: There have been significant advances in the diagnosis and treatment for hepatocellular carcinoma in recent years, however, progressive disease remains difficult to cure. Consequently, there is a growing need for biochemical markers which will potentially detect disease progression after treatment, and guide decisions to switch therapy.

Methods: This was a single center, retrospective analytical cohort study. Data was collected from Early, Intermediate or Advanced stage HCC patients, who received: Ablation, transarterial chemoembolization, resection, tyrosine kinase inhibitors, or atezolizumab + bevacizumab. Baseline demographics were taken. Pre and post treatment AFP and PIVKA II levels were then gathered. Comparisons of PIVKA-II and AFP across cohort characteristics were performed using Spearman's (rho) correlation coefficients. Analyses were performed using IBM SPSS 22 with $p < 0.05$ deemed to be indicative of statistical significance.

Results: Results show a concordance of PIVKA II levels with treatments responses by mRECIST criteria. A significant difference was seen in the pre-treatment and post-treatment PIVKA II levels in patients who underwent resection and received tyrosine kinase inhibitors. A positive relationship between PIVKA-II with the size of the largest HCC lesion by imaging was depicted.

Participants were predominantly male with non-viral causes as etiology.

Conclusions: Our study reveals an association of PIVKA II with tumor size and its concordance with treatment response by imaging criteria. Using AFP alone may not discriminate between pre and post treatment responses but the addition of PIVKA II or the use of PIVKA II alone may serve as a better predictor of response to treatment.

Abstract Submission No. 101074

P-0540

The change of hepatic function after RFA/MWA to early stage HCC in patients with CSPH assumed by LSM

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Background: Ablation treatment such as radiofrequency ablation (RFA) or microwave ablation (MWA) for early stage hepatocellular carcinoma (HCC) thought to have little effect on liver function. However, it is unclear whether ablation does not affect liver function even in patients with clinical significant portal hypertension (CSPH). We aimed to investigate whether ablation treatment reduces liver function in patients with CSPH assumed by liver stiffness measurement (LSM) of transient elastography.

Methods: 71 cases with CSPH in which ablation treatment was performed for early stage HCC were retrospectively analyzed. The diagnosis of CSPH was defined according to the BAVENO VII criteria as cases that met either of the following: (1) $LSM \geq 25kPa$, (2) $LSM 20-25kPa$ and platelet value $<15 \times 10^9/L$, and (3) $LSM 15-20kPa$ and platelet value $<12 \times 10^9/L$. Changes in liver function was examined using data before and 6 months after treatment.

Results: The median age was 71 years, and LSM was 23.6 kPa. 14 patients (19.7%) had Child-Pugh Grade B. Changes in parameters after 6 months of treatment were: PT%: 81.2% to 80.0% (median change: -0.6%, $p = 0.258$), ALBI score: -2.36 to -2.34 (+0.02, $p = 0.188$) and no significant changes were observed. Although FIB4 increased from

5.94 to 6.41 (+0.30, $p = 0.028$), FIB3 did not significantly decrease from 4.95 to 5.13 (+0.04, $p = 0.203$), suggesting the influence of aging. In the analysis of pre-treatment factors that contribute to deterioration of liver function after ablation treatment using ALBI score, significant factors were not extracted.

Conclusion: RFA/MWA does not affect liver function in patients with CSPH assumed by LSM.

Abstract Submission No. 101083

P-0541

4D ULTRASONOGRAPHY FOR THERAPEUTIC RADIOFREQUENCY ABLATION FOR HEPATOCELLULAR CARCINOMA**Naoki Hotta¹**¹masuko memorial hospital JAPAN Japan

INTRODUCTION: Studies to evaluate the tumor vascularity in HCC have been done extensively with various imaging modalities because the finding of the vascularity is helpful to evaluate the biological features of the tumor. In the present study, we investigated whether 4D real-time flow imaging is useful to display the accurate position of percutaneous radiofrequency ablation (RFA) needle in the tumor and evaluated the efficacy of RFA therapy in patients with HCC. **MATERIALS** All patients gave written informed consent and this protocol had been approved by the Human Studies Committee at Masuko Memorial Hospital. **US imaging** We used VOLUSON730 (GE Medical systems, Milwaukee), APLIO XG (Toshiba Medical Systems) and IU22 (Phillips) for RFA therapy with a convex probe as US system. APLIO and VOLUSON machine probe is mechanical probe and IU22 probe is matrix array probe. **4D Real-time** refers here to the display of 3-dimensional moving images composed of 3 orthogonally intersecting scans in the transverse, longitudinal and horizontal planes. RF ablation was carried out under a real-time US guidance.

RESULTS: We confirmed by various angles that the needle was inserted into the center of tumor nodule. The simultaneous study before RFA therapy showed the inflow of arterial blood and tumor stain. And importantly it appeared that 4D real-time US provided much perceptible information on the spatial relationship between RFA needle and the target lesion, and resulted in accurate treatment. We experienced the treatment of 58 patients with HCC by RFA using 4D real-time ultrasound system. Application of this method allowed a more accurate cauterization of the tumor.

Abstract Submission No. 101096

P-0542

Performances of GAAD Score, PIVKA-II, and AFP for Hepatocellular Carcinoma Surveillance

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Background: Hepatocellular carcinoma (HCC) is an important burden in chronic liver diseases (CLD). According to APASL guidelines, the recommended approach for HCC surveillance is a biannual combination of ultrasonography (US) and serum alpha-fetoprotein (AFP).

Prothrombin induced by vitamin K absence-II (PIVKA-II) represents a novel HCC biomarker, and the GAAD score is calculated based on gender, age, AFP, and PIVKA-II. This study aimed to assess the clinical performance of GAAD score, PIVKA-II, and AFP for HCC surveillance.

Method: This cross-sectional study was conducted at Siriraj Hospital, Thailand, between May and October 2023, included CLD patients at risk for HCC, both post-treatment and without HCC history. US, along with AFP and PIVKA-II was used for surveillance. HCC was diagnosed based on CT/MRI or histology in patients with new lesions or abnormal biomarkers.

Results: There were 77 enrolled patients, with 11 patients (14.3%) diagnosed with HCC, one newly diagnosed, and 10 post-treatment HCC. The mean age was 66.29±10.12 years, and 55.8% had cirrhosis. The etiologies of CLD were mainly chronic hepatitis B (CHB), followed by hepatitis C. At baseline, cirrhotic patients, CHB, and alcoholism were significantly more prevalent in HCC group compared to non-HCC group. The sensitivity for HCC detection was highest in the GAAD score (63.6%), followed by PIVKA-II (54.5%) and AFP (45.5%), all of which had high specificity (>85%). Moreover, ROC analysis revealed that the GAAD score showed high performance in distinguishing HCC from non-HCC group.

Conclusion: The GAAD score demonstrated high performance in HCC detection among patients with CLD.

Abstract Submission No. 101100

P-0543

Clinical features of HCC patients treated with RFA, in whom immunoadjuvant therapy should be used

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Background/Aim: The IMbrave050 trial (IM050) reported a significant reduction in recurrence of hepatocellular carcinoma (HCC) with atezolizumab plus bevacizumab (Atez/Bev) after curative therapies, but the prognostic value of this treatment is unknown. Although the indication of radiofrequency ablation (RFA) is wider than that of resection, adjuvant treatment can be problematic in terms of cost and risk of side effects. The clinical factors that should be aggressively treated with adjuvant therapy after RFA are identified, with a focus on recurrence beyond the Milan Criteria (MC), because the recurrence beyond MC makes curative treatments unfeasible and shortens the prognosis.

Materials/methods: From 2000 to July 2023, 528 patients with Child-Pugh A, who were diagnosed and treated at our hospital and who underwent radical treatment (resection/RFA) and met the tumor criteria for RFA of IM050 were enrolled, after excluding cases with missing data and cases with autoimmune disease. Risk factors for recurrence of MC deviation were examined retrospectively (IRB No. 26-11).

Results: The Cox proportional hazards univariate analysis showed that the risk factors for recurrence beyond MC were HCV positivity (HR 1.61), HBV positivity (HR 0.54), AFP (>100ng/mL) (HR 1.58), L3 (>10%) (HR 2.0), PIVKA-II (>100mAU/mL) (HR 1.86) (each P<0.05) and multivariate analysis showed that the risk factors for recurrence beyond MC were HCV positive in multivariate analysis (HR 1.53), L3 (>10%) (HR 1.8), PIVKA-II (>100mAU/mL) (HR 1.81) (each P<0.05). Each factor was scored as 1 point. Median period for recurrence beyond MC (months) for scores 0/1/2 or higher was not reached/103/49, median period for first recurrence (months) was 42/29/22, median overall survival (months) was 118/85/59. In resected patients, hepatic vein invasion, portal vein invasion, and poorly-

differentiation were 0/1.1/6.6/15.8% each for scores 0/1/2/3, 2.0/12.1/14.1/31.6%, and 6.0/6.7/15.3/15.8%, respectively (each <0.01).

Conclusion: As scores increase, both time to first recurrence and time to recurrence beyond MC became shorter. Patients with a score of 2 or more in MC who undergo RFA should aggressively consider Atez/Bev adjuvant therapy, as it might prolong time to recurrence beyond MC by suppressing recurrence.

Abstract Submission No. 101111

P-0544

Changes in systemic chemotherapy for unresectable HCC and its effect on overall survival

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Background/Aims: In 2009, sorafenib (SOR), the first molecular target agent (MTA), was approved for the treatment of unresectable hepatocellular carcinoma (uHCC). Then there was a long gap until lenvatinib (LEN) in 2018. Since then, a series of regimens including five MTAs and two immune checkpoint inhibitors (ICIs) have been introduced and made available. This study aims to elucidate the evolution of systemic pharmacotherapy in a community hospital.

Material/Methods: We included 220 patients with uHCC who received initial systemic chemotherapy at our hospital from May 2009 to August 2023. In according with the advent of new drugs, we divided 2009-2023 into four groups as follows: group G1 (n=47: 2009-2013), group G2 (n=71: 2014-2017), group G3 (n=57: 2018-2020), and group G4 (n=45: 2021-2023). Clinical background and number of used lines at the time of initial systemic chemotherapy induction in each group were analyzed retrospectively.

Results: There were significant differences in the proportion of males (G1/G2/G3/G4=95.7/84.5/73.7/82.2 %, P=0.027), Alb (3.7/3.9/3.7/4.0 g/dL, P=0.032), mALBI 1 ratio (29.8/54.9/42.1/46.7 %, P=0.017), AFP (289/99/98/13 ng/mL, P=0.014), PIVKA-II (2387/180/292/104 mAU/mL, P<0.001) and BCLC stage B ratio (21.3/46.5/49.1/35.6 %, P=0.016). There were no significant differences in age (70/71/73/72 years), ALBI score (-2.48/-2.65/-2.53/-2.60), PT (87.4/88.0/87.0/86.0 %), platelet count (13.6/12.7/13.6/14.1 x104/mL), PS, maximum diameter of intrahepatic tumor and number of intrahepatic tumors. The most frequently used drugs by group were G1/G2/G3/G4 (%)=SOR (100)/SOR (94.4)/LEN (47.4)/Atez/Bev (82.2) (P<0.001), and the mean number of lines was G1/G2/G3/G4=1/1.42/1.86/1.49, P<0.001. Median overall survival (OS) was G1 vs. G2 vs. G3 =11.5 vs. 23.6 vs. 21.6 months, indicating a prolonged prognosis (21.3 months for G4, where most patients are currently continuing treatment). OS (median) for patients with mALBI 1/2a was G1 vs. G2 vs. G3 =12.6 vs. 25.8 vs. 29.5 months, indicating improved prognosis.

Conclusion: As the concept of TACE refractoriness/unsuitability became more widespread and the timing of systemic chemotherapy introduction became earlier, the number of patients with good liver reserve function and BCLC stage B patients increased. As a result, the number of available regimens increased, and the number of used lines increased, resulting in improved OS in patients with good liver reserve function. The ICI regimen, which is expected to be more effective, has become the mainstream regimen, and is expected to further improve OS in the future.

Abstract Submission No. 101112

P-0545

Cause of Death Analysis in Patients with Metastatic Liver Cancer Treated with Local Therapy

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Objective: In our hospital, local therapy such as radiofrequency or microwave ablation is aggressively applied to patients whose prognosis is determined by the progression of liver metastases, regardless of the size or number of tumors. There is an accepted opinion that local therapy for liver metastases is ineffective because Stage IVB is a systemic disease, but we attempted to verify this opinion based on the actual causes of death of patients treated with local therapy.

Methods: We included 450 patients with metastatic liver cancer treated locally between April 2006 and December 2020. The primary tumors included 28 organs: colorectal cancer (59%). 371 patients died, and the cause of death was classified into cancer and non-cancer deaths, and cancer deaths were classified into liver-related and non-liver-related deaths. There were 128 deaths in our hospital, and the cause of death was identified comprehensively, including imaging and blood tests. For deaths occurring outside the hospital, the institution was asked to provide the cause of death, if known, and a written response was obtained.

Results: There were 115 patients with unknown cause of death, and these were excluded from the analysis of 256 patients. Of the 114 patients who died in our hospital, 38 (33%) died of liver-related causes, and of the 142 patients who died outside our hospital, 73 (51%) died of liver-related causes.

Conclusion: It was possible to estimate that local therapy prolonged life in at least one-third of patients who died after receiving local therapy for liver metastases.

Abstract Submission No. 101127

P-0546

Efficacy of Immunotherapy and Targeted Therapy for Unresectable HCC: Analysis of Survival Curves

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Background and objectives: Hepatocellular carcinoma is the third-leading cause of cancer-related death worldwide. We used parametric survival models to assess the efficacy of immunotherapy and targeted therapy as first-line strategies for treating unresectable hepatocellular carcinoma, based on an analysis of the evidence from phase III trials.

Methods: The PubMed, Embase, and Cochrane Library databases were searched for studies reporting patient data of overall survival (OS) and progression-free survival (PFS) as Kaplan-Meier curves. Data was obtained from the curves using a digitization software. A pooled analysis of the parametric survival curves was performed using a Bayesian framework.

Results: Twelve randomized controlled trials were included, and log-normal and log-logistic distributions provided the best fits for the OS and PFS data, respectively, suggesting that the proportional hazard assumption is not valid. The sintilimab plus bevacizumab biosimilar therapy achieved superior OS and PFS compared to other treatments. The efficacy of the sintilimab plus bevacizumab biosimilar was typically ranked first within previous studies.

Conclusions: The hazard ratios are not constant over time. Sintilimab plus bevacizumab biosimilar therapy is more efficacious than other treatments in terms of OS and PFS during the first 60 months of treatment.

Keywords: Unresectable hepatocellular carcinoma, Immunotherapy, Targeted therapy, Tyrosine kinase inhibitor, Immune checkpoint inhibitor, Parametric survival analysis

Abstract Submission No. 101141

P-0547

Expression of ESPL1 Gene in HCC Tissue and Its Prognostic Role in HCC

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Aim: This study aimed to investigate the expression of the ESPL1 gene in hepatocellular carcinoma (HCC) and its impact on clinical prognosis.

Methods: We obtained expression data and clinical information of ESPL1 from HCC patients in the TCGA database. Comparative analysis was performed on ESPL1 expression in cancerous, adjacent non-cancerous, and normal tissues. COX regression and Kaplan-Meier analyses were used to assess the association between ESPL1 expression levels and patient prognosis. ESPL1 mutation analysis was carried out using the cBioportal online tool, and a protein interaction network for ESPL1 was constructed using the STRING database for GO/KEGG enrichment analysis to elucidate its molecular functions.

Results: ESPL1 expression levels were significantly higher in HCC tissues compared to adjacent non-cancerous and normal tissues. Additionally, higher ESPL1 levels were observed in HBV-related HCC cases. Primary tumor stage and ESPL1 expression were identified as independent risk factors for the prognosis of HCC patients, with higher ESPL1 expression associated with poorer prognosis. The mutation rate of ESPL1 in HCC patients was approximately 1%, and patients with mutations had a significantly poorer prognosis. Enrichment analysis indicated that ESPL1 is primarily involved in biological functions related to the cell cycle, mitosis, and chromosome segregation.

Conclusion: Our findings suggest that ESPL1 is upregulated in HCC, particularly in cases related to HBV infection, and high expression of ESPL1 is associated with poor prognosis in HCC patients. Therefore, ESPL1 may potentially serve as a biomarker for adverse prognosis in HCC patients.

Abstract Submission No. 101151

P-0548

Epidemiology of Hepatocellular Carcinoma in Taiwan

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Background: Hepatocellular Carcinoma (HCC) is a major contributor to the world's cancer burden and incidence rates have increased in many countries. In recent decades. In more recent years, however, the increase in some countries, such as the US, has abated. It is interesting to understand HCC incidence rate in Taiwan.

Methods: We searched the database of NHI, which covers over 99% of the Taiwanese population, for patients who diagnosis as HCC and listed in Registry for catastrophic illness patients during years 2013-2020. The systemic therapy usage and heart failure/chronic kidney disease comorbidity were also studied.

Results: The incidence rate of HCC in Taiwan was decreasing from 57.8 in a hundred thousand in year 2013 to 48.1 in a hundred thousand in year 2020. Among these HCC patients, the percentage of patients were receiving systemic therapy was increasing from 24.4% in year 2013 to 26.3% in year 2020. The comorbidity in HCC patients were about 9.8%-11.9% in heart failure and 17.9%-22.5% in chronic kidney disease among years 2013-2020.

Conclusions: The incidence rate of HCC was slightly decreasing in Taiwan. Additional studies are needed to improve prevention strategies and advance management of patients with HCC, especially in the field of tumor regression therapies.

Abstract Submission No. 101191
P-0549

Clinical Outcomes of Atezolizumab plus Bevacizumab in Patients with Child-Pugh Classification B

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Purpose: Atezolizumab plus Bevacizumab (Ate/Bev) is widely used as the first-line therapy for unresectable hepatocellular carcinoma (uHCC). The IMbrave150 study was conducted in patients with Child-Pugh classification A (CP-A) uHCC. However, some patients with Child-Pugh classification B (CP-B) have also received Ate/Bev in a natural clinical setting. This study evaluated the outcomes of Ate/Bev in patients with CP-B uHCC.

Methods: From October 2020 to Aug 2023, 52 patients received Ate/Bev for uHCC in our hospital. Of these, 38 were CP-A patients, and 14 were CP-B patients. Clinical features, OS, PFS, therapeutic response, and changes in liver function of each group were examined.

Results: Median OS was 18.4 months in CP-A vs. 7.3 months in CP-B ($p=0.418$), and median PFS was 6.1 months in CP-A vs. 3.7 months in CP-B ($p=0.34$). OS and PFS tended to be longer in CP-A, but no significant difference was observed. ORR was 22.5% in CP-A vs. 18.2% in CP-B, and DCR was 71.0% in CP-A vs. 72.7% in CP-B, not significantly different. ALBI scores were -2.40 before treatment and -2.16 after 6 weeks in CP-A, and -1.71 and -1.71 in CP-B. The rate of change was 9.9% in CP-A and 17.0% in CP-B, with a slightly higher trend toward worsening in CP-B, although the difference was not significant.

Conclusion: Although patients should be carefully selected, some therapeutic effects of Ate/Bev can be expected in patients with CP-B.

Abstract Submission No. 101195
P-0550

Association between early job loss and prognosis among hepatocellular carcinoma survivors

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Background: given the high probability of unemployment or job loss among hepatocellular carcinoma (HCC) survivors, studies investigating the health effects of the loss of economic activity among patients with HCC are necessary. This study aims to examine the risk of all-cause mortality by early job loss among HCC survivors.

Methods: This retrospective cohort study from National Health Insurance Service data in Korea recruited patients aged 35–54 who diagnosed with HCC and had undergone either surgical procedure or local ablation between January 2009 to December 2015. The primary and secondary outcomes were all-cause mortality and HCC recurrence, respectively. Early job loss was defined as a change in insurance type from economic active status to dependent within 1 year from the treatment date. Adjusted hazard ratio (HR) and 95% confidence interval (CI) were estimated using multivariable Cox regression models. Subgroup analyses were further performed.

Results: Among 4,578 patients (median follow-up, 8.3 years), 1,189 patients (26.0%) died: 989 (24.7%) in the Job-maintained group and 200 (35.0%) in the Early Job loss group ($p<0.001$). Early job loss was significantly associated with the increased risk of all-cause mortality, but not that of HCC recurrence (adjusted HR [95% CI] 1.52 [1.30–1.78] and 1.07 [0.91–1.25], respectively). Subgroup analyses presented individuals with middle-income level, non-liver cirrhosis, non-alcoholism, or surgical resection have a prominently higher risk of all-cause mortality.

Conclusion: Our study found a significant association between increased risk of all-cause mortality and early job loss among HCC survivors undergoing curative treatment.

Abstract Submission No. 101197
P-0551

Efficacy/safety of sequential therapy with short-term LEN followed by TACE for unresectable HCC

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Background: The TACTICS-L trial reported the efficacy and safety of lenvatinib (LEN)- hepatic artery chemoembolization (TACE) sequential therapy, in which LEN is administered for 15-21 days followed by TACE. However, the duration of LEN before TACE is controversial. In this study, we performed TACE after short-term (7-day) administration of LEN (short-term LEN-TACE), and examined its effectiveness and safety.

Methods: Patients with unresectable HCC, BCLC stage A or B, maximum tumor diameter <7 cm and Child A liver reserve were included in this study. TACE was performed after taking LEN for 7 days and a 2-day break, and LEN was restarted after TACE. Approximately 4

weeks after TACE, dynamic CT was taken to evaluate efficacy of short-term LEN-TACE.

Results: Thirteen patients underwent short-term LEN-TACE. Ten cases were male, median age was 80 years, 12 cases were recurrent cases. Nine cases within Up-to-7 criteria, median AFP (ng/mL)/PIVKA-II (mAU/mL) 9.4/86. No adverse events of grade 3 or higher were observed, and TACE was performed as scheduled in all cases. Efficacy was evaluated in 10 patients: complete response (CR)/partial response (PR)/progressive disease; 7/2/1. CR was achieved in 4 of the 5 patients in whom decreased intratumor blood flow was observed during CTHA immediately before TACE, and bile duct dilatation without infection occurred after TACE in 3 CR cases.

Conclusions: This study suggested that even after 7 days of LEN administration, changes in intrahepatic hemodynamics occurred, which affected the efficacy of TACE. Short-term LEN-TACE is an effective and safe treatment for unresectable HCC.

Abstract Submission No. 101214
P-0552

Nomograms for Non-Surgical HCC Patients of Asian Descent Undergoing Chemotherapy: A SEER Study

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Background: Non-surgically treated Asian HCC patients receiving chemotherapy are uncommon in clinical practice. This study aims to establish and validate a prognostic nomogram model for predicting overall survival (OS) and cancer-specific survival (CSS) in this patient group.

Methods: Patient data diagnosed with HCC between 2004 and 2015 were extracted from the Surveillance, Epidemiology, and End Results (SEER) database. These patients were randomly divided into a training cohort (n=1868) and a validation cohort (n=802). Prognostic nomograms predicting OS and CSS were constructed based on independent prognostic variables identified from univariate and multivariate Cox regression analyses. The nomograms' effectiveness was assessed using the concordance index (C-index), receiver operating characteristic curve (ROC), and calibration curve, while clinical utility was evaluated using decision curve analysis (DCA).

Results: The independent prognostic factors for OS included age, metastasis, AJCC stage, tumor size, and AFP, while for CSS they were AJCC stage and tumor size. These variables were used to construct nomograms. In the training cohort, the C-indices for the OS and CSS nomograms were 0.712 (0.699-0.725) and 0.728 (0.715-0.741), respectively. The AUC values for predicting 1-, 3-, and 5-year OS were 0.80, 0.78, and 0.77, and for predicting 1-, 3-, and 5-year CSS were 0.82, 0.79, and 0.77, respectively. The calibration curves indicated good performance of the prediction models, and DCA curves demonstrated good clinical utility.

Conclusion: Nomograms for predicting OS and CSS in Asian HCC patients receiving chemotherapy without surgical treatment were developed and validated using the SEER database. These nomograms demonstrated excellent predictive accuracy and clinical utility.

Abstract Submission No. 101350
P-0553

NLR as a predictor of tumor-associated neutrophil activity based on tumor size of HCC

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Introduction: One of the most common malignant tumors worldwide is HCC. Its morbidity and mortality have both recently increased. Neutrophil play important role as known as tumor-associated neutrophil (TAN) activity, which lead to increase size of tumor although the exact relationship isn't fully understood. We elaborate NLR as the representative predictor of TAN activity based on tumor size in HCC.

Objective: This study aimed to determine the role of NLR as predictor of TAN activity based on tumor size and progression in HCC patients.

Method: This is a prospective study involving 93 patients, done at Mohammad Hoesin Hospital Palembang from January to August 2023. Laboratory and imaging examinations were done on each patient.

Results: 93 HCC patients consist of 72 males (77.4%) and 21 females (22.6%) with an average age of 53.47±11.28 years. The majority of causes of HCC are hepatitis B virus (62.4%), hepatitis C virus (5.4%), and other causes (32.3%). Based on the ALBI ratio, Grade 1: 69.9%, Grade 2: 28.0%, and Grade 3: 2.2%. A total of 75.3% participant present with large tumor (≥ 5 cm) and 62.4% participant present with multiple nodules. NLR has a significant positive correlation to tumor size ($r = 0.399$; $p < 0.001$) and metastasis ($r = 0.284$; $p = 0.002$). NLR has a significant negative correlation to survival rate ($r = -0.344$; $p = 0.001$).

Conclusion: NLR is a significant factor influencing tumor size, metastasis, and survival rate of HCC patients. NLR potentially incorporated into the prognostication tool for HCC.

Abstract Submission No. 101354
P-0554

Evolution of Etiologies and Prognosis of Hepatocellular Carcinomas in Lebanon

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Viral hepatitis, once the dominant cause (80%) of hepatocellular carcinoma (HCC), is now overshadowed by metabolic dysfunction-associated steatohepatitis (MASH) due to improved vaccination efforts.

This study aimed to track the evolution of HCC etiologies and patient outcomes in Lebanon across different periods.

This is a monocentric observational study of HCC cases diagnosed in Lebanon between 2000 and 2023 distributed over three periods: P1 (2000-2005), P2 (2006-2015), and P3 (2015-2023).

The study population consists of 275 patients. Sociodemographic data and characteristics of liver diseases and etiologies of HCC, are represented in table 1.

67 (40.9%) patients were not treated, 54 (32.9%) received curative treatment such as hepatectomy, transplantation, radiofrequency, or a combination, and 43 (26.2%) received non-curative treatment including chemotherapy, immunotherapy, chemoembolization, or a combination. P2 has the best survival with an average of 25.6±30.5 months, followed by P1 with 15.4±21.5 months and P3 with 13.0±15.9 months. Survival with curative treatment is 33.3±31.1 compared to 12.0 ±15.4 months in untreated or non-curatively treated patients. Survival according to the therapeutic approach is shown in graph 1. There is a reduction in the survival of HCC diagnosed from 2019 (average 9.7±12.1 months).

In Lebanon, there is a decline in viral-linked HCC due to improved hepatitis programs, and a rise in MASH-related cases. The reduced incidence of HCC as the initial sign of liver disease indicates effective HCC screening in cirrhotics. Patient survival declined between 2019 and 2023, a period marked by the economic crisis of the country and the Covid-19 pandemic; causality to be proven by further studies.

Abstract Submission No. 101356
P-0555

Identification of high-risk groups for non-viral HCC using the FIB-3 index

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Introduction: In recent years, the incidence of non-viral hepatocellular carcinoma (HCC) has been increasing, while viral HCC has been decreasing. Non-viral HCC is not under surveillance and is often diagnosed at an advanced stage. We have recently developed a liver fibrosis prediction score, FIB-3 index. Here we examine the utility of FIB-3 index for identifying high-risk groups for non-viral HCC.

Methods: The subjects were 195 patients with stage 1, early non-B non-C HCC and 82 non-HCC diabetic control patients attending diabetic clinics. Using ROC analysis with HCC as the outcome variable and FIB-3 index, FIB-4 index, APRI, AAR, and AP20 as explanatory variables, we examined the ability to predict high-risk groups for non-viral HCC.

Results: Patient backgrounds were as follows for HCC (N=195) and non-HCC (N=82) groups: age 70 vs 63.5 years ($p=0.001$), male 69.2% vs 54.9% ($p=0.027$), BMI 24.4 vs 24.5 ($p=0.698$), platelets 124,000 vs 237,000/ μ L ($p<0.0001$), AST 38 vs 23 IU/L ($p<0.0001$), ALT 28 vs 21.5 IU/L ($p<0.0001$), showing significant differences. For predicting high-risk non-viral HCC, AUROC was 0.893 for FIB-3 index, 0.889 for FIB-4 index, 0.875 for APRI, 0.712 for AAR, and 0.885 for AP20, with FIB-3 index having the highest value. Dividing subjects at 60 years, FIB-3 index showed similar cutoff values (2.443 vs 2.642) in both age groups, with AUROC 0.888 and 0.897. In contrast, FIB-4 index showed AUROC 0.889 and 0.895 in the two groups, but cutoff values differed greatly (2.416 vs 1.607). APRI and AP20 also showed large differences in cutoff values between age groups. AAR had low AUROC and was not useful for predicting non-viral HCC risk.

Conclusion: FIB-3 index may be useful for identifying high-risk groups for non-viral HCC using a single cutoff value regardless of age.

Abstract Submission No. 101399
P-0556

Serum 25-hydroxylated vitamin D level and prognosis of non-viral hepatocellular carcinoma

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Background: Vitamin D deficiency has been associated with various cancers, including hepatocellular carcinoma (HCC). This study aimed to investigate the association between serum 25-hydroxylated vitamin D [25(OH)D] levels and the prognosis of non-viral HCC.

Methods: Among 713 patients with newly diagnosed non-viral HCC from 1994 to 2019, 119 patients with measurable 25(OH)D levels before initial treatment were included. The patients were divided into four groups based on quartiles of serum 25(OH)D concentration (Q1–Q4), and Kaplan-Meier analysis was used to assess the overall survival. The association between serum 25(OH)D concentration and prognosis was evaluated using Cox proportional hazards models.

Results: The median age of the 119 patients (89 males, 30 females) was 70 years. BCLC stage 0/A/B/C/D were 29/42/35/10/3 patients, and Child-Pugh classification A/B/C were 86/30/3. The median serum 25(OH)D concentration was 12.9 ng/mL, with 89% classified as vitamin D deficient (< 20 ng/mL). No significant differences were observed in BCLC classification ($P = 0.36$), but Q1 showed a trend of fewer Child A in Child-Pugh classification ($P = 0.07$). The median overall survival for Q1, Q2, Q3, and Q4 were 3.6, 4.8, 3.4, and 6.8 years, respectively ($P = 0.4$). Multivariate analysis adjusted for age, sex, Child-Pugh classification, BCLC classification, and AFP (>100 ng/mL) revealed significantly better overall survival in Q4 (adjusted hazard ratio vs. Q1: 0.48, 95% confidence interval 0.23–0.99, $P = 0.0497$).

Conclusion: Serum 25(OH)D concentration was identified as an independent prognostic factor in patients with non-viral HCC. Further accumulation of cases and additional investigations are necessary.

Abstract Submission No. 101416
P-0557

The efficacy of Atezolizumab plus Bevacizumab according to viral etiology of HCC

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Background & Aims: This real-world study compared the efficacy of first-line atezolizumab plus bevacizumab (Atezo/Bev) according to viral etiology of hepatocellular carcinoma (HCC).

Methods: We retrospectively reviewed consecutive 395 patients with intermediate ($n=55$) and advanced-stage HCC ($n=340$) treated by Atezo/Bev as primary systemic treatment between 2018 and 2022 at Asan Medical Center. Patients were divided into an intention-to-treat (ITT) group (patients treated at least one cycle of Atezo/Bev), and a per-protocol (PP) analysis group (patients with at least one measurable target lesion and treated with ≥ 3 cycles of Atezo/Bev), who included survival and response analyses, respectively.

Results: The ITT and PP groups included 376 and 284 patients, respectively. In the PP group, there were 90 patients with hepatitis B virus (HBV)-infected HCC and 68 with nonviral-related HCC. RECIST-based objective response rates did not differ significantly between the HBV (8.2% and 18.0%) and non-HBV groups (20.0% and 25.6%) and between the viral (9.7% and 19.0%) and nonviral groups (19.1% and 25.0%) at initial and best responses, respectively. The ITT analysis showed that progression-free survival was longer in HBV carriers than the counterpart ($p=0.01$ by log-rank test), as was not overall survival ($p=0.06$). However, after adjusting confounders in multivariate Cox regression, the difference in progression-free survival remained to be no longer significant. Similar trends in both endpoints were noted for viral versus nonviral subsets of patients.

Conclusions: Our real-world data indicate that HBV or viral etiology may not be associated with clinical outcomes in Atezo/Bev-treated patients with unresectable HCC.

Abstract Submission No. 101426
P-0558

Radiofrequency Ablation Therapy for Hepatocellular Carcinoma Using a 15G Variable Needle

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Introduction: The 15G variable needle radiofrequency ablation system released in 2022 by STARmed is reported to achieve larger ablation zones and more spherical ablation fields compared to conventional 17G variable needles. Here we report our experience using this system.

Methods: The subjects were 9 cases where this system was used from November 2022 to November 2023. Ease of needle insertion, ablation characteristics, ablation effects, and complications were examined. Four grounding pads were placed on the back and abdomen.

Results: Ease of needle insertion was similar to 17G needles, with good controllability and suitability even for difficult insertions requiring delicate manipulation. Needle tip visualization on ultrasound was comparable to 17G needles, clearly visible even in deep regions. Ablation ultrasound images were also similar to 17G needles, but using identical 17G protocols resulted in larger gas formation, necessitating care with ablation endpoint determination. With 30mm active tip exposure, a single ablation achieved approximately 40mm spherical ablation zones. Ablation times with back and abdominal grounding pads were 3-5 minutes for 30mm active tips. Complications were comparable to conventional 17G needles, with only mild fever and hepatic dysfunction.

Conclusions: The 15G variable needle is a new option for radiofrequency ablation, and may enable more aggressive treatment of larger HCC tumors.

Abstract Submission No. 101438
P-0559

Extracellular Vesicle-Derived miRNAs as Diagnostic and Prognostic Biomarkers for NBNC-HCC

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Introduction: Extracellular vesicle-derived microRNAs (EV-miRNAs) are promising circulating biomarkers for chronic liver disease. In this study, we explored the potential significance of plasma EV-miRNAs in non-hepatitis B-, non-hepatitis C-related HCC (NBNC-HCC).

Methods: We compared, using the NanoString method, plasma EV-miRNA profiles between NBNC-HCC and control groups including patients with non-alcoholic fatty liver disease (NAFLD) and healthy controls. The differentially expressed EV-miRNAs were validated in another set of plasma samples by qRT-PCR.

Results: A total of 66 significantly differentially expressed EV-miRNAs between the HCC and the control groups were identified in the discovery set. In the validation cohort, including plasma samples of 70 NBNC-HCC patients, 70 NAFLD patients, and 35 healthy controls, 5 plasma EV-miRNAs were significantly elevated in HCC, which included miR-19-3p, miR-16-5p, miR-223-3p, miR-30d-5p, and miR-451a. These miRNAs were found to participate in several cancer-related signaling pathways based on bioinformatic analysis. Among them, EV-miR-19-3p exhibited the best diagnostic performance and displayed a high sensitivity for detecting alpha-fetoprotein-negative HCC and early-stage HCC. In multivariate analysis, a high EV-miR-19-3p level was demonstrated as an independently unfavorable predictor of overall survival in patients with NBNC-HCC.

Conclusions: In conclusion, our data have indicated, for the first time, that EV-miR-19-3p could serve as a novel circulating biomarker for the diagnosis and prognosis of NBNC-HCC.

Abstract Submission No. 101446
P-0560

A Retrospective Cohort Study on Microwave Ablation and Lenvatinib on Hepatocellular Carcinoma

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Background: Systemic therapy has been used as a first-line treatment for intermediate-stage HCC, especially for larger (≥ 5 cm) or multiple lesions. Based on the REFLECT trial, lenvatinib has been approved as a first-line treatment for unresectable HCC in different parts of the world. Lenvatinib has exhibited favorable results in inhibiting tumor angiogenesis and tumor growth. The present study aimed to evaluate efficacy of combined percutaneous microwave ablation therapy and lenvatinib in patients with intermediate hepatocellular carcinoma.

Methods: Thirteen patients with Child Pugh B-HCC were included in the study. The patients had no prior history of systemic treatment. Of them, 4 received both PMAT and Lenvatinib, while 9 of them received PMAT monotherapy. The clinical outcomes used to evaluate treatment included tumor size, MELD Na, and Child Pugh Class.

Results: The 2 treatment arms were followed up on a monthly basis for the 6 months, there was no significant difference on MELD Na scores (p value<0.05) and tumor size progression on both treatment arms (p value<0.05). For the first 5 months of the study, there was no significant difference on Child Pugh Classes, however on the 6th month, there was significant increase on the CPC of monotherapy arm in comparison with combination therapy, PMAT + Lenvatinib (p value<0.05) which has stable CPC.

Conclusion: Our newly proposed combination therapy may potentially be effective in patients with Child Pugh B- HCC. A larger scale, multicenter, prospective study is warranted to confirm the findings.

Keywords: microwave ablation, Lenvatinib, hepatocellular carcinoma, intermediate-stage

Abstract Submission No. 101562
P-0561

First clinical experience of STRIDE regimen for Advanced HCCs in our hospital.

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Background Advanced HCC (BCLC -B, C) systemic chemotherapy was advanced in recent years. Eight regimens were available in Japan in 2023 September. STRIDE regimen was introduced to our hospital In 2023 May. I report first introduced advanced HCC patients who received STRIDE regimens.

Methods Five patients were treated by STRIDE regimen from May 2023 to October 2023. 4 patients were BCLC stage-C and 1 patient is BCLC stage B. Gender were 5 men and Age was range (64-79). One patient had PVTT and another patient had Bile duct invasion. One patient was 1st line chemotherapy. Two patients were 2nd line chemotherapy The other 2 patents were 3rd line chemotherapy. Chemotherapy effects were evaluated by m-RECIST. IrAE side effects were observed by doctors, hospital pharmacists and hospital nurses.

Results First evaluation of STRIDE resion PR was 2 patients, SD was 2patients, PD was 1 patient. 1 patient of PD was died 4 months later because of tumor growth. IrAE side effect were autoimmune liver dysfunction (grade 3) and another patient had erythema multiforme and was treated by prednisolone and ACTH isolated deficiency occurred one after another and treated by cortisone acetate.

Conclusions STRIDE resimens for 2nd a3rd line regimen was effective for 40% of Advanced HCC. But irAE managements on STRIDE were important for HCC patients.

Abstract Submission No. 101585

P-0562

Prognosis Of Patients with Hepatocellular Carcinoma based on Differentially Expressed Genes

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Background: Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related deaths globally. Prediction of prognosis in patients with HCC remains challenging due to heterogeneity in etiology of liver disease, tumor biology, and liver function. Hence, we aim to investigate gene expression profiles in patients with HCC to develop accurate models for prognosis prediction.

Methods: RNA was extracted from frozen liver tissue samples of HCC and paired non-tumorous tissues from 106 patients with HCC (68 viral-related HCC, 38 non-alcoholic steatohepatitis (NASH)-related HCC). The developmental and immune gene expression profiles, including over 700 genes, were analyzed via the nCounter platform (NanoString Technologies). Differentially expressed genes (DEGs) (defined as $p < 0.05$ and large fold change > 1.0 standard deviation (SD)) were identified. Subsequently, prognostically important DEGs with a significant impact on overall survival (OS) and/ or recurrence-free survival (RFS) were selected using adaptive Lasso-based Cox regression.

Results: 86 DEGs and 152 DEGs were identified in the analysis of samples from NASH-related and viral-related HCC respectively. Adaptive Lasso-based Cox regression selected 13 prognostically important DEGs. The 13-gene model was used to stratify patients into "high-risk", "medium-risk", and "low-risk" groups using the most parsimonious percentile cut-offs, and there was significant difference in 10-year OS between high-, medium-, and low-risk groups (Log-rank $p < 0.001$).

Conclusion: Developmental and immune gene expression profiles are potentially useful in the development of accurate prognostic markers and offer insights into future therapeutic targets.

Abstract Submission No. 101614

P-0563

Differential lung ventilated percutaneous ablation for hepatocellular carcinoma

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Background: We have been performing percutaneous radiofrequency ablation (RFA) since December 2001 for hepatocellular carcinoma (HCC). In April 2018, we introduced next-generation microwave ablation therapy (MWA). Here, we report percutaneous ablation under differential lung ventilation (DLV).

Methods: We examined patient background, tumor factors, treatments, and therapeutic efficacy of percutaneous ablation under DLV in patients treated between December 2020 and November 2023.

Results: Five patients with HCC (4 males and 1 female) ranged in age from 69 to 83 years (average 75.6); 2 cases were recurrences. Background liver disease included 2 cases of non-B non-C cirrhosis and 3 cases of post-SVR type C cirrhosis. Child-Pugh scores ranged from 5 to 9. BMI was $25 \leq < 30$ in 2 patients and ≥ 30 in 1. Four patients had 1 tumor and 1 patient had 2 tumors; the maximum diameters were 14 to 27 mm (average 20.6) and the location was S8 in 4 cases and S7 in 1 case. The tumors could not be depicted by ultrasonography before treatment in 3 patients, and were difficult to depict in 2. In 4 cases, contrast-enhanced ultrasound (CEUS) was performed preoperatively, but in 2 cases, it was difficult to delineate. There was 1 RFA was performed in 1 patients and MWA in 4. Three patients received artificial pleural effusion using 1700 to 2000 ml, and 2 only DLV. DLV was performed in combination with CEUS in 1 patient, and in B mode in 4 patients. Treatment time ranged from 20 to 77 minutes, (average 55.6). All had no complications.

Conclusion: Percutaneous ablation under DLV can be expected to have a safe and reliable therapeutic effect on cases that are difficult to depict with extracorporeal ultrasound.

Abstract Submission No. 101636

P-0564

Mechanisms of Jiedu prescription in treating hepatocellular carcinoma based on network pharmacology

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Objective: Yangyin Fuzheng Jiedu Prescription (YFJP) is an empirical prescription with excellent clinical efficacy. However, the specific target and mechanism of Traditional Chinese medicine (TCM) are still unclear. This study aimed to explore the key herbs of YFJP in the treatment of HCC using a network pharmacology method.

Methods: We retrospectively included 1021 HCC patients; 481 had received YFJP treatment and 540 had received comprehensive Western medicine treatment without TCM. Network pharmacological methods were applied to explore the key components and Chinese herbs of YFJP treatment of HCC and the core components and targets of the key herbs in the Jiedu prescription (JDP) treatment of HCC.

Results: Compared to those in the control group, HCC patients in the YFJP group had longer OS and PFS rates, higher CD8⁺T cell counts,

and lower levels of CRP ($p < 0.05$). The YFJP-HCC overlapping target network were established, revealed that YFJP compounds for HCC were mainly from JDP. The key compounds and core targets of JDP for the treatment of HCC were identified using network pharmacological analysis. Molecular docking showed that the ligands of the four compounds had strong binding effects with the four core targets. Immunohistochemical analysis showed that JDP could decrease the expression of IL-6, STAT3, VEGF and TNF- α in tumor tissues.

Conclusion: YFJP adjuvant therapy can improve HCC patients' OS rate. JDP is a key component of YFJP in the treatment of HCC. JDP can inhibit inflammation and delay HCC progression by regulating IL-6, STAT3, TNF- α , and VEGF.

Abstract Submission No. 101640

P-0565

Therapeutic Effectiveness of Early Additional cTACE after DEB-TACE for Hepatocellular Carcinoma

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Purpose: We have previously reported that early additional cTACE after drug-eluting beads TACE (DEB-TACE) significantly increased the CR rate compared to patients treated with DEB-TACE alone. In the present study, we investigated how early additional cTACE should be performed after DEB-TACE in patients with hepatocellular carcinoma (HCC) at a multicenter setting.

Methods: Twenty-seven patients with unresectable hepatocellular carcinoma (HCC) with a maximum tumor diameter of 30 mm or greater, Child-Pugh classification A-B, and ECOG-PS 0-2, who were treated at four institutions including our hospital between July 2014 and November 2022, were included in this study. The subjects undergone DEB-TACE first and cTACE as the second treatment. The overall response rate (ORR) and disease control rate (DCR) were evaluated retrospectively by mRECIST.

Results: The overall evaluation by initial DEB-TACE was CR/PR/SD/PD=0/27/0/0, and the overall response rate and disease control rate were 100%. The overall response rate was 75.0% and disease control rate was 91.7% in the group that received the next cTACE treatment earlier than DEB-TACE (CR/PR/SD/PD=1/8/2/1), whereas the overall response rate and disease control rate in the group that received the next cTACE treatment more than 3 months after conventional DEB-TACE were The overall response rate, CR/PR/SD/PD=2/3/6/4, overall response rate, and disease control rate were 33.3% and 73.3%, respectively, indicating a significant difference in overall response rate between the two groups ($p=0.031$). **Conclusion:** In unresectable hepatocellular carcinoma, early additional cTACE after DEB-TACE can bring better therapeutic effect.

Abstract Submission No. 101661

P-0566

Percutaneous radiofrequency ablation in early-stage hepatocellular carcinoma

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Radiofrequency ablation (RFA) is a minimally invasive treatment widely performed for the treatment of liver neoplasms. Recently, resulting of long prognosis has made by ablation in the clinical practice. In Japan, JSH consensus statements and recommendations 2021, Resection and RFA are equally recommended as first-line therapy in patients of less than 3cm, 3 nodules HCC in the result of a head-to-head randomized controlled trial (SURF trial).

We introduced adjustable RFA electrode needle (VIVARF system) which became usable from 2015 in order to improve therapeutic results of RFA. In 125 patients with liver cancer. The 5-year survival rate of RFA at our institution is 70%. Although local recurrence rate after curative RFA is as low as 6.0%, the intrahepatic distant metastasis is as high as 70% at 5 years. Complications were skin burned in 4.2% due to cause by needle damage from induction needle. We use a variety of techniques such as artificial pleural effusion, artificial ascites, under sedation to improve the effectiveness of our treatments.

After the treatment, the prevention of intrahepatic distant recurrence by direct-acting antivirals (DAAs) is very important.

Abstract Submission No. 101685

P-0567

Efficacy of Conversion therapy after chemotherapy for unresectable hepatocellular carcinoma

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Background: The efficacy chemotherapy followed by conversion therapy for unresectable hepatocellular carcinoma (HCC) has been reported, but there are insufficient reports on the long-term outcomes and progress after conversion therapy.

Patient and Methods: We retrospectively analyzed 17 cases of unresectable HCC treated with chemotherapy followed by conversion therapy at our hospital between April 2010 and April 2023.

Results: Conversion therapy included liver resection in 7 patients, radiofrequency ablation in 6 patients, TACE in 3 patients, and radiotherapy in 1 patient. Median survival from the start of chemotherapy was 41.1 months, and median survival after conversion was 26.0 months. After conversion therapy, 12 patients (71%) had recurrence, and the median recurrence-free period was 5.4 months. Four patients had extrahepatic recurrence (3 pulmonary, 1 bone, and 1 peritoneal, with overlap) and 8 patients had new intrahepatic lesions. Recurrent treatment for new intrahepatic lesions included hepatectomy in 1 case, RFA in 1 case, TACE in 4 cases, and chemotherapy in 2 cases. The median survival after conversion was 41.3 months in patients who remained tumor-free for more than 3 months after conversion, compared with 19.9 months in patients who had a recurrence within 3 months ($P=0.01$).

Conclusion: Conversion therapy after chemotherapy for unresectable HCC resulted in long-term survival. Careful evaluation, including search for extrahepatic lesions, should be performed before conversion therapy.

Abstract Submission No. 101704

P-0568

Characteristics of hepatocellular carcinoma treated with drug therapy followed by conversion therapy

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Objective: To analyze the characteristics of CR hepatocellular carcinoma treated with drug therapy and followed by conversion therapy.

Methods: Sixty-three with BCLC-B stage HCC who started drug therapy at our hospital between January 2016 and March 2023, age 77 years $\pm$ 6.12, 51 males, Child Pugh A 52 B 7, tumor diameter 23 mm $\pm$ 24.67 (8-130 mm), tumor number 4 or more 48, up to 7 in 24, Sorafenib 30 Lenvatinib 20, Atezolizumab+Bevacizumab 13, observation period 19.5 months $\pm$ 11.82.

Results: After the initiation therapy, treatment was changed in 40: 23 received TKI, 10 received TACE, 4 received RFA (MWA), and 3 received radiation. The final efficacy evaluation showed 6 of CR (9.5%), 12 of PR (19%), 13 of SD (20.6%), and 32 of PD (50.8%). Cumulative survival rate for all were 61% at 1 yr, 41.7% at 2 yr, and 26.9% at 3 yr. 6 had CR, 1 with ATZ/Bv only, 4 with RFA (MWA) after LEN, and 1 with additional TACE after LEN. AFP 4.34 ng/ml $\pm$ 1.61, PIVKAI 60.4 $\pm$ 43.7, Child-Pugh A in 5 Maximum tumor diameter 16 mm $\pm$ 2.33, next tumor diameter 8.7 mm $\pm$ 1.67, tumor number 6.2 $\pm$ 2.2 up to 7 The number of tumors was 6.2 $\pm$ 2.2, up to 7. In multivariate analysis, the factor contributing to CR was tumor diameter of 15 mm or less.

Conclusion: it is important to select a treatment with conversion therapy, in case of unresectable HCC with a diameter of 15 mm or less.

Abstract Submission No. 101708

P-0569

Real world outcomes in HCC patients within or outside the IMbrave 150 Study Criteria

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Objective: Atezolizumab/bevacizumab (Atezo/Bev) combination therapy for unresectable hepatocellular carcinoma (HCC) is now implemented in clinical practice post IMbrave150 trial. This study compares outcomes of patients not meeting IMbrave150 trial criteria.

Methods: Out of 975 patients treated with Atezo/Bev for HCC between May 2018 and October 2023, 936 were analyzed, excluding clinical trial participants and those with missing data. Patient characteristics: Age: 74.0 (68.0-80.0) years, Sex (Male/Female): 740/196, PS (0/1/2 or more): 782/126/28, mALBI grade (1/2a/2b/3): 332/242/348/14, BCLC stage (0/A/B/C/D): 14/69/346/504/3, AFP: 30.7 (5.9-517.5) ng/mL. Median observation period: 12.8 (6.9-21.3) months (continuous variables: median, interquartile range).

Results: 404 (43.2%) were within, and 532 (56.8%) were outside IMbrave150 study criteria. Median PFS (95% CI): 7.4 (6.5-8.8)/5.8 (5.1-6.5) months (p=0.002), OS: 26.5 (24.9-NA)/18.8 (16.5-22.1) months (p<0.001). Multivariate analysis revealed significant factors for PFS (NBNC HR: 1.17, CD HR: 1.32, AFP >100 HR: 1.47, mALBI 2b&3 HR: 1.47) and OS (PS >2 HR: 1.99, AFP >100 HR: 1.48, mALBI 2b&3 HR: 2.04). Best response rate (ORR/DCR): 29.7/25.9% (p=0.220), 80.5/78.0% (p=0.399). The only significant adverse event difference was hypertension (all grades): 85 (21.0%)/77 (14.5%) (p=0.009). Subgroup analysis showed no significant PFS and OS differences, especially in mALBI 1&2a patients.

Conclusion: In the real world, cases meeting criteria show longer prognoses than IMbrave150 cases. Additionally, mALBI 1&2a patients, even if outside standard cases, exhibit better prognoses than IMbrave150 counterparts

Abstract Submission No. 101712

P-0570

Encephalitis induced by atezolizumab plus bevacizumab in a patient with hepatocellular carcinoma

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Introduction: Atezolizumab plus Bevacizumab (Atz+Bev) therapy is a first-line systemic therapy in patients with unresectable hepatocellular carcinoma (HCC). Neurological immune-related adverse events (irAEs) are rare, but high mortality has been reported.

Case Presentation: A 65-year-old man was diagnosed with hepatocellular carcinoma, and he was treated with transarterial chemoembolization. Lenvatinib therapy was initiated because he developed lung metastasis. After 2 months of lenvatinib therapy, he developed bone metastasis. Atz+Bev therapy was initiated as second-line therapy. Two weeks after first administration of Atz+Bev, the patient showed language disorder, walking disorder and headache. Imaging studies did not show findings of stroke and metastatic brain tumor. Cerebrospinal fluid tests showed elevated protein and cell counts. After admission, he developed coma. We initiated intravenous methylprednisolone (1g/day), intravenous acyclovir, and intravenous piperacillin/tazobactam therapy. Blood tests did not show antibodies associated with infection or paraneoplastic neurological syndrome. Cerebrospinal fluid culture and polymerase chain reaction did not detect bacteria or virus. He was diagnosed as encephalitis induced by Atz+Bev. His consciousness was improved the next day, and the patient was discharged 31 days after admission.

Conclusions: We experienced a case of encephalitis that developed after treatment with Atz+Bev. In our case, immediate high-dose corticosteroids therapy may help improvement of patient's neurological symptoms.

Abstract Submission No. 101736

P-0571

Pre-Sarcopenia predicts the outcome of hepatocellular carcinoma patients with first-line Lenvatinib

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Aim: Muscle volume loss (Pre-sarcopenia) is linked to an unfavorable prognosis in individuals diagnosed with hepatocellular carcinoma (HCC). This study was to elucidate the clinical importance of pre-sarcopenia in patients receiving first-line lenvatinib for unresectable HCC in real world.

Methods: We retrospectively evaluated patients with unresectable HCC who had undergone lenvatinib as first-line treatment between January 2018 and Dec 2021. Pre-sarcopenia was diagnosed based on a previously reported cut-off value calculation formula [psoas muscle area at level of middle of third lumbar vertebra (cm²)/height (m)²]. Treatment response was assessed by radiologic imaging according to the Response Evaluation Criteria in Solid Tumors versions 1.1. (RECIST1.1)

Results: A total of 171 patients (Male/Female: 124/47, mean age: 65.9 years) were recruited including 52 (30.4%) patients with pre-

sarcopenia and 119 (69.6%) patients with non pre-sarcopenia. The overall survival (OS) and progression free survival (PFS) was 18.2 months and 6.5 months, respectively. Pre-sarcopenia group had a significant poorer PFS (4.7 vs 6.8 months, $p=0.026$) and OS (7.6 vs 22.4 months, $p<0.001$) than Non pre-sarcopenia group. Also, at the time of lenvatinib termination, higher percentage of patients without pre-sarcopenia could maintain a better liver function reserve to afford sequential therapies than those with pre-sarcopenia (58% vs 26.5%, $p<0.001$). Moreover, multivariate analysis showed pre-sarcopenia (Hazard Ratio: 2.025, 95% Confidence Interval (1.222–3.335); $p=.006$) was associated with mortality after adjusting post-treatment and alpha-fetoprotein.

Conclusions: In clinical practice, pre-sarcopenia was shown to be a significant prognostic factor in patients treated with first-line lenvatinib for unresectable HCC.

Abstract Submission No. 101748
P-0572

Vascular endothelial growth factor receptors peptide vaccines generate peptide-specific CTLs for HCC

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Aim: Vascular endothelial growth factor receptor (VEGFR)-specific cytotoxic T lymphocytes (CTLs) can theoretically be expected to cause damage to not only VEGFR-expressing tumor cells but tumor vascular endothelial cells. In this study, we evaluated the safety and efficacy of a vascular endothelial growth factor receptor (VEGFR)-targeted peptide vaccine in patients with unresectable hepatocellular carcinoma who had responded to transcatheter arterial chemoembolization.

Methods: Twenty-two patients were randomized 1:1 to receive VEGFR-targeted peptides (VEGFR1 1mg and VEGFR2 1mg) or placebo. The primary endpoint was immunological safety evaluation. Secondary endpoints were immunological response and clinical outcome. To assess specific CTL responses, ELISpot assays were performed after in vitro growth.

RESULTS: No serious adverse events were observed. Of the 12 patients in the vaccine group, VEGFR1-specific CTL responses were induced in 8 patients (66.7%) and VEGFR2-specific CTL responses in 10 patients (83.3%). When divided into two groups according to immunoreactivity, the median PFS for patients with an immune response to VEGFR1 was 7.4 and 2.7 months ($P=0.019$) and for patients with an immune response to VEGFR2 was 10.6 and 2.7 months ($P=0.001$).

Conclusions: Immunotherapy with peptide vaccines targeting VEGFR1 and VEGFR2 were well tolerated without serious adverse events. The peptide vaccines also effectively induced peptide-specific CTLs in patients with unresectable hepatocellular carcinoma.

Abstract Submission No. 101787
P-0573

Results of Atezolizumab plus Bevacizumab for advanced hepatocellular carcinoma in Vietnam

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Backgrounds: Atezolizumab plus bevacizumab was approved in 2022 in Vietnam as a first-line treatment for advanced hepatocellular carcinoma (HCC). The purpose of this study was to assess the curative effect and tolerability of the combination treatment in advanced HCC.

Methods: Retrospective study, single-arm, single center of patients aged 18 years or older with advanced HCC defined as the Barcelona clinic liver cancer staging system (BCLC) stage B was unsuitable or failed with local interventions or metastatic disease (BCLC stage C) received systemic therapy with Atezolizumab plus Bevacizumab intravenously on days 1 of a 21-day cycle at National Cancer Hospital Vietnam from May 2022 to March 2023. The outcomes included pooled overall response (OR), complete response (CR), partial response (PR), median overall survival (mOS), median progression-free survival (mPFS), and adverse events (AEs).

Results: Thirty-one patients were enrolled. The OR, CR, and PR rates of the therapy response based on Response Evaluation Criteria in Solid Tumors (RECIST) were 41.9%, 3.2%, and 38.7%, respectively. Median progressive-free survival (PFS) was 5 months and median overall survival (OS) was 15.5 months. During the treatment, 38.7% and 9.7% of patients experienced any grade AEs and grade 3 and above AEs, respectively including hypertension, increased liver enzymes and thrombocytopenia.

Conclusions: Atezolizumab in combination with Bevacizumab is effective and well-tolerated in patients with advanced or metastatic HCC in Vietnam. Need to further research for this confirmation.

Abstract Submission No. 101800
P-0574

Epidemiology and clinical manifestations of HCC in patients Mongolia and Russia

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Objective: The current study is aimed at determining differences of epidemiological and clinical profiles associated with HCC in patients belonging to ethnic groups of Asians from Mongolia and Caucasians from Asian region of Russia.

Materials and methods: The studies were carried out in the cross-border regions of Mongolia and Asian part of Russia (Irkutsk region). 300 patients with HCC of the Caucasian and Mongolian races were enrolled in the study. The level of AFP in the serum was determined by the chemiluminescence technique.

Results: The long-term dynamics of the HCC incidence shows more unfavourable trends in the territory of Mongolia compared to Irkutsk region. In both groups, male patients over 60 years of age predominated. Patients from Mongolia often have a history of jaundice and alcohol abuse. Out of the etiological factors, HCC is more often associated with the HBV in Mongolia than in the Asian part of Russia. At the same time, in Caucasians, HCC develops primarily on the background of liver cirrhosis. In patients with HCC, AFP level higher than

20 ng/ml were significantly more frequent in the ethnic group of Caucasoids than in Mongoloids.

Conclusions: In Mongolia, among the risk factors for the development of the disease, hepatitis B virus plays a major role, which significantly differs from the Asian part of Russia. For the purpose of early diagnosis of HCC, it is necessary to search for new molecular markers or their combinations due to the insufficient diagnostic efficiency of AFP determination.

Abstract Submission No. 101815
P-0575

Differential expression of Telomerase reverse transcriptase and cytokine in hepatocellular carcinoma

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Background: Telomerase reverse transcriptase (TERT) abnormalities are the most common altered pathway in hepatocellular carcinoma (HCC), an inflammation-induced cancer. HCC is characterized by male predominance in incidence, with an estimated male-to-female ratio of 3-4:1. Little is known regarding the role of TERT abnormalities and inflammatory cytokines in hepatocarcinogenesis. This study aimed to investigate the association of the TERT and cytokines with gender disparity in HCC.

Method: The study included a total of 357 HCC patients with stored liver tissues or serum. TERT expression was measured by qRT-PCR, and multiple cytokines were detected by multiplex immunoassay.

Results: Overall, TERT expression was higher in HCC than in Non-HCC tissues ($P=0.0001$). Among HCC patients, males had higher TERT expression than females ($P=0.0001$). The levels of cytokines, such as INF- γ , IL-10, IL-12, IL-17, IL-2, IL-6, and TNF- α were not different between genders. When analyzed within patients with HBV-associated HCC, males had higher levels of both IL-6 and TERT expression than females. Among the cytokines, only IL-6 positively correlated with TERT expression in males, but not in females. The correlation between serum IL-6 and tumor TERT levels appeared to be stronger in patients with HBV-associated HCC than in those with non-HBV-associated HCC ($r=0.373$, $p=0.001$ for HBV-HCC; $r=0.012$, $p=0.957$ for non-HBV-HCC).

Conclusion: TERT and IL-6 are differentially expressed between male and female HCC patients, with a positive correlation only in male patients or those with HBV-associated HCC. These results give insight into the potential mechanism of TERT-IL-6 axis involved in gender disparity in liver carcinogenesis.

Abstract Submission No. 101818
P-0576

Case reports: durable response of systemic therapy for hepatocellular carcinoma with bone metastasis

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Bone is the second most common site for hepatocellular carcinoma (HCC) metastasis. Patients with HCC and bone metastasis face a grim prognosis, with a median survival time of only 4.6 months. Unfortunately, therapy for such cases often yields poor responses, posing challenges for disease control. Here, we present two cases of HCC with bone metastasis that demonstrated durable responses to chemotherapy and immunotherapy, respectively.

A 67-year-old male, diagnosed with HCC involving major vein invasion and bone metastases in the right iliac region, initially underwent sorafenib and regorafenib along with radiotherapy. Despite these interventions, disease progression persisted. Switching to palliative chemotherapy involving cisplatin and 5-fluorouracil, followed by tegafur, resulted in a durable partial response, extending overall survival to over 45 months (Figure 1 and 2). A notable decrease in alpha-fetoprotein levels was observed (12369 to 3.27 ng/mL) after a 2-year course of chemotherapy. In another case, a 64-year-old male with HCC rupture and bone metastasis experienced disease progression following sorafenib, radiotherapy, transcatheter arterial chemoembolization, and S4 hepatectomy. Nivolumab, initiated as a second-line treatment, led to a durable partial response, with an overall survival exceeding 61 months (Figure 3 and 4). A significant reduction in alpha-fetoprotein levels was noted (38200 to 3.16 ng/mL) after a 6-month course of immunotherapy.

While HCC with bone metastasis typically carries a poor prognosis and shows limited response to systemic treatment, these cases underscore that specific patients can exhibit promising therapeutic efficacy with not only immunotherapy but also chemotherapy following the unsuccessful outcome of initial systemic treatment.

Abstract Submission No. 101834
P-0577

A Study of Combination Therapy with SBRT for HCC with Macrovascular Invasion at Our Institution.

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Backgrounds: Effective treatment for hepatocellular carcinoma with macrovascular invasion (MVI-HCC) has not yet been established. In this study, we reviewed combination therapy of unresectable MVI-HCC with stereotactic body radiation therapy (SBRT) at our institution.

Methods: We included 28 patients with unresectable MVI-HCC treated with SBRT from August 2012 to November 2022 in this study. 1) The safety and efficacy of SBRT were evaluated. 2) 25 patients were treated with hepatic transcatheter arterial infusion chemotherapy with cisplatin (CDDP-TAI), continuous hepatic arterial infusion chemotherapy (HAIC), and Lenvatinib, and the patient backgrounds and outcomes of these three groups were compared.

Results: 1) Median age: 69(48-81) years, male/female: 21/7 cases, inferior vena cava thrombus: 5 cases, portal vein tumor thrombus (Vp 2/3/4): 2/10/13 cases. Combination therapies included CDDP-TAI in 10 patients, continuous HAIC in 7, Lenvatinib in 8, Sorafenib in 2, and Atezolizumab/Bevacizumab in 1. The MST for all patients was 18.6 months. Tumor thrombi were enlarged in 4 patients, with the median

time to enlargement of 2.4 (1.4-13.6) months. SBRT caused no gastrointestinal disorders, and 2 patients developed bile duct stenosis. 2) Comparison of patient backgrounds showed significant differences in Child-Pugh classification, tumor occupancy, platelet count, and albumin. MST for CDDP-TAI/continuous HAIC/Lenvatinib was 16.0/18.6/24.1 months, not significantly different. In univariate analysis of OS, DCP>10,000 mAU/ml was a significant poor prognostic factor ($p=0.008$).

Conclusions: SBRT for MVI-HCC was performed safely and effectively at our institution. There were no significant differences in OS despite the different treatments depending on liver function and tumor occupancy.

Abstract Submission No. 101847

P-0578

Duration of Response and Factors associated with sustained response to ATZ/BEV therapy

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Background and aims: In systemic chemotherapy for malignant tumors, disease progression is often observed even after a good treatment effect has been achieved. The aim of this study was to examine the duration of response (DOR) and factors associated with sustained response of atezolizumab plus bevacizumab (ATZ/BEV) combination therapy in patients with unresectable hepatocellular carcinoma (HCC).

Methods: This is a multicenter study conducted between October 2020 and June 2023. A total of 343 HCC patients who received ATZ/BEV combination therapy as first-line chemotherapy were included.

Results: The objective response rate (ORR) was 39.1%. The disease control rate (DCR) was 77.7%. The progression free survival (PFS) was 7.6 months. The overall survival (OS) was 22.5 months. The DOR was 6.9 months. In patients who have a good therapeutic effect (complete or partial response), the OS of patients who lead to disease progression and who didn't was 19.0 months and 30.0 months, respectively ($P=0.051$). Multivariate analysis revealed that non-viral liver disease (OR 3.74, 95% confidence interval [CI] 1.0-13, $P<0.050$) and LCA-reactive α -fetoprotein isoform (AFP-L3) at best response $\leq 5\%$ (OR 4.23, 95% CI 0.95-19, $P=0.059$) as predictive factors for the sustained response.

Conclusion: ATZ/BEV combination therapy in unresectable HCC can achieve longer survival in patients who continue to good respond. However, patients who have non-viral liver disease or whose AFP-L3 is not sufficiently reduced by treatment are more likely to convert to progression disease.

Abstract Submission No. 101848

P-0579

Impacts of muscle and adipose mass on male hepatocellular carcinoma patients undergoing resection

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Background & Aims: Body composition is an objective assessment reflecting nutritional status and liver reserves. Curative resection, the standard treatment for early-staged hepatocellular carcinoma (HCC) is an energy-consuming major operation that would affect body composition. In this study, we aimed to investigate the impact of muscle and adipose tissue on the outcome of HCC after curative resection in male patients.

Method: From January 2013 to December 2016, 229 consecutive female patients undergoing curative resection for HCC in Taipei Veterans General Hospital were retrospectively reviewed. Skeletal muscle index (SMI), subcutaneous, visceral, intramuscular, and total adipose tissue index (SATI, VATI, IMATI, TATI) were calculated at L3 vertebral level from pre-operative computed tomography scan using Slice-O-matic software. Factors associated with survivals were analyzed.

Results: A significantly worse overall survival (OS) was noted in patients with pre-surgical lower SMI ($p<0.001$), higher IMATI ($p<0.001$), and lower SATI ($p=0.005$). Otherwise, the OS could not be differentiated by VATI or TATI. Besides, baseline ALBI grade $>$ (Hazard ratio [HR]: 1.889, $p=0.035$), poorly differentiated tumor histology (HR: 2.748, $p=0.001$), lower SMI ($\leq 46.6 \text{ cm}^2/\text{m}^2$) (HR: 2.103, $p=0.020$), higher IMATI ($> 2.9 \text{ cm}^2/\text{m}^2$) (HR: 3.719, $p<0.001$), and lower SATI ($\leq 38.0 \text{ cm}^2/\text{m}^2$) (HR: 2.416, $p=0.029$) were independent predictors of a worse OS.

Conclusion: Sarcopenia, myosteatosis, and subcutaneous adipopenia can independently predict survival in male HCC patients undergoing surgical resection. These findings help to establish surveillance and nutrition support strategies to optimize patients' outcomes.

Abstract Submission No. 101849

P-0580

Prognostic impact of muscle loss during atezolizumab/bevacizumab combination therapy

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Aim: The purpose was to examine the significance of changes in muscle volume during atezolizumab/bevacizumab combination therapy (AB therapy).

Method: The prognostic impact of changes in muscle volume after AB therapy was examined in 171 patients whose efficacy could be determined by CT after the start of AB therapy in a retrospective, multicenter study.

The psoas muscle area index (PI) was calculated from CT findings. At the first CT after starting atezolizumab bevacizumab, cases with a decrease in PI from before treatment were designated "decrease group" and those with an increase were designated "increase group".

Result: The pre-treatment median PI was 5.01 for men and 3.55 for women. The median overall survival (OS) was not reached and the

median progression-free survival (PFS) was 210 days. The objective response rate (ORR) was 30.9% and disease control rate (DCR) was 79.5%. There were 98 patients in the decreased group and 73 in the increased group.

The ORR was 24.4% in the decrease group and 38.8% in the increase group ($p=0.04$), and the DCR was 73.4% in the decrease group and 87.5% in the increase group ($p=0.03$), both significantly better in the increase group. Median OS was 731 days in the decrease group and not reached in the increase group ($p=0.097$), and median PFS was 162 days in the decrease group and 322 days in the increase group, significantly better in the increase group ($p=0.02$).

Discussion: The prognosis and effectiveness of treatment are poor in cases of reduced muscle mass after AB therapy.

Abstract Submission No. 101878

P-0581

Systemic treatment in patients with unresectable hepatocellular carcinoma in Child-Pugh class B.

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Background: Systemic treatment is generally recommended for unresectable hepatocellular carcinoma (uHCC) patients with Child-Pugh (CP)-A status. Given the urgent need for effective therapeutic strategies to treat u-HCC patients with CP-B, this study was conducted to compare the efficacy of lenvatinib (LEN) with that of atezolizumab plus bevacizumab (Atez/Bev).

Methods: A total of 145 uHCC patients with ECOG performance status 0 or 1 and CP-B liver function who received Atez/Bev ($n=53$) or LEN ($n=92$) as initial systemic treatment from April 2018 to December 2022 were enrolled. Therapeutic response as well as clinical features and prognosis were retrospectively evaluated.

Results: Median age for all patients was 71 years (interquartile range 61-77) and 113 (77.9%) were male. CP score was 7 for 105, 8 for 31, and 9 for 9 patients. The Atez/Bev and LEN groups did not differ significantly for best response (complete response:partial response:stable disease:progressive disease = 0:12:20:12 vs. 5:22:24:19, $p=0.265$). There was no significant difference for progression-free survival (PFS) between them [median 5.7 (95% CI 3.6-7.9) vs. 4.4 (95% CI 3.5-5.9) months, $p=0.581$]. Adverse events (AEs) (any grade/ $\geq$ grade 3) were observed in 83.0%/36.4% ($n=44/16$) of the Atez/Bev group and 78.3%/36.1% ($n=72/26$) of the LEN group ($p=0.53$ and $p=1.0$, respectively).

Conclusion: PFS, post-progression treatment rate, and incidence of AEs were not significantly different between the Atez/Bev and LEN groups. Although both treatments showed equivalent effects, neither demonstrated sufficient therapeutic efficacy in the present cases. Development of an effective systemic therapy for uHCC patients with CP-B is needed in the near future.

Abstract Submission No. 101890

P-0582

1 year mortality rate of patients with high PIVKA-II values in Mongolia

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1 year mortality rate of patients with high PIVKA-II values in Mongolia

Introduction: There are two commonly used HCC tumor markers widely used in Mongolia which are AFP and PIVKA-II, and we decided to assess mortality among patients with values higher than 300 mAU PIVKA-II markers.

Methods: Out of a total of 1015 people tested, 318 people had a higher than normal values of PIVKA-II, and 103 patients had value higher than 300 mAU/ml, out of which 54 people were contacted to take an retrospective anamnesis by telephone.

The result: Of the total of 54 people, 1 year mortality rate was 31.4% ($n=17$), and the marker value of PIVKA- II in these patients ranged between 708- 30'000 mAU/ml. We chose cut off value of 300mAU/ml because of lower false positivity rate.

Conclusion: 60% of deceased patients who had PIVKA-II marker value above 300 mAU/ml were tested 5-8 months prior to the survey, and 70% of them died within 3-4 months after the testing.

Abstract Submission No. 101896

P-0583

Multidisciplinary Treatment for Patients with Advanced Hepatocellular Carcinoma

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Introduction: Various treatments are available for treating hepatocellular carcinoma (HCC). Among HCC, Vp4 portal vein tumor thrombosis (PVTT) has a poor prognosis. There have been reports of treatment with molecularly targeted agents in combination with hepatic arterial infusion chemotherapy (HAIC) and radiotherapy (RT) in HCC patients with Vp4 PVTT, but none with atezolizumab, the immune checkpoint inhibitor. Here, we present cases of unresectable HCC with Vp4 PVTT that were treated with the combination atezolizumab and bevacizumab (Atezo+Bev) after HAIC and RT.

Patients: 66-year-old man, 74-year-old man, 83-year-old man, 69-year-old man, 62-year-old man and 85-year-old woman were diagnosed with HCC with Vp4 PVTT. Cirrhosis was classified as Child-Pugh class A or B. HCC was diagnosed as TNM stage IVa or IVb. RT for PVTT was performed the same day or the day after HAIC. Atezo+Bev was started at least 1 week after RT was completed.

Result: Death was confirmed in 4 of the 6 patients; the median overall survival time was not reached. The survival times of the 4 patients were 18.7, 12.5, 5.1, and 1.7 months. Based on the mRECIST criteria, the objective response rate of patients with best tumor response to Atezo+Bev therapy was 66.7%, and that of patients with best response of PVTT to Atezo+Bev was 66.7%.

Conclusion: These cases showed that in HCC with Vp4 PVTT, HAIC and RT before Atezo+Bev may be useful to prolong survival.

Abstract Submission No. 101900

P-0584

Atezolizumab+bevacizumab during anti-platelet/anti-coagulation therapy in hepatocellular carcinoma

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Background & Aims: This study aimed to determine the safety and efficacy of atezolizumab + bevacizumab therapy in hepatocellular carcinoma patients receiving anti-platelet agents or anticoagulants.

Methods: The patients were divided into those using (IM out) and those not using (IM in) anti-platelet agents or anticoagulants, which violated the exclusion criteria of the IMbrave150 trial, and were retrospectively examined.

Results: The study included 114 patients (IM in: 95; IM out: 19). For first-line treatment, the progression-free survival was 206 days for IM in and 307 days for IM out ($p=0.245$), and the overall survival was 685 days for IM in and not reached for IM out ($p=0.610$), with no significant difference between the two groups. Similarly, there were no significant between-group differences in progression-free survival and overall survival for later-line treatment. Hemorrhagic adverse events of $\geq$ grade 3 were observed in 7 IM in patients and 3 IM out patients. No significant factors associated with hemorrhagic adverse events of $\geq$ grade 3 were identified in the multivariate analysis including a factor for IM in/out group. No deaths were directly attributable to bleeding events or exacerbations of thrombosis.

Conclusion: Atezolizumab + bevacizumab therapy shows almost the same safety and efficacy in hepatocellular carcinoma patients receiving and those not receiving anti-platelet agents or anticoagulants. It is desirable that this issue will be examined in more cases and prospective studies.

Abstract Submission No. 101910
P-0585

Impact of DAAs on the Clinical Prognosis of Japanese Patients with HCC Caused by Hepatitis C Virus

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Background/Aim: Direct acting antivirals (DAAs) capable of eliminating hepatitis C virus (HCV) sustained virological response SVR at a higher rate than interferon therapy have been available in Japan since 2014. This study examined the clinical impact of DAAs for hepatocellular carcinoma (HCC) due to HCV before and after the advent of these drugs.

Methods: Enrolled were 1982 patients with HCC due to HCV treated at our institutions in Japan from January 2000 to January 2023. They were divided into two groups based on before and after DAA availability; pre-DAA (before 2013, $n=1181$) and post-DAA (after 2014, $n=801$). Changes in clinical features and prognoses were evaluated in a retrospective manner.

Results: The groups did not show significant differences for Liver Cancer Study Group of Japan tumor node metastasis stage or Japan integrated staging (JIS) score. However, the post-DAA group had higher frequencies of patients with SVR from anti-viral treatments (45.9% vs. 10.1%), elderly age (73 vs. 69 years old), lower AST (40 vs. 56 IU/L), ALT (31 vs. 46 IU/L), and AFP (11.2 vs. 23.6 ng/mL) levels, higher platelet count (13.6 vs. 10.8 / μ L), longer prothrombin time (88.0% vs. 81.9%), better ALBI score (-2.53 vs. -2.36), and higher rate of curative treatment (surgical resection or radio frequency ablation) (73.7% vs. 65.0%) ($p<0.001$, for all). Also, recurrence-free survival (RFS) after curative treatment was significantly better in the post-DAA group (median 2.9 vs. 2.1 years) as was overall survival (OS) [median: not applicable (NA) vs. 5.5 years] ($p<0.001$, for all). After inverse probability weighting (IPW) adjustment using propensity scores based on multivariate analysis, OS was also better in the post-DAA group (median 7.0 vs. 5.7 years, $p<0.001$). As a sub-analysis, comparisons of prognosis among three groups after dividing the post-DAA group into non-SVR ($n=307$), pre-SVR (HCC developed after SVR, $n=368$), and post-SVR (SVR developed after HCC, $n=126$) showed that OS for the non-SVR group was significantly shorter (median 3.2 years vs. NA vs. NA, $P<0.001$), with no significant difference noted between the pre- and post-SVR groups ($p=0.19$).

Conclusion: The prognosis of patients with HCC due to HCV was greatly improved after introduction of DAAs, with the resultant high rate of HCV elimination dramatically changing clinical practice for HCV-related HCC cases.

Abstract Submission No. 101922
P-0586

Prognostic Assessment Using the GNRI in Atezolizumab Plus Bevacizumab Therapy for HCC

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Background/Aim: The geriatric nutritional risk index (GNRI) is an easy-to-use tool for assessing nutritional status based on body weight and serum albumin. This study aimed to evaluate the prognostic predictive ability of GNRI in patients with hepatocellular carcinoma (HCC) treated with atezolizumab plus bevacizumab (Atz/Bv).

Materials/Methods: The study included 525 HCC patients who received Atz/Bv as a first-line systemic chemotherapy. GNRI was used to evaluate prognosis, and patients were classified based on normal, mild-decline, moderate-decline, and severe-decline GNRI values. Muscle volume decline (MVD) was also evaluated as a sub-analysis.

Results: Prognoses (median progression-free survival (mPFS)/median overall survival (mOS)) were stratified according to GNRI status (normal vs. mild vs. moderate vs. severe decline=8.3/21.4 vs. 6.7/17.0 vs. 5.3/11.5 vs. 2.4/7.3 months) ($P<0.001$). The mPFS and mOS according to Child-Pugh class (A, B, and C) were 7.0/19.1, 4.3/6.4 and 0.4/1.1 months ($P<0.001$), while those according to albumin-bilirubin (ALBI) grade (1, 2, and 3) were 9.3/21.4, 6.0/14.5 and 3.0/7.3 months ($P<0.001$). The c-index values of GNRI for predicting PFS and OS

were higher than those of Child-Pugh class and ALBI grade (0.574/0.632 vs. 0.527/0.570 vs. 0.565/0.629). GNRI, Child-Pugh class, and ALBI grade were analyzed for time dependent receiver operating characteristic curve (ROC) analysis to evaluate the area under the curve (AUC) for PFS and OS at 6 and 12 months. The AUC for PFS at 6 and 12 months were 0.616 and 0.594 for GNRI, 0.533 for Child-Pugh class, and 0.607 and 0.591 for ALBI grade, respectively. The AUC for OS at 6 and 12 months were 0.669 and 0.667 for GNRI, 0.622 and 0.580 for Child-Pugh class, and 0.654 and 0.661 for ALBI grade, respectively. The frequency of MVD increased as GNRI values declined (GNRI status: normal vs. mild vs. moderate vs. severe decline=17.6% vs. 29.2% vs. 41.2% vs. 57.9%, $P<0.001$), and a GNRI value of 97.8 was predictive of its occurrence (AUC 0.715, 95%CI 0.649-0.781, specificity/sensitivity=0.644/0.688). There were significant relationships between GNRI and SMI in both genders (Male: $r=0.42$, 95%CI 0.302-0.526, $P<0.001$, Female: $r=0.438$, 95%CI 0.169-0.646, $P=0.002$).

Conclusion: The results of this study suggest that GNRI is a useful prognostic tool for predicting both prognosis and MVD in HCC patients treated with Atz/Bv.

Abstract Submission No. 101943
P-0587

Clinical Profile of Non-Viral and Viral Hepatocellular Carcinoma in a Tertiary Hospital in Indonesia

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Background: With the introduction of national hepatitis B vaccination program and direct-acting antivirals for hepatitis C virus, viral-related hepatocellular carcinoma (HCC) is predicted to decrease in the future, while non-viral HCC may increase. This study aims to compare the clinical characteristic of patients with viral and non-viral HCC.

Methods: This is a descriptive study using HCC patient registry in our hospital. Clinical characteristics according to the etiologic agent of HCC were assessed. Patients were classified as non-viral HCC when HBsAg and anti-HCV results were negative.

Results: Between January 2015 and December 2021, 799 individuals received an HCC diagnosis, with 743 participants being part of the study. Exclusion of 56 patients occurred due to incomplete data on the etiologic agent. The study comprised 650 individuals in the viral group and 93 in the non-viral group. Notably, Hepatitis B stood out as the primary etiologic agent, contributing to HCC in 500 patients. Patients with non-viral HCC were significantly older than viral HCC (median age 65 (IQR 20) vs. 59.5 (IQR 16), $p<0.001$). A higher proportion of non-viral HCC patients displayed AFP levels below 200 ng/mL. Nevertheless, non-viral HCC patients were less frequently associated with BCLC stage A and radiofrequency ablation (RFA) treatment compared to their viral HCC counterparts.

Conclusion: Non-viral HCC patients presented at an older age, lower AFP level, and a more advanced tumor stage compared to those with viral HCC.

Abstract Submission No. 101952
P-0588

Impact of locoregional therapy on hepatocellular carcinoma treated with atezolizumab and bevacizumab

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Background: Atezolizumab plus bevacizumab (Atez/Bev) therapy is extremely effective and has a high response rate in hepatocellular carcinoma (HCC) treatment. Here, we investigated the efficacy of adding locoregional therapy with Atez/Bev therapy for non-complete response (CR) HCC cases.

Patients and Methods: Twenty-eight HCC patients in non-CR during Atez/Bev therapy received locoregional therapy, and treatment efficacy was evaluated based on a modified RECIST assessment.

Results: There were 23 male and five female participants with a mean age of 73.5 years. In the Atez/Bev therapy combined with locoregional therapy effective group, both transcatheter arterial chemoembolization (TACE) and radiofrequency ablation (RFA) were combined in all patients. A significant reduction in neutrophil-to-lymphocyte ratio (NLR) was observed after adding locoregional therapy ($p=0.039$). Moreover, a combination of TACE and RFA was performed for all patients in the CR group. When assessing the add-on effect of the combination of TACE and RFA in the progressive disease (PD) group, seven patients were found to achieve non-PD after adding locoregional therapy. For patients who achieved non-PD, significant NLR reduction was noted after the addition of locoregional therapy.

Conclusion: Adding locoregional therapy such as TACE/RFA was found to exert an effect even in non-CR patients who had received Atez/Bev therapy. An NLR reduction after adding locoregional therapy was noted. Even when a response is not obtained during Atez/Bev therapy, it is important to avail the option to add locoregional therapy as it may contribute to improved prognosis via immune modulation with tolerable adverse reactions.

Abstract Submission No. 101992
P-0589

The effect of YangYinFuZhengJieDu decoction with HBV-HCC: a prospective, randomized clinical trial

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Retrospective study found that the YangYinFuZhengJieDu decoction (YYFZJD) can delay tumor progression and prolong the survival time of hepatitis B virus-related Hepatocellular Carcinoma (HBV-HCC) patients. In mice, we found that YYFZJD exerted anti-tumor effects by alleviating T cell exhaustion and immune suppression. In this study, we aim to evaluate the efficacy and safety of YYFZJD and verify its anti-tumor immune response. 132 patients with HBV-HCC were conducted and assigned to receive either YYFZJD or no YYFZJD (control) in a 1:1 ratio. They were followed up for 96 weeks. At a follow-up of 96 weeks, the overall survival rate of patients in YYFZJD and Control group was 65.2% and 50%, respectively (Log-rank $P<0.05$). And the progression-free survival rate was 57.6% and 40.9%, respectively (Log-rank $P<0.05$). The AFP level decreased in the YYFZJD group ($P=0.027$). The PD-1+TIM-3+CD8+T cells significantly decreased in YYFZJD group, and the anti-tumor cytokine IFN- γ increased ($P<0.05$). However, in comparison with the control group, we found no significant difference in the incidence of liver dysfunction

in the YYFZJD group ($p \geq 0.05$). In conclusion, YangYinFuZhengJieDu decoction can reduced mortality in HBV-HCC patients and delay tumor progression by regulating the immune suppression. At the same time, YYFZJD has good safety. Future multi-center trials with larger sample sizes are required to verify these findings. Clinical trial registration: www.ClinicalTrials.gov NCT02927626.

Abstract Submission No. 102035

P-0590

Changing epidemiology of HCC in the United States: a population-based study from 2000-2017

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Background: HCC is the 6th deadliest cancer in the US, and it is unclear if there has been significant improvement in survival in recent years, especially for HCC patients with nonviral liver disease.

Aims and Method: To investigate the survival trends of HCC patients over time and by etiology using the U.S. population-based Surveillance, Epidemiology, and End Results–Medicare (2000-2017).

Results: The study included 52,698 HCC patients. Viral HCC patients were more likely to be Asian (18.0% vs. 10%) or Black (17.9% vs. 7.0%) and with early HCC stage I/II (52.0% vs. 43.0%), and to have higher 5-year survival (16.4% vs. 12.0%) (all $P < 0.001$). Viral HCC patients also had higher 5-year survival than nonviral HCC patients in both the pre and post 12/2013 periods (Figure 1A). Additionally, though survival increased for both groups over time (Figure 1B) survival rates increased more for viral HCC (44.2% increase, from 14.7% to 21.2%) as compared to nonviral HCC (33.6% increase, from 10.7% to 14.3%). On multivariable Cox's regression analysis adjusting for age, sex, race and ethnicity, tumor stage, cirrhosis status, HCC treatment, and time period, viral (vs. nonviral) etiology was independently associated with higher survival (adjusted hazard ratio [aHR]=1.25, 95%CI 1.23-1.28, $P < 0.001$). HCC diagnosis after 12/2013 was also associated with higher survival compared to before (aHR=1.27, 95%CI 1.24-1.30, $P < 0.001$).

Conclusion: Despite some improvement over time, overall 5-year survival rates remain low at only 21.2% for viral HCC and 14.3% for nonviral HCC. Further efforts are needed to improve HCC surveillance and treatment.

Abstract Submission No. 102038

P-0591

Multidisciplinary treatment strategy for macroscopic portal vein tumor thrombus

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Background: Hepatocellular carcinoma (HCC) with a tumor thrombus extending to the first branch (Vp3) or main trunk (Vp4) of the portal vein is considered an end-stage condition with an extremely poor

prognosis with few treatment options. The present study aimed to analyze the optimal treatment for Vp3/4 HCC.

Subjects: One hundred patients who underwent hepatectomy for Vp3/4 HCC and 26 patients who underwent chemotherapy (lenvatinib (LEN: n=10) and atezolizumab/bevacizumab combination therapy (A/B: n=16))

Results: The median survival (MST) of all 100 patients who underwent hepatectomy for Vp3/4 HCC was 14.5 months. The MSTs of patients with Vp3 (n = 37) and Vp4 (n = 63) were 16.1 months and 14.3 months, respectively, without significant difference ($P = 0.7098$). Any tumor factor, including Vp status (Vp3 or 4), the type of resection (curative or reductive), intrahepatic maximal tumor size, intrahepatic tumor number, and the existence of extrahepatic metastasis, did not influence overall survival.

The MST of all 26 patients who underwent chemotherapy was 9.8 months (A/B: 15.0 months and LEN: 9.8 months). The objective response rates (CR+PR) by mRECIST and RECIST were 37.5% and 25.0% in the LEN group and 50.0% and 37.5% in the A/B group, respectively. The proportions of patients with a decrease in tumor markers from baseline (AFP day30/before<1) at 1 month after the start of chemotherapy were 62.5% in the LEN group and 69.2% in the A/B group. Of the 26 patients, none were eligible for conversion hepatectomy, but 5 patients in the A/B group were recurrence-free with drug fee.

Conclusion: For Vp3/4 HCC, hepatectomy tended to have a better prognosis than chemotherapy. Future studies are needed to determine the possibility of long-term prognosis for patients in the chemotherapy group who can be treated with conversion therapy.

Abstract Submission No. 102041

P-0592

Safety and Efficacy of Atezo/Bev in Combination with Radiation Therapy in HCC with Vp4 PVTT

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Background: Hepatocellular carcinoma (HCC) with portal vein tumor thrombus (PVTT) generally has a poor prognosis, but the efficacy of atezolizumab plus bevacizumab (ATZ/BEV) therapy in Vp4 PVTT cases has been reported. Previous studies have demonstrated the therapeutic effects of radiation therapy (RT) in Vp4 cases. This study investigates the combination of ATZ/BEV and RT in Vp4 cases.

Methods: This study included unresectable HCC patients who received ATZ/BEV in our hospital from October 2020 to September 2023. Vp4 cases who started treatment after September 2022 were treated with RT.

Results: During the period, 63 cases received ATZ/BEV treatment, including 8 Vp4 cases, with RT administered in 4 cases. RT was performed on the PVTT with a planned total dose of 25 Gy in 5 fractions. Of the 4 RT cases, 3 received RT before starting ATZ/BEV therapy, and 1 received RT between the second and third courses. No side effects leading to discontinuation were observed in the combined RT group, and there was no significant difference in liver reserve before and after RT. One case in the combined RT group had PVTT extending to the SMV. After RT, ATZ/BEV was started, and the first imaging assessment was CR, with tumor markers also becoming negative. ATZ/BEV administration was discontinued after 18 courses, and the patient has been recurrence-free since.

Conclusions: The combination of ATZ/BEV and RT in Vp4 cases was safely administered. Some cases showed good treatment outcomes, suggesting the potential for improved treatment efficacy.

Abstract Submission No. 102068
P-0593

Hepatectomy using a right thoracotomy and continuous oblique incision -our experience-

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Introduction: Even with advances in laparoscopic hepatectomy and robotic surgery, there are still cases in which open hepatectomy is necessary. Hepatectomy using a right thoracotomy and continuous oblique incision makes it easy to cut and suture the right and short hepatic veins with retroperitoneal dissection. It is useful and safe for wide posterior segmentectomy including the caudate lobe, resection of recurrent lesions around the right adrenal gland, and cases where severe adhesions are observed at the hepatic hilum or anterior surface during repeated hepatectomy.

Subjects: Since 2005, 26 patients (group O) underwent hepatectomy using this approach. Seven cases (26.9%) among them underwent repeated hepatectomy.

Perioperative outcomes were compared with 81 cases of right lobe hepatectomy (Group J) performed during the same period using a supine J-shaped incision.

Results: The breakdown of right hepatectomy in groups O/J was 7/17 cases of right lobectomy and extended right lobectomy, and 19/64 cases of segmentectomy and partial resection. The operative time, intraoperative blood loss, and postoperative hospital stay were 270/314 minutes ($p < 0.05$), 991/1151 ml, and 19/19 days, respectively. Complications of Clavien-Dindo 2 $\leq$ were observed in 6/30 cases. Comparing only right and extend right lobectomy, the operative time, intraoperative blood loss, and postoperative hospital stay were 226/382 minutes ($p < 0.05$), 1101/1701 ml, and 13/30 days ($p < 0.05$), respectively. Complications were observed in 1/14 cases ($p < 0.01$).

Conclusion: Hepatectomy through right thoracotomy and continuous oblique incision remains an effective surgical technique for resection of lesions, which is expected to be difficult with laparoscopic liver resection or a frontal

Abstract Submission No. 102076
P-0594

AWGC's Novel Cachexia Criteria: A Prognostic Guide for Unresectable Hepatocellular Carcinoma

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Background: Cachexia, marked by aggressive dysfunction and muscle mass loss despite standard nutritional support, significantly impacts chemotherapy response, adverse events, and prognosis. The Asian Working Group of Cachexia (AWGC) introduced novel criteria for Asian populations in 2023. This study evaluated cachexia prevalence and its prognostic influence in unresectable HCC patients undergoing systemic chemotherapy.

Methods: Retrospectively analyzing 185 HCC patients receiving systemic chemotherapy at Gifu university hospital from July 2009 to July 2023, cachexia was defined by AWGC criteria (Weight loss $>2\%/3-6$ months or low BMI ($<21 \text{ kg/m}^2$) with anorexia, decreased grip strength,

or elevated CRP $\geq 0.5 \text{ mg/dL}$). Overall survival (OS) and progression-free survival (PFS) were assessed using a log-rank test and Cox proportional hazards model. Mann-Whitney U-test evaluated differences in continuous variables.

Results: Patient characteristics are detailed in Table 1. Cachexia, diagnosed in 47 patients (25.4%), correlated with a higher percentage of females, higher ALBI scores and lower immunotherapy usage. Tumor factors exhibited no significant differences. Both OS (median 11.1 vs. 20.5 months, $p = 0.02$) and PFS (median 6.0 vs. 8.3 months, $p = 0.002$) significantly shorter in the cachexia group. Multivariate analysis identified cachexia as an independent unfavorable factor for OS (HR 1.60; 95%CI 1.01-2.46, $p = 0.03$) and PFS (HR 1.61; 95%CI 1.12-2.33, $p = 0.01$).

Conclusions: Cachexia, by AWGC criteria, prevailed in 25.4% of unresectable HCC patients, emerging as a significant prognostic factor, irrespective of liver function and tumor factors. Cachexia assessment should precede systemic therapy administration.

Abstract Submission No. 200000
P-0595

Comparison between nivolumab and regorafenib after sorafenib failure for hepatocellular carcinoma

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Background and Aims: Nivolumab and regorafenib are used as second-line therapies for patients with advanced hepatocellular carcinoma (HCC). We aimed to compare the effectiveness of nivolumab to regorafenib.

Method: We retrospectively reviewed HCC patients treated with nivolumab or regorafenib after sorafenib failure. Progression-free survival (PFS) and overall survival (OS) were analyzed. Inverse probability of treatment weighting (IPTW) using the propensity score (PS) was conducted to reduce treatment selection bias.

Results: Among the recruited 189 patients, 137 and 52 patients received regorafenib and nivolumab after sorafenib failure, respectively. Nivolumab users showed higher Child-Pugh B patients (42.3% vs. 24.1%) and shorter median sorafenib maintenance (2.2 vs. 3.5 months) compared to regorafenib users. Compared to regorafenib users, nivolumab users showed shorter median OS (4.2 vs. 7.4 months, $P = 0.045$) and similar median PFS (1.8 vs. 2.7 months, $P = 0.070$), respectively. However, median OS and PFS were not different between the two treatment groups after 1:1 PS matching yielded 34 pairs (log-rank $P = 0.810$ and 0.810 , respectively), and after stabilized IPTW (log-rank $P = 0.445$ and 0.878 , respectively). In addition, covariate-adjusted Cox regression analyses showed that the nivolumab (vs. regorafenib) use was not significantly associated with the PFS and OS after 1:1 PS matching and stabilized IPTW (all $P > 0.05$).

Conclusion: Clinical outcomes in patients treated with nivolumab and regorafenib after sorafenib failure did not differ significantly.

Abstract Submission No. 200049
P-0596

Effect of Marital and Insurance Status on the Survival of Elderly Patients with HCC

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Background: Among various types of cancer, marital and insurance status are considered important prognostic factors. However, how these factors affect elderly HCC patients remains unexplored. The purpose of this study was to reveal the role of marital status and insurance in the survival of elderly HCC patients.

Methods: We retrieved data for patients diagnosed with HCC between 2010 and 2016 from the Surveillance, Epidemiology, and End Results (SEER) database. Our analysis of the clinicopathological features, overall survival (OS), and cancer-specific survival (CSS) was based on marital and insurance status.

Results: A total of 10,620 elderly HCC patients received complete information from SEER. The OS and CSS of the nonmarried group were worse than those of the married group. The OS and CSS of the uninsured group were lower than those of both the insured and Medicaid groups. The results suggest that marital status and insurance may affect the long-term survival of elderly HCC patients. The subgroup survival analyses revealed the lowest risk for death among the insured married group based on the comparison of the OS and CSS across all other groups. Moreover, univariate and multivariate analyses revealed race, insurance, surgery, and chemotherapy as independent predictors for OS, whereas sex, insurance, surgery, radiotherapy, and chemotherapy were independent predictors for CSS in elderly HCC patients.

Conclusion: Marital status and insurance status have a great influence on the survival of elderly HCC patients. Therefore, it is necessary to provide more support to this lonely and uninsured vulnerable group of patients.

Abstract Submission No. 200050
P-0597

A predictive nomogram for venous thromboembolism in patients with primary liver cancer

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Background: Cancer often leads to venous thromboembolism (VTE), which is the primary reason for cancer-related mortality, this study aimed to develop a nomogram chart model capable of accurately predicting the probability of venous thromboembolism (VTE) in patients diagnosed with primary liver cancer (PLC) within the overall population. Doctors can accurately identify VTE patients by utilizing this model and apply early prevention and therapeutic strategies to decrease the likelihood of thrombosis.

Method: Using data collected from patients diagnosed with PLC at Chongqing University Cancer Hospital in China, logistic invariant and multivariate analysis techniques were employed to identify the independent risk factors associated with VTE. An integrated nomogram was then constructed for internal verification. The effectiveness of the Nomogram prediction is assessed through the receiver operating characteristic curve (ROC) and calibration curve.

Result: 1565 patients diagnosed with PLC were analyzed. In total, the nomogram integrated eight risk factors for VTE that were independent, namely activated partial thromboplastin time (APTT) ($P=0.007$), D-dimer ($P=0.019$), lymphocyte count (LYM) ($P=0.012$), monocyte count (MONO) ($P=0.002$), transarterial chemoembolization (TACE) ($P<0.001$), surgical intervention ($P=0.010$), and immunotherapy ($P=0.010$). The nomogram model demonstrated a strong discriminatory ability with C indices of 0.753 and 0.710 in the training and verification queues, respectively. The nomogram's calibration chart demonstrates a strong correlation between the estimated probability and the real probabilities.

Conclusion: In this study, we developed and verified a new nomogram to estimate the likelihood of VTE in individuals diagnosed with PLC. By utilizing the nomogram model, it is possible to accurately

assess the risk of VTE in PLC patients on an individual basis and identify those at high risk who require a targeted preventive treatment approach.

Abstract Submission No. 200088
P-0598

Efficacy combine DEXA with N-Actylecyteine to prevent post embolization Syndrome after TACE

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100 patient were enrolled : 50 patient were assigned randomly to dexamethasone plus NAC and placebo, DEXA+ NAC were significantly lower developed PES than placebo group (6% VS 80% , $P<0.001$) and multivariate analysis dexamethasone+NAC is a protective factor against PES with Abd OR of 0.04 ($P<0.001$) . Post -TACE liver decompensation was documented in 7 from 50 (14%) in control group as opposed to DEXA+NAC no developed (14% VS 0%) but multivariate analysis no statistically significant due to low incidence of liver decompensation , ALBI >0.5 increased is significant predictor for liver decompensation

Abstract Submission No. 200089
P-0599

Real world of curative stage hepatocellular carcinoma, A multicenter study

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Over thousand ($n=1145$) HCC patient's data from 2 tertiary center for ten years periods. CP-A, CP-B, CP-C were 48.7, 34.4 and 15.1% with mean MELD score of 12.6. Etiology were hepatitis B, NASH, hepatitis C and alcohol; 33, 27.1, 25.8, 17.3% respectively. At the time of HCC diagnosis by application of BCLC Criteria, 470 patients (41%) were in curative stage of BCLC- 0 ($n=244$; 21.31%) and Stage of BCLC- A ($n=226$; 19.73 %). Over six-hundred patients ($n=675$) were diagnosed with non-curative stage [BCLC- B: ($n=417$; 36.41%), BCLC-C: ($n=102$; 8.9%) and BCLC-D: ($n=156$; 13.62%)]. Within 470 HCC at BCLC stage 0-A categorized treatment modality of curative HCC, radiofrequency ablation ; RFA ($n=188$), resection ($n=98$) and trans-arterial chemoembolization; TACE ($n=109$). Our comparative study between RFA and resection found a higher proportion of CP- B and tumor size of equal or less than 2 cm were selected to RFA treatment (RFA: $n=55$; 29.3% vs Resection $n=7$; 7.1%, $p<0.001$) and (RFA: 63.6% vs Resection 31.5%; $p<0.001$). Selection to liver resection has a characteristic of CP-A (Resection: $n=90$; 91.8% vs RFA: $n=131$; 69.7%, $p<0.001$)

Abstract Submission No. 200104
P-0600

Sarcopenia and Prognosis in Hepatocellular Carcinoma Patients Treated with Atezolizumab/Bevacizumab

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Objective: Although there have been advances in the prevention and diagnosis of hepatocellular carcinoma (HCC), many HCC patients are diagnosed with advanced stage. Atezolizumab plus bevacizumab (atezo/bev) is recommended as first-line treatment for unresectable HCC (uHCC). Recently, sarcopenia-related factors, including decreased skeletal muscle index (SMI), have been reported to be associated with prognosis in uHCC patients. There are few reports on grip strength (GS) despite their importance in accurate sarcopenia diagnosis, and furthermore, there is no evidence regarding atezo/bev. We investigated whether sarcopenia affects the clinical outcome of atezo/bev.

Methods: This study included 64 uHCC patients on atezo/bev and assessed their GS and SMI, and SMI was measured using bioelectrical impedance analysis (BIA). We diagnosed sarcopenia based on GS and BIA-SMI and compared the sarcopenia and non-sarcopenia groups.

Results: Of these patients, 28 had sarcopenia, and 36 had non-sarcopenia. Adverse events (AEs) frequently occurred, and the albumin-bilirubin score significantly decreased after atezo/bev in the sarcopenia group than in the non-sarcopenia group. The median progression-free survival was 4.7 (0.4–26.4) and 10.6 (1.1–24.5) months in the sarcopenia and non-sarcopenia groups, respectively. The median overall survival (OS) was 12.6 (1.4–27.7) months in the sarcopenia group and was not reached in the non-sarcopenia group, indicating a significant difference ($p < 0.01$). In multivariate analysis, sarcopenia was significantly associated with OS.

Conclusion: Sarcopenia was associated with poor clinical outcomes based on the occurrence of AEs and decreased liver function in uHCC patients on atezo/bev. GS and SMI are important parameters for accurately diagnosing sarcopenia.

Abstract Submission No. 200171
P-0601

Fatty acid metabolism related genes predict prognosis in Hepatocellular carcinoma

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Background: Hepatocellular carcinoma (HCC) is associated with high morbidity and mortality. Alterations in fatty acid metabolism promote tumor progression. Herein, we aimed to investigate the association between fatty acid metabolism related genes (FAMRGs) expression and HCC.

Methods: FAMRGs were obtained from the MsigDB, and HCC samples information were obtained from the TCGA and GEO database. Based on the expression profiles of FAMRGs, we classified HCC samples into different clusters. Based on differentially expressed genes (DEGs) between clusters, we established the prognostic risk model and nomogram using LASSO and multivariate COX regression analyses, and validated the effectiveness of the model. Subsequently, we explore the differences in gene mutation characteristics, infiltrating immune cells, tumor microenvironment score and drug sensitivity between the high-and low-risk groups. Finally, the immunohistochemistry staining was utilized to confirm the expression of the prognostic related genes in HCC.

Results: The HCC samples were divided into three clusters based on the expression profiles of the FAMRGs. 4 DEGs among clusters to construct prognostic risk model, which displays good prognostic efficacy. And we found patients in the high-risk group had worse overall survival, an immunosuppressive microenvironment, and worse sensitivity to anti-cancer drug treatment. The results of

immunohistochemical staining showed that the expression of prognostic related genes was significantly different between HCC and normal tissues.

Conclusion: In summary, we establish a prognostic risk model based on FAMRGs to proof fatty acid metabolism is related to the prognosis of HCC, and provide a new insight for predicting HCC prognosis and clinical treatment.

Abstract Submission No. 200175
P-0602

Towards Tumorized Therapies: Dynamics of Wnt/β-catenin Oncogenic Variants in multiple HCC nodules

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Aim: Tumor nodules carrying Wnt/β-catenin signaling pathway abnormalities were shown to have unique features of pathology (rich bile production/pseudo tubular formation), of imaging findings (EOB-MRI high) and of poor ICI response. However, HCC occurrence is multicentric and metachronous in many occasions. In this communication, we disclosed the spectrum of dynamic changes among nodules with Wnt/β-catenin abnormalities.

Methods: Surgically resected 313 tumor nodules from 190 patients were laser micro-dissected and NG-sequenced by in-house panel (72 genes, spanning 177,048 nt) including 5 (*CTNNB1*, *AXIN*, *APC*, *NCOR1*, *FGF19*) genes of Wnt/β-catenin signaling pathways.

Results: We first revealed the involvement of Wnt/β-catenin signaling pathways abnormalities in 122 patients with solitary nodules. In 44 of 122 (36%), abnormality of the pathway was detected. We then studied 68 cases with multiple recurrence of HCC (194 nodules). Of these 194 nodules, only 38 (19%) had Wnt/β-catenin abnormalities. Of the 68 cases, 30 cases (44%) had at least one nodule having Wnt/β-catenin abnormality, but only 4 cases (13%) constantly had Wnt/β-catenin signaling pathway abnormality thereafter and the remaining 87% (26 cases) had other types of “drivers” in recurrent nodules.

Conclusion: In real life, serial occurrence of HCC is so common. This study indicates the change or switching of the drivers to promote carcinogenesis occurs from nodules to nodules. Only in 13% of cases they are constantly showing Wnt/β-catenin abnormality and others had different drivers. For the future, appropriate tumorized therapy is needed.

Abstract Submission No. 200181
P-0603

Clinical and genomic Characterization of HCC nodules after SVR achievement

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Aim: The advent of direct-acting antivirals (DAAs) has reduced HCC by achieving sustained virologic response (SVR). Despite this, reports of HCC post-SVR have emerged. This study scrutinizes the genomic and clinical features of HCC post-DAA treatment.

Methods: Among 689 DAA cases from July 2013 to November 2023, we examined 59 post-DAA HCC cases, comparing tumor size and number with 371 non-DAA cases. Genomic analysis used an in-house HCC panel (72 SMGs: 59,016 aa). OncoKB annotated oncogenic variants. We assessed WNT/ β -catenin abnormalities in these cases, comparing with 134 non-DAA HCC cases. In 11 post-DAA multiple HCC cases, tumors with shared oncogenic variants were defined as intrahepatic metastasis (IM), while those without were considered multicentric origin (MC). Clonality was evaluated and compared with 53 non-DAA multiple HCC cases.

Results: After SVR, 40 patients had 58 nodules, with an average of 1.3 and a median tumor size of 2.0 cm (0.5-9.0). In non-DAA cases (n=371), the average was 1.8, with a median size of 3.8 cm (0.8-21.9). Among post-SVR HCC cases, 26% demonstrated WNT/ β -catenin abnormalities, while non-SVR cases showed abnormalities in 29%. In post-SVR multiple HCC, 18% had IM&MC, and 82% had MC. In non-DAA cases, 32% showed IM, 15% showed IM&MC, and 53% showed MC.

Conclusion: Post-SVR HCCs tend to be smaller and fewer, suggesting a favorable prognosis. The frequency of WNT pathway abnormalities shows no significant difference between SVR and non-SVR cases. However, there is a significantly higher prevalence of MC in post-SVR multiple cases than non-SVR cases.

Abstract Submission No. 200183

P-0604

Serum ATX forecast postoperative recurrence in patients with HBV associated liver cancer

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Objective: To explore the role of of serum secretion of motor factors (ATX) predict postoperative recurrence in patients with HBV associated liver cancer (HBV-HCC).

Methods: Forty patients who met the indications of HBV-HCC surgical treatment and underwent surgical resection were enrolled. Based on the results at one-year, the patients were divided into a recurrence group (18 cases) and a non recurrence group (22 cases). Univariate and multivariate regression was used to identify the impact factors associated with postoperative recurrence. The area under the receiver operating characteristic curve (AUROC) was used to assess the prediction for postoperative recurrence.

Results: The serum ATX levels of the recurrent group were significantly higher than those non recurrent group. Univariate and multivariate analysis showed that the maximum tumor diameter (p=0.011), serum ATX (p=0.036), and number of tumors (p=0.010) were independent predictors for postoperative recurrence in patients with HBV-HCC. ROC analysis showed that serum ATX has high value in predicting postoperative recurrence of HBV-HCC, with an area under the curve of 0.774 (95% CI: 0.610-0.938). Combining ATX, maximum tumor diameter, and number of tumors has higher value in predicting postoperative recurrence of HBV-HCC, with an area under the curve of 0.924 (95% CI: 0.844-1.000).

Conclusion: The serum ATX levels, maximum tumor diameter, and number of tumors in patients with HBV-HCC could be used as an important predictors for postoperative recurrence. The serum ATX levels could be used as an early serum predictor of postoperative recurrence.

Abstract Submission No. 200190

P-0605

The Importance of Hepatic Reserve in Sequential Therapy for Unresectable Hepatocellular Carcinoma

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Functional hepatic reserve is important when considering sequential systemic therapy for patients with unresectable hepatocellular carcinoma (uHCC). However, there have been few reports on the relationship between the change in hepatic reserve and the timing of switching to the sequential therapy. In this study, we examined the so-called "albumin-bilirubin (ALBI) curve", or the change in ALBI score during Lenvatinib (LEN) treatment.

We assessed ALBI score as indices of liver function during LEN treatment. Thirty-eight Child-Pugh A patients who received LEN from April 2018 to August 2023 were included in the study. From those, 20 received the sequential systemic therapy after LEN discontinuation (sequential group) and 18 patients cannot be treated (non-sequential group). The "ALBI curves" during LEN treatment in each group were examined.

Among 38 patients, median age was 74 years (43-89), 33 male-patients (86.8%), ALBI score was -2.26 (-3.19 to -1.57) at starting of LEN treatment, mALBI grade 1/2a/2b were 7/12/19 patients, and the duration of LEN treatment was 255 days (48-1180). ALBI scores for the sequential vs. non-sequential group were -2.19 vs -1.66 (p=0.0033) at LEN discontinuation, -2.20 vs -1.47 (p=0.0079), -2.27 vs -2.11 (ns) and -2.22 vs -2.05 (ns) at 4 weeks, 8 weeks and at 12 weeks before discontinuation, respectively. Moreover, at 4 weeks before discontinuation in the non-sequential group ALBI scores worsened to -1.47.

Our results suggest that LEN treatment should be discontinued or switched to the sequential therapy when the ALBI score worsens to -1.47 during the course of treatment in CTP-A uHCC patients.

Abstract Submission No. 200197

P-0606

Network pharmacology to reveal the mechanism of Fufang Banmao capsule for treating unresectable PLC

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Our objective is to utilize network pharmacology to investigate the bioactive ingredients and mechanism of Fufang Banmao capsules (FFBM). The bioactive ingredients for the FFBM were screened using the SwissTargetPrediction database, while the FFBM components were sourced from the HERB database. Targets and differentially expressed genes (DEGs) for FFBM and PLC were obtained using PharmMapper and the GEO database, respectively. Common targets were identified through the use of Venn diagrams. Enrichment analysis and protein-protein interaction (PPI) were carried out, and the Cytoscape software was employed to identify Hub genes and construct the ingredient-target-pathway network. Retrospectively collected data on

patients diagnosed with unresectable PLC from January 2008 to December 2019 were then analyzed. Finally, Cox analysis was used to elucidate the role of FFBM in the treatment of unresectable PLC. There were a total of 20 common targets, among which, MET, FGFR1, MDM2, HSP90AA1, SRC, and KDR were identified as hub genes. Enrichment analysis showed a significant association between the use of FFBM for treating PLC and various signaling pathways, such as chemical carcinogenesis, PI3K-AKT, Rap1, FoxO, MAPK, and VEGF. Clinic data revealed that FFBM significantly improved the prognosis of unresectable PLC.

Abstract Submission No. 200213
P-0607

Comparison of Prediction Models Based on Sonovue/Sonazoid-CEUS for Pathologic Grade and MVI in HCC

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Background: This study aimed to develop and compare the prediction model based on Sonovue and Sonazoid contrast enhanced ultrasound (CEUS) for pathologic grade and microvascular invasion (MVI) of hepatocellular carcinoma (HCC). And to investigate whether Kupffer phase images have additional predictive value for the above pathological features.

Methods: 90 patients diagnosed as primary HCC and received curative hepatectomy were prospectively enrolled. All patients underwent conventional ultrasound (CUS), Sonovue and Sonazoid-CEUS examination preoperatively. Clinical, radiological and pathological features including pathologic grade, MVI and CD68 expression were collected. We developed prediction models composing of clinical, CUS and CEUS (Sonovue and Sonazoid, respectively) features for pathologic grade and MVI with both logistic regression and machine learning (ML) method.

Results: 41 (45.6%) patients were poorly differentiated HCC (p-HCC) and 37(41.1%) were MVI positive. For pathologic grade, logistic model based on Sonazoid-CEUS had significant better performance than which based on Sonovue-CEUS (area under curve (AUC), 0.929 versus 0.848, $P=0.035$). While for MVI, these two models had similar accuracy (AUC, 0.810 versus 0.786, $P=0.068$). Meanwhile, we found well-differentiated HCC tends to have higher enhancement ratio in 6-12 minutes during Kupffer phase of Sonazoid-CEUS, as well as higher CD68 expression compared with p-HCC. Besides, all of these models can effectively predict the risk of recurrence ($P < 0.05$).

Conclusion: Sonovue-CEUS and Sonazoid-CEUS showed comparable excellence in predicting MVI, while Sonazoid-CEUS was superior to Sonovue-CEUS in predicting pathologic grade due to the Kupffer phase. Enhancement ratio in Kupffer phase have additional predictive value for pathologic grade prediction.

Abstract Submission No. 200250
P-0608

Point shear wave elastography in local treatments for HCC and liver metastases.

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BACKGROUND AND AIM: Liver fibrosis could impact the response to oncological therapies and it correlates with the stiffness of the parenchyma. Aim of our study was to explore the role of point shear wave elastosonography (pSWE) in predicting the response to local treatments for hepatocellular carcinoma (HCC) or liver metastases (METs).

MATERIAL AND METHODS: A prospective single-center study was conducted. We included all patients with HCC or METs treated by percutaneous ablation, trans arterial chemo-embolization, and external radiotherapy between September 2022 and March 2023. pSWE measurements were performed at the enrollment on the liver free from nodules, and on the targeted nodules. Results were expressed in m/sec. Patients were then followed at three and six months by computed tomography or magnetic resonance imaging, evaluated by a radiologist blind to elastosonographic data.

RESULTS: 43 patients were enrolled: 22 HCCs, and 21 liver METs of different etiologies. Among the 22 HCC patients, 19 patients (86.4%) suffered of liver cirrhosis. As expected, liver stiffness in cirrhotic patients was significantly higher than in non-cirrhotic patients (2.19 m/s [IQR 0.81] vs. 1.28 m/s [IQR 0.71], $p < 0.0001$). ARFI of the liver was sensitive and specific in predicting response to treatments at the six months follow-up, identifying a cut-off of 1.58 m/s associated with a lack of therapeutic response (AUC 0.73; 95% CI 0.54 – 0.92; $p = 0.033$).

CONCLUSION: Our study is a “proof of concept” about the role of pSWE, in the assessment of response to loco-regional treatments in case of malignant liver nodules.

Abstract Submission No. 200253
P-0609

Trance Arterial Chemoembolization (TACE) Treatment Option as Per Request of Patient

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INTRODUCTION: Hepatocellular cancer is second most common cause of death in males. It has strong association with hepatitis B and C. Best treatment option is stage dependent. Surgical option is the best way to treat the cancer. Sometimes patients do not opt the surgical option and they prefer non surgical methods. TACE Trance arterial Chemoembolization is one of them.

AIM: TACE can control the severity of HCC.

CASE REPORT: A 55 Years old male with previous history of .Hepatitis b and treated irregularly presented with complained of pain abdomen. His laboratory and radiological investigations were showing as if he is Child A. His ct scan was showing 4 cm tumor in segment 6. Patient was offered surgical resection but he opted TACE. He underwent 3 cycles of TACE and his AFP came down from 50 to 15. After one year his ct scan was showing again active disease. AFP had raised to 30.

RESULT: TACE Controlled the disease partially in this case.

DISCUSSION: Best treatment option is surgical in case of HCC. Sometimes we have to take care of wish of patients considering his financial status and other concerns. In these cases we have left no other choice except non surgical options. TACE is good option for time gaining or reducing the severity of cancer.

Abstract Submission No. 200260

P-0610

Identification of CT values that could be predictive of necrosis in HCC after lenvatinib treatment

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Purpose: To assess the utility of measurement of the computed tomography (CT) attenuation value (CTav) in predicting tumor necrosis in hepatocellular carcinoma (HCC) patients who achieve a complete response (CR), defined using modified Response Evaluation Criteria in Solid Tumors (mRECIST), after lenvatinib treatment.

Method: We compared CTav in arterial phase CT images with post-operative histopathology in four patients who underwent HCC resection after lenvatinib treatment, to determine CTav thresholds indicative of histological necrosis (N-CTav). Next, we confirmed the accuracy of the determined N-CTav in 15 cases with histopathologically proven necrosis in surgical specimens. Furthermore, the percentage of the tumor with N-CTav, i.e. the N-CTav occupancy rate, assessed using Image J software in 30 tumors in 12 patients with CR out of 571 HCC patients treated with lenvatinib, and its correlation with local recurrence following CR were examined.

Results: Receiver operating characteristic (ROC) curve analysis revealed an optimal cut-off value of CTav of 30.2 HU, with 90.0% specificity and 65.0% sensitivity in discriminating between pathologically identified necrosis and degeneration, with a CTav of less than 30.2 HU indicating necrosis after lenvatinib treatment (N30-CTav). Furthermore, the optimal cut-off value of 30.6% for the N30-CTav occupancy rate by ROC analysis was a significant indicator of local recurrence following CR with 76.9% specificity and sensitivity (area under the ROC curve; 0.939), with the CR group with high N30-CTav occupancy ($\geq 30.6\%$) after lenvatinib treatment showing significantly lower local recurrence (8.3% at 1 year) compared with the low ($<30.6\%$) N30-CTav group ($P < 0.001$, 61.5% at 1 year).

Conclusion: The cut-off value of 30.2 HU for CTav (N30-CTav) might be appropriate for identifying post-lenvatinib necrosis in HCC, and an N30-CTav occupancy rate of $>30.6\%$ might be a predictor of maintenance of CR. Use of these indicators have the potential to impact systemic chemotherapy for HCC.

Abstract Submission No. 200271

P-0611

Surgery or RFA is a curative conversion therapy for patients with HCC treated with ATZ plus BV

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Background and Aims: We aimed to validate the predictive factors for tumor response and the prognostic impact of conversion therapy aimed at cancer- and drug-free states in patients with unresectable hepatocellular carcinoma (u-HCC) undergoing atezolizumab plus bevacizumab (Atez/Bev) therapy.

Methods: This retrospective study enrolled 156 patients who were Child-Pugh class A with u-HCC treated using Atez/Beva. The profile of objective response was investigated using decision-tree analysis. Progression-free, recurrence-free, and overall survival were assessed.

Results: The progression-free and overall survival were 6.1 and 18.0 months, respectively. Objective response and disease control rates were 32.0% and 84.0%, respectively. Decision-tree analysis revealed that neutrophil-to-lymphocyte ratio (NLR) <3 , modified albumin-bilirubin grade (m-ALBI) 1 or 2a, and age <75 were sequential splitting variables for the objective response, respectively. In the multivariate analysis, NLR <3 and m-ALBI grade 1 or 2a were identified as predictive factors for objective response. We successfully achieved eligibility for conversion therapy in 17 patients after Atez/Bev therapy significant response. Following conversion therapy, the curative therapy group, including surgical resection or radiofrequency ablation (RFA), had significantly higher recurrence-free survival than did the transcatheter arterial chemoembolization (TACE) and Atez/Bev discontinuation (surgical resection or RFA; not reached vs. TACE; 5.3 months, $p = 0.008$, Atez/Bev discontinuation; 3.9 months, $p = 0.048$, respectively) groups.

Conclusions: NLR <3 and m-ALBI grade 1 or 2a were predictive factors for conversion therapy, leading to cancer- and drug-free states in patients with u-HCC undergoing Atez/Bev therapy. Moreover, surgery or RFA may be suitable for conversion therapy for cancer-free status.

Abstract Submission No. 100053

P-0612

Correlation between LSM, but not CAP on Fibroscan with mortality- a NHANES database study

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Background: Vibration-controlled transient elastography is a noninvasive diagnostic ultrasound-based device gaining popularity in measuring liver stiffness and fibrosis. It has been reported both controlled attenuation parameter (CAP), indicating steatosis, and liver stiffness measurement (LSM), indicating fibrosis, independently correlated with overall mortality over three-year follow-up.¹

Method: We accessed NHANES database and performed population selection. Univariate Cox proportional hazard model was used to calculate hazard ratio (HR) for all-cause death in CAP and LSM. Cox regression of CAP and LSM was performed with supplementing overlay of P values as Z-axis.

Results: After excluding 2853 patients, 3821 patients were included. Univariate Cox proportional hazard model showed a nonsignificant HR for all-cause death in CAP (every 10 dB/m) of 1.03 (95% CI 0.98-1.08, $P=0.264$). The results did not change when adjusted for interaction term with LSM with HR of 1.01 (95% CI 0.96-1.06, $P=0.662$). For LSM (every 1 kPa), univariate analysis showed an HR of 1.04 (95% CI 1.02-1.06, $P<0.001$), which adjusted to 1.01 (95% CI 0.93-1.09, $P=0.856$) after accounting for the interaction term.

Figure showed Cox regression of CAP and LSM, the P value markedly lost statistical significance with an increase in CAP, though not LSM. This suggests a more robust association of LSM with mortality, echoing the established concept that fibrosis is a more potent predictor of mortality than steatosis.^{2,4}

Conclusion: There is a robust correlation between fibrosis and mortality, but not steatosis, different from the recent article. Further research is needed on this topic with larger samples in independent cohorts.

Abstract Submission No. 100148

P-0613

Gadoxetate disodium-enhanced MRI for HCC: Value of late portal venous phase for enhancing capsule

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Purpose: To investigate added value of late portal venous phase (LPVP) for identification of enhancing capsule (EC) on gadoxetate disodium-enhanced MRI (GD-MRI) for diagnosing hepatocellular carcinoma (HCC) in patients with chronic liver disease (CLD).

Methods: This retrospective study comprised 116 high-risk patients with 128 pathologically proven HCCs who underwent GD-MRI including arterial phase, conventional portal venous phase (CPVP, 60 s), LPVP (mean, 104.4 ± 6.7 s; range, 90–119 s), and transitional phase (TP, 3 min). Two independent radiologists assessed the presence or absence of major HCC features, including EC on CPVP and/or TP (CPVP/TP) and EC on LPVP. Frequency of EC was compared on GD-MRI between with and without inclusion of LPVP. The radiologists assigned Liver Imaging Reporting and Data System (LI-RADS) v2018 categories on GD-MRI before and after identifying EC on LPVP.

Results: Of 128 HCCs, seven (5.5%) revealed EC on LPVP but not on CPVP/TP (Reviewer 1, 57.8% [74/128] vs. 63.3% [81/128]; Reviewer 2, 57.0% [73/128] vs. 62.5% [80/128]; $P=0.016$, respectively). Sensitivities of LR-5 assignment for diagnosing HCCs were not significantly different in GD-MRI with or without LPVP for identification of EC (Reviewer 1, 71.9% [92/128] vs. 72.7% [93/128]; Reviewer 2, 75.0% [96/128] vs. 75.8% [97/128]; $P=1.000$, respectively).

Conclusion: Including the LPVP in GD-MRI may improve identification of EC of HCC in patients with CLD. However, LI-RADS v2018 using GD-MRI showed comparable sensitivity for diagnosing HCC regardless of applying LPVP for EC.

Abstract Submission No. 100202

P-0614

Hepatic steatosis assessment through 3D organ segmentation from virtual noncontrast dual-energy CT

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Purpose: To evaluate the efficacy of volumetric CT attenuation parameters derived from automated 3D organ segmentation on virtual non-contrast (VNC) images from dual-energy CT (DECT) in the assessment of hepatic steatosis, using MRI proton density fat fraction (MRI-PDFF) as the reference standard.

Methods: This retrospective study included 252 living liver donor candidates who had undergone preoperative liver DECT scans and MRI-PDFF assessments. A deep learning-based 3D organ segmentation algorithm was used to automatically segment the liver and spleen from VNC images obtained through contrast-enhanced DECT. Mean volumetric CT attenuation values of each segmented liver (L) and spleen (S) were then measured, allowing for the calculation of liver attenuation index (LAI), defined as L minus S. Correlation between VNC parameters for hepatic steatosis (L_{VNC} and LAI_{VNC}) and MRI-PDFF values was assessed using Pearson correlation coefficient. Agreements of VNC and true non-contrast (TNC) parameters were assessed using intraclass correlation coefficients (ICC). Performance of VNC parameters for identifying MRI-PDFF $\geq 5\%$ and $\geq 10\%$ were evaluated using receiver operating characteristic (ROC) curve analysis.

Results: Both L_{VNC} and LAI_{VNC} showed significant correlations with MRI-PDFF values ($r=-0.585$ and -0.588 , $P<0.001$) and excellent agreements with L_{TNC} and LAI_{TNC} ($ICC=0.957$ and 0.968), respectively. L_{VNC} and LAI_{VNC} exhibited similar areas under the ROC curve (AUCs) of 0.795 and 0.806 for MRI-PDFF $\geq 5\%$; and 0.916 and 0.932, for MRI-PDFF $\geq 10\%$, respectively.

Conclusion: CT attenuation parameters from DECT-derived VNC images, automatically measured through 3D organ segmentation, can be useful for opportunistic hepatic steatosis screening without the need for additional TNC imaging.

Abstract Submission No. 100263

P-0615

Correlation of R2 from multiecho MRS and R2* from MRI-PDFF for measuring hepatic iron deposition

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Purpose: R2 and R2* are two MRI parameters that can assess hepatic iron concentration. The relationship between the R2* obtained from multiecho PDFF and HIC is relatively well evaluated. However, the threshold of R2 obtained by multiecho MRS is not well known. The aim of this study is to compare and correlate R2 with R2* in liver transplant donor candidates and recipients who have already undergone transplantation.

Methods: 175 participants, comprising 115 potential donors and 60 recipients, underwent multiecho MRS and MRI-PDFF for hepatic fat signal fraction evaluation using three 3T MRIs. To correct hepatic iron deposition, R2 values in multiecho MRS and R2* values for PDFF were calculated. In each participant, two distinct R2* values were derived: 1) from a segmented liver volume auto-segmented by software (R2*-seg), and 2) from an ROI equivalent to MRS (R2*-ROI). We correlated R2 and R2* values using simple correlation analysis. Also, we calculated mean values and standard deviation of R2 and R2* values.

Results: Mean R2, R2*-seg, R2*-ROI were 38.0 ± 5.2 (16.7-50.8), 55.3 ± 13.7 (6.2-95.4) and 44.1 ± 15.1 (15.1-125.2), respectively. Correlation coefficients were 0.5676 between R2 and R2*-seg, 0.5724 between R2 and R2*-ROI and 0.6076 between R2*-seg and R2*-ROI. Between R2 and R2* values, correlation graph shows curved shape correlation.

Conclusion: R2 measured by Multiecho MRS and R2* measured by PDFF were positively correlated. As R2* values, which has already

proven useful, R2 values measured by multiecho MRS has the potential to be used to diagnose hepatic iron storage disease.

Abstract Submission No. 100568
P-0616

PREDICTORS OF AT-RISK LIVER STIFFNESS IN THE POINT-OF-CARE COMMUNITY LIVER SCREENING PROGRAM SIRIUS

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Background: Liver fibrosis is the critical driver of increased mortality in advanced chronic liver disease (ACLD). Screening programs are promising tools for the identification of cases with asymptomatic ACLD with liver stiffness (LS) as its established surrogate.

Methods: The SIRIUS project is a liver screening program. From 08/2022-06/2023 we visited 25 communities offering liver examination including medical history, AUDIT-C, anthropometrics, liver stiffness (Fibroscan, Echosense), and point-of-care laboratory parameters (POCLP). Baveno VII-derived cut-offs of LS were used: >10 kPa as moderate-risk and >15 kPa as advanced-risk. Independent predictors of at-risk stiffness were identified in the logistic regression with $P < 0.05$ and AUROC.

Results: 2314 individuals were examined, 2164 having complete data, 1664 (76.9%) a valid POCLP (Labs group), M/F 39/61%, median age 54y, BMI 27, 16.9% of smokers, history of liver disease, arterial hypertension, diabetes, and cancer in 8.0, 34.2, 6.9, and 5.6%, at-risk alcohol consumption in 14.9%, the LS >8, >10, and >15 kPa in 12.2, 5.9, and 1.8%.

Predictors of moderate-risk: age (1.05, 1.03-1.07), history of liver disease (3.7, 2.32-5.91), BMI 1.12 (1.09-1.16), employed status (2.03, 1.21-3.41), diabetes (2.36, 1.41-3.95) and AUDIT-C 2nd question (2.01, 1.43-2.81), (AUROC=0.786, 0.768-0.803), in the Labs group: age (OR=1.03, 95%CI 1.12-1.05), history of liver disease (2.74, 1.57-4.76), GGT (1.01, 1.01-1.012), BMI (1.11, 1.07-1.16), conjugated bilirubin (1.09, 1.01-1.19), HDL cholesterol (0.49, 0.26-0.96), AUROC=0.784 (0.763-0.803).

Predictors of advanced-risk: age (1.04, 1.01-1.07), waist circumference (1.03, 1.00-1.05), history of liver disease (6.78, 3.42-13.43) and AUDIT-C 2nd question (2.74, 1.66-4.52), (AUROC=0.795, 0.778-0.812), in the Labs group: age (1.04, 1.01-1.08), history of liver disease (4.00, 1.77-9.06), GGT (1.01, 1.0-1.012), and HDL (0.31, 0.11-0.85) (AUROC=0.795, 0.775-0.814).

Conclusion: The SIRIUS project identified individuals with moderate or advanced-risk stiffness in 5.9% and 1.8%. The accuracy of predictive models was good regardless of valid POCLP. This evidence serves to develop a comprehensive national liver screening program.

Abstract Submission No. 100813
P-0617

Identification of liver malignant nodules using DCE-US combined with LR-M classification criteria

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Objective: Explore the diagnostic value of DCE-US quantitative parameters for liver malignant nodules with high-risk factors for HCC, and combine them with LR-M to differentiate between HCC and non-HCC malignant nodules.

Method: According to the pathological results, the nodules were divided into HCC and non-HCC malignant group, and each nodule was classified by CEUS LI-RADS 2017. Using VueBox® Quantitative analysis software performs CEUS quantitative analysis for each nodule, compares the differences in quantitative parameters between HCC and non-HCC malignant nodules.

Result: Among 186 patients with 190 liver malignant nodules, there are 137 HCC and 53 non-HCC malignant nodules. The median values of quantitative parameters RT, TTP, mTTI, and FT in the non-HCC malignant group were lower than those in the HCC group, with $P < 0.05$. There was a statistically significant difference in WiAUC, WoAUC, WiWoAUC, and WoR values between HCC and non-HCC malignant groups, with $P < 0.05$. Washout within 60s and $FT \leq 21.15s$ is the new diagnostic standard of LR-M, and the sensitivity, specificity, and positive predictive value of LR-5 for HCC are 83.94%, 96.23%, and 98.29%, respectively.

Conclusion: DCE-US can help to distinguish between HCC and non-HCC malignant nodules. The diagnostic standard of washout within 60s and quantitative parameter $FT \leq 21.15s$ can significantly improve the diagnostic sensitivity of LR-5 for HCC.

Abstract Submission No. 101118
P-0618

Gadolinium loaded-chitosan Nanoparticles for Contrast Enhanced MRI Diagnosis of Liver Disease

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Background: Precisely diagnosing the liver fibrosis by a non-invasive way still suffers big challenges. Magnetic resonance-based methods have multiple advantages on diagnosing liver fibrosis. The purpose of this study is to develop gadolinium loaded-chitosan nanoparticles (Gd-CSNPs) as MRI contrast agent to diagnose liver fibrosis in vivo.

Methods: The Gd-CSNPs were prepared by the method of cross linking, which followed by the modification of surface with DTPA by NHS-EDC. The physical characterizations of Gd-CSNPs were obtained by TEM, dynamic light scattering instrument and XPS analysis. The cell toxicity of Gd-CSNPs was evaluated on mouse melanoma A375 cells. Liver fibrosis mice models were constructed via intraperitoneal injecting 10 % CCl₄ twice a week for 12 weeks. T1 signals of MRI by using Gd-CSNPs were measured in vitro and in vivo at different concentrations and time intervals.

Results: Gd-CSNPs were synthesized by chitosan and TPP at a mass ratio of 5:1, with the size of about 10nm. XPS analysis confirmed the presence of element Gd in Gd-CSNPs. Compared with FDA-approved magnevist, Gd-CSNPs showed no cytotoxicity in vitro. T1 relaxivity of Gd-CSNPs was significantly stronger than that of magnevist in vitro and vivo. The T1 signal of Gd-CSNPs was the strongest an hour after injection in mice and it could remain stable for at least 3 hours.

Conclusion: Gd-CSNPs show stronger and more stable MRI signals in liver than that of Magnevist and may be used as a contrast agent in MRI for diagnosis of liver fibrosis via a non-invasion means.

Abstract Submission No. 101184
P-0619

The usefulness of hepatic fibrosis markers for hepatocarcinogenesis in patients with MASLD/MASH

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Background And Aims: Several non-invasive fibrosis markers for the degree of hepatic fibrosis in patients with chronic hepatitis have been reported. The hepatic fibrosis is correlated with hepatocarcinogenesis, therefore, these non-invasive markers are useful for the prediction of hepatocarcinogenesis. However, which non-invasive markers have been the most useful marker is controversial. The aim of this study was to clarify the diagnostic ability for the prediction of hepatocarcinogenesis using Fib-4 index, Fib-3 index and Vibration-controlled Transient Elastography(VCTE).

Methods: The 728 MASLD/MASH consecutive patients from October 2014 to June 2022 who underwent VCTE and blood examination were included in this retrospective cohort study. The males were 335(46.0%), the median age was 56 years old. The patients within six months at least in observation periods were excluded.

Results: 14 out of 714 patients with MASLD/MASH(2.0%) have been developed hepatocellular carcinoma(HCC). The cumulative hepatocarcinogenesis rate were 1.0, 1.7, 2.0% in 1, 3, 5 years, respectively. Hazard ratio(HR) for hepatocarcinogenesis with cut off value of 1.30 and 2.67 in Fib-4 index were 7.13(95%CI; 1.593-31.86) (p=0.010) and 15.85 (95%CI; 4.82-51.08) (p<0.001), respectively. C-index with cut off value of 1.30 and 2.67 in Fib-4 index were 0.685 and 0.752. Hazard ratio(HR) for hepatocarcinogenesis with cut off value of 1.57 and 3.50 in Fib-3 index were 6.85(95%CI; 1.907-24.62)(p=0.003) and 7.69 (95%CI; 2.654-22.28)(p<0.001), respectively. C-index with cut off value of 1.57 and 3.50 in Fib-3 index were 0.691 and 0.669. Hazard ratio(HR) for hepatocarcinogenesis with cut off value of 7.6(kPa) and 9.6(kPa) in VCTE were 6.22(95%CI; 2.083-18.60)(p=0.001) and 10.27 (95%CI; 3.434-30.69)(p<0.001), respectively. C-index with cut off value of 7.6(kPa) and 9.6(kPa) in VCTE were 0.671 and 0.708.

Conclusion: Fib-4 index, Fib-3 index and VCTE were useful non-invasive hepatic fibrosis markers for the prediction of hepatocarcinogenesis in MASLD/MASH patients. MASLD/MASH patients with higher cut off value in each non-invasive marker should be carefully follow-up.

Abstract Submission No. 101216
P-0620

Ultrasonic image analysis of the left lobe of the liver in patients with NAFLD using deep learning.

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Purpose: Elastography increased diagnostic accuracy of liver fibrosis. However, several challenges persist, including the widespread

utilization of equipment, difficulties in measuring certain cases, and the influence of viscosity factors. Rough surface and a blunted hepatic margin have long been acknowledged as valuable characteristics indicative of hepatic fibrosis. The objective of this study was to conduct image analysis and quantitative assessment of the contour of the sagittal section of the left lobe of the liver.

Methods: Between February and October 2020, 458 consecutive outpatients underwent ultrasound examinations at our hospital. A total of 214 images were manually annotated by delineating the liver contour to create annotation images. U-Net was employed for liver segmentation, with the dataset divided into training (n=128), testing (n=42), and validation (n=44) subsets. Additionally, 23 NAFLD cases with pathology data between 2015 and 2020 were included. Segmentation was performed using the program developed in the first step. Subsequently, shape analysis was conducted using ImageJ.

Results: Liver segmentation exhibited high accuracy, as indicated by Dice loss of 0.044, Intersection over Union of 0.935, and an F score of 0.966. While no findings demonstrated a correlation with fibrosis stage, some exhibited a trend towards correlation. Area (p=0.056), MinFerret (p=0.068), and Minor (p=0.060) each displayed a particularly low score at F4.

Conclusion: Deep learning segmentation of the sagittal cross-sectional contour of the left lobe of the liver demonstrated commendable accuracy. Thin shape with smaller areas were associated with F4. However, given the limited cases, more images are needed to improve accuracy.

Abstract Submission No. 101284
P-0621

THE INVESTIGATION OF LIVER STIFFNESS MEASUREMENT BY ELASTOGRAPHY IN THE PRESENCE OF INFLAMMATION

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Background: Liver stiffness measurement (LSM) has been reported to be affected by inflammation. However, the details have not been well established. In the current study, we aimed to develop strategy for the best use of elastography in the presence of inflammation.

Methods: We retrospectively recruited 290 patients who underwent liver biopsies performed since January 2018 in our institution approved by local institutional IRB (no. 20170202). Histological assessment was evaluated according to the METAVIR score and we defined active inflammation as A2 and 3 grade. We assessed the diagnostic performance of Vibration-Controlled Transient Elastography(VCTE) using by ROC analysis.

Results: METAVIR fibrosis stage was F0 (30%), F1 (17%), F2 (14%), F3 (11%), F4 (27%). The AUROC of VCTE index for each fibrosis stage F=0 vs F≥1, F≤1 vs F≥2, F≤2 vs F≥3, F≤3 vs F4 were 0.89, 0.93, 0.92, 0.92. In cases with active inflammation, AUROC of VCTE didn't significantly decrease by 0.89, 0.94, 0.90, 0.90. On the other hand, LSM values tended to increase at the presence of inflammation especially in mild fibrosis stage; A0,1 vs A2,3 was 6.3 vs 8.0 kPa (P=0.0005) in F0 stage, 7.6 vs 11.5 (P=0.064), F1, 12.2 vs 15.9 (P=0.062) in F2, 16.0 vs 15.8 (P=0.810) in F3, 33.4 vs 27.7 (P=0.728) in F4.

Conclusion: Since overestimation of liver stiffness induced by inflammation occurs only in mild fibrosis stage, the risk of overestimation can be avoided by raising cut-off value in such specific cases.

Abstract Submission No. 101317
P-0622

Spleen Stiffness Measurement using New Spleen-Dedicated Fibroscan: Intra/Interobserver Repeatability

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Background: Bleeding from esophageal varix is one of the most life-threatening complications of portal hypertension, which is a major consequence of liver cirrhosis. The spleen stiffness measurement (SSM) by standard Fibroscan® (SSM@50Hz) has been evaluated as the non-invasive diagnostic tool for esophageal varix. Recently, the SSM using a novel spleen-dedicated Fibroscan® (SSM@100Hz) has been developed and found to have a better accuracy than SSM@50Hz. The aim of this research was to evaluate the intra- and interobserver repeatability of SSM@100Hz.

Methods: Eighty-four patients with chronic liver disease were randomly allocated to group 1 (for evaluation of intraobserver repeatability) or group 2 (for evaluation of interobserver repeatability), respectively. In group 1, both of two sessions of SSM@100Hz were performed by one radiologist. In group 2, the first session of SSM@100Hz was performed by one radiologist and the second session of SSM@100Hz was performed by another radiologist without the information about the result of the first session.

Results: Overall success rate of SSM@100Hz was 94% (79/84). Median SSM of total patients was 16.7 kPa (interquartile range [IQR] 13.2 - 19.9kPa) with 17.4 kPa (IQR 13.3 - 20.3kPa) in group 1 and 16.2 kPa (IQR 13.0 - 19.9kPa) in group 2, respectively. The intraobserver repeatability in group 1 revealed a high intra-class correlation coefficient (ICC) (0.977, 95% confidence interval [CI]: 0.955, 0.988) and, in group 2, interobserver repeatability also showed a high ICC (0.958, 95% CI: 0.919, 0.978).

Conclusions: SSM@100Hz is a feasible and highly reproducible tool in patients with chronic liver disease.

Abstract Submission No. 101522
P-0623

SPECT Identifies Compensated Cirrhotics with Higher Accuracy than Blood Tests

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Background: Chronic liver disease is staged into fibrosis categories F0 to F4. Due to the liver's ability to compensate some F4 patients may live for years. Others may decompensate and need a transplant. Decompensation is detected by abnormal blood tests or clinical manifestations. Some institutions use quantitative liver function deterioration for an early indication of decompensation. SPECT imaging provides quantitative liver function (PHM), steatosis, portal hypertension and alcoholic hepatitis. Hoefs Physiologic Stage captures these disease processes into six categories H0 to H5. We hypothesized that cirrhotic patients who have PHM $\geq$ 75 are likely compensated cirrhotics.

Methods: Hypothesis was tested with 46 sequential cirrhotic patients, confirmed using liver biopsies, shear wave velocity, and nodular liver surface. Patients were grouped into: CC - Compensated Cirrhotics (N=33) and DC - Decompensated Cirrhotics (N=13).

Results: Of 35 patients with PHM $\geq$ 75, 31 were in Group CC and 4 in Group DC. Of 11 patients with PHM<75, 9 were in Group DC and 2 in Group CC. Ability of PHM to predict compensated cirrhosis were: PPV =89%, NPV = 82%, Sensitivity = 94% and Specificity = 69%. Blood tests were compared to PHM. PHM was best with Accuracy 87%, followed by Albumin 83%, Bilirubin 76%, and INR 74%

Conclusions:

1. PHM identified compensated cirrhotics with a high PPV and NPV.
2. PHM was more accurate than blood tests and may be more reliable in setting monitoring intervals.
3. H3 patients may be monitored less often than H4 patients thus reducing healthcare costs.

Abstract Submission No. 101622
P-0624

Usefulness of shear wave elastography for evaluation of HCC recurrence after ablation

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Background: Although shear wave elastography (SWE) is useful method for liver fibrosis assessment, its usefulness in the recurrence risk evaluation of hepatocellular carcinoma (HCC) is unknown. Therefore, we evaluated the usefulness of SWE in risk assessment of the HCC recurrence after ablation therapy.

Methods: We retrospectively analyzed the relationship between HCC recurrence and liver stiffness (LS) in 43 HCC patients who underwent ablation therapy. The average age 69 years, M/F 34/9, background liver disease is HCV/HBV/NASH/alcohol/others 16/2/9/12/3, tumor diameter is 2.2 cm. The shear wave propagation velocity (Vs) was measured in the right lobe of liver. The diagnostic accuracy was evaluated by ROC curve analysis. The recurrence-free survival (RFS) was evaluated by the Kaplan-Meier method.

Results: The Vs value was 2.11 $\pm$ 0.79/2.65 $\pm$ 0.95 m/sec in the non-recurrence group/recurrence group (p < 0.05). In the evaluation of HCC recurrence, when the cut-off value of Vs was 1.81, the sensitivity was 0.88, the specificity was 0.57, and the area under the ROC curve was 0.724. The RFS of low Vs group was significantly longer than that of high Vs group (p = 0.002).

Conclusions: LS measured by SWE is useful for assessment of HCC recurrence risk after ablation therapy.

Abstract Submission No. 101734
P-0625

A novel multiomic model for analyzing the intratumor heterogeneity in hepatocellular carcinoma

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The impact of intratumor heterogeneity (ITH) on clinical outcomes and treatment responses is substantial, especially in hepatocellular carcinoma (HCC), which is considered to present high ITH. However, the accuracy of widely used techniques for assessing ITH, which relies on

small tissue samples from pathological slides or genetic sequencing, may be compromised by potential sampling biases. Such invasive procedures may also cause unexpected damage to patients. To address this, we have developed a novel radiomics approach, which can non-invasively analyze the whole of the tumor, using a radio-multiomic dataset of HCC in Sir Run Run Shaw Hospital (n = 368). This dataset encompasses radiomic features obtained from dynamic multi-parameter magnetic resonance imaging. Our findings in HCC demonstrate a correlation between imaging ITH (IITH) and both pathological and genetic ITH, each independently associated with an unfavorable prognosis. Furthermore, our multiomic analysis reveals that high-IITH tumors exhibit active carcinogenic pathways and metabolic reprogramming. Collectively, these studies underscore the superiority of radiomics in capturing ITH and provide insights into the molecular foundations of ITH, along with proposing treatment strategies for HCC with high IITH.

Abstract Submission No. 101795
P-0626

Erythropoietic protoporphyria with characteristic MRI findings during exacerbation of liver injury

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Introduction: Erythropoietic protoporphyria (EPP) is an autosomal overt inherited disorder caused by a decrease in the activity of ferrochelatase (FECH), an enzyme that catalyzes the insertion of iron into protoporphyrin IX. EPP usually consists of skin lesions and has a good prognosis. However, we report a case of EPP with acute liver damage and characteristic imaging findings on EOB-MRI.

Case: A 34-year-old man had been diagnosed with myeloid protoporphyria from birth. The patient was referred to our hospital for upper abdominal pain. Severe liver injury and jaundice were observed with markedly high levels of protoporphyrin in blood and stool. Gd-EOB-DTPA-Enhanced Magnetic Resonance Imaging (EOB-MRI) revealed no noticeable deformation in the liver, and the hepatic parenchymal contrast effect was unevenly attenuated. Even 60 minutes after EOB administration, the uptake of EOB into the liver parenchyma remained attenuated.

In Liver Histopathological findings, the lobular structure of the liver was generally preserved, but many brownish porphyrin crystals with red auto-luminescence were observed in hepatocytes and sinusoids. He improved with conservative treatment with ursodeoxycholic acid. After the improvement of symptoms, the deposition of porphyrin crystals in the liver tissue and the MRI findings also improved.

Conclusion: There are no case reports of attenuation of the signal enhancement effect of EOB-MRI during hepatic injury exacerbation in patients with EPP, and the EOB MRI may be useful for evaluating disease status.

Abstract Submission No. 101954
P-0627

A case of liver cyst rupture that was mistaken for liver metastasis

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A 68YO Chinese Male with a history of heavy ethanol consumption was admitted for epigastric and right hypochondrial pain, black stools and a drop in his hemoglobin level from 14 to 12.2g/dL. His liver function test (LFT) showed mildly raised total bilirubin of 33µmol/L, and elevated alanine transaminase (406U/L) and aspartate transaminase (80U/L). Oesophagogastroduodenoscopy showed a Forrest 3 duodenal ulcer; however, that did not explain his LFT. A CT Abdomen was performed, which showed multiple liver cysts and small ill-defined hypodense liver lesions (biggest was 1.2cm in diameter), suspicious for liver metastases. CT Thorax/Pelvis and colonoscopy were done to evaluate for the source of liver metastases, but were unyielding. Biopsies of the liver metastases were performed, which showed cholesterol clefts and aggregates of histiocytes / multinucleated giant cells (CD168 positive, MNF116 negative), in keeping with cholesterol granuloma, but no features of hepatocellular neoplasm were seen. His LFT also normalised 2 months later.

The liver lesions were further evaluated with an MRI Liver (with Primovist). The previously visualized suspicious lesions were reported to be smaller, and there was no evidence of metastases. Overall radiological findings were in keeping with adult polycystic liver disease.

The diagnosis is that the liver cyst might have ruptured and bled, causing the enhancement seen on the CT Abdomen. The presence of cholesterol clefts and granuloma is non-specific, and is likely secondary to inflammation or bleeding after a hepatic cyst rupture. This case illustrates how rim enhancement due to cysts rupture/hemorrhage can be mistaken for liver metastases.

Abstract Submission No. 102046
P-0628

Enhancing Deep-seated Hepatocellular Carcinoma Detection in contrast enhanced ultrasound

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Background: Sonazoid contrast-enhanced ultrasound (CEUS) is effective for detection of liver lesion like hepatocellular carcinoma (HCC). However, detecting deep-seated HCCs poses significant challenges due to acoustic attenuation occurring in the far field of ultrasound. Accordingly, this study aimed to explore the role of the mechanical index (MI) setting in enhancing the detection of deep-seated HCCs and develop an innovative methodology for the utilization of that.

Methods: 682 successive patients with 805 pathologically or radiologically confirmed hypervascularity HCC lesions larger than 10mm were included. All the patients underwent B-mode ultrasound and CEUS examinations with both low and high MI settings of post-vascular phase (PVP). Propensity score matching (PSM) and logistic regression were employed to address confounding 10 variables. The univariate and multivariate analyses were conducted for statistical assessment.

Results: For the overall population, the depth, echogenicity, and size of the lesions were identified to be independent indicators for enhanced detection through the additional high MI setting (odds ratio, OR: 1.495, 95% confidence interval, CI: 1.345-1.661, OR: 4.708, 95% CI: 2.779-7.974, and OR: 0.965, 95% CI: 0.940-0.990, respectively). After accounting for the effects of confounding variables by PSM,

lesions that were undetected under the low MI setting but became detectable under the additional high MI setting during PVP exhibited significantly greater depth compared to lesions that did not benefit from the additional high MI setting (8.39 ± 2.46 cm vs. 6.42 ± 2.54 cm, $p < 0.001$).

Conclusion: For hypervascularity HCCs larger than 10 mm, the additional high MI setting during PVP improved the detection of deep-seated lesions.

Abstract Submission No. 200154

P-0629

Using SWE to differentiate fibrotic stenosis from inflammatory stenosis in Crohn's disease

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Abstract

Objective: To assess the feasibility of utilizing shear-wave elastography to distinguish between fibrotic strictures and inflammatory strictures in patients with Crohn's disease.

Methods: Retrospectively analyze patients who have progressed to stricturing Crohn's disease and have underwent SWE in a close period of time. The materials, including computed tomography enterography or magnetic resonance enterography-based radiological materials, endoscopic appearance, histopathologies of endoscopic biopsy and treatment responses, are synthesized to establish a novel comprehensive score, namely fibrotic score which divides patients into two separate groups—the inflammatory primary group and the fibrotically primary group. The SWE value of the stenotic bowel walls is compared.

Result: Sixty patients are enrolled, of which forty-three are divided into inflammatory primary group and seventeen into fibrotically primary group. The mean SWE value of stenotic bowel walls in the fibrotically primary group (24.1 ± 12 kPa) is significantly higher than that in the inflammatory primary group (12.5 ± 6.0 kPa). According to the maximum Youden index, 15.9 kPa as the cut-off to differentiate fibrotic lesions from inflammatory lesions is determined. The corresponding sensitivity is 82.4% (95% CI 0.558 to 0.953) and specificity is 79.1% (95% CI 0.635 to 0.894) while the area under the receiver operating characteristic curve is 0.85 (95% CI 0.740 to 0.952, $P < 0.001$).

Conclusion: Shear-wave elastography is feasible in detecting fibrotic bowel walls in patients with stricturing Crohn's disease and is helpful for their clinical strategies being made.

Abstract Submission No. 100054

P-0630

Incidental Finding of Metastatic Medullary Thyroid Cancer after Liver Transplant: A Case Report

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A 61-year-old male with history of coronary artery disease, type 2 diabetes, hypertension, dyslipidemia, paroxysmal atrial fibrillation, and

gastroesophageal reflux underwent liver transplantation due to decompensated cirrhosis due to MAFLD complicated by ascites, esophageal ulcer bleeding post banding. Review of patient's explant revealed an incidental finding of a 1.4 cm nodule located in the segment II of left liver lobe. The immunohistochemical profile of the tumor cells was suspicious for metastatic medullary carcinoma of thyroid origin. Further evaluation revealed elevated serum calcitonin at 325 pg/mL (normal ≤ 14.3 pg/mL) and chest CT scan noted an 8 mm nodule in the right thyroid gland with adjacent 5 mm lymph nodes. Following evaluation with thyroid ultrasound confirmed 1.1 cm right upper lobe thyroid nodule. Fine needle aspiration biopsy of nodule was consistent with medullary carcinoma. Subsequently, the patient underwent total thyroidectomy. Postoperatively, the patient's condition was closely monitored to evaluate the response to treatment. Laboratory results following surgery include calcitonin of 143 pg/mL, ≤ 14.3 pg/mL; CEA of 4.4 ng/mL, 0-2.9 ng/mL, and elevated TSH levels with normal T4 levels.

Current pre-liver transplant evaluation cancer screening usually includes screening for colon cancer, lung cancer, cervical cancer, breast cancer, and prostate cancer. This case presented an incidental finding of metastatic medullary thyroid cancer, accounting for only 2-3% of thyroid malignancies, on liver explant. Due to its rareness, screening for this type of cancer might not be cost-effective pre liver transplant. But this case highlighted timely intervention can significantly impact patient outcomes and guide appropriate management strategies.

Abstract Submission No. 100200

P-0631

Comparing Thermal & Non-Thermal Ablation with Immune Checkpoints for Enhanced Tumor Immune Response

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Background and Objective: The combination of ablation therapies and immune checkpoint inhibitors (ICIs) potentiates tumor immunity and anti-tumor effects, producing a heightened abscopal effect. The object was to compare the therapeutic impacts of ICIs combined with two distinct ablation treatments: radiofrequency ablation (RFA) and irreversible electroporation (IRE).

Methods: 1. Two groups—treatment and control—were inoculated with Hep55.1c cells on the intracutaneous right flank on Day 0. The treatment group underwent either RFA or IRE on Day 7, exhibiting no tumor recurrence by Day 35. Subsequently, both groups were rechallenged with cell injections on their left flank. The groups were further subdivided based on the administration of an anti-CD8 antibody or its absence.

2. Mice received Hep55.1c cell injections in the right flank on Day 0 (primary lesion) and left flank on Day 6 (metastatic nest). Four groups were formed: control, ICI, ablation (RFA or IRE), and combination therapy (ICI with RFA or IRE). Primary lesion received ablation on Day 7, and treatment effects were evaluated.

Results: (1) Mice treated with ablation therapy (RFA or IRE) displayed resistance to tumor engraftment. Conversely, in mice administered the anti-CD8 antibody, tumor recurrence and growth were observed. (2) ICI and ablation therapy slowed metastatic tumor growth

significantly versus ablation alone. RFA tended to outperform IRE in tumor suppression.

Conclusion: While ablation therapy alone evoked an immunostimulatory effect, the addition of ICIs further curtailed tumor growth. In conclusion, the combination of ablation therapy and ICIs produced a synergistic effect and holds potential clinical value.

Abstract Submission No. 100585
P-0632

Impact of conversion surgery in patients with advanced intrahepatic cholangiocarcinoma

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Background: The impact of conversion surgery (CS) has not been well studied in patients with advanced intrahepatic cholangiocarcinoma (ICC). This study aimed to evaluate outcomes of patients who received CS and those who did not.

Methods: We retrospectively reviewed patients with unresectable or recurrent ICC who were treated at our institution between January 2015 and December 2022. Baseline characteristics and outcomes were compared between patients who received CS and those who did not. Cox proportional hazards model was used to identify prognostic factors for survival.

Results: Among 91 patients (locally advanced/metastatic/recurrent 10/60/21), nine patients (locally advanced/metastatic/recurrent 2/4/3) underwent CS after chemotherapy. There were no significant differences in baseline characteristics between the two groups. Objective response to chemotherapy was more frequently observed in the CS group (78% vs. 17%, $P < 0.001$). Median time to surgery and median relapse-free survival were 6.1 months and 13.7 months, respectively, in the CS group. Median overall survival was significantly longer in the CS group (50.0 vs. 13.5 months, $P < 0.001$). Age < 75 years, performance status of 0, modified Glasgow prognostic score of 0, carcinoembryonic antigen < 10 ng/mL were identified as significant prognostic factors for survival and every patient who underwent CS met three or four of these prognostic factors.

Conclusions: CS was performed in 9.9% of patients with unresectable or recurrent ICC. CS in highly selected patients was associated with a long median overall survival.

Abstract Submission No. 100630
P-0633

A Multicenter Study on Hepatocellular Adenomas in Korea: Clinicopathologic and imaging features

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Background: Clinicopathologic and imaging features of hepatocellular adenomas (HCA) in Eastern countries have not been well evaluated.

Purpose: To conduct a comprehensive analysis of clinicopathologic and imaging features of HCAs in Korea and to present an imaging-based method to differentiate β -catenin mutated HCA (β HCA) from other subtypes.

Methods: This retrospective multicenter study included pathologically confirmed HCAs from three tertiary institutions in Korea between January 2010 and March 2023. HCA subtypes were classified using the current WHO classification through pathologic analysis including complete immunohistochemical staining panels. Two abdominal radiologists reviewed multiphase CT and gadopentetic acid-enhanced MRI images. Clinical characteristics and imaging features of HCA subtypes were compared. A scoring system for β HCA was developed and validated using subdivided cohorts: development (January 2010-April 2021) and validation (May 2021-March 2023) cohorts.

Results: 121 patients (47 men; mean age, 39.0 years $\pm$ 13.5) with 138 HCAs were included in the study. HCAs in Korea displayed characteristic clinicopathologic features, including a high proportion of male (38.8%), obesity (35.5%), inflammatory subtype as the most common subtype (38.4%), and a low percentage of oral contraceptive use (5.0%). Each HCA subtype demonstrated distinct clinical and imaging features. The scoring system for differentiating β HCA exhibited high performance in both the development cohort (AUC 0.92, 95% CI: 0.87-0.97) and the validation cohort (AUC 0.91, 95% CI: 0.77-1.00).

Conclusion: The comprehensive analysis of clinicopathologic and imaging features of HCAs in Korea can add insights regarding the nature of HCAs across different geographic regions. The imaging-based scoring system effectively differentiates β HCA.

Abstract Submission No. 100810
P-0634

The impact of percutaneous ablation therapy for liver metastases of non- colorectal cancer

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Background/aims: According to the Clinical practice guidelines for the management of liver metastases from extrahepatic primary cancers 2021 (The Japanese Society of Hepato-Biliary-Pancreatic Surgery), local ablation therapy is not recommended for non-colorectal liver metastases (CRLM). Percutaneous ablation therapy (PAT) for non-CRLM was retrospectively investigated in terms of local control and overall survival (OS) in the single center.

Subjects/Method: From June 2004 to December 2022, 128 cases and 183 nodules treated with PAT for non-CRLMs were enrolled for the present study. The factors related to local recurrence free survival (LRFS) and OS were analyzed using univariate (Logrank) and multivariate analysis (Cox proportional hazards method).

Results: OS of all cases was 42.3% at 3 years, 18.9% at 5 years, and median OS was 28.1 months. As a factor related to OS, univariate analysis showed significant differences in the presence/absence of extrahepatic metastasis (58/70, $p < 0.001$) and the primary tumor in the pancreas/non-pancreas (30/98, $p = 0.002$). Multivariate analysis showed that extrahepatic metastasis (HR 0.510, $p = 0.011$) was an independent factor for poor prognosis. LRFS was 70.6% at 1 year, median 11.0 months. Univariate analysis showed that the primary tumor was pancreatic/non-pancreatic (48/135, $p < 0.001$), ablation margin $\geq < 5$ mm (41/142, $p = 0.0168$), and tumor diameter $> < 18$ mm (62/121, $p < 0.001$). As a result of multivariate analysis, the primary tumor was pancreatic/non-pancreatic (HR 3.647, $p < 0.001$) and tumor diameter > 18 mm or less (HR 3.162, $p < 0.001$) were independent factors of LRFS.

Conclusion: Percutaneous ablation therapy for non-CRLMs may contribute to the prognosis in non-pancreatic primary tumors, and local control of 18 mm or less in diameter is good indication.

Abstract Submission No. 100923
P-0635

Compound X from *Coptidis Rhizoma* suppresses epithelial-mesenchymal transition of colorectal cancer.

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The current study aimed to investigate the anti-hepatic metastasis effect of compound X, a main active compound of *Coptidis Rhizoma*, in animal model, and the underlying mechanisms. A murine colon carcinoma (CT26) tumor tissue was implanted in cecum of Balb/c mouse with/without oral administration of compound X (100 mg/kg) for evaluation anti-colon-liver metastatic outcome. Regarding the pharmacological actions of compound X, the anti-metastatic behaviors were evaluated using 5-fluorouracil-resistant colon cancer cell (HCT116/R). The administration of compound X significantly inhibited the hepatic metastasis by modulated EMT markers (E-cadherin, vimentin, Snail) and decreased inflammatory cytokine (TGF- β , TNF- α , IL-6, IL-1 β). In HCT116/R cell model, compound X significantly inhibited migration and invasion by modulating EMT markers. In conclusion, compound X evidently possess an anti-colon-liver metastatic effect, and its underlying mechanisms involve inhibition of epithelial-mesenchymal transition (EMT) through TGF- β signaling pathway. Thus, compound X can be a potential candidate in drug development against hepatic metastasis from CRC.

Abstract Submission No. 100926
P-0636

Risk of Development of ACLF and Mortality among NASH Cirrhosis Patients with Acute Decompensation

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Background: Non-alcoholic steatohepatitis (NASH) is now the leading cause of cirrhosis. Studies have shown that Acute-on-Chronic Liver Failure (ACLF) incidence and mortality due to NASH is lower when compared to other etiologies.

Method: Retrospective-prospective cohort study from Thailand. A total of 626 hospitalized cirrhotic patients [acute liver decompensation (AD)=278 patients, ACLF=348 patients] from January 2010 to June 2020 were enrolled. This study aimed to identify the predictive factors for ACLF development and mortality among NASH cirrhosis (NC) during AD.

Results: There were 55 patients with NC and 571 patients with non-NASH cirrhosis (NNC). 22 NC patients (40.0%) and 326 (57.1%) of NNC developed ACLF ($p=0.016$). 412 patients (65.8%) were male. The mean age of NC and NNC groups was 72.0 $\pm$ 10.6 and 57.3 $\pm$ 13.6 years ($p<0.001$). CTP score, MELD, and CLIF-C OF score were higher in NNC group 10.3 $\pm$ 2.9 vs 9.4 $\pm$ 3.3 ($p=0.035$), 22.6 $\pm$ 9.1 vs 18.0 $\pm$ 7.4 ($p<0.001$), 8.9 $\pm$ 2.7 vs 7.3 $\pm$ 2.6 ($p<0.001$). All-cause mortality at 28-day and 90-day were similar in both groups (NC 41.8%, 58.2%; NNC 42.8%, 56.4%). Factors for predicting ACLF among NC patients were elevated hemoglobin levels [OR 2.138 (95%CI 1.120-4.080, $p=0.021$), elevated serum creatinine [OR 56.113 (3.360-937.166, $p=0.005$), and a high international normalized ratio (INR) [OR 4.273 (1.158-15.763, $p=0.029$)]. Bacterial infection was a significant predictor for 28 and 90-day mortality [OR 4.735 (1.007-22.277, $p=0.049$) and OR 5.329 (1.432-19.834, $p=0.013$)].

Conclusion: The incidence of ACLF is lower in NC compared to NNC patients but the mortality rate was indifferent. Bacterial infection remains the major predictor for mortality.

Abstract Submission No. 101814
P-0637

Liver resection for non-colorectal, non-neuroendocrine liver metastases in our hospital

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Background: While the advantages of liver resection for liver metastases from colorectal cancer or neuroendocrine tumors are widely recognized, the significance of resection for liver metastases from non-colorectal non-neuroendocrine tumors (NCNNLM) remains uncertain. This study investigates the outcomes of liver resection for NCNNLM at our hospital.

Methods: We conducted a retrospective analysis of short-term outcomes and long-term prognoses in 50 patients who underwent liver resection for NCNNLM between 1995 and 2021.

Results: The primary cancer sites in 50 cases include stomach ($n=26$), esophagus ($n=7$), breast ($n=4$), prostate ($n=2$), uterus ($n=2$), gallbladder ($n=2$), and other sites ($n=7$). Primary histology types were adenocarcinoma ($n=35$), squamous cell ($n=7$), gastrointestinal stromal tumor ($n=7$), solid-pseudopapillary neoplasm ($n=1$). There was no perioperative mortality and significant complications (Clavien-Dindo Grade III or more) were occurred in 6 patients (12%). The 1-, 3-, and 5-year survival rates were 66%, 31%, and 25%, respectively, and time of metastasis, localization were correlated with prognoses. In patients with metachronous metastasis and localization in either lobe, the 1-, 3-, and 5-year survival rates were 74%, 49%, and 40%, respectively. Especially in patients with synchronous metastases and localization in bilobar, the 3-year survival rates were 0%. Long-term survival was not possible.

Conclusion: Liver resection for NCNNLM is a safe treatment option. Although it is necessary to carefully consider and select individual

cases, there is a possibility that prolonged survival can be achieved by performing liver resection even in patients with NCNNLM.

Abstract Submission No. 200066
P-0638

Outcome of percutaneous transhepatic biliary stent in malignant biliary obstruction in Thailand

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Background: Malignant biliary obstruction(MBO) is likely to be in-operative at first presentation. Palliative biliary drainage is essential to increase overall survival. Percutaneous transhepatic biliary stent(PTBS) is effective and safe procedure of biliary drainage in MBO. However, there is no previous study in outcome of PTBS insertion in MBO in Thailand.

Objective: To determine outcome, success rate and complications of PTBS insertion in MBO.

Methods: A retrospective study was performed on 41 patients with MBO underwent PTBS insertion from 2015-2021. Technical data, success rate, and outcome(survival analysis and complications) were analyzed.

Results: Of 41 patients, PTBS insertion had technical success 82.93% and functional success 70.59%. Median survival time of patients was 95 days (IQR 50-147 days). Occlusion rate occurred in only 22.6% of patients and all of them underwent percutaneous transhepatic biliary drainage (PTBD) as alternative palliative biliary drainage. Mean occlusion free survival time was 77.14 days (SD 51.68 days). Most of patients (79.4%) did not have PTBS-related complications. The most common complication was acute cholangitis that found in 6 patients (17.6%). Median complication free survival was 91 days (IQR 60-155 days). For patients with functional success after PTBS insertion, the cumulative survival rates in 30-day,120-day, and 390-day and cumulative occlusion-free survival rates were statistically significantly better than those with functional failure ($p=0.030$, $p=0.007$).

Conclusion: Outcome and success rate of PTBS insertion were 82.93% in technical success and 70.59% in functional success. Functional success of PTBS insertion was the most important issue that related with better cumulative survival and occlusion-free survival.

Abstract Submission No. 200096
P-0639

Durvalumab plus gemcitabine and cisplatin combination therapy in unresectable biliary tract cancer

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Introduction and Aims: Durvalumab, an immune checkpoint inhibitor, was approved for unresectable biliary tract cancer in December 2022, but the actual situation in clinical practice remains unclear.

Gemcitabine, cisplatin, and S-1 combination therapy(GCS) was considered one of the options for primary chemotherapy for unresectable biliary tract cancer. We compared and investigated the actual clinical use of gemcitabine, cisplatin, and durvalumab combination therapy (GCD) and GCS therapy, including their effectiveness.

Methods: 28 patients who started GCD combination therapy (March 2023 to October 2023) and 45 patients who started GCS combination therapy (January 2019 to October 2023) for unresectable biliary tract cancer at our hospital. A retrospective analysis was conducted targeting the month of the month. Differences in patient background were corrected using propensity score matching (PSM), and overall survival (OS) and progression-free survival (PFS) were compared.

Results: After PSM, 13 cases were selected in each case. When PFS was compared, the GCS group was significantly better (2.7 months (95% CI: 1.5-2.8) vs. 7.0 months (4.9-9.2), $p=0.0038$), but when OS was compared, there was a no significant difference(not reached (4.7-), vs 16.2 months (3.6-20.3), $p=0.6027$).

Conclusion: According to our study, in actual clinical practice, the GCD group has inferior PFS compared to the GCS group, but there is no significant difference in OS, and the long tail effect, which is a characteristic of immune checkpoint inhibitors, can be obtained. Whether this is the case will need to be carefully observed in the future.

Abstract Submission No. 200139
P-0640

A Case of Hepatic Epithelioid Hemangioendothelioma Diagnosed with Sonazoid CEUS Guided Biopsy

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Background: Hepatic epithelioid hemangioendothelioma (EHE) is a rare non-epithelial tumor of vascular endothelial origin, demonstrating a slow growth tendency and representing a low to moderate-grade malignant tumor. Radiologically, it resembles metastatic liver tumors and intrahepatic cholangiocarcinoma, requiring a definitive diagnosis through histopathological examination via biopsy. In this report, we present a case of EHE in which percutaneous needle biopsy under Sonazoid contrast-enhanced ultrasound was diagnostically valuable.

Case: 32 years old, female

Chief complaint: None (visited for the investigation of liver tumors)
Medical history: While residing in the United States, an abdominal contrast-enhanced CT scan was performed following a traffic accident, revealing multiple liver tumors of approximately 10 mm in the right hepatic lobe.

Findings: Abdominal contrast-enhanced CT: Multiple liver tumors of approximately 10 mm in the right hepatic lobe. Based on the contrast findings, metastatic liver cancer or hepatic epithelioid hemangioendothelioma was suspected.

Abdominal ultrasound: The liver tumors identified on CT were challenging to recognize with B-mode ultrasound. However, Sonazoid contrast-enhanced ultrasound low-contrast findings in the post-vascular phase, enabling recognition and identification.

Blood test: No abnormalities were observed in liver and biliary enzymes or tumor markers.

Pathological examination: Hepatic epithelioid hemangioendothelioma.

Discussion: In this case, Hepatic epithelioid hemangioendothelioma may be challenging to identify with B-mode ultrasound. Sonazoid

contrast-enhanced ultrasound-guided biopsy proves to be extremely useful for a definitive diagnosis in such cases.

Abstract Submission No. 200283
P-0641

A rare case of MTX-LPD (large B-cell lymphoma) appeared as multiple hepatic tumors

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Case: A 60-year-old woman with multiple hepatic tumors was admitted. The patient was diagnosed as rheumatoid arthritis in her thirties and had oral methotrexate (MTX) for 10 years. As AST/ALT levels were elevated 4 years earlier, ursodeoxycholic acid was administered. g-GTP levels slightly increased thereafter. The MRI revealed multiple hepatic tumors (max. 59 mm, and three other tumors). Enhanced CT showed hypo-vascular tumors, suggestive of metastases. However, upper/lower endoscopy revealed no primary lesions, MTX was withdrawn. On admission; g-GTP 70 U/L, LDH 435 U/L, sIL-2R 2153 U/ml, hepatitis viruses and tumor markers negative, and EBV-DNA 60000 copies/ml. PET-CT showed FDG uptake in the right pharynx and liver. Histopathology from both biopsies indicated large atypical cells within the small lymphocyte. Immunohistochemical findings yielded a diagnosis of MTX-associated lymphoproliferative disorders (MTX-LPD); large B-cell lymphoma. Hepatic tumor was reduced (39.7mm) on ultrasonography. LDH and sIL-2R also decreased (178 U/L and 957 U/mL, respectively), 1 month later MTX withdrawal. At 4 months, tumor decreased further (26.2 mm) and sIL-2R was normalized. At 15 months to date, there has been no evidence of relapse.

Conclusion: We have presented a rare case in which MTX-LPD-associated primary multiple hepatic tumors, regressed after MTX withdrawal. To find good patient outcomes earlier, changes in peripheral lymphocyte counts (Tokuhira, 2020) and LDH/sIL-2R levels along with ultrasonographic findings may be important.

Abstract Submission No. 100151
P-0642

The spike of SARS-CoV-2 induces IL-8 secretion of human hepatocytes and promotes NETosis

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The emergence of SARS-CoV-2 was responsible for the COVID-19 pandemic. Despite primarily as a respiratory virus, the presence of SARS-CoV-2 has been detected in liver tissue with a significant percentage of COVID-19 patients experiencing liver damage, having raised questions about its impact on the liver. In this study, we simulated SARS-CoV-2 infection in human liver cells by transfecting the SARS-CoV-2 spike plasmid and explored their pathological effect in hepatocytes. We found that the spike protein could be located in both the cell cytosol and membrane with the observation of the syncytia, potentially indicating interaction with nearby cells to help the virus transmission. Additionally, the spike protein increased reactive oxygen species (ROS) levels and lipid accumulation, possibly contributing to oxidative stress and inflammation. We also revealed heightened interleukin-8 (IL-8) secretion by spike-expressing liver cells. Importantly, spike-expressing Huh7 activated human neutrophils adhesion, forming neutrophil extracellular traps (NETs) in coculture model. Moreover,

the purified NETs induced IL-8 secretion of Huh7, suggesting a feedback loop between NETs and IL-8 secretion was observed.

Abstract Submission No. 100446
P-0643

Seroprevalence of enteric hepatitis A and E viruses among general residents in Binh Thuan, Vietnam

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Background: In developing countries with poor sanitation and limited access to clean water, hepatitis A virus (HAV) and hepatitis E virus (HEV) are the main causes of acute viral hepatitis. Although Vietnam exhibits a notable liver mortality rate, the prevalence of HAV and HEV among the general population remains limited. This study aims to determine the prevalence and genotype of HAV and HEV using stocked serum.

Methods: A total of 504 stocked serum collected from residents in Vietnam, by multi-stage random sampling in 2012 was used to detect total anti-HAV and anti-HEV IgG using the in-house ELISA method. HAV and HEV RNA screening was done by nested RT-PCR using a universal primer set targeting nonstructural protein 2A, 2B of HAV, and ORF1 of HEV. Genotyping was done by phylogenetic tree analysis. **Results:** The seroprevalence of total anti-HAV was 93.8% and anti-HEV-IgG was 31.9% with no significant difference by sex and age except anti-HEV IgG which positivity was significantly lower in <40 years old adults (20%). HAV RNA was detected in 27 anti-HAV positives (5.6%) while no HEV RNA was found in 162 anti-HEV positives. By phylogenetic tree analysis, all HAV strains were genotype IA and close to HAV strains from China and Japan.

Conclusion: Our study revealed that over 90% of residents were immune to HAV whilst 31.9% were immune to HEV especially in the young adults <40 years old. Considering the herd immunity of HAV, a prevention measure and improved sanitation is required to prevent the potential sporadic outbreak of HEV in Vietnam.

Abstract Submission No. 101422
P-0644

Drug-resistant organism colonization in patients with cirrhosis admitted to ICU

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Introduction: The burden of drug-resistant organisms is rising and screening for drug-resistant organism colonizers may aid in the

appropriate management of the patients and prevent transmission especially in patients with cirrhosis.

Methods: Patients with cirrhosis who were admitted to ICU with a recent exposure to more than one antibiotic or those referred from other hospitals were included. The established hospital screening protocol is to perform nasal, rectal, axillary and groin swabs for methicillin-resistant staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), carbapenem-resistant enterococci (CRE) and *Candida auris* colonization in patients. Those positive are isolated and provided one-to-one nursing care.

Results: Seventy-five patients were screened over last 6 months. Of them, 85.3% (n=64) were males and the commonest etiology was alcohol, and 38 (50.6%) were ACLF. Approximately 46 (61.3%) patients had 59 swabs positive. The commonest was CRE, which was positive in 49.3% of patients, followed by VRE in 22.6%. Interestingly, 15% of swab positive and 13.8% of swab negative had positive blood culture. Two patients in the swab positive and 1 in swab negative had culture positive SBP (P=0.67). There were no differences in the etiology, liver function tests and severity scores among swab positive and negative groups. Furthermore, the mortality in those with swab positivity was 43.5% compared to 44.8% in those without (P=0.54).

Conclusion: Colonization in cirrhosis is common due to recurrent hospitalization, frequent antibiotic exposure, and immune dysfunction. Appropriate hand hygiene, regular sanitization of ICUs, aseptic precautions during procedures and screening for colonizers can reduce burden of MDR infections.

Abstract Submission No. 101436

P-0645

Clinical Characteristics and Treatment Outcomes of Patients with HCV/HIV Coinfection in Korea

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Background/aims: Because of the very low incidence of human immunodeficiency virus (HIV) infection in Korea, the epidemiologic data on hepatitis C virus (HCV)/HIV coinfection are limited. We investigated the clinical characteristics and treatment outcomes of patients with HCV/HIV coinfection in Korea.

Methods: We collected retrospectively data of patients diagnosed with HCV/HIV coinfection at 12 academic hospitals in Korea from 2009 to 2020.

Results: A total of 124 patients were included. Male gender was predominant (n=113, 91.1%), and the mean age was 46.5 ± 13.5 years. Of them, 11 patients (8.9%) had cirrhosis and 7 (5.6%) was positive HBsAg. During follow up, 2 patients (1.6%) developed HCC and 9 (7.3%) died. Among the 112 patients (90.3%) who were performed with HCV genotype test, most were genotype 2 (n=53, 47.3%) and

genotype 1b (n=41, 36.6%). In particular, the genotype 1a was 12.5% (n= 14). Ninety-one patients (73.4%) were treated with antiviral agents and a total of 104 antiviral treatments were administered. The sustained virologic response rate of the patients receiving pegylated interferon-based treatment was greater than that of those receiving DAA treatment (58.1% vs 89.0%, $P < 0.001$).

Conclusion: In Korea, patients with HCV/HIV co-infection were predominantly male, younger, and had a higher prevalence of genotype 1a compared to the known patients with HCV mono-infection. They had a better treatment response to DAA treatment than that to interferon-based treatment.

Abstract Submission No. 101462

P-0646

Inhibition of hepatitis E virus replication by FDA-Approved RdRp inhibitors

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Hepatitis E virus (HEV) is primarily a hepatotropic virus that is responsible for acute hepatitis E in the general population and for chronic hepatitis in immunocompromised individuals. In the absence of a globally accessible vaccine, pegylated interferon- α and ribavirin are the only antiviral agents available for the treatment of chronic patients. As viral RNA-dependent RNA polymerases (RdRps) are indispensable for RNA replication, they are considered potential drug targets. In this study, we screened some well-known RdRp inhibitor molecules, notably, favipiravir, sofosbuvir, remdesivir, filibuvir, and tegobuvir. Of these, monotherapy with favipiravir and sofosbuvir inhibited the RdRp activity with an IC₅₀ value of 10.2 ± 4.9 and 5.2 ± 2.9 μ M, respectively, compared to the reference drug ribavirin (3.5 ± 1.6 μ M). Further investigation of the combination therapy showed a reduction in viral RNA copy numbers by approximately 90%. Therefore, favipiravir has an additive effect when used with sofosbuvir. Therefore, we propose that favipiravir is a promising anti-HEV drug that can be used in combination with sofosbuvir.

Abstract Submission No. 101688

P-0647

nonalcoholic steatohepatitis-related cirrhosis complicated by sepsis-induced liver dysfunction

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It is sometimes difficult to diagnose cholangitis lenta and sepsis-induced liver dysfunction due to phlegmonous gastritis clinically. We herein present a rare autopsy case. A 60-year-old man had been treated for nonalcoholic steatohepatitis-related cirrhosis. One month before admission to our hospital, he developed Miller-Fisher syndrome as a complicating condition. He was admitted to our hospital for the treatment of cirrhosis and rehabilitation. He remained on the waiting list for the hepatic transplant and we were in contact with the transplant department. The patient died of hepatic failure two weeks after exacerbation of anorexia and rapid progression of liver dysfunction.

Autopsy revealed cholangitis lenta and sepsis-induced liver dysfunction, which was attributed to phlegmonous gastritis due to *Moraxella (Branhamella) catarrhalis*. Acute cholangitis by *B. catarrhalis* has never been reported previously. In histological examination, numerous bile thrombi, neutrophils and lymphocytes were found to proliferate the canals of Hering, indicating the sepsis-related cholangitis lenta. Moreover, *B. catarrhalis* existed with neutrophils in all layers of the stomach. Thus, it was most likely that phlegmonous gastritis was orally developed, which caused sepsis and then cholangitis. Phlegmonous gastritis has seldom been reported in patients with liver cirrhosis. We believe the importance of keeping in mind that phlegmonous gastritis could be one of the complications of advanced liver cirrhosis and cause sepsis-induced liver dysfunction.

Abstract Submission No. 101701

P-0648

Clinical characteristics of 44 cases of liver abscess: A single center study

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Background: Hepatic abscess is a rare disease, but it sometimes has a poor prognosis. In this study, we reviewed our experience with liver abscesses in our hospital.

Methods: We retrospectively reviewed the clinical characteristics of a total of 44 patients who were diagnosed with liver abscess by CT or MRI scan and hospitalized for treatment between October 2013 and July 2023.

Results: The median age was 74 years. The backgrounds of the patients were as follows: 12 were obese with BMI over 25, 16 had a history of smoking, 7 were heavy alcohol drinkers, 18 had hypertension, 9 had diabetes mellitus, and 11 had dyslipidemia. The positive rate of blood cultures was 31%, and the positive rate of cultures of percutaneous drainage fluid was 67%. Of the 27 cases in which pathogenic bacteria could be identified, 11 were *Klebsiella pneumoniae* and 6 were *Escherichia coli*. 5 of the 6 *Escherichia coli* cases had biliary tract disease/post-biliary reconstruction. Patients in whom abscess drainage was performed, compared to patients in whom drainage was not performed, had a significantly larger maximum diameter abscess (65.5 vs. 38.0 mm, $P<0.001$) and higher CRP on admission (20.2 vs. 11.8 mg/dL, $P=0.003$). The number of days of hospitalization was significantly positively correlated with the maximum diameter of the abscess and CRP on admission ($P<0.001$). There were 5 recurrent cases, 4 of which had biliary disease/post-biliary reconstruction, and 1 of which had all 6 lifestyle-related factors.

Conclusions: Percutaneous drainage was performed in severe cases, leading to an improved bacterial identification rate, but there were cases of recurrence in patients with biliary disease/post-biliary reconstructive surgery. Post-treatment follow-up was considered important.

Abstract Submission No. 101714

P-0649

Clinical characteristics of 44 cases of liver abscess: A single center study

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Conclusions: Percutaneous drainage was performed in severe cases, leading to an improved bacterial identification rate, but there were cases of recurrence in patients with biliary disease/post-biliary reconstructive surgery. Post-treatment follow-up was considered important.

Abstract Submission No. 101902

P-0650

To present a clinical, paraclinical, and microbiological profile of patients with liver abscesses

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: This retrospective cross-sectional investigation examined 196 patients diagnosed with hepatic abscesses treated at Hospital 108 from January 2018 to August 2023.

Results: The average age of the individuals in the study was 57.8 ± 16.0 years, with a male-to-female ratio of 3.1/1. Frequently associated comorbidities included diabetes mellitus (28.1%), hypertension (14.3%), and gallstones (7.8%). Epidemiological risk factors within the study population encompassed irregular deworming practices (99%), consumption of raw vegetables (49%), intake of raw salads (44.9%), and inadequate hand hygiene following restroom use (44.9%). The classic Fontan's triad was identified in 26% of patients. Among the 196 patients, 57.15% exhibited anemia, 70.9% displayed an elevated white blood cell count (with 73% indicating an increase in neutrophil counts and 26.0% showing an elevation in eosinophil counts), and 98.2% had elevated Procalcitonin levels. Liver abscesses were predominantly situated in the right lobe (74.0%), primarily as solitary abscesses (82.6%), with an average size of 63.3 ± 29.1 mm, and the largest documented abscess measured 172 mm. Bacterial isolates were

detected in 63 patients, with *Klebsiella* being the most prevalent (80.9%), followed by *E. coli* (7.9%). In conclusion, liver abscess is an acute infectious condition, typically found in elderly individuals with underlying diseases, more common in males, and directly related to unsanitary lifestyle habits. The primary cause is Gram-negative bacteria, and imaging diagnosis is an effective diagnostic tool.

Abstract Submission No. 101994
P-0651

Changing Hepatitis A Serology in A Hepatitis B Hyperendemic Region in Asia

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Background: Acute Hepatitis A generally has a self-limiting and benign course in the general population. There is, however, potential for increased morbidity in patients with underlying liver disease. There is a limited updated Hepatitis A serology data in the Philippines, a hepatitis B hyperendemic region.

Methods: Hepatitis A serology data of 750 individuals from the "Early Cancer Detection in the Liver of Filipinos with Chronic Hepatitis B using AI-driven integration of clinical and genomic biomarkers (CAN-DLE Study)" were analyzed.

Results: The cohort was 76% HBsAg positive and across all ages 57.47% were found to have AntiHAV IgG positivity. There was increasing seropositivity at increasing age, with anti HAV IgG positivity rates of 6.26%, 32.95%, and 60.79% in those 18-25, 25-35, and > 35 years of age, respectively. AntiHAV Ig G positivity was also noted in high risk populations: 88.77% in HBsAg + Cirrhotic patients, 47.13% in patients with HCC, and 74.5% in HBsAg patients with Steatotic Liver Disease.

Conclusions: Data from our study shows some change in the AntiHAV IGG seropositivity data by age, with note of decreased positivity by age as compared to published data before the year 2000. This reinforces the recommendation to do baseline AntiHAV IgG testing and possibly vaccinating at baseline assessment of Filipinos with chronic liver disease.

Abstract Submission No. 200057
P-0652

SEROPREVALENCE OF HEPATITIS A VIRUS INFECTION IN VIETNAM: INTERIM RESULTS FROM 2023

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Background: The incidence of Hepatitis A Virus (HAV) is closely associated with socioeconomic factors, access to clean drinking water, and improved sanitation. In Vietnam, epidemiologic data of HAV is lacking over the past two decades. The objective of this study is to assess age-specific HAV seroprevalence and evaluate risk factors associated with HAV seropositivity in Vietnam.

Methods: A cross-sectional seroprevalence study was conducted in two contrasting areas (urban and rural) in Vietnam. Serological testing for anti-HAV IgG antibodies (Roche test kit) and socio-demographic questionnaire interviews were done in all participants. The age at midpoint of population immunity (AMPI) was determined.

Results: In this interim analysis, 882 participants aged 1 to >50 were tested (518 urban, 364 rural). Participants aged <15 years comprised 24.5% of the sample. Total HAV seropositivity in the interim population was 62.7%. Anti-HAV seropositivity was 50.8% in urban areas; significantly lower than in rural areas (79.7%), $p < 0.001$. Univariate analysis revealed that a main factor associated with higher risk of HAV infection included residing in a rural area during first 5 years. Participants with a higher education level, having knowledge of Hepatitis A /infectious disease, using piped water in dwellings, and washing their hands after defecation had a lower association to HAV seropositivity. Initial AMPI was 36 years, indicating potential low endemicity.

Conclusions: Initial findings show differences in HAV seroprevalence between urban and rural areas. These data are important for policy-makers to determine prevention strategies, such as national immunization programs, to reduce HAV infections and disease burden.

Funding: GlaxoSmithKline Biologicals SA (GSK study identifier: 216938).

Abstract Submission No. 200149
P-0653

Unraveling Hepatic Tuberculosis: Recurrent Fever, Jaundice & Tea-Colored Urine in a 32-Year-Old Male

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This case report details the diagnostic journey of a 32-year-old male with a perplexing three-year history of recurrent fever, jaundice, tea-colored urine, and occasional acholic stools, each episode spontaneously resolving. Exhaustive investigations initially yielded inconclusive results, challenging the conventional diagnostic paradigm. Subsequent evaluation, including liver function tests and imaging studies, revealed subtle abnormalities, prompting a reevaluation of potential infectious etiologies.

The breakthrough in diagnosis came with a positive result in the QuantiFERON-TB Gold+, unveiling the presence of Tuberculosis as an underlying cause for the recurrent symptomatic episodes. Additional confirmation came along with the resolution of the symptoms when Anti-Koch's treatment was initiated. This rare manifestation of extrapulmonary tuberculosis highlights the importance of considering atypical presentations, especially in regions where tuberculosis is endemic.

The report discusses the challenges faced in diagnosing Hepatic Tuberculosis, emphasizing the need for heightened clinical suspicion and a comprehensive diagnostic approach. It also underscores the importance of timely identification and initiation of appropriate anti-tubercular therapy to prevent further complications and improve patient outcomes.

This case serves as a poignant reminder of the diverse clinical presentations of tuberculosis, urging clinicians to maintain a broad differential diagnosis and consider rare manifestations in the pursuit of resolving diagnostic conundrums associated with recurrent fever, jaundice, and tea-colored urine.

Abstract Submission No. 100149
P-0654

Complications Associated with Living Donor in Liver Transplant: A Global Analysis of 60,829 Donors

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Introduction: Living donor liver transplantation (LDLT) is a major life-saving procedure but it is not without risks to the donor. Particularly in the east where deceased donor organs are less available, understanding the incidence and types of complications in LDLT is crucial for both donor safety and optimizing transplant outcomes.

Methods: A comprehensive meta-analysis was conducted by searching Medline and Embase databases for relevant articles published until July 2022. These studies evaluated the incidence of complications among LDLT donors, categorized by organ systems. The analysis utilized statistical models with Clopper-Pearson intervals.

Results: The overall pooled incidence of complications in LDLT donors was 24.7% (95% CI: 21.6% to 28.1%). Minor complications occurred in 17.3%, while major complications were less frequent at 5.5%. Clavien-Dindo classification revealed Grade I (10.9%), Grade II (5.7%), and Grade III (5.4%) complications. Grade III was subdivided into IIIa (3.2%) and IIIb (1.9%), with Grade IV (0.2%) complications posing life-threatening risks. Remarkably, the overall pooled incidence of donor mortality (Grade V) was 0.06%. Right lobe donation had the highest complication rate (26.6%), with the highest major complication rate (6.6%) compared to left lobe (12.3%) and left lateral section donation (12.7%). Complications were further categorized by organ systems, with psychological (7.6%), wound-related (5.2%), and respiratory (4.9%) complications being most prevalent. Cardiovascular complications were least common (0.8%).

Conclusion: This comprehensive analysis emphasizes the need for careful assessment and monitoring of LDLT donors, shedding light on the incidence and types of complications they may encounter during the transplant process.

Abstract Submission No. 100951
P-0655

PERCUTANEOUS TREATMENT OF LIVER CYSTIC ECHINOCOCCOSIS

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Objective: to analyze the effectiveness of the treatment of liver cystic echinococcosis by PAIR method.

Methods: We analyzed the outcome of 133 patients with active echinococcal liver cysts who underwent percutaneous and transhepatic echinococcectomy during the period from January 2017 to August 2023. Staging was carried out according to WHO-IWGE Classification Images of Cystic Echinococcosis. Prior to the PAIR procedure, patients taking 800 mg of Albendazole for 7 days, and in the postoperative period, 800 mg of Albendazole for 2 months continuously. Ultrasound control was performed every 1, 3, 6, 9, 12 months, CT after 1 year.

Results: The postoperative stay of patients in the pair was 3.8 (1-19) days. The follow-up time averaged 39.9 months $\pm$ 21 (min. 2 - max. 79 months). During the PAIR procedure, a biliary fistula occurred in 3.7%, the operation ended with the abandonment of Pigtail-type drainage tubes 8.5Fr., also intraoperatively, anaphylactic reaction occurred in 5.2%, which were successfully resolved. In the long-term period, suppuration of the residual cavity after PAIR occurred in 6.01% of patients who were drained under local anesthesia, whose cysts were larger than 12 cm during the PAIR procedure, and 6 (5.1%) relapses occurred during the PAIR procedure.

Conclusion: In cysts CE1 and CE3a, the optimal volume is PAIR, characterized by a smaller postoperative stay, early recovery, the effectiveness is comparable to "open" surgery.

Abstract Submission No. 100957
P-0656

Results of liver transplantation in NSCS named after A.N. Syzganov

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Aim: To analyze the results of liver transplantation (LT) in our clinic.

Methods: From December 2011 to September 2023 we performed 256 LT on adults and children in the Syzganovs NSCS. LT from a living related donor was performed in 230 (89.8%) patients, including pediatric liver transplantation in 44 (17.1%) cases, from a deceased donor in 26 (10.1%) cases.

Indications for liver transplantation were cirrhosis in outcome: HCV- 22, HBV- 26, HBV+HDV- 83, primary biliary cirrhosis- 33, autoimmune hepatitis- 4, cryptogenic cirrhosis- 9, myofibroblastic tumor- 1, steatohepatitis- 2, Budd-Chiari disease-1, Wilson-Konovalov disease- 1, alimentary toxic hepatitis-2, biliary atresia-44, secondary biliary cirrhosis-2. Clinical outcomes were retrospectively analyzed.

Results: The overall survival rates of patients after LDLT were: 5 years- 74.3%; 10 years-71.7%. Postoperative complications were 85 cases as follows: biliary complications 31 (36.4%), bleeding 15 (17.6%), relaparotomy 20 (23.5%), rejections were observed in 10 (11.7%) cases, non compliance 9 (10.5%) cases. Also analyzed 118 donor for adult recipients, 10 (8.4%) non-life threatening complications were identified. Such as portal vein thrombosis Yerdel grade - I 1(0.8%) case, bleeding 1 (0.8%) case and 8 (6.7%) cases of biliary complications.

Conclusion: We have problems in the development of liver transplantation from a deceased donor, therefore we perform LDLT up to 90%.

Abstract Submission No. 100997
P-0657

The Liver Transplantation Economic Analysis in Asia

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Globally, Asia and Pacific region accounts for 62.6% of all liver disease deaths, especially 54.3% of cirrhosis-related deaths and 72.7% of HCC-related deaths. In Asia, a shortage of deceased donor liver grafts is the universal problem to be faced with in all transplant centres. This

study focuses on what factors affect liver transplantation in Asian countries, specifically on health economics side.

Using data obtained from the Global Observatory on Donation and Transplantation and the World Bank, 8 countries of Asia were selected to see how the economic growth, health expenditure, average protein supply, and Prevalence of anemia among women of reproductive age (15-49 years) affect the liver transplantation. This study employed data from 2010-2019 and then analyzed using Panel Data analysis.

From the results of the panel data regression, it is known that variables of economic growth, health expenditure have a significantly positive influence on liver transplantation. Meanwhile, the variable of the average food supply has a negative influence and the prevalence of anemia among women of reproductive age (15-49 years) insignificant influence. The result indicates health expenditure can increase the liver transplantation by 3%. The rise of economic growth also can increase liver transplantation. If economic growth rises by 1%, it is followed by an increase in the liver transplantation by as much as 1%. In addition, the average food supply can be determined as a factor that affects liver transplantation.

Abstract Submission No. 101134
P-0658

Acute and chronic rejection after Liver Transplantation: experience of single center in Kazakhstan

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Introduction: Organ transplantation is the treatment of choice for patients with end-stage liver diseases. Patients with ESLD in Kazakhstan has an access to Liver Transplant program which started in early 2000's. Despite the advances in immunosuppression regimens acute and chronic allograft rejection remains one of the challenges of LT.

Method: Consecutive LT recipients who underwent surgery in our institution from 2013 to 2023 were evaluated recipients for clinical, laboratory and liver histology signs of rejection.

Result: In total 55 patients were included in this analysis, LDLT cases is the predominantly done surgery = 36 cases, DDLT - 19 cases. Period of 2013 to 2023 total of 9 rejections observed, 6 episodes of acute rejection and 3 episodes of chronic rejection observed. Of these, all acute rejection cases were responsive to methylprednisolone, they were all during early post-transplant period and in 3 cases donor's age was younger than 23 years old and longer cold ischemic time. Among late acute rejection of 3 recipients (50%) that developed after mean of 1,4 years 2 of them were responsive to methylprednisolone bolus. Chronic rejection was observed in 3 recipients (33%) were treated by adjusting the dosage of immunosuppressive agents, and 1 of them received retransplantation and died after 6 month due to sepsis & multi-organ failure.

Conclusion: Acute rejection (10.9%) in our study occurred both during early post-transplant and late periods. In all cases CMV, EBV, viral A, B,D,C infections and other vascular causes excluded, biopsy confirmed with Banff criteria and we observed death of 4 (44%) recipients.

Abstract Submission No. 101231
P-0659

SINGLE ORIFICE OUTFLOW RECONSTRUCTION IN RIGHT LOBE GRAFT LIVING DONOR LIVER TRANSPLANTATION

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Introduction: Outflow reconstruction is one of the key requirements of successful living donor liver transplantation. The aim of study is to evaluate the technical characteristics and outcomes of single orifice outflow reconstruction in living donor liver transplantation using right lobe graft in a center in Vietnam.

Method: The prospective study was performed on 52 cases of living donor liver transplantation using right lobe graft at 108 Military Central Hospital from January 2019 to December 2020. Polyester prostheses were used in reconstructing the MHV when the remnant liver volume was less than 35% of the donor liver volume. Venous branches with diameter ≥ 5 mm were preserved and anastomosed to the prosthesis.

Result: There were 42 cases of using the extended lobe living donor liver transplant including the middle hepatic vein (HV) (80.8%) and 10 cases of the modified right lobe graft with the middle HV reconstructed from the V5 and/ or V8 branches (19.2%) by using polytetrafluoroethylene artificial vessels. We conjoined the MHV and RHV as a single orifice hepatic vein. The HV were enlarged to the left and downwards at the orifice of the recipient's right hepatic vein, with a mean incision length of 14 mm and 9.7 mm, respectively. There were 1 cases of middle hepatic vein obstruction (1.7%). The mortality rate of hepatic venous outflow obstruction was 1.9%. The caliber of HV anastomosis (< 30 mm) was an independent risk factor for hepatic venous outflow obstruction.

Conclusion: The single orifice hepatic vein reconstruction in LDLT using a right lobe graft is a simple and feasible surgical technique, and it does not require cadaveric vessels.

Abstract Submission No. 101236
P-0660

DONORS BILIARY VARIATION AND BILIARY COMPLICATIONS IN 150 CASES OF LIVING DONOR LIVER TRANSPLANT

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Introduction: Living donor liver transplant (LDLT)) has developed tremendously as a savage therapy for chronic liver disease and malignancy. Our study aims to evaluate the biliary anatomy variation according to Varoti classification and its correlation with surgical outcomes for both donors and recipients undergoing LDLT.

Method: The prospective study was performed on cases of living donor liver transplantation using right lobe graft at 108 Military Central Hospital from October 2017 to December 2022. Donors' and recipients' demographic data, clinical data, operative details and postoperative course information were collected. We also reviewed the management and outcomes of BCs.

Result: 150 cases of LDLT at 108 Military Central Hospital from October 2017 to December 2022 were included in our study. Among the donors, the mean age was 30.89 ± 7.23 , with male predominance (77.3%). The prevalence of type 1 biliary anatomy was 84.67%. Type 2, 3a, 3b, 4a, and 4b accounted for 5.33%, 2.67%, 5.33%, 0.67%, and 1.33% of cases, respectively. Donors' complications were witnessed in 7 cases (4.67%), and all needed intervention (Clavien Dindo grade 3). Biliary complications were found in 36 (24.0%) recipients, with 22 (14.67%) cases of biliary stenosis and 16 (10.67%) cases of biliary leak, including 2 cases encountering both complications. Cold ischemia time significantly increased the biliary complication rate.

Conclusion: According to our study, biliary variant anatomy is common in liver transplantation donors. However, such variations should not be considered a contraindication to donation but require accurate pre- and intraoperative radiologic and surgical evaluations to plan a careful reconstruction.

Abstract Submission No. 101238

P-0661

Evaluation of early results in right donor hepatectomy for living donor liver transplantation

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Introduction: To evaluate the early results in donor right hepatectomy for living donor liver transplantation in 108 Military Central Hospital.

Method: Retrospective study of 127 donors cases who underwent right hepatectomy from October 2017 to June 2022 in 108 Military Central Hospital.

Result: The average age was 56.2 ± 12 years, and 80.3 % of the donor were male. The remnant left liver volume: $37.86 \pm 4.28\%$, right liver resection with middle hepatic vein accounted for the majority with 56.7%, graft size: 660.7 ± 107.9 g, operative time: 281.3 ± 50.0 minutes, blood loss: 313.7 ± 169.2 ml. There was no donor mortality, and the overall morbidity rate was 7.9%. Most of the complications of donors were either grade II or III, and biliary complications were the most common complications, with an incidence of 4.7%. The percentage of left liver volume increased after 07 days: $64.68 \pm 23.1\%$ and the average length of hospital stay was 11.2 ± 3.0 days.

Conclusion: With careful donor selection, right donor hepatectomy for living donor liver transplantation gives good results with a low complication rate.

Abstract Submission No. 101737

P-0662

Two cases of laparoscopic liver resection with incidental ICG mapping due to cholestasis

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Background: We employ 3D simulations using software to create images depicting the abdominal relationships of vascular structures and tumors, allowing for the planning of surgical strategies before Laparoscopic Hepatectomy (LH). In recent years, real-time intraoperative navigation using indocyanine green (ICG) staining has been explored. ICG is typically intravenously injected before surgery to identify tumors. Usually, ICG is intravenously injected before surgery to identify the tumor, but there are cases in which the liver is stained in areas.

Methods: From October 2020 to September 2023, 158 cases of LH were conducted at our institutions. ICG is routinely administered 2-14 days before the surgery date. In two of these cases, preoperatively administered ICG induced fluorescence not only in the tumor but also in an area corresponding to the planned resection area. We present findings from these cases.

Results: The first case involved a 68-year-old man diagnosed with hepatocellular carcinoma (S6, $\Phi 35$ mm). The second case featured a 74-year-old woman diagnosed with metastatic hepatocellular carcinoma (S3, $\Phi 30$ mm). The observed ICG fluorescence area during surgery resulted from the preoperatively administered ICG stagnating and coincidentally aligning with the resection area planned in the preoperative individual simulation. Following liver resection according to the fluorescent region, no bile leak or recurrence was observed. Observation using a fluorescence microscope revealed no malignant findings in the fluorescent rim. Pathologically, liver resection with fluorescent margins was deemed reasonable.

Conclusion: In cases where preoperatively administered ICG stagnates and aligns with the resection site in the preoperative patient-specific simulation, it may contribute to the surgical outcome of LH.

Abstract Submission No. 101785

P-0663

Change of HCC transplant candidates' prioritization policy leads to organ utilization improvement

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Introduction: Prioritization of HCC patients on the waiting list brings reduced access of non-HCC patients to liver transplantation (LT). New policy was adopted in Israel in March 2016. Patients with one tumor ≤ 3 cm were defined as "low risk" and received MELD 18 without increment, all other HCC patients were defined as "high risk" and received traditional prioritization.

Methods: Retrospective analysis of the National Transplant Center data for patients listed for LT from January 2010 to December 2021 before and after policy change (period A and period B respectively)

Results: Proportion of HCC patients listed in period B significantly decreased compared to period A (109/910 (12%) vs 155/755 (21%), ($p < 0.001$), due to lower amount of "low risk" patients 23/109 (21.1%) vs 63/155 (40.6%), ($p < 0.001$)

Waiting time to transplantation in HCC patients was significantly longer in period B than in period A (12.3 ± 9.3 vs 10.23 ± 6.2 months respectively, $p = 0.008$) that was explained by elongation of waiting time in low vs high risk group (17.6 ± 13.8 vs 11.3 ± 7.9 , $p = 0.002$) during period B. But transplantation rate and wait list mortality remains unchanged ($128/155$ vs $97/109$ ($p = 0.14$) and $17/155$ vs $4/109$ ($p = 0.06$)).

In the group of non-HCC patients transplant rate didn't change $299/600$ vs $379/801$, $p = 0.35$, but wait list mortality significantly decreased ($219/900$ vs $120/801$, for period A vs B ($p < 0.001$))

Conclusion: Changing allocation policy lead to increase in HCC patients waiting time without impairing their transplantation chance and survival. Due to significant decrease in number of listed HCC patients after policy change further follow up needed for final conclusions.

Abstract Submission No. 101799

P-0664

Near-infrared fluorescent imaging for tumor detection and securing surgical margin RFA

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Abstract

Background and Objective: Radiofrequency ablation (RFA) has been performed for liver tumors. However, some paper reported liver resection of local recurrence after RFA has a poor prognosis due to local progression of tumors or tumor progression with unclear boundaries. This study investigated the pathological features using near-infrared fluorescent imaging for local recurrence after RFA.

Patients and Methods: In this retrospective study, we included seven patients who underwent liver resection for local recurrence of hepatocellular carcinoma (HCC, n=6) or liver metastasis (colorectal liver metastasis (CRLM), n=4) or lung carcinoid liver metastasis (n=1)) after RFA at our department between 2011 and 2020. Histopathological specimens were evaluated using fluorescent microscopy (BZ-X800; Keyence).

Results: Pathological findings revealed negative surgical margin in all patients. The fluorescence patterns of HCC were as follows: partial fluorescent type and combined type (Partial + Rim). Conversely, the fluorescence pattern of liver metastasis was rim fluorescent type (A fluorescence signal only surrounding the tumor) in all cases.

In the rim positive cases of both HCC and liver metastasis, under fluorescence microscope, the viable tumors located inside the fluorescence rim and no malignant finding was detected in the fluorescence rim surrounding the tumor. It was suggested that non-fluorescent signal area showed the curative parts with coagulative necrosis treated by RFA.

Conclusion: The histopathological findings suggested near-infrared fluorescent imaging is a useful navigation tool for detecting tumors and identifying boundary between tumor and non-tumor in liver resection for local recurrence of liver tumors after RFA.

Abstract Submission No. 101827

P-0665

Laparoscopic resection of segment 4 & ventral area of right anterior section

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Introduction: Based on the anatomy of ventral-dorsal ramification of the right anterior portal vein, only ventral area of right anterior section can be removed, leaving portal branches to the dorsal area intact. By this procedure half of the volume of right anterior section can be saved. Short-term results of laparoscopic resection of segment 4 & ventral area (LLR S4 + ventral area) were studied.

Method: During the period from November 2018 to November 2022, the authors performed 5 cases of LLR S4 + ventral area. Mean age was 62 years. All the 5 patients were male. The diagnosis was HCC in 4 and combined hepatocellular cholangiocarcinoma in 1. One patients had 2 tumors and RFA was done for the 1.5cm sized tumor in segment 5/6 before the laparoscopic surgery. Mean tumor size was 2.75cm (range, 2.0 ~4.7cm). Mean BMI was 23.39 (range 21.02 ~ 25.29). Underlying liver was chronic hepatitis in 2 and cirrhosis in 3. Four patients were positive for HBsAg. Mean liver elasticity was 6.65 kPa (range, 4.4 ~ 11.8 kPa) on Fibroscan.

Result: Mean operation time was 321 minutes. Mean estimated blood loss was 400 ml. Mean Pringle time was 75 minutes. No patient received blood transfusion. Mean postoperative hospital stay was 7.4 days. There was no postoperative complication or readmission within 60 days.

Conclusion: LLR S4 + ventral area is easier to perform than laparoscopic central bisectectomy. Tumor adherent to the middle hepatic vein is a good indication for this operation.

Abstract Submission No. 101828

P-0666

VIBRATION-CONTROLLED TRANSIENT ELASTOGRAPHY TO EXCLUDE STEATOSIS IN LIVING-LIVER DONOR EVALUATION

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Background: Using vibration-controlled transient elastography (VCTE) with controlled attenuation parameter (CAP) as an assessment of hepatic steatosis for living donor evaluation might eliminate necessity for invasive liver biopsies. This study aimed to evaluate correlation between CAP and histologic amount and percentage of liver fat and between CAP and magnetic resonance imaging fat signal fraction (MRI-FSF).

Materials and methods: This was a retrospective study of subjects who were living donors for living donor liver transplantation (LDLT) from January 2019 to June 2023. The histopathological report was obtained during pre-LDLT evaluation or surgery. The receiver operating characteristic (ROC) analysis was used to predict hepatic steatosis with appropriate sensitivity, specificity, and the Youden's Index for liver donor screening.

Results: Fifty-three subjects were living donors, including 15 (28.3%) men with a mean age of 31.9±6.9 years. The area under the curve (AUC) for CAP to predict hepatic steatosis ≥5% by histology was 0.851, 95%CI 0.727–0.974, p<0.001. The optimal cutoff value of CAP was ≥240 dB/m to detect histologic steatosis ≥5%, with sensitivity of 72.7% and specificity of 83.3%. To predict hepatic steatosis >5% by MRI-FSF, the AUC for CAP was 0.771, 95%CI 0.609–0.933, p=0.004. The optimal cutoff value of CAP was ≥254 dB/m to detect MRI-FSF >5%, with sensitivity of 61.5% and specificity of 92.1%.

Conclusions: VCTE is a non-invasive test that could be used for hepatic steatosis assessment in living donors for LDLT evaluation. Subjects evaluated for living donors with CAP <240 dB/m could avoid liver biopsy.

Abstract Submission No. 101957

P-0667

Extended Left Lobe Graft for Adult-to-adult LDLT for donor safety and recipient outcome

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Background: Donor hepatectomy carries a significant risk for the donor. In LDLT where donor safety is most important, considering the use of the left lobe is an essential option for donor safety. This study aims to assess the safety of donors and the outcomes for recipients when using an extended left lobe graft.

Patients and methods: From January 2018 to August 2022, LDLT was performed on 225 patients at our center. Among them, 32 patients underwent LDLT using an extended left lobe (ELL) graft and 193 patients underwent LDLT using a modified right lobe (MRL) graft. In these two groups, donor safety was first compared, and then, the recipient outcomes were compared according to the type of graft.

Results: Due to the volume problem of the graft, the ELL group had a male ratio of 93.8%, which was higher than that of the MRL group. The complication rate of Clavien-Dindo IIIa or more was the same in both groups, but peak total bilirubin and peak PT INR after donor hepatectomy were both significantly higher in the MRL group. Normalization of total bilirubin and PT were also earlier in the ELL group. For the recipients, there was no difference between the two groups in vascular complications, biliary complications and overall survival.

Conclusions: The use of ELL grafts in adult LDLT protects donor well-being while not negatively impacting recipient outcomes. In adult-to-adult LDLT, it is recommended to consider the use of ELL grafts as long as they are available in adequate volume.

Abstract Submission No. 102059
P-0668

Right priority approach in laparoscopic total caudal lobectomy for hepatocellular carcinoma

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Owing to its special location and anatomical characteristics, the caudate lobe (CL) resection is the most complex and difficult liver surgery. The portal vein, biliary tract, and artery of the total CL do not always walk in Glissonean pedicle together; the portal vein branches are complex and irregular, and the outflow of the CL is also diverse. Effective anatomical criteria and technical means to clearly define the right and ventral margins of the CL are still lacking. The complete right liver mobilization through right priority approach can help safely dissect the right hepatic short veins and caudate process hepatic pedicle (G1C), and the right CL resection plane can be identified using Peng's line or right paracaval plane as landmarks. This study reports the technical criteria for the right priority approach and good postoperative outcomes.

Abstract Submission No. 102085
P-0669

The safety and efficacy of laparoscopic repeat hepatectomy for recurrent hepatocellular carcinoma

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Background: Repeat hepatectomy is often technically difficult because of severe postoperative adhesion and deviation of the remnant liver caused by the previous liver resection. This study aimed to report perioperative outcomes of laparoscopic repeat hepatectomy (LRH) compared with those of open repeat hepatectomy (ORH).

Methods: One hundred and forty-two patients who underwent repeat hepatectomy for hepatocellular carcinoma (HCC) between April 2016 and August 2022 were enrolled. Of these patients, 102 and 40 patients underwent ORH and LRH, respectively. The clinical characteristics and perioperative outcomes of the groups were compared using propensity score matching (ORH-PSM group *versus* LRH-PSM group).

Results: Propensity score matching showed 18 patients in each of these groups. There were no significant differences in patient characteristics and tumor factors between the groups. Intraoperative blood loss ($P=0.005$) was lower and the operating time ($P=0.03$) and postoperative hospital stay ($P=0.001$) were shorter in the LRH-PSM group than in the ORH-PSM group.

Conclusion: LRH is a safe approach for recurrent HCC in selected patients.

Abstract Submission No. 102088
P-0670

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Abstract Submission No. 200010
P-0671

Direct estimation of the future remnant liver function reserve intraoperatively for predicting POPF

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Background: The prediction of post-hepatectomy liver failure (PHLF) based on remnant liver function reserve is crucial for the success of hepatectomy. In patients with perihilar cholangiocarcinoma, a disparity between indirect and direct estimation of future remnant liver function may be observed. The objective of this study was to investigate whether intraoperative measurement of indocyanine green (ICG) clearance in a future remnant liver could serve as a predictor of PHLF.

Methods: This retrospective study included 49 consecutive patients who underwent anatomical hepatectomy between June 2016 and August 2022. Intraoperative ICG plasma disappearance rate (int-ICG-PDR) was measured after clamping the selective hepatic inflow to the liver that was to be resected. Logistic regression analysis for predicting PHLF grade B/C was employed to identify independent predictors.

Results: The median age of the population was 69 (62-74, IQR). Of the operations performed, 89.8% were major hepatectomies. PHLF Grade

B/C was observed in nine patients (18.4%) with no mortality. Stepwise multivariate logistic analysis confirmed that int-ICG-PDR ($p=0.015$) was an independent predictor for PHLF B/C. ROC analysis showed an AUROC of the int-ICG-PDR was 0.80. A subgroup analysis of patients with preoperative biliary drainage showed that the AUROC of int-ICG-PDR increased to 0.92.

Conclusions:

Int-ICG-PDR was a promising predictor for PHLF in patients undergoing anatomical hepatectomy.

Abstract Submission No. 200109

P-0672

Post liver transplantation infection in Mongolia

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Introduction: Liver transplantation (LT) is the definitive treatment for patients with end stage of liver disease. Infections are common consequences of organ transplantation resulting from immune suppression and prolonged hospitalization.

Aims: to determine incidence, demography, risk factors, timeline and characteristics of post-liver transplantation infections at our center.

Materials and methods: This retrospective cohort study examined the records of all liver transplant recipients under 65 years of age in First Central Hospital of Mongolia from August 2016 to February 2023. Demographic, laboratory, and clinical data and the administered medications were recorded.

Results: All recipients with at least 12 months of follow up were enrolled ($n=180$ M-89, F-91, average age 44). Bacterial infection incidence was 75%: gram-negative- 41.3% and gram-positive- 58.6%. Surgical site infections (SSI) were the commonest (41.6%), followed by urinary tract infections (UTI) (10.9%), sepsis [u1] [u2] (11.9%) and respiratory infections (27.2%). The length of hospitalization, re-hospitalization was significantly higher in the infected group than in non-infected group. The median isolation time of Gram-negative bacteria was 14.5 ± 7.3 , of gram-positive rods 15 ± 6.4 days after LT.

This study shows 8.77% of total infections were multidrug resistant. Among the MDR bacterial 43.7[u3] % and 43.7 of gram-negative bacteria were ESBL and MDR-GNB respectively, and 12.5% was CRE. There were 3 cases of active TB and which was developed 1.3 years after LT.

Conclusion: SSI were more common sources of infection and most infections were detected in the early period after LT.

Abstract Submission No. 200118

P-0673

Split liver transplantation plus domino liver transplantation

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Split left and right liver transplantation plus domino liver transplantation with one donor liver and three simultaneous recipients is a

complex but feasible allocation scheme to alleviate donor liver shortage. Donor liver shortage has remained the main obstacle in liver transplantation. Split liver transplantation and domino liver transplantation can alleviate the problem of donor liver shortage and shorten the waiting time of recipients, which have been implemented in many transplant centers. However, domino liver transplantation with split liver transplantation is rarely reported. This paper reported a case of cadaver donor liver split liver transplantation (right half liver) and a case of domino liver transplantation (domino liver). Patient 1 was diagnosed with hepatitis B cirrhosis (decompensated stage) and received split liver transplantation (right half liver). Patient 2 was diagnosed with familial hypercholesterolemia and underwent split liver transplantation (left half liver). Patient 3 was diagnosed with liver malignancies and hepatitis B cirrhosis. The diseased liver of patient 2 was implanted as a domino donor liver to complete domino liver transplantation, thus realizing a cadaver donor liver. Hence, three cases of liver transplantation were completed, and all patients recovered smoothly after surgery. In summary, split and domino liver transplantations provide a new approach to maximize organ utilization and achieve three or more recipients for one liver.

Abstract Submission No. 200119

P-0674

Parental and domino auxiliary liver transplantation for Crigler-Najjar syndrome

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Background: In this research, the surgical procedure, prognosis, and prognostic of parental liver transplantation (LT) in combination with domino auxiliary liver transplantation (DALT) were evaluated.

Case presentation: Here, we describe a case of parental LT paired with DALT. We observed the overall outcomes, postoperative issues, and postoperative recuperation of the donors and recipients.

Methods: The domino donor was released four weeks after surgery, and the parental LT donor recovered without incident. On the sixth day after surgery, the blood flow ratio of the domino recipient was checked, and it showed a declining trend. As an emergency measure, a portal vein stent was implanted together with a portal vein balloon dilatation and a portal vein embolization. Following the intervention, the child's blood flow improved, and the patient was discharged three weeks after the operation.

Conclusion: Children with liver transplants may now get innovative therapy for metabolic problems that combine parental LT and DALT, giving them the same development possibilities as healthy children.

Abstract Submission No. 200133

P-0675

Successful downstaging is a good prognostic for unresectable HCC after conversion therapy

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Background and objective: The prognosis of unresectable advanced hepatocellular carcinoma (HCC) is poor. The advances in local therapy

and rapid development of systemic therapy have brought hope for curative resection after conversion therapy to these patients. This study retrospectively analyzed the prognosis and influencing factors of unresectable HCC patients who underwent conversion therapy and surgical resection.

Materials and Methods: From January 2020 to December 2022, a total of 56 patients with unresectable or recurrent HCC after resection were treated with surgical resection after targeted drugs, immune checkpoint inhibitors combined or not combined with local treatment, which included hepatectomy in 31 cases, liver transplantation in 18 cases and extrahepatic metastasis resection in 7 cases. The follow-up was until December 25, 2023 or death, with a median follow-up time of 22.5 months.

RESULTS: There were 47 males and 9 females in the 56 patients, with an average age of 56.9 years (36-78 years). According to surgical pathology, 25 cases had a downstaging of the tumor BCLC stage at the time of surgery, 28 cases had unchanged stage and 3 cases experienced tumor progression. Since the date of surgery, the median overall survival time was not reached, and the 1-, 2- and 3-year survival rates were 96.4%, 79.3% and 61.3%, respectively. Non-downstaging, abnormal AFP levels and microvascular invasion after conversion therapy were poor factors that affect prognosis ($p < 0.05$), and the non-downstaging was an independent risk factor of prognosis ($P = 0.011$). The 3-year survival rate of was 95.7% in the patients with successful downstaging (25 cases). The median disease-free survival (DFS) was 23.9 months. HBsAg positive, non-downstaging and abnormal AFP levels after conversion therapy and pathological microvascular invasion were poor influencing factors of DFS ($p < 0.05$), and abnormal AFP levels after conversion therapy was an independent risk factor of DFS ($p = 0.007$).

Conclusion: Unresectable advanced HCC patients who underwent surgery after systemic therapy combined or not combined with local therapy had a better prognosis, especially those with successful downstaging. The abnormal AFP levels after conversion therapy was an independent risk factor of DFS.

Key words: hepatocellular carcinoma, unresectable; conversion therapy; liver resection; liver transplantation; systemic therapy; local therapy; prognosis

Abstract Submission No. 200142

P-0676

Hemorrhagic complications after hepatectomy in patients receiving antithrombotic therapy

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Background: In recent years, the number of patients taking oral antithrombotic drugs has increased. In the present study, we used propensity score matching (PSM) to investigate the effect of antithrombotic medication on perioperative outcomes in patients undergoing liver resection.

Methods: Patients were divided into two groups: antithrombotic group (127 patients, 17.5%) and non- antithrombotic group (548 patients, 82.5%). Sex, age, body mass index, history of liver resection, presence or absence of laparotomy, operative technique and presence or absence of biliary reconstruction were used as covariates and a propensity score was calculated by logistic regression. Postoperative complications were compared after matching in both groups.

Results: The mean operative time, intra-operative blood loss and transfusion rate in all patients were 285 min, 383 ml and 23.5% respectively, and the postoperative complication rate (CD classification $\geq$ III) was 23.7%. Compared to the oral antithrombotic group and the non- antithrombotic therapy group, the mean age (75.1 vs. 67.3 years, $p < 0.001$) and male ratio (89.8% vs. 69.4%, $p < 0.001$) were higher in the antithrombotic therapy group. The postoperative complication rate (CD classification $\geq$ Grade III) was higher in the antithrombotic therapy group (31.5% vs. 19.9%, $p = 0.009$), but PSM analysis between the two groups showed no significant difference in postoperative complication rates. Analysis focusing on the rates of hemorrhagic and thrombotic complications also showed no significant differences.

Conclusions: Antithrombotic therapy was not found to be an independent risk factor for post-operative complications, including hemorrhagic and thrombotic complications.

Abstract Submission No. 100674

P-0677

Efficacy and Safety of Atezolizumab-Bevacizumab Therapy for Advanced Hepatocellular Carcinoma

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Backgrounds: Atezolizumab-bevacizumab combination therapy has been approved for first-line systemic chemotherapy in advanced hepatocellular carcinoma. Real-world retrospective analysis was performed to evaluate the effectiveness and safety of the chemotherapy.

Methods: A single-center, retrospective cohort study was performed. Between January 2020 and July 2023, patients with advanced hepatocellular carcinoma who received atezolizumab-bevacizumab systemic therapy were enrolled. Response to the therapy was assessed with mRECIST criteria. Evaluation of first radiologic response, best overall response, progression-free survival, and overall survival was done. Also, prognostic factors for first radiologic response, progression-free survival, and overall survival were also assessed.

Results: A total of 70 patients were investigated. Baseline characteristics showed a median age of 63 years, male dominance (89%), and viral etiology (84%). Four patients achieved complete response and 19 reached partial response when evaluated by best overall response. Response duration was 4.7 months (range 1.5-25.5). Median progression-free survival was 4.1 months (95% CI, 3.7-6.7), and median overall survival was 24.6 months (95% CI, 11.6-). Age and tumor extent of over 50% of the liver was predictive of progression-free survival ($p = 0.009$ and $p = 0.007$, respectively) Tumor extent of over 50% of the liver and albumin-bilirubin (ALBI) score were predictive of overall survival ($p = 0.025$ and $p = 0.004$, respectively). A total of 120 adverse events occurred and event grades over 3 accounted for 24% ($n = 29$).

Conclusion: Atezolizumab-bevacizumab therapy showed comparable results in advanced HCC patients and safety profiles were similar to previous studies.

Abstract Submission No. 101058

P-0678

Treatment Outcomes of Unresectable Intrahepatic Cholangiocarcinoma

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Aim: In recent years, pemigatinib, an FGFR inhibitor, and Durvalumab, anti-PD-L1 antibody has been approved for unresectable intrahepatic cholangiocarcinoma (ICC). In this study, we evaluated the treatment outcomes of ICC at our hospital and also reported on the treatment efficacy and safety of GCD (gemcitabine+cisplatin+Durvalumab) therapy and pemigatinib.

Methods: The study included 22 cases of ICC treated at our hospital (average age 70 years, M:F=13:9, stage II:III:IVA:IVB=3:1:9:9). We conducted an evaluation of treatment outcomes and prognosis for these cases.

Results: Primary treatment consisted of GC therapy in 17 cases and GCD therapy in 5 cases. The response rate was 17.6%, and disease control rate was 58.8%. In the patients who received GCD therapy, 3 cases showed PR, and 2 cases showed SD. None of the cases exhibited severe side effects. Seven of all patients received CGP (comprehensive genome profile) test, with two cases showed positive for FGFR fusion genes, leading to the introduction of pemigatinib (one case was introduced at another institution). In cases where pemigatinib was initiated at our hospital, disease control has been maintained for six months after initiation, and the patient is still alive after more than two years from the initial diagnosis. However, the overall survival was poor at 13.5 months, and long-term survival was observed in cases where SD or better treatment outcomes were achieved with primary chemotherapy.

Conclusion: The prognosis for unresectable intrahepatic cholangiocarcinoma is extremely poor, and achieving SD or better treatment outcomes in primary therapy has been identified as a factor contributing to long-term survival.

Abstract Submission No. 101240
P-0679

Referral to a hepatologists may prolong OS of patients with malignancies treated by ICI

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Background: The occurrence of liver dysfunction, an immune-related adverse event (irAE) caused by immune checkpoint inhibitors (ICIs), and treatment efficacy is not clear. We investigated the relationship between the occurrence of hepatic dysfunction and treatment response in patients treated with ICIs at our hospital.

Method: We studied 813 patients treated with ICI between November 2014 and August 2023 for the occurrence of irAEs and compared survival (OS) with and without treatment continuation due to liver dysfunction.

Results: Of the patients treated with ICI, 309 (38%) developed irAE and 42 (5.2%) developed hepatic dysfunction.

The median (range) ALT and T-Bil of patients who discontinued ICI treatment were 359 (53-1388) U/mL and 1.15 (0.44-12.41) mg/dL, respectively. Of the discontinued cases, 20 (47.6%) had Grade 3/4 ALT/AST elevation, only 3 had T-Bil Grade 3, and only 7 had prolonged prothrombin time, a sign of liver failure. The median OS with and without continuation of ICI treatment due to development of hepatic dysfunction was 32.8 months in the continuation group and 11.5 months in the discontinuation group (P=0.246). The median OS for all irAE-expressing groups (n=309) was 32.0 months, and 12.6 months for non-expressing groups (n=504) (P<0.001).

Conclusion: In patients who developed hepatic dysfunction, OS tended to be prolonged in the continued treatment group compared to

the discontinued treatment group. Most patients who develop liver dysfunction with ICI treatment have elevated transaminases, and OS may be prolonged by referral to a hepatologist for a comprehensive evaluation of severity.

Abstract Submission No. 101418
P-0680

Durvalumab plus Tremelimumab treatment in patients with unresectable HCC; an early experience.

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Background: Durvalumab + tremelimumab (Dur+Tre), a new first-line drug combination for unresectable hepatocellular carcinoma, has become available in Japan from April 2023. We investigated the efficacy and safety of Dur+Tre treatment at our hospital.

Methods: Seven patients with unresectable hepatocellular carcinoma who received Dur+Tre treatment from April 2023 to November 2023 were enrolled and evaluated for their clinical background, treatment response (radiological evaluation by RECIST v1.1, and changes in tumor markers), and adverse events (according to CTCAE ver. 5.0).

Results: The median age of the patients was 72 (43-81) years. The median ALBI score was -2.16 and four patients were classified in modified ALBI grades 2b and 3. One and six patients had BCLC stage B and C, respectively. Treatment lines varied from 1st (n=2), 2nd (n=4), and 3rd (n=1). 5 patients continued treatment; the number of courses was 6 (n=1), 5 (n=2), 3 (n=1), and 2 (n=1). Clinical responses were observed in these 5 patients; three were judged as PR by RECIST v1.1, while decreases in tumor markers were demonstrated in 4 patients. Only one patient had a grade 3 or higher irAE (fever).

Conclusions: Although 6 out of 7 cases were BCLC-C, PR were found in 3. Dur+Tre treatment seemed to be a useful treatment option for unresectable HCC.

Abstract Submission No. 101588
P-0681

Interstitial Pneumonia During Atezolizumab/Bevacizumab Therapy for Unresectable HCC

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Aim: We investigated the occurrence of interstitial pneumonia after Atezolizumab/bevacizumab (Atz/Bev) introduction for unresectable hepatocellular carcinoma (HCC) and its anti-tumor effect.

Methods: From October 2020 to May 2023, 124 patients with advanced HCC who received Atz/Bev in our hospital were enrolled. KL-6 and SP-D levels were regularly measured. The median age was 75 years, 24 patients had lung metastases, the median KL-6 was 258.5, and the median SP-D was 54.6 at baseline.

Results: Eight patients (6.5%) developed interstitial pneumonia after a median follow-up of 275 days. The median time to onset of interstitial pneumonia was 105 days, and the cumulative incidence of interstitial pneumonia was 6.5% at six months and 7.9% at one year. The best antitumor response in the 8 patients who developed interstitial

pneumonia was 0 for CR, 4 for PR, 3 for SD and 1 for PD according to RECIST. Factors at baseline associated with the development of interstitial pneumonia was the presence of lung metastases. There was no association between changes in KL-6 and SP-D during the first 6 weeks. In the 8 patients who developed interstitial pneumonia, KL-6 was significantly elevated from 6 weeks before onset to 3 weeks before onset; SP-D was significantly elevated from 6 weeks before onset to 3 weeks before onset and from 6 weeks before onset to onset.

Conclusion: Periodic measurement of KL-6 and SP-D levels and their trends were considered useful for predicting the development of interstitial pneumonia and for early detection.

Abstract Submission No. 101667
P-0682

Effect of atezolizumab bevacizumab combination therapy on skeletal muscle mass and cardiac function

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Background: We reported that sorafenib, an anti-VEGF inhibitor, may reduce skeletal muscle mass by suppressing carnitine absorption in patients with liver cancer (Anticancer Res 2020 40:4173-4182). However, the effects of the monoclonal antibody VEGF inhibitor Bevacizumab have not been reported.

Aim: Objective: To clarify the age-dependent effects of atezolizumab + bevacizumab (AteBev) combination therapy on skeletal muscle mass and cardiac function in patients with hepatocellular carcinoma (HCC). **Methods:** Eighty-three HCC patients treated with AteBev combination therapy in our department were included. Before treatment and 3 weeks after treatment, blood samples were collected. Abdominal CT examination was performed 6 weeks after treatment, and the therapeutic effect was evaluated using mRECIST, and PMI was calculated from the iliopsoas muscle area. In addition, left ventricular systolic function was evaluated using global longitudinal strain (GLS) in echocardiography.

Results: There were 16 middle-aged patients, 25 early-elderly patients, and 42 late-elderly patients. In the study of skeletal muscle mass, PMI after 6 weeks of treatment showed significant changes in middle-aged and early-elderly patients. A significant decrease was observed in the late-elderly patients, although no cardiac function studies showed no significant changes in %Ejection Fraction and GLS after 3 weeks of treatment in middle-aged patients, but significant decreases in early- and late-elderly patients.

Conclusion: Cardiac function decline was confirmed in the elderly patients after 3 weeks of treatment in AteBev therapy. In this case, it was considered important to actively introduce nutrition and exercise therapy to maintain not only skeletal muscle mass but also cardiac function.

Abstract Submission No. 101694
P-0683

Synergistic Anticancer Effects of Combined Immunotherapy and PI3Kγ Inhibitors in Liver Cancer

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Background and Aims: Immune checkpoint inhibitors (ICIs)-based combination therapies in hepatocellular carcinoma (HCC) patients are effective for some patients. PI3Kγ inhibition can target suppressive macrophages, potentially enhancing efficacy of ICIs. This study investigated how PI3Kγ inhibitors function within HCC microenvironments (TME) to activate specific immune cells in murine models.

Method: The novel PI3Kγ inhibitor, AZD3458 was evaluated for its antitumor effects in both murine HCC cell lines (BNL and RIL-175) and BNL syngeneic model, as well as human HCC cell lines (Huh7 and Hep3B) and human peripheral blood mononuclear cells (PBMCs) *in vitro*. We used PI3Kγ inhibitor (AZD3458; 30 mg/kg, orally, daily), tyrosine kinase inhibitor (TKI; lenvatinib; 10 mg/kg, orally, daily), and ICI (anti-PD-1 mAb; 10 mg/kg, intraperitoneally, daily).

Results: AZD3458 enhanced antitumor activity of the ICI-TKI combinations in BNL, RIL-175, and BNL syngeneic models, increasing natural killer (NK) cell activity. Co-treatment of AZD3458 enhanced the cytotoxicity of the ICI-TKI combinations against human HCC cell lines and human PBMCs *in vitro*. AZD3458 increased the expression of activation cytokines for NK cells and decreased the expression of inhibitory cytokines for NK cells in human PBMC-derived M2-polarized macrophages. Furthermore, the inhibitors both increased and decreased the expression levels of the M1 macrophage marker inducible nitric oxide synthase and the M2 macrophage marker Arg1, respectively.

Conclusion: The PI3Kγ inhibitor specifically targets TAMs and alters their function to achieve anti-tumor effects. These findings suggest that inhibiting PI3Kγ could be a crucial part of the combined anti-tumor treatment using ICI and TKI in HCC.

Abstract Submission No. 102066
P-0684

Analysis of disease progression in patients who were evaluated as complete response (CR) by mRECIST

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Background: The mRECIST is widely used as a criterion for evaluating response to therapy in hepatocellular carcinoma. However, the clinical significance of CR is not well understood.

Methods: We analyzed patients with advanced hepatocellular carcinoma who received systemic chemotherapy at our institute from June 2018 to July 2023. We selected patients evaluated as CR by mRECIST, and we analyzed whether the patients subsequently became Progressive Disease (PD) and the associated factors.

Results: 21 patients were evaluated as CR by mRECIST. Lenvatinib was performed in 8 patients (total 98 cases) and atezolizumab plus bevacizumab in 13 patients (total 78 cases). 18 patients were studied excluding 3 patients who underwent LEN-TACE. Mean age was 75.0±7.3 years, Male/Female 15/3, HBV/HCV/NBNC 2/4/12, BCLC stage A/B1/B2/C 2/1/10/5. Evaluation by RECIST was CR/PR/SD/PD 3/12/3/0. After a mean follow-up of 1.7 years, 11 patients (61%) were evaluated as PD. The proportion of PD was 4/5 (80%) in the lenvatinib group, significantly higher than 7/13 (54%) in the atezolizumab plus bevacizumab group. The proportion of PD were CR 2/3 (67%), PR 6/12 (50%) and SD 3/3 (100%) when grouped by RECIST. In the group that continued chemotherapy, the rate was 5/9 (56%), and in the group that completed chemotherapy, the rate was 6/9 (67%). There was no significant difference between the groups.

Conclusion: Of patients evaluated as CR by mRECIST, 61% had disease progression. The proportion of PD was significantly higher in the

lenvatinib group, suggesting the need for additional therapy or close follow-up.

Abstract Submission No. 200164
P-0685

A case of hemophagocytic syndrome after pembrolizumab treatment for breast cancer

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A 52-year-old woman was diagnosed with right breast cancer (ER, PgR, HER-2/neu) in June 2023 and preoperative chemotherapy (pembrolizumab + carboplatin + paclitaxel) was started in July. The tumor subsequently shrank, but a Grade 3 liver injury appeared, and the patient was referred to the hepatology clinic in November. Preoperative chemotherapy was stopped, but liver injury did not improve, and the patient was admitted to our department with fever and worsening liver injury. Pembrolizumab-related immune-related adverse event was suspected, and the patient was started on prednisolone (2 mg/kg body weight). However, marked thrombocytopenia, leukopenia, and hyperferritinemia were noted, and hemophagocytic syndrome (HPS) was suspected. Bone-marrow puncture revealed hemophagocytosis and a diagnosis of HPS was made. Steroid pulse therapy was administered for 3 days, and prednisolone was resumed thereafter. Liver injury improved quickly, but thrombocytopenia persisted, thus second bone marrow puncture was performed on the 25th day. There was no hemophagocytosis, and megakaryocytes were increased in the bone marrow. In addition, hyperferritinemia was also improved. The patient is currently under observation while tapering off prednisolone. HPS is a systemic inflammatory disease characterized by macrophage hemophagocytosis in the bone marrow, with a variety of symptoms including fever, liver damage, pancytopenia, coagulation abnormalities, elevated LDH levels, and hyperferritinemia. In Japan, as of September 2018, there were 6,421 cases of adverse reactions due to immune checkpoint inhibitors, of which HPS was reported in 11 cases (about 0.2%), which is very rare.

Abstract Submission No. 100565
P-0686

Cardiovascular Risk Factors Are Associated With Hepatic Encephalopathy After TIPS Insertion

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Background: Transjugular intra-hepatic porto-systemic shunt (TIPSS) is a well-established intervention for reducing portal hypertension for treatment of refractory ascites and variceal bleeding. Previous studies on post-TIPSS complications were predominantly done in Western populations, and mostly included patients with alcohol or

viral etiology of liver disease. We hence aimed to evaluate the prevalence and risk factors of major post-TIPSS complications in a tertiary centre in Singapore.

Methods: A retrospective observational cohort study involving 61 patients who underwent TIPSS at National University Hospital, Singapore between 1 January 2014 to 31 December 2021 was performed. The proportion of patients who developed hepatic encephalopathy (HE) and fluid overload after TIPSS was evaluated. Risk factors for these complications were interrogated through odds ratios (OR) using logistic regression.

Results: 26 patients (42.6%) developed HE and 8 patients (13.1%) developed fluid overload. Adjusting for age, gender, ethnicity, Child-Pugh Score and Model for End-Stage Liver Disease score, multivariate logistic regression analysis found that diabetes mellitus (OR 8.56, 95% CI 1.84-39.9, $p=0.006$), hypertension (OR 4.1, 95% CI 1.21-13.9, $p=0.024$), higher body mass index (OR 1.14, 95% CI 1.01-1.29, $p=0.039$), and coronary artery disease (OR 7.01, 95% CI 1.26-39.1, $p=0.026$) were associated with development of HE. Additionally, low HDL (OR 17.29, 95%CI 1.70-175.76, $p=0.016$) was associated with development of fluid overload.

Conclusion: Presence of cardiovascular risk factors was associated with development of post-TIPSS HE. Given the rising prevalence of metabolic dysfunction-associated steatotic liver disease, further research to evaluate this association is crucial to optimise patient selection for TIPSS.

Abstract Submission No. 100728
P-0687

Hepatic Artery Pseudoaneurysm, a Rare Fatal Complication of Cholecystectomy: A case report

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Background and Significance: Hepatic artery aneurysm is rare with an incidence of 0.03% and the second most common type of visceral aneurysm. Pseudoaneurysm of the hepatic artery is caused by injuries in the hepatobiliary system with cholecystectomy as the most common cause. Hepatic artery aneurysm is an emergency due to the risk of exsanguination and the treatment of choice is angioembolization. Due to its rarity and high mortality, we present a case of hepatic artery pseudoaneurysm in a female with history of cholecystectomy.

Case: A 48 year old female with a history of laparoscopic cholecystectomy (2018) presented with one month history of melena associated with epigastric pain. Gastroscopy showed no ulcers or other source of bleeding. Contrast abdominal CT scan showed biliary ectasia, however, contrast MRCP done showed a right hepatic artery pseudoaneurysm with probable duodenal fistula thus was advised angioembolization at our institution. Hepatic angiogram showed a bleeding focus (pseudoaneurysm) seen arising from a branch in direct communication with the proximal right hepatic artery adjacent to the cholecystectomy clips (see figure 1). Transcatheter coil embolization of left hepatic artery branches and covered stent placement across the right hepatic artery was done (see figure 2). Final angiogram showed cessation of active extravasation. No recurrence of bleeding thereafter thus the patient was discharged well.

Conclusion: Hepatic artery pseudoaneurysm is a rare but established complication of cholecystectomy. It is associated with high mortality thus prompt recognition is warranted. Initial diagnosis is via CT angiography and treatment is via endovascular intervention.

Abstract Submission No. 100876
P-0688

Anti-coagulation Therapy Do Not Improve Patency Rate in BCS After Interventional Recanalization.

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Budd-Chiari syndrome(BCS) is a kind of syndrome with hepatic out-flow obstruction. The etiology is quite different between eastern and western populations. Recent guidelines suggest patients with BCS need long-term anticoagulation after diagnosis, but whether anticoagulation is needed for Asian people with less hypercoagulable factors needs further discussion.

We consecutively enrolled patients diagnosed as BCS and underwent vascular interventional surgery (balloon/stent) in our hospital from January 2009 to March 2023. During the follow-up, we mainly focus on the condition of postoperative anticoagulation and vascular patency. Meanwhile, we recorded all bleeding-related events and survival.

A total of 244 patients were included and divided into two groups (standard anticoagulation and non-standard anticoagulation) according to whether they use anticoagulation drugs regularly. Within the cohort, only 1/111 patient was JAK2V 617F positive and none was positive with MPL/CALR/Factor II G 20210A/Factor V G1691A. K-M survival analysis showed that there was no difference in the incidence of vascular restenosis between the two groups with a median restenosis time 28.956 months (25.099,32.814) vs 25.065 months (21.438,28.692) (P=0.698). There was no significant difference in survival. During anticoagulation, there were 4 cases with major bleeding, of which 3 took warfarin and 1 took rivaroxaban. There was no statistical difference in the occurrence of all bleeding events between patients who used different drugs.

In our cohort, anticoagulation therapy after interventional recanalization does not improve postoperative vascular patency and survival while some of the patients got massive bleeding during medication. Whether long-term anticoagulation is needed for every BCS patient needs further discussion.

Abstract Submission No. 101689
P-0689

OUTCOME OF PERCUTANEOUS TRANS-HEPATIC VARICEAL OBLITERATION FOR GASTRIC VARICEAL BLEEDING

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Background: We evaluated the efficacy and safety of percutaneous trans-hepatic or trans-splenic variceal obliteration (PTVO) as an alternative for management of GVB when BRTO is impossible.

Methods: Seventeen patients (mean age 59 years, 13 men) with liver cirrhosis who received PTVO for uncontrolled GVB from October 2017 to January 2023 were retrospectively examined. Efficacy was evaluated by the rate of successful prevention of rebleeding during follow-up, and improvement of liver function based on Child-Pugh (CP) class. Safety was evaluated by the rate of postprocedural complications.

Results: The causes of cirrhosis were hepatitis B (n=3), hepatitis C (n=2), alcohol consumption (n=4), autoimmune hepatitis (n=2), and a combination of factors (n=6). Before procedure, eight had CP class A, seven had CP B, and two had CP C. The PTVO was performed using a trans-splenic approach (n=7) or a trans-hepatic approach (n=10), and

was successful in all patients. However, two experienced rebleeding during hospitalization; one was considered irrecoverable and expired and the other received embolization. CP class improved in 3 patients (33.3%) and remained the same in 6 patients (66.7%) at 1 to 3 months. CP class improved in 1 patient (14.3%), remained the same in 5 patients (71.4%), and worsened in 1 patient (14.3%) at 6 months.

Conclusion: PTVO of patients with cirrhosis led to no significant deterioration in liver function or procedure-related complications. This procedure can be considered an effective and safe option for patients with GVB when a conventional approach is not possible.

Abstract Submission No. 102089
P-0690

Safety and Usefulness of Transbrachial Angiography in digestive system disease

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BACKGROUND/AIM: Transbrachial method is advantageous in that it does not necessitate prolonged rest in the hospital room, thereby reducing the need for nursing assistance, although technically, the procedure is more difficult to perform than via the transfemoral arterial approach. In this study, we determined the usefulness of this method for abdominal angiography.

METHODS: We began to employ this method as first choice for abdominal angiography at our hospital since May 2012. We have so far conducted the procedure in 240 times as part of the patient workup for digestive system disease.

RESULTS: There were no cases in which the arterial puncture failed, although it was found to be impossible to insert the catheter into the peritoneal cavity in one patient with a severely deformed aortic arch. After the patients returned to their rooms, re-bleeding from the puncture site occurred in one patient, but the bleeding could be controlled uneventfully by compression of the site. None of the cases required readmission because of Re-admission due to these complications or the development of pulmonary embolism occurred. This method also allowed the concomitant performance of Computed-Tomographic-angiography and smooth treatment procedures, such as embolization of the hepatic artery and hemostatic treatments with metal coils and partial splenic arterial embolization and others.

CONCLUSION: Transbrachial Brachial Arterial Angiography on the left side is of great value in the clinical setting and may be employed as can be the first procedure of choice for abdominal angiography and the treatment of digestive system disease.

Abstract Submission No. 102096
P-0691

Transcatheter arterial chemoembolization by radial artery approach as a minimally invasive treatment

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Background: Computed tomography during arterial portography (CTAP) and Computed tomography during hepatic arteriography (CTHA) provide high accuracy for the diagnosis of hepatocellular carcinoma (HCC). Still, their use is limited due to their invasiveness. Especially in the elderly patients, a minimally invasive TACE by the radial artery approach is expected. The current status of treatment from the radial artery approach TACE was studied.

Method: Twelve patients underwent TACE by radial artery approach between November 2021 and July 2023 at our hospital. Regarding patient age, indication for radial access, selectivity, procedure duration, vascular access site complications were investigated.

Result: The mean patient age was 73.8 years. Transradial approach was selected because of hepatic encephalopathy in 4 cases, advanced age or dementia in 5 cases, ascites effusion in 2 cases, and patient preference in 1 case. Selectivity included segmental embolization in 3 cases, lobar in 3 cases, and whole liver in 4 cases. There were no vascular access site complications, and RFA was added in 10 of the 12 patients with HCC. There was also one case of repeat treatment during the study, but no vascular damage was observed.

Conclusion: Transradial approach TACE with CT angiography can be a minimally invasive treatment for elderly patients with HCC. Further case accumulation and long-term follow-up are needed.

Abstract Submission No. 200048

P-0692

Application of swan neck microcatheter superselective catheterization in TACE of liver cancer

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Background: TACE is currently recognized as the first choice therapy for patients with unresectable liver cancer, super-selective catheterization is a pivotal. The soft swan neck tip can be used as an effective alternative for those who have difficulty in superselective catheterization.

Methods: The clinical data of patients who used Maestro swan neck microcatheter and stride microcatheter combined with streaming microcatheter for liver cancer superselective chemoembolization in hospital were collected. Analyze the advantages and disadvantages of the swan neck microcatheter over the conventional straight-tip catheter superselection.

Results: In the swan neck microcatheter group, 467 cases underwent conventional hepatic artery chemoembolization, with a total of 926 blood supply arteries in the liver. Among them, 132 patients had extrahepatic feeding arteries. The 322 target arteries originated from the main artery at an acute angle, and 165 arteries present a "hairpin" pattern. WHISPER MS micro-guide wire were used in 52 patients. In the conventional straight-tip catheter group, 617 cases underwent conventional hepatic artery chemoembolization, with a total of 1052 intrahepatic arteries. Among them, 189 patients had extrahepatic feeding arteries. The 382 target arteries originated from the main vessel at an acute angle, forming a "hairpin" pattern with 178 blood vessels. Among them, 12 patients did not complete super-selective catheterization. The X-ray exposure time of the swan neck microcatheter group was shorter and the X-ray exposure dose was reduced.

Conclusion: The swan neck microcatheter can improve the success rate of interventional superselective catheterization, shorten the X-ray exposure time, reduce the X-ray exposure dose, and the catheterization is easier.

Abstract Submission No. 200225

P-0693

Durvalumab plus HAIC and TKIs in combination with for advanced biliary tract cancers

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Background: The TOPAZ-1 study showed that durvalumab(D) plus gemcitabine and cisplatin(GC) significantly improved OS for BTC patients. Recent studies found that TKIs could modify tumor immune microenvironment. And hepatic arterial infusion chemotherapy (HAIC) could improve the survival in BTC patients while reduce systemic toxicity. Here we evaluated the efficacy and safety of Durvalumab plus HAIC and TKIs for advanced BTC patients.

Methods: In this single arm, retrospective study, advanced BTC patients who received D+HAIC+TKIs from January 2022 to September 2023 were screened. The gemcitabine and oxaliplatin was administered Q6W on day 1. Intravenous D was administered Q3W on day 4 or 5 after HAIC or day 1. TKIs regimens was administered daily. After a maximum of 6 cycles HAIC, patients received D plus TKIs every 3 weeks as maintenance treatment. The ORR, PFS, OS and safety were evaluated.

Results: A total of 20 patients were enrolled. 19 (95%) patients were stage 3b or above and 8(40%) patients had distant metastasis. And 5 patients received second-line D+HAIC+TKI treatment. 14 patients achieved partial response, 4 patients had stable disease, resulting in an ORR 70% and disease control rate 90%(RECIST v1.1). The median PFS, and OS were not reached. The most common adverse events was platelet count decreased (5, 25%) and nausea(2, 10%). None of the patients had treatment-related grade 3~4 toxicities.

Conclusions: The results suggest that HAIC plus durvalumab and TKIs could achieve a promising tumor response and manageable safety profile in patients with advanced BTC. Survival outcomes warrant long term follow up.

Abstract Submission No. 100119

P-0694

Screening of Hub genes analysis with immune infiltration in liver failure based on machine learning

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Abstract

Objective: Key regulatory genes of Hepatitis B Virus(HBV)-related liver failure were screened by machine learning approach to analyze their correlation with immune cell infiltration to provide a new theoretical basis for HBV-related liver failure related mechanisms.

Method: HBV-related liver failure related expression microarrays were obtained in Gene Expression Omnibus(GEO)database and analyzed. The integrated microarrays were subjected to differential analysis and functional enrichment analysis. Differentially expressed genes (DEGs) were identified using LASSO regression algorithm (selection operator) and support vector machine recursive feature elimination (SVM-RFE) algorithm, among which the hub genes were screened using protein-protein interaction networks (PPI) and analyzed for their correlation with immune cell infiltration using CIBERSORT inverse convolutional integration algorithm.

Results: A total of 652 Genes were screened and further screening identified 28 potential candidate genes using LASSO regression analysis and SVM-RFE algorithm.

PPI analysis revealed that C8B, CPB2 and MASP2 were HBV-related liver failure hub genes. Further analysis found C8B, CPB2 and MASP2 showed significant correlation with immune cell infiltration, including M2 macrophages.

Conclusion: Bioinformatics analysis of HBV-related liver failure microarrays revealed that C8B, CPB2 and MASP2 play crucial roles in the regulation of HBV-related liver failure and are significantly associated with immune cells, such as M2 macrophages.

Keyword: HBV-related liver failure; Immune cell infiltration; machine learning

Abstract Submission No. 100264

P-0695

Mesenchymal stem cell's exosome exerts cytoprotective effects in acute liver failure via NEMO/NF- κ B

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Background and Aims: Balancing the death and proliferation of hepatocytes is crucial in developing non-transplantation treatments for acute liver failure (ALF), a condition with a high short-term mortality rate. Previous research has confirmed that small extracellular vesicles (sEVs) derived from mesenchymal stem cells (MSCs) can regulate proliferation and apoptosis of endogenous cells, but it is unclear whether they can promote proliferation and apoptosis of hepatocytes in acute liver failure.

Method: To establish the ALF cell model of L02/THLE2 cell lines induced by H₂O₂ and ALF mouse model induced by GalN/LPS, collect and identify MSC-sEVs, and co-culture with ALF hepatocytes, then detected the proliferation and apoptosis of hepatocytes in ALF cell model by fluorescent labeling technique, meanwhile, detected the expressions of NEMO, c-FLIP, inhibitor κ B (I κ B), pI κ B, and NF- κ Bp65 by western blot. Lastly, MSC-sEVs were injected into ALF mouse through the tail vein to evaluate the effect in vivo.

Results: The MSC-sEVs were combined with the ALF cell model, resulting in heightened activity of the hepatocytes within the ALF cell model. MSC-sEV-treated mice with ALF had higher 24 h survival rates and more significant reductions in liver injury than mice treated with sEV-free concentrated medium. Meanwhile, MSC-sEVs could upregulate NEMO, c-FLIP and pI κ B, NF- κ Bp65 nuclear expression increased, and Bcl-2, Bax and cleaved caspase-3 expression decreased in vivo and in vitro.

Conclusion: The application of BMSC-sEVs showed a positive impact by preventing the development of ALF. NEMO/NF- κ B signaling pathway plays an important role in liver protection from ALF by BMSC-sEVs.

Abstract Submission No. 100282

P-0696

Serum ammonia variation predicts mortality in patients with hepatitis B virus-related ACLF

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Background: Hyperammonemia is critical to the development of hepatic encephalopathy (HE) and is associated with mortality in end-stage liver disease. This study investigated the clinical value of ammonia variation in hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF) patients.

Methods: A total of 276 patients with HBV-ACLF were retrospectively recruited. Patients' ammonia levels were serially documented. Baseline ammonia, Peak ammonia (Highest level), and Trough ammonia (Lowest level) were particularly corrected to the upper limit of normal (AMM-ULN). The primary endpoint was 28-day mortality.

Results: The 28-day, 3-month, and 12-month mortality were 19.2%, 25.7%, and 28.2%, respectively. 51 (18.4%) patients had overt HE (grade 2/3/4). Patients with higher grades possessed higher ammonia levels. Peak AMM-ULN was significantly higher in patients with overt HE and non-survivors compared with their counterpart ($P < 0.001$). Following adjustment for significant confounders, high Peak AMM-ULN was an independent predictor of overt HE (hazard ratio, 1.031, $P < 0.001$) and 28-day mortality (hazard ratio, 1.026, $P < 0.001$). The cut-off of Peak AMM-ULN was 1.8 determined by using X-tile. Patients with Peak AMM-ULN appearing at day 1-3 after admission had a higher proportion of overt HE and mortality compared to other groups. Patients with decreased ammonia levels within 7 days had better clinical outcomes than those with increased ammonia.

Conclusions: Serum Peak ammonia was independently associated with overt HE and mortality in HBV-ACLF patients. Serial serum ammonia may have prognostic value.

Abstract Submission No. 100299

P-0697

Mesenchymal Stem Cell Derived EVs Promote Efferocytosis In Acute-on-Chronic Liver Failure

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Background: ACLF is a severe clinical syndrome with a high mortality rate. We previously found that in vitro infusion of BM-MSCs can improve the survival rate of patients with ACLF patients, and had a high expression of MerTK, which is essential in the efferocytosis process. In this study, we aim to evaluate the efficacy and safety of the BM-MSC EVs treatment in ACLF mouse model, explore how it affects the efferocytosis of macrophages.

Method: ACLF mouse were divided into EV group and PBS control group. After 24 hours, mouse liver tissue and serum were collected. HE staining was performed to compare the inflammation status, and ELISA was used to compare the liver function. Immunofluorescence staining was performed. Briefly, CD86 labeled M1 macrophages and CD206 labeled M2 macrophages, then the ratio of M1/M2 macrophages were compared. Next, we performed TUNEL staining on apoptotic cells, the number of apoptotic cells between different groups were counted. Western blot was performed to detect the expression of MerTK.

Results: Compared with the control group, the EV group showed a mild degree of inflammation in HE staining and a better improvement in liver function; The immunofluorescence results showed that the liver tissue of mouse in the EV group expressed more CD206 and less CD86, indicating that the M2 polarization of macrophages in the EV group; TUNEL staining showed that there were fewer apoptotic cells in the EV group, indicating increased efferocytosis. Western blotting of the liver tissue showed that MerTK expressed more in the EV group.

Conclusion: The treatment of ACLF with BM-MSC evs can promote efferocytosis, and improve the inflammatory response of liver tissue. Mertk protein may play a very important role in this process.

Abstract Submission No. 100329
P-0698

DDX3X Regulates the Function of Endoplasmic Reticulum Stress in Acute on Chronic Liver Failure

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The functional transition of endoplasmic reticulum (ER) stress plays a critical role in the progression of acute-on-chronic liver failure (ACLF), but the underlying mechanisms remain unclear. Here, we explored DDX3X and its mechanisms in the functional transition of ER stress. DDX3X increased with prolonged-ER stress, and its deficiency promoted apoptosis under short-term ER stress but protected cells from prolonged ER stress *in vitro* and *in vivo*. Cytoplasm DDX3X interacted with PPARα to translationally activated TFEB expression under short-term ER stress, and phosphorylated DDX3X increased nuclear translocation to initiate cell apoptosis under prolonged ER stress. Serum DDX3X was increased in HBV-ACLF patients, and its fluctuations was related with the disease prognosis. We clarified the molecular mechanism for dual functions of DDX3X in ER stress functional transition.

Abstract Submission No. 100535
P-0699

The long-term efficacy and safety of TAF in HBV-ACLF patients: A propensity score-matching analysis

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Background & Aims: The objective of this study was to evaluate the long-term efficacy and safety of Tenofovir alafenamide (TAF) in patients with hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF) in China, considering the limited knowledge on the subject.

Methods: Patients with HBV-ACLF who received TAF or ETV monotherapy were recruited. They were prospectively followed up and the primary endpoint was liver transplant-free survival at week 96.

Results: A total of 133 patients were enrolled, and propensity score matching produced 40 patients in each group. At week 96, 26 of the TAF group (65.0%) and 28 of the ETV group (70.0%) survived, with no significant difference in long-term liver transplant-free survival ($p = 0.701$). Each group displayed a noteworthy decline in HBV DNA loads. Although virus load reduction and HBV DNA undetectable rates resulted in no statistical significance, TAF group showed a slightly higher HBV DNA undetectable rate after 24 weeks of treatment. At week 48, the HBV DNA undetectable rate in the TAF group was 82.6%, surpassing that of the ETV group (76.0%, $p = 0.791$). Liver function showed improvement in both groups throughout the study period. In

comparison to the ETV group, patients in the TAF group showed less elevation in creatinine and a milder decrease in eGFR, especially at week 4. Within 96 weeks of observation, no drug-related adverse events were noted.

Conclusions: TAF showed favorable long-term efficacy and safety for HBV-ACLF and may offer advantages in terms of protecting renal function and improving long-term virologic response.

Abstract Submission No. 100631
P-0700

A prognostic model based on apolipoprotein C-2 for HBV-related acute-on-chronic liver failure

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Background & Aims: Hepatitis B virus (HBV)-related acute-on-chronic liver failure (ACLF) characterized by short-term high mortality. Then it is crucial for calling for robust prognostic biomarker and developing an effective model for initial risk stratification.

Methods: The predictive performance of apolipoprotein C-2 (APOC2) was validated in 2 prospective cohort and a longitudinal cohort for the mortality of HBV-related ACLF, and incorporated with clinical data to develop a new prognostic model.

Results: APOC2 as a prognostic biomarker for patients with HBV-related ACLF was verified in the training cohort, and low-APOC2 level increased the incidence of complications. Further validation with an external cohort ($n = 143$) indicated that baseline APOC2 levels were significantly lower ($p < 0.001$) in patients with non-survivor than in these with survivor. The cumulative survival duration of patients with low APOC2 levels was significantly shorter ($p < 0.001$) than that of patients with high APOC2 levels in two cohorts. Additionally, we constructed the nomogram and developed a new scoring model called ACID-B, which incorporated APOC2, age, diabetes, international normalized ratio, alpha-fetoprotein, ammonia, C-reactive protein, and HBsAg. The ACID-B score was significantly superior to the Child-Turcotte-Pugh, Model for End-stage Liver Disease (MELD), MELD-sodium, and Chinese Group on the Study of Severe Hepatitis B scores (all $p < 0.05$). The external validation group further confirmed the earlier results. Meanwhile, the increase of APOC2 level reflected the improvement of the patient during hospitalization in the longitudinal cohort.

Conclusions: APOC2 is a promising prognostic biomarker for HBV-related ACLF. A new prognostic model based on APOC2 is a high-performance prognostic score for HBV-related ACLF.

Abstract Submission No. 100774
P-0701

IFI16 as a biomarker for complications of HBV-related acute-on-chronic liver failure

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Background: IFI16, as a novel DNA sensor, plays an important role in viral infection, but it has rarely been reported in HBV-associated acute-on-chronic liver failure. The purpose of this study was to investigate the effects of IFI16 on different stages and complications of HBV-associated acute-on-chronic liver failure.

Methods: This study consecutively collected 40 patients diagnosed with HBV-associated acute-on-chronic liver failure from July 2023 to August 2023 attending The Third Affiliated Hospital of Sun Yat-sen. A retrospective comparison of the clinical data of the three groups (Early-stage, Mid-stage, End-stage) of patients was performed. IFI16 in peripheral blood plasma was determined by ELISA kit. Bivariate correlation analysis was used to analyze the association of IFI16 with clinical laboratory tests and complications and disease progression.

Results: The differences in clinical and anatomical features among three groups were statistically significant in terms of male percentage, IB, PTA, INR, MELD score. IFI16 were significantly and positively correlated with complications of HBV-associated acute-on-chronic liver failure in infection and gastrointestinal hemorrhage.

Conclusion: IFI16 were significantly correlated with complications of HBV-associated acute-on-chronic liver failure.

Abstract Submission No. 100794

P-0702

Midtrimester Termination of Pregnancy with IUFD in a case of Dengue Related Acute Liver Failure

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Background: Dengue is an important mosquito borne disease in an endemic area like Nepal. Dengue infection in pregnancy carries the risk for both mother and newborn. This paper reports a case of survival of pregnant woman with dengue related acute liver failure.

Clinical significance: Early diagnosis and proper treatment of dengue related acute liver failure along with IUFD in pregnancy can reduce the mortality.

Case Description: A 26yr G2P1L1 at 26weeks and 5days of gestation was brought to Emergency department with complain of high grade fever, abdominal pain, icterus and not perceiving fetal movements. Urgent investigations and treatment was started that included ionotropes, blood products, IV fluids and high grade antibiotics. Clinical features and blood reports were suggestive of Dengue related acute liver failure with intrauterine fetal death. On second day of admission patient was intubated for respiratory distress and poor GCS, along with vaginal termination of pregnancy using inducing agent, misoprostol. Patient was extubated after 7th day of intubation. With success of vaginal delivery and continuous conservative treatment, patient clinical features and reports parameters were improved. On 18th day of admission patient was discharged.

Conclusion: Dengue related acute liver failure in pregnancy is very rare with high mortality rate. Early diagnosis and treatment is crucial mostly in critical phase of dengue. Dengue should be kept in the differential diagnosis of pregnant women with fever during epidemics in endemic areas and quick intervention can lead to reduced mortality.

Abstract Submission No. 100875

P-0703

Differences between variceal and non-variceal gastrointestinal bleeding in decompensated cirrhosis

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Background and Aims: Gastrointestinal bleeding (GIB) including variceal bleeding (VB) and non-variceal gastrointestinal bleeding (NVB) is a major complication in patient with chronic liver disease, especially liver cirrhosis. Recent studies reported that there were no differences in clinical outcomes between VB and NVB. However, larger scale, multicenter, prospective studies were warranted to confirm this results because there was different pathogenic mechanism of development between VB and NVB. We aimed to investigate differences of clinical outcomes and risk factor in cirrhotic patients with GIB.

Method: The prospective Korean Acute-On-Chronic Liver Failure (KACLiF) cohort consisted of 1,773 patients who were hospitalized with acute decompensation of chronic liver disease, from July 2015 to August 2018. We enrolled a total of 490 cirrhotic patient with GIB after excluding non-cirrhotic patients. Patients were then regularly evaluated for adverse outcomes (liver transplantation and death) every 3 month during follow-up period.

Results: A total of 490 cirrhotic patient with GIB were included, 414 with VB and 76 with NVB. Patients with NVB had poorer underlying liver function than those with VB (bilirubin 4.49 ± 3.96 vs 2.86 ± 3.64 mg/dL, $p < 0.001$; Child-Pugh score 8(5-14) vs 7(5-15), $p < 0.001$; MELD 16.6(7-41) vs 13.6(7-54), $p = 0.004$; MELD-Na 19.2(8-41) vs 15.3 (7-50), $p < 0.001$). Patients with VB and NVB had similar 28-day adverse outcome (death or liver transplantation) (4.6% vs 6.6%, $p = 0.460$), 90-day adverse outcome (7.5% vs 13.2%, $p = 0.101$), 1-year adverse outcome (18.4% vs 19.7%, $p = 0.177$). MELD was only one predictor for 28-day, 90-day, and 1-year adverse outcome in patients with VB if factors were analysed with ACLF. However, cardiac failure and/or respiratory failure were additional risk factors for 28-day, 90-day, and 1-year adverse outcomes in patients with VB if factors were analysed each statistically important organ failure. Compared to results in patients with VB, MELD was an important predictor for 28-day and 90-day adverse outcomes in patients with NVB.

Conclusion: Our results showed no statistically difference of adverse outcomes in cirrhotic patients with VB and NVB. However, there were differences of major predictor for short-term and long-term adverse outcomes between patients with VB and NVB.

Abstract Submission No. 100911

P-0704

Targeting transglutaminase 2-mediated inflammatory response in sepsis-induced liver injury

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Background: Sepsis is a major cause of death in hospitals and involves an uncontrolled inflammatory response to infection, leading to multiple organ dysfunction, including acute liver failure. Transglutaminase 2 (TG2) is a crosslinking enzyme involved in diverse cellular processes, such as cytoskeletal function, signal transduction, and cell survival.

Methods: Sepsis mice were established by intraperitoneal injection of lipopolysaccharide (LPS) or cecal ligation and puncture. In vitro and ex vivo transamidase activity of TG2 was measured based on the incorporation of 5-biotinamidopentylamine, a biotinylated substrate for TG2. Loss-of-function analysis was performed with TG2 inhibitor cystamine (CTM), clodronate liposome for macrophage depletion, and siRNA against vimentin. LC-MS/MS-based proteome analysis and RNA-seq transcriptome analysis was applied to explore the underlying mechanism. Streptavidin-conjugated magnetic bead was used to isolate biotinylated substrate of TG2. RAW264 cell was introduced for in vitro validation.

Results: Pharmacological inhibition of TG2 activity with CTM improved the survival of sepsis mice and ameliorated LPS-induced liver injury. Omics analysis showed that CTM inhibited LPS-induced inflammation especially in the livers of sepsis mice. Increased TG2 activity was mainly observed in TG2-expressing and F4/80-positive midzonal M1 macrophages in the livers of sepsis mice. Macrophage depletion ameliorated LPS-induced liver inflammation. Vimentin was identified as a substrate crosslinked by TG2 and knockdown of vimentin inhibited LPS-induced cytokine expression in RAW264 cells.

Conclusion: This study elucidated the role of TG2 in mediating sepsis-induced inflammation by facilitating the crosslinking of vimentin in macrophage and the therapeutic potential of TG2 as a molecular target for sepsis-associated liver injury.

Abstract Submission No. 100959
P-0705

How to Cure Depression in Patients after CLD Transplantation? Systematic Literature Review.

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Depression is when a person experiences anxiety, feels uneasy, and so on. Depression can affect anyone, including patients with Chronic Liver Disease and Liver Transplants. This article aims to determine whether depression influences a person's long-term survival after Liver Transplantation (LT). What are the actions taken to reduce depression?

This abstract uses a literature study from PubMed using the keywords depression, chronic liver disease, and liver transplantation.

The results of a literature review study found that patients prone to depression are Chronic Liver Disease (CLD) patients with chronic hepatitis C due to the use of interferon therapy. OLT patients with depression have a higher mortality rate than patients who are not depressed; appropriate use of anti-depressants will reverse this effect. Selective serotonin reuptake inhibitors (SSRIs) and selective noradrenaline reuptake inhibitors (SNRIs) are effective and generally safe in patients with CLD and OLT. Second, depressive symptoms and grades can be measured by the Beck Depression Inventory (BDI) score during the first year post-transplant; depression usually occurs during the first year after L-TX (liver transplant). Third, the consumption of anti-depressants

It is hoped that in the future, researchers will be able to find out more about how bad the impact of depression is on daily life, identify early and developing depressive symptoms, or screening.

Abstract Submission No. 101234
P-0706

Applying new criteria to evaluate outcomes of living-donor liver transplant for ACLF

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Aim: Recently, new diagnostic criteria for acute-on-chronic liver failure (ACLF) were established in Japan. However, there is little evidence regarding the feasibility of classifying patients undergoing living-donor liver transplantation (LDLT). The aim of this study was to re-evaluate the impact of these new diagnostic criteria on ACLF and the severity classification of patients undergoing LDLT.

Methods: We collected data of recipients who underwent LDLT for liver failure between 2017 and 2022 and reviewed it retrospectively.

Results: Of the 59 patients with liver failure, 54 (91.5%) were diagnosed with ACLF; Grade 0 (n = 4), Grade 1 (n = 24), Grade 2 (n = 19), and Grade 3 (n = 9). There was no substantial difference in overall survival (OS) and the occurrence of postoperative complications between liver failure patients with and without ACLF. The OS after LDLT was significantly different among the four groups of ACLF patients (P < 0.001). Interestingly, ACLF Grade 3 patients had substantially lower OS compared to other ACLF groups even after LDLT (P = .006; 5-year OS rates, 33.3% vs. 85.9%).

Conclusion: Proper use of the new diagnostic criteria for ACLF in Japan demonstrated that the presence and severity of ACLF, especially the presence of multiple organ failures, leads to morbidity and mortality even in an LDLT setting. Considering that the patients with ACLF Grade 3 do not have the favorable outcomes of LDLT, deceased-donor liver transplantation usage, or LDLT before reaching the severity of Grade 3 may be suitable for further research.

Abstract Submission No. 101320
P-0707

Development of an Innovative Prognostic Model for Predicting Mortality in Patients with ACLF

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Background: Acute-on-chronic liver failure (ACLF) presents with elevated short-term mortality rates, necessitating intensive care unit (ICU) admission. Accurate prognostication is essential for timely liver transplantation referrals. Despite widespread use, the superiority of the CLIF-C ACLF score in Asian ICU patients remains inconclusive compared to other scoring systems. This study aims to (i) compare the predictive performance of original MELD, MELD-Lactate, CLIF-C ACLF, CLIF-C ACLF-Lactate, and APACHE-II scores for short-term mortality, and (ii) develop and validate a novel scoring system, assessing its predictive efficacy against the original five scores.

Methods: A cohort of 265 consecutive cirrhotic ACLF patients admitted to the ICU was enrolled. Prognostic values for mortality were evaluated through ROC analysis. A novel model was developed and internally validated using 5-fold cross-validation. Additionally, external validation was performed in another ICU with 40 ACLF patients.

Results: Alcohol abuse emerged as the primary cirrhosis etiology. The AUROC of the five prognostic scores in predicting one-month mortality did not significantly differ. However, the newly developed model, incorporating age, A-a gradient, BUN, total bilirubin, INR, and HE grades, demonstrated significantly improved performance with AUROC of 0.863 and 0.829 for one-month and three-month mortality, respectively, surpassing the original five prognostic scores. External

validation in another ICU with 40 ACLF patients further supported its efficacy.

Conclusions: The novel ACLF model outperforms established scores in predicting short-term mortality for ICU-admitted ACLF patients. Rigorous external validation is warranted to affirm its clinical utility.

Abstract Submission No. 101495

P-0708

Persistent systemic inflammation is important driver of acute-on-chronic liver failure

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Background/Aims: We aimed to investigate the association between acute-on-chronic liver failure (ACLF) development and systemic inflammatory markers in acutely decompensated chronic liver disease patients.

Methods: We enrolled 1,249 patients without ACLF at baseline in Korean ACLF cohort. Organ failure and ACLF were defined by European Association for the Study of the Liver-Chronic liver failure (EASL-CLIF) criteria. Primary outcome was ACLF development and new organ failure development within 1 year.

Results: Most common etiology of chronic liver disease was alcohol (66.1%), followed by viral hepatitis (15.5%). Mean model for end-stage liver disease and CLIF-C AD score were 16.3 ± 5.4 and 49.7 ± 9.3 , respectively. Patients with high C-reactive protein (CRP) (≥ 1.0 mg/dL), white blood cell count (WBC) ($\geq 10.0 \times 10^9/\text{mm}^3$), procalcitonin level (1.0 mg/dL) showed significantly higher 1-year ACLF development rate than patients with low CRP ($P < 0.001$), WBC ($P = 0.004$) and procalcitonin ($P = 0.014$), respectively. Those with systemic inflammatory response syndrome (SIRS) also had significantly higher ACLF development rate than those without SIRS ($P = 0.045$). Cox proportional hazard regression model showed that SIRS, bacterial infection, low albumin and Na levels, high bilirubin, international normalized ratio (INR), CRP, creatinine, and procalcitonin levels were significant factors in univariate analysis, and bilirubin (Hazard ratio (HR) 2.266, $P = 0.012$), INR (HR 6.047, $P < 0.001$), CRP (HR 2.242, $P = 0.011$), and procalcitonin (HR = 2.437, $P = 0.011$) level were independent factors for ACLF development. Those with high CRP level had significantly higher renal ($P < 0.001$), coagulation ($P < 0.001$), cerebral ($P = 0.013$), circulatory ($P = 0.009$) failure development ($P = 0.001$) than those with low CRP, and those with high procalcitonin had significantly higher renal failure development rate ($P = 0.032$). The ACLF development rate of the patients with low CRP at baseline but high CRP at 7th day was significantly higher than that of the patients with high CRP at baseline but low CRP at 7th day ($P = 0.01$) and similar to that of the patients with persistently high CRP ($P = 0.629$). The change of the SIRS also showed similar results to the CRP change.

Conclusion: Persistent or worsening systemic inflammation is a main driver for development of organ failure and ACLF. The resolution of

inflammation could reduce the ACLF development. Reducing systemic inflammation can be a treatment target to prevent disease progression.

Abstract Submission No. 101527

P-0709

Effect of glucocorticoids on survival in liver failure: A Systematic Review and Meta-Analysis

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Background and aim: Glucocorticoids have been used for treating liver failure, but this strategy remains controversial. Current clinical studies have little effective evidence for its therapeutic effect, and results are inconsistent. This study aims to estimate the effect of glucocorticoids on survival in patients with liver failure.

Methods: Randomized clinical trials and observational studies, comparing glucocorticoid vs conventional therapies in patients with LF, were identified from public databases from its inception to 1 August 2022. The primary outcome was the survival rate, defined as survival without transplantation or death.

Results: In total, we included eleven studies. 1267 patients participated in the study, of which 604 (47.67%) received glucocorticoid therapy. The meta-analysis revealed that glucocorticoids increased the survival rate of liver failure patients by 20% (RR: 1.20, 95% CI: 1.01-1.42, $P = 0.034$). Furthermore, glucocorticoid therapy did not increase the risk of infection and bleeding (RR: 1.31, 95% CI: 0.70-2.42, $P = 0.395$; RR: 1.57, 95% CI: 0.93-2.65, $P = 0.089$).

Conclusion: Our meta-analysis reported glucocorticoids improved survival in liver failure patients without increasing the risk of infection and bleeding.

Abstract Submission No. 101544

P-0710

Study on predicting the efficacy of glucocorticoids in treating hepatitis B-induced ACLF

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Objective: To discover the optimal indications of intervention with glucocorticoids (GCs) in patients with HBV-induced HBV-ACLF, and to establish a model of predicting the efficacy of steroids therapy (PEST) in HBV-ACLF.

Methods: The baseline characteristics of 112 patients of HBV-ACLF with GCs from Southwest hospital were retrospectively analyzed to find some independent factors associated with the efficacy of steroids therapy, and a model for PEST was established for predicting the effect of GCs therapy. The predictive accuracy of PEST model and other models was compared using the area under the receiver ROC curve (auROC), and was validated by 64 patients from our hospital.

Results: Multivariate logistic regression analysis showed that INR, TBil, cirrhosis and albumin were the best predictors of the therapeutic efficacy of steroids in HBV-ACLF. $PEST = e^x / (1 + e^x)$, $X = 0.253 \times ALB - 2.333 \times INR - 0.097 \times TBil - 2.695 \times Cirrhosis$ (yes=1, no=0)-1.486. The auROC of PEST model was 0.958, and significantly higher than MELD, MELD-Na, CTP and ZHY, $P < 0.05$. An analysis of 64 patients

with HBV-ACLF from our hospital had similar verified results. The 90-day transplantation-free survival rate was 95.1% in cases with INR <1.50, or 98.0% in cases with PEST $\geq$ 0.70, and 83.8% in cases with INR $\geq$ 1.5 and PEST $\geq$ 0.40, but only 4.0% in cases with INR $\geq$ 2.6 and PEST <0.40.

Conclusion: Our novel PEST model established in this study had an excellent performance in predicting the therapeutic effect of GCs in patients with HBV-ACLF. Patients with INR <1.50 or PEST $\geq$ 0.70 were considered to be the optimal cases of GCs intervention. Patients with INR $\geq$ 2.60 and PEST <0.40 were considered to be the worst indication of GCs intervention.

Abstract Submission No. 101596

P-0711

Metabolomics study of HBV ACLF patients with different precipitating events

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Methods: 96 patients with HBV-ACLF hospitalized were prospectively included and divided into the hepatotropic virus insult precipitating events group (HVI group) and the non-hepatotropic virus insult precipitating events group (NVI group). The serum specimens from the study population and the control population were examined using a UPLC-LTQ Orbitrap XL ultra performance liquid chromatography and mass spectrometry system. The metabolic profile was described, and a model was developed to differentiate between HBV-ACLF due to hepatotropic and non-hepatotropic viral insult precipitating events, to screen for specific metabolic ions at the metabolomic level in patients with HBV-ACLF due to hepatotropic viral insult and non-hepatotropic viral insult precipitating events, to identify the possible potential for differences in the prognosis of HBV-ACLF due to different precipitating events.

Results: Preliminary metabolomic analysis revealed significant differences in serum metabolite profiles between the hepatotropic virus insult-induced HBV-ACLF (HVI-HBV-ACLF) group, the non-hepatotropic virus insult-induced HBV-ACLF (NVI-HBV-ACLF) group. Based on the differences, orthogonal partial least squares (OPLS-DA) models were established between the HVI-HBV-ACLF group and the NVI-HBV-ACLF group. The characteristic metabolic ions between the HVI-HBV-ACLF group and the NVI-HBV-ACLF group were identified. The results were oleamide, kynurenine, sodium glycocholate, glycocholate, glutamate betaine, leukotriene E3, 12-keto-tetrahydro-leukotriene B4, and dihydroxyacetone phosphate, respectively.

Conclusions: There were significant differences in serum metabolite profiles between the HVI-HBV-ACLF and the NVI-HBV-ACLF. The prognostic differences between the HVI-HBV-ACLF and NVI-HBV-ACLF groups may be explained by the fact that the immunometabolic imbalance was more pronounced in the HVI-HBV-ACLF.

Keywords: acute-on-chronic liver failure, precipitating events, metabolomics

Abstract Submission No. 101629

P-0712

The ratio of VWF to ADAMTS13: Usefulness as a prognostic biomarker in acute-on-chronic liver failure

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Background/Aims: ACLF has a high risk of short-term mortality. A disintegrin-like and metalloproteinase with thrombospondin type-1 motifs 13 (ADAMTS13) is a metalloproteinase that specifically cleaves multimeric von Willebrand factor (VWF). Imbalance between ADAMTS13 and VWF is associated with portal hypertension, which induces ACLF development. A previous study reported that ADAMTS13 activity (ADAMTS13:AC) and VWF antigen (VWF:Ag) are predictive biomarkers of ACLF development in patients with cirrhosis. This study investigated the changes in ADAMTS13:AC and VWF:Ag level from before to after the development of ACLF to determine their usefulness as a prognostic biomarker in patients with ACLF.

Methods: A total of 101 patients with cirrhosis were enrolled in this study. ADAMTS13:AC and VWF:Ag was determined by an enzyme-linked immunosorbent assay. Cox proportional hazards regression analysis was conducted to determine independent prognostic factors for patients with liver cirrhosis in the post-ACLF group.

Results: ADAMTS13:AC gradually decreased in the order of non-ACLF group, pre-ACLF group, and finally post-ACLF group. VWF:Ag and the ratio of VWF:Ag to ADAMTS13:AC (VWF:Ag/ADAMTS13:AC) gradually increased in the order of non-ACLF group, pre-ACLF group, followed by post-ACLF group. VWF:Ag/ADAMTS13:AC and CLIF-C ACLF score were associated with prognosis in the post-ACLF group in multivariate analysis. The cumulative survival of the post-ACLF group was significantly lower for patients with high VWF:Ag/ADAMTS13:AC (>9) compared with those with low VWF:Ag/ADAMTS13:AC ($\leq$ 9) (HR: 10.72, 95% confidence interval: 1.39–82.78, $P < 0.05$).

Conclusions: The VWF:Ag/ADAMTS13:AC increased according to the progression of ACLF in patients with cirrhosis and predicted prognosis in patients with cirrhosis with ACLF.

Abstract Submission No. 101663

P-0713

Successful Therapeutic Plasma Exchange (TPE) in Lymphoma-associated Acute Liver Failure

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Acute liver failure (ALF) secondary to malignant infiltration of the liver is rare and associated with poor survival without prompt recognition and treatment.

We report a case of a well 45-year-old Chinese male who presented with fever and jaundice. Physical examination showed scleral icterus, hepatosplenomegaly and non-tender cervical lymphadenopathy with no encephalopathy. Blood investigations revealed severe acute liver injury (Alb 21g/L, bil 130 μ mol/L, ALP 788U/L, ALT 68U/L, AST 77U/L, PT 20.4 sec). Computed tomography imaging confirmed

hepatosplenomegaly and lymphadenopathy with no biliary obstruction. Oncology was consulted and the working diagnosis was a lymphoproliferative disorder with malignant liver infiltration.

An excision biopsy of a cervical lymph node was performed and he was started on intravenous Dexamethasone for hemophagocytic lymphohistiocytosis (HLH). However, while awaiting histology, he developed encephalopathy and acute liver failure on Day 5 requiring intubation. Therapeutic plasma exchange (TPE) was promptly initiated as a bridge to initiation of curative-intent chemotherapy. He underwent 2 sessions of TPE (5-6 litres each session), with improvement in biochemical indices and mentation. Once diagnosis of peripheral T-cell lymphoma was confirmed, he received Gemcitabine and Carboplatin. He responded well to chemotherapy with significant improvement in liver function, and was extubated 4 days later.

This case highlights the utility of TPE as a life-saving bridging therapy in patients with suspected lymphoma-associated acute liver failure prior to histological confirmation, given the chemo-sensitive nature of the disease. To the best of our knowledge, this is the first reported case of successful TPE in lymphoma-associated ALF.

Abstract Submission No. 101741

P-0714

Current status and treatment with artificial liver support system for ALF and ACLF in our hospital

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Background: The efficacy of online hemodiafiltration (online HDF) for acute liver failure (ALF) and Acute-on-Chronic Liver Failure (ACLF) as an artificial liver support system (ALSS) has been reported. In addition to online HDF, our hospital has used continuous plasma filtration with dialysis (CPDF). We investigated the current status and treatment of ALF and ACLF in our hospital.

Methods: The backgrounds and prognoses of ALF or ACLF patients who received either or both online HDF and CPDF in our hospital were retrospectively evaluated.

Results: Of the 12 cases, 7 were ALF (HAV 1 case, HBV 2 cases, AIH 1 case, drug 1 case, unknown 2 cases), and 5 were ACLF whose exacerbating factors are infection 2 cases, drug 2 cases, and unknown 1 case. Liver transplantation was performed in 4 of the eight surviving cases, and the four deceased cases were considered liver transplantation ineligible for various reasons. Among five ACLF patients, three had liver transplantation, one died, and one recovered. The median treatment duration with ALSS was 9 (2-27) days; three of seven patients starting CPDF had recovered before day 3; however, three of the remaining required changes to online HDF until day 3. Blood ammonia levels and the severity of hepatic encephalopathy at the time of ALSS indication tend to lower in patients started with CPDF compared to online HDF.

Conclusions: CPDF may contribute to the prognosis of some ALF or ACLF patients. Further investigation might be needed to make a strategy to improve their prognosis.

Abstract Submission No. 101861

P-0715

Plasma exchange improve short term mortality in steroid ineligible alcoholic (ACLF) patients

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Background and Aims: Acute on chronic liver failure patients has high short-term mortality. Therapeutic plasma exchange is a modality of treatment in acute liver failure patients, but its efficacy in steroid ineligible alcoholic ACLF has seldomly studied. We aimed that therapeutic plasma exchange improves 30-day mortality thus it can help as a bridge therapy to liver transplantation.

Methods: Patients of steroid ineligible alcoholic ACLF patients n-1424, out of which 182 receive plasma exchange. We compared the 30 day and 90-day mortality in these patients.

Results: Baseline investigations were comparable in the patients who received plasma exchange or standard medical treatment. Out of 182 patients who received plasma exchange, 120 (66 %) patients survived at 30 days as compared to who did not received plasma exchange 638/1242 (51%) survived was significant with p value <0.001. Nearly 77/182 patient (42%) survived in plasma exchange group as compared to 586/1242 patients (46 %) with p value 0.09 at 90 days. High baseline MELD score, MELD Na, CTP score, AARC score, number of days of hospital stay has correlated with poor survival outcome.

Conclusion: Plasma exchange is an effective modality in improving short term mortality in alcoholic ACLF patients and can serve as a bridge to liver transplantation.

Abstract Submission No. 101946

P-0716

MSC-exo alleviate IL-17 mediated immune damage in acute liver failure via RXRG/FOXP3 signaling

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Background and Aims: Acute liver failure is a severe immune injury caused by an inflammatory storm involving multiple cytokines in liver tissue and can be life threatening. In the circumstance of liver donors scarcity, it is crucial to find effective non-transplant treatment methods. Previously, we found that human bone marrow mesenchymal stem cell exosomes can alleviate liver injury in acute liver failure mice, but the key molecular mechanisms by which they regulate the liver immune microenvironment remain unclear.

Methods: To establish the ALF cell model and ALF mouse model induced by GalN/LPS, randomly divided into blank control group, ALF group, and MSC-exo treated ALF group (n=6), detect the expression of IL-17, RXRG, and FOXP3 by western blotting.

Results: The MSC-exo treated ALF cell model showed a significant increase in RXRG and FOXP3 expression, while IL-17 showed the opposite.

Conclusion: MSC-exo can reduces IL-17 levels and alleviates liver inflammatory response in ALF by upregulate RXRG in infiltrating Th cells of the liver to enhancing the inhibitory effect of FOXP3 on ROR γ .

Abstract Submission No. 101951

P-0717

Predictors of ACLF in patients with compensated liver cirrhosis presented by variceal bleeding

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Background: ACLF is an emergency hepatic condition. Acute variceal bleeding is one of the acute insults for development of ACLF. We aimed to investigate the incidence and predictors for development of ACLF after acute variceal bleeding in cirrhotic compensated patients.

Materials and methods: The study included 310 patients with compensated liver cirrhosis presented by acute variceal bleeding. The patients subjected to complete history taking, full examination, laboratory, and radiological investigations. Child Turcott Pugh score (CTP). Upper gastrointestinal endoscopy done with endoscopic management of variceal bleeding, after proper resuscitation and administration of vasopressors and PPIs. Patients were followed up at 2 weeks of admission, 4 weeks, 3 months by clinical and laboratory evaluation to detect signs of development of ACLF.

Results: Among 310 patients included in the study, 17 (5.5%) patients developed ACLF and 14 (82.3) of which died and 3 patient survived ACLF at last follow up. The main predictors were: haemodynamic instability (p 0.019), bleeding on endoscopy (p 0.001), rebreeding within one week (p 0.001), emergent endoscopy (p 0.028), higher INR (p 0.029), leucocytosis (p 0.001), rising creatinine (p 0.004), low albumin level (p 0.001).

Conclusion: The incidence of ACLF in our study was (5.5%). With high mortality rate. Severity of the bleeding, timing of endoscopy, high baseline INR, low baseline albumin, rising serum creatinine, leucocytosis were the main predictors for development of ACLF in cirrhotic compensated patients. Early prediction and treatment of those patients could prevent development of ACLF.

Abstract Submission No. 200023

P-0718

YGF promotes mitophagy by regulating the S100A9/RAGE signaling pathway to ameliorate ACLF

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Background: Mitophagy dysregulation significantly contributes to the pathogenesis of acute and chronic liver failure (ACLF). The JianPi LiShi YangGan formula (YGF) can improve ACLF by promoting autophagy. However, the precise mechanism underlying this effect remains unknown.

Purpose: To investigate the effect of YGF on hepatocyte mitophagy in ACLF mice and elucidate its molecular mechanism.

Methods: The ACLF mouse model was established using carbon tetrachloride, lipopolysaccharide, and D-galactose. Hematoxylin and eosin staining were employed to evaluate the hepatoprotective effect of YGF in ACLF mice. Mitochondrial damage was assessed using transmission electron microscopy. The mechanism of action of YGF was explored by analyzing transcriptomics data and employing wb, immunohistochemistry, and immunofluorescence.

Results: In ACLF mice hepatocytes, YGF reduced mitochondrial damage, enhanced mitophagy. However, 3-Methyladenine (3-MA) treatment in ACLF mice weakened the protective effect of YGF against hepatocyte damage and pro-mitophagy. Transcriptome sequencing data and experiments validated that YGF inhibited S100A9/RAGE pathway activation in ACLF mice hepatocytes. In

AIM12 cells overexpressing RAGE, recombinant S100A9 protein inhibited CCCP-induced mitophagy. Additionally, treatments with S100A9 and RAGE inhibitors ameliorated liver injury in ACLF mice, and enhancing the co-localization of Lamp2 with COX-IV. However, pretreatment with 3-MA partially reversed the protective effects and pro-mitophagy.

Conclusion: YGF promotes mitophagy in ACLF mouse hepatocytes, attenuating hepatocyte injury. Its mechanism may partially regulate the S100A9/RAGE pathway, inhibiting mitophagy. The impairment of mitophagy in hepatocytes mediated by S100A9/RAGE may contribute significantly to ACLF progression. Inhibiting its pathway to promote mitophagy may be a prospective therapeutic strategy for ACLF.

Abstract Submission No. 200195

P-0719

MSC-sEVs attenuated macrophage-related inflammation in ACLF via connexin43

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Background and Aims: Acute-on-chronic liver failure (ACLF) is a clinical syndrome with high short-term mortality but lack of effective medical treatment. Previous studies have demonstrated the attenuating effect of mesenchymal stem cell-derived small extracellular vesicles (MSC-sEVs) on macrophage-related inflammation process of ACLF. However, whether the underlying mechanism involves connexin43 (Cx43) gap junction between macrophages remains poorly understood. In this study, we explored the gap junction-related mechanism by which MSC-sEVs attenuated macrophage-related inflammation in ACLF.

Methods: Mouse bone marrow derived MSC-sEVs were cocultured with RAW264.7 macrophages that were stimulated with 1µg/ml LPS for 24h to induce macrophage M1 polarization. Cell viability was assayed by CCK8 and cell proliferation was detected by EdU staining. Protein and mRNA expression of Cx43 was determined by qPCR and western blot.

Results: Cell viability and proliferation decreased after stimulated with LPS. MSC-sEVs treatment reversed the cell viability and proliferation of M1 polarized macrophages. Western blotting and qPCR demonstrated reduced protein and mRNA expression of Cx43 in M1 macrophages in MSC-sEVs treated group, compared to PBS control group.

Conclusion: MSC-sEVs attenuated macrophage-related inflammation by inhibiting connexin43 in M1 polarized macrophages.

Abstract Submission No. 100409

P-0720

Durvalumab in Combination with Gemcitabine and Cisplatin for Biliary Tract Cancer at Our Hospital

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Background: Advanced biliary tract cancer (BTC) generally presents a grim prognosis. The TOPAZ-1 trial recently indicated a significant

benefit of combining durvalumab with chemotherapy in such cases. This study aimed to evaluate the efficacy and safety of durvalumab, gemcitabine, and cisplatin in treating patients with advanced BTC at our institution.

Methods: We retrospectively reviewed six patients diagnosed with either unresectable or metastatic BTC, treated with durvalumab, gemcitabine, and cisplatin from January to October 2023. The parameters examined included patient characteristics, treatment responses, duration of follow-up, and any adverse events encountered.

Results: The cohort comprised patients with a median age of 69.5 years. There were 4 males and 2 females. Primary sites were intrahepatic cholangiocarcinoma (n = 2), hilar cholangiocarcinoma (n = 3), and gallbladder carcinoma (n = 1). The treatment yielded an overall response rate of 14% and a disease control rate of 50% during a median follow-up of 4.7 months. One patient developed interstitial pneumonia. Hematological adverse events were the most common but were generally controllable through dosage reduction, and no toxicity-related death was observed.

Conclusion: The regimen of durvalumab, gemcitabine, and cisplatin demonstrated a tolerable safety profile and encouraging preliminary efficacy in our cohort of advanced BTC patients.

Abstract Submission No. 100805

P-0721

The Role of Antiviral Therapy in HBV-associated Patients with Intrahepatic Cholangiocarcinoma

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Background: Cholangiocarcinoma (CCA) is a deadly hepatobiliary tumor categorized into intrahepatic (iCCA), perihilar (pCCA), and extrahepatic (eCCA) groups. Previous studies highlight viral hepatitis as a significant risk factor for iCCA prognosis, yet the connection between HBV-related iCCA and antiviral management in Taiwan remains unclear.

Methods: We conducted a retrospective review of CCA patients records at MacKay Memorial Hospital from Jan. 1, 2015, to Dec. 31, 2021. We enrolled patients with histologically confirmed CCA and analyzed the prognosis of HBV-associated patients with iCCA.

Result: A total of 152 patients with confirmed pathology were included, with 25 of these patients diagnosed with iCCA and HBV infection. Additionally, we enrolled 17 patients who exhibited detectable viral loads (>20 IU/mL). These patients were split into two groups: one receiving antiviral therapy (n = 13) and the other without it (n = 4). There were no significant differences between the two groups in the patient's characteristics (Table 1). Within the group underwent antiviral therapy, 46.2% of the patients were deemed resectable; 76.9% of the patients underwent chemotherapy. Within the group without antiviral therapy, 75% of the patients were deemed resectable. There was no disparity found in the survival curves for patients in the groups receiving antiviral therapy compared to those without it ($p=0.172$) (Figure 1).

Conclusion: Our retrospective data demonstrated the HBV-associated patients with iCCA receiving antiviral therapy did not affect the survival rate. Further prospective studies are necessary to draw a definitive conclusion.

Abstract Submission No. 100998

P-0722

Sex Disparities in Gallbladder and Biliary Tract Cancer Across a Decade in the Asia-Pacific Region

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Background: Gallbladder and biliary tract cancer represent an escalating global health threat, particularly in the Asia-Pacific region, where comprehensive research on sex disparities is lacking. This study aims to address this gap by examining sex differences in gallbladder and biliary tract cancer in Asia over 10-year period.

Method: Utilizing data from the Global Burden of Disease Study 2019, our analysis scrutinizes temporal trends in gallbladder and biliary tract cancer across the Asia-Pacific. We calculate annual frequencies and age-standardized rates (ASRs) for incidence, death, and disability-adjusted life-years (DALYs), categorized by sex. The annual percent change (APC) is calculated to assess alterations in ASRs over time.

Result: A consistently higher age-standardized incidence rate (ASIR) is observed in females in the SEA (Southeast Asia) region, while the Western Pacific region displays the opposite trend over the past decade. Males exhibit a 30% lower ASIR for gallbladder and biliary tract cancer compared to females in SEA, but conversely, males show a 30% higher ASIR for these cancers in the Western Pacific compared to females. Notably, a higher increase is observed in females in SEA, with an upward trend noted in both genders. Conversely, a more substantial decrease is observed in females in the Western Pacific region, with a decline noted for both genders. Similar patterns are discerned in age-standardized death rates (ASDR) and age-standardized DALYs rates.

Conclusion: Our study underscores a significant sex difference in gallbladder and biliary tract cancer in Asia-Pacific region, emphasizing the imperative to scrutinize the differing presentations between the two regions.

Abstract Submission No. 101119

P-0723

A Novel Model of Intrahepatic Cholangiocarcinoma Using Obese Mice and Carcinogen

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Background: Cholangiocarcinoma (CCA) is the second most common primary cancer of the liver and has a poor prognosis. Various animal models, including carcinogen-induced and genetically engineered rodent models, have been established to clarify the mechanisms underlying cholangiocarcinoma development, but an appropriate mouse model for CCA has not been established.

Methods: Male obese db/db and control C57BL/6/J mice were used. Azoxymethane (AOM) or saline was intraperitoneally administered once a week for 4 weeks, and then 8 weeks later, all mice were sacrificed.

Results: The relative liver weights of the mice treated with AOM were lower than those of the mice without AOM treatment. Liver damage and oxidative stress were observed in mice given AOM and were

exacerbated in obese mice. A histopathological analysis revealed atypical biliary duct epithelium in the liver of both the AOM-administered obese and control mice. The hepatic lesions were stained with CK19 and appeared to be an intrahepatic cholangiocarcinoma with higher tumor incidence, shorter experimental duration, and a markedly increased incidence in obese mice. Molecular markers analyzed using a microarray and qPCR indicated that the cancerous lesions originated from the cholangiocytes and developed in the inflamed livers. These findings indicated that this is a novel mouse model of intrahepatic cholangiocarcinoma in the context of steatohepatitis.

Conclusions: We established a novel mouse model of intrahepatic CCA in obese db/db mice administered with AOM. This model will help elucidate the pathogenic mechanism of CCA and establish novel preventive and therapeutic strategies for this disease.

Abstract Submission No. 101598

P-0724

From Outside: A Case Series on Lemmel's Syndrome

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Lemmel's Syndrome is a rare disease characterized by obstructive jaundice in the absence of choledocholithiasis or pancreaticobiliary/periampullary tumors, periampullary diverticulum is a usual cause. This report can increase the knowledge in the diagnosis and management of this disease.

Case 1 is a 74 year old female, presenting with one-week dull right upper quadrant pain, fever and jaundice. Work up revealed Direct hyperbilirubinemia (Total Bilirubin 12.72mg/dl) ALP 135U/L, ALT 610mg/dl. MRCP showed: paravaterian diverticulum(AP-1.6cm) with mass effect on the distal common bile duct(CBD) and resultant upstream dilation (CBD: 1.1cm) until the central intrahepatic ducts. ERCP showed: paravaterian diverticulum, no intraluminal filling defects, and a dilated CBD(1cm). Sphincterotomy and balloon sweeping was done yielding purulent bile. Biliary stent insertion was done as well as initiation of antibiotics. One-month after, her bilirubin levels are normal and is asymptomatic.

Case 2 is an 88 year old male, presenting with 4-day sub-xiphoid dull pain. Icteresia was noted on admission. Work up revealed: Direct hyperbilirubinemia (Total Bilirubin: 4.33mg/dl), ALP 144U/L, ALT 193mg/dl. Contrast Abdominal CT scan showed: large paravaterian diverticulum(AP-4.8cm) compressing the distal CBD with resultant upstream dilation (CBD:1.2cm) until the proximal intrahepatic ducts. UDCA 300mg/cap thrice daily was started. After two-weeks on UDCA, he is asymptomatic and with normal bilirubin levels.

Work up in these patient should be prompt to prevent complications such as cholangitis. No single definitive management is currently recommended. Conservative or medical management is an option in mildly symptomatic cases and more invasive therapy can be done in patients who develop complications

Abstract Submission No. 101845

P-0725

Association of *IDH1* Mutations with Survival and Recurrence in Intrahepatic Cholangiocarcinoma

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Purpose: *IDH1* mutations are causal in tumor development and progression; however, their association with disease characteristics, prognosis and therapy response in patients with resected intrahepatic cholangiocarcinoma (ICC) remains controversial.

Experimental Design: In this cohort study, we recruited 803 patients who underwent curative resection for ICC at a single hospital in China. We performed whole-exome sequencing and Sanger sequencing to identify *IDH1* mutations. We used the Kaplan-Meier method and log-rank test to compare overall survival (OS) and disease-free survival (DFS).

Results: A total of 5 different subtypes of *IDH1* somatic mutation affecting 94 (11.7%) patients were identified. Across all patients considered, those received adjuvant chemotherapy were significantly associated with superior OS and DFS when compared with patients not received adjuvant chemotherapy. In the whole ICC cohort, patients with *IDH1* mutations showed no significant difference in OS ($P=0.86$) or DFS ($P=0.64$) compared with those with wild-type *IDH1*. When we looked at patients received or not received adjuvant chemotherapy, separately, univariate and multivariable analysis revealed that *IDH1* mutations were significantly associated with superior OS ($P=0.03$) and DFS ($P=0.02$) in patients received adjuvant chemotherapy, but were marginal associated with worse OS ($P=0.09$) and DFS ($P=0.15$) in patients not received adjuvant chemotherapy.

Conclusions: We characterized the distribution of *IDH1* mutations in a large cohort of patients with ICC from China. The presence of *IDH1* mutations was associated with better survival and decreased risk of recurrence in resected ICC received adjuvant chemotherapy.

Abstract Submission No. 102095

P-0726

Not All Hilar Masses are Klatskin Tumor, Isolated Hepatobiliary Tuberculosis : A Case Report

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Isolated Hepatobiliary Tuberculosis is a rare entity. Diagnosis is difficult to achieve due to the insidious nature of the disease and non specific clinical as well as radiological findings. Here we report a case of a 47 year old female with Hepatobiliary tuberculosis, who presented with right upper quadrant pain. Patient is a HIV infected individual on Anti retroviral therapy for the past 13 years. Patient had no evidence of pulmonary or extra pulmonary tuberculosis on routine investigations. Patient was found to have a mass lesion at the hilum of the liver with focal lesions in the liver parenchyma as well on imaging and was suspected to have hilar cholangiocarcinoma. The diagnosis of tuberculosis was confirmed after a trans jugular biopsy of the liver lesion.

Clinical significance : In endemic areas with appropriate clinical and imaging findings the possibility of hepatic tuberculosis should be considered and tissue diagnosis should achieved considering good response to intervention for Hepatobiliary tuberculosis.

Abstract Submission No. 200069

P-0727

mALBI is not the prognostic factor in patients with unresectable biliary tract cancer

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Background: Although modified albumin-biliubin model (mMLBI) is useful as an assessment of liver function in antitumor therapy for hepatocellular carcinoma, its usefulness in biliary tract cancer (BTC) is not clear. Herein, we conducted this retrospective analysis of the associations of mMLBI and prognosis in patients with unresectable BTC. **Methods:** All consecutive patients who underwent palliative chemotherapy for unresectable BTC at Nihon University Hospital were retrospectively studied. mMLBI was calculated using pre-treatment data. Progression free survival (PFS) was evaluated using Kaplan-Meier methods. Multivariable hazard regression models were used to evaluate the prognostic factors in patients with unresectable BTC.

Results: Twenty-two patients included in the analysis with a median age of 75, male gender in 73%, Intrahepatic cholangiocarcinoma/Hilar cholangiocarcinoma/distal BTC/duodenal papillary cancer/Gallbladder cancer in 18/32/9/5/36%, metastatic disease in 64%, biliary drainage in 59%, median CA19-9 value of 133 IU/L, combination chemotherapy (Gemcitabine+Cisplatin+Dulvalumab, Gemcitabine+Cisplatin+S-1 and Gemcitabine+Cisplatin) in 64%, and mALBI 1/2a/2b/3 in 18/32/45/5%. 2 cycle completion rate was 86%. The median PFS was 4.6 (95%CI, 3.3-7.1) months in response rate 5% and disease control rate 75%. The multivariate analysis revealed Gallbladder cancer (hazard ratio [HR] 28.1, 95%CI, 1.85-1450.9, $p < 0.01$) as independent prognostic factors for PFS, but mALBI 2a/2b/3 (HR 0.29, 95%CI, 0.02-3.81, $p = 0.33$) was not.

Conclusion: mALBI was not associated with PFS in patients with unresectable BTC.

Abstract Submission No. 200100

P-0728

Villous Adenoma of the Common Bile Duct Co-existing with a Pancreatic Head Mass: A Case Report

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Introduction: Villous adenomas are benign lesions typically found in the colon, and rarely seen in the biliary tree. Histopathology is necessary to confirm the diagnosis. We report a case of a villous adenoma in the CBD co-existing with a pancreatic head mass, causing obstructive jaundice.

Case Report: A 78-year-old female presented with a three week history of obstructive jaundice. Triphasic CT scan showed dilated intrahepatic ducts down to the distal CBD, with tapering of its distal end, with no radiopaque lithiasis. ERCP revealed a dilated CBD (1.5 cm) with a distal CBD stricture (1 cm). Brush cytology showed biliary epithelium with low grade dysplasia consistent with villous adenoma. EUS demonstrated a distal CBD stricture and pancreatic body cyst, which was not biopsied. MRI showed a lobulated mass (3.2 x 3.0 cm) involving the pancreatic head, causing distal CBD obstruction with extrahepatic and intrahepatic biliary ductal dilatation. Repeat ERCP was done and cholangioscopy revealed ulceronodular lesions at the distal CBD. Histopathology showed fibrocollagenous tissue with mild chronic inflammation. Patient underwent Whipple surgery with loop gastrojejunostomy and jejunostomy. Histopathology showed well differentiated ductal adenocarcinoma of the pancreatic head. The tumor invaded the duodenal wall up to muscularis propria, ampulla of Vater, and peripancreatic soft tissue. The omentum, gallbladder, CBD margins were negative for tumor.

Conclusion: Though villous adenoma is rarely found in the biliary tree, clinicians should consider this as a differential diagnosis in patients

presenting with obstructive jaundice. These premalignant tumors require surgical resection to rule out malignancy.

Abstract Submission No. 200129

P-0729

The Possibility of 5-aminolevulinic acid mediated photodynamic diagnosis in cholangiocarcinoma

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The diagnostic accuracy of cholangiocarcinoma is still insufficient, which is less than 80%, and new diagnostic methods are urgently needed. 5-Aminolevulinic acid (5-ALA) is a natural amino acid that is utilized in the mitochondrial heme synthesis pathway producing the intermediate metabolite protoporphyrin IX (Pp IX). Pp IX is a photosensitizer emitting red fluorescence upon exposure to blue light. While it is rapidly metabolized to heme in normal cells, it accumulates in cancer cells due to reprogramming of heme metabolism. The photodynamic diagnosis by using 5-ALA (5-ALA-PDD) has already been implemented in glioma and bladder cancer. However, its utility in cholangiocarcinoma remains uncertain. In this study, we aimed to elucidate the utility of 5-ALA in the diagnosis of cholangiocarcinoma using patient-derived organoids. We established organoids from four samples of cholangiocarcinoma, including surgical specimens and biopsies obtained during endoscopic retrograde cholangiopancreatography. Additionally, tissues were collected from the peritumoral region, and we also established organoids derived from non-cancerous bile ducts in two cases. These organoids faithfully recapitulated the characteristics of the primary tissues in terms of histology and gene expression patterns. After administration of 5-ALA, fluorescence microscopic analysis revealed that Pp IX accumulation levels were higher in organoids derived from bile duct cancer (40-71%), compared to organoids from non-cancerous bile ducts (<4%). Our findings provide a possibility of 5-ALA-PDD in cholangiocarcinoma, leading to the microscopic or endoscopic strategies.

Abstract Submission No. 200251

P-0730

Clinical significance of lymph-nodes of the hepatic hilum in primary biliary cholangitis.

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BACKGROUND AND AIM: Primary biliary cholangitis (PBC) is a rare chronic liver disease. The lymph nodes at the hepatic hilum, are indicative of non-specific necroinflammatory activity. The aim of our

study was to evaluate the significance of the peri-hepatic lymph nodes, identified during liver ultrasound, in a population of PBC patients on specific therapy according to treatment guidelines.

MATERIALS AND METHODS: All patients affected by PBC were retrospectively analysed. The data were compared with a population of patients suffering from liver disease of different etiology, undergoing to liver ultrasound in our outpatients clinic consecutively, in the same observation period.

RESULTS: 140 patients were included, of which 46 suffered from "pure" PBC. In the non-CBP population, there were 19 patients affected by PBC in overlap with autoimmune hepatitis or metabolic steatohepatitis, and the seroprevalence of anti-mitochondrial antibodies (AMA) was 13.8% (vs 69.5% in the CBP population). The overall prevalence of lymph nodes detected by ultrasound was 34.3%, with the presence of ultrasound signs of liver fibrosis in 46.4%. The prevalence of lymph nodes in PBC patients was significantly higher than in non-PBC patients: 25/46 patients (54%) vs 23/94 patients (24%) [$P < .0001$]. All patients receiving obeticholic acid therapy (as monotherapy or therapy of association with ursodeoxycholic acid and/or fibrate), presented single or multiple lymph nodes at the hepatic hilum.

Furthermore, regardless of the etiology of the liver disease, lymph nodes were more frequent in patients with ultrasound signs of liver fibrosis: 29/65 patients (45%) vs 19/75 patients (25%) [$P = .021$].

CONCLUSIONS: The presence of lymph nodes at the hepatic hilum during a liver ultrasound could suggest the diagnosis of PBC. The lymph nodes are more frequent in case of ultrasound signs of liver fibrotic evolution.

Abstract Submission No. 200272
P-0731

Clinical Strategy Approach in Managing Complex Biliary Cases

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In the era of laparoscopic procedure, there are innovations on non-surgical management approaches for managing biliary tract disorders, such as therapeutic endoscopic retrograde cholangiopancreatography (ERCP) and interventional endoscopic ultrasound (EUS). There is still no clear consensus yet in step-approach for managing difficult biliary disorders. A retrospective endoscopy database study was conducted. Complex biliary cases which included in this study, where multi-management approach is needed, biliary obstruction accompanied with cholangitis or biliary sepsis, difficult CBD stone, recurrent CBD stone, or advanced progressive malignant biliary obstruction. Sixty-one subjects in this retrospective database study were considered as complex biliary cases. In this study, 16.4% of the subjects underwent combination of therapeutic ERCP and EUS in one session based on the complexity of the case; and 8.2% of the subjects underwent therapeutic ERCP with additional single operator cholangioscopy procedure. One subject underwent rendezvous ERCP procedure through percutaneous approach. Around 4.9% of the subjects underwent EUS-guided biliary drainage procedure. The technical success rate of all procedures was 100%. Four subjects (6.6%) died within one month after procedure. One patient died due to procedure-related events, while the other cases of death were due to the malignant process of the diseases. It was demonstrated that no significant association was observed between all mortality outcomes and baseline characteristics of the patients. Complex biliary cases require a good clinical approach algorithm to decide

which procedure comes first based on comprehensive evaluation consists of patient's factor, expertise, cost, and the risk of complications.

Abstract Submission No. 100042
P-0732

A Case of Acute Liver Failure in an Elderly HBV Carrier Without Apparent Trigger

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Patient: 78-year-old female

Chief Complaint: Appetite loss, nausea

History of Present Illness: The patient complained symptoms as above while hospitalized in an orthopedic hospital. Blood tests revealed severe liver injury and positive for HBs antigen, therefore she was referred to our institution.

Clinical Course: CT examination upon admission showed marked liver atrophy and massive ascites. Blood tests showed elevated AST and ALT levels, decreased PT% value, high HBV-DNA titer, while negative for IgM-HBc, denying the initial HBV infection. Consciousness was maintained with normal ammonia level, and there were no evident flapping tremors. The patient had a past history of pneumonia four months prior. She was positive for HBs antigen while ALT level was normal at that time. Based on these findings, we diagnosed this case as acute liver failure with the background of HBV asymptomatic carrier. Intensive therapies, including plasma exchange, steroid pulse therapy, and administration of tenofovir alafenamide, were initiated. However, her status of liver failure worsened, and she died on day 19 of hospitalization. Liver necropsy revealed a sub-massive liver necrosis histologically. The formations of elastic fibers, which generally appear in the late stage of liver fibrosis, were only partially observed. That was consistent with the onset from a healthy carrier. Findings of liver regeneration were hardly observed.

Conclusions: Acute liver failure without any trigger is considered extremely rare in elderly HBV carriers. The delayed liver regeneration due to advanced age may have contributed to the fatal outcome in this case.

Abstract Submission No. 100048
P-0733

XANTHOGRANULOMATOUS CHOLECYSTITIS MASQUERADING AS COLON CANCER: A CASE REPORT

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Significance: Xanthogranulomatous cholecystitis (XGC) is a rare form of chronic cholecystitis commonly mistaken for gallbladder cancer. We present a case of XGC that masqueraded as colon cancer. There has been no report to date where XGC propounded as such. Familiarity of this presentation may contribute to prompt diagnosis and adequate treatment.

Case presentation: A 59-year-old male, with remote history of cholelithiasis removed by endoscopic retrograde cholangiopancreatography, presented with anorexia, weight loss, chronic right upper quadrant pain and a palpable mass.

Management: Abdominal CT revealed an ill-defined hepatic flexure mass intimately related to the gallbladder, with loss of delineation of the gallbladder from the liver bed. Colonoscopy was done revealing a nodular, ill-defined mass at the hepatic flexure. Biopsies of this lesion revealed chronic active colitis with reactive epithelial changes, and an ulcer with granulation tissue. A multidisciplinary team was convened to manage the case. The patient successfully underwent laparotomy, extended right hemicolectomy, and en-bloc cholecystectomy with liver resection. Gross examination of the specimen showed a cholecystocolic fistula. Final histopathologic examination, however, revealed xanthogranulomatous cholecystitis with adenomyomatosis, without evidence of malignancy.

Recommendation: This report shows that XGC can potentially masquerade as colon cancer. A high index of suspicion and multidisciplinary approach are critical to properly manage a perplexing case. Extensive surgery may be reasonable where there is suspicion for malignancy and/or multiorgan involvement.

Abstract Submission No. 100071

P-0734

Zollinger-Ellison syndrome: A rare clinical case of Hepatic gastrinoma

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Clinical Case Summary: Zollinger-Ellison syndrome (ZES) is a rare syndrome that includes non-specific symptoms in the context of excessive gastric acid secretion. We report a rare case of a 38-year-old male patient with abdominal pain, dyspepsia, and diarrhea lasting more than 10 years who was treated at multiple hospitals in many countries without a definitive diagnosis of ZES, making the treatment ineffective, greatly affecting the patient's quality of life.

At our hospital, clinical examination revealed no special abnormalities. Laboratory tests showed the blood count, liver and kidney function, electrolytes within normal limits. Abdominal ultrasound only showed a 18x16 mm echogenic nodule in the liver.

Colonoscopy showed no abnormality. Gastroscopy showed Grade B reflux esophagitis, enlarged gastric folds and many ulcers in the D2 of duodenum with *Helicobacter pylori*-negative.

Because of the above-mentioned signs on endoscopic images combined with clinical manifestations, we suspected that the patient had ZES and conducted a fasting serum gastrin test, the result was 839 pg/ml which was very high compared to the normal threshold of <100 pg/ml. Moreover, abdominal MRI showed the hepatic nodule with atypical enhancement; the histopathological result of liver biopsy was Gastrinoma.

After having definitive diagnosis of Hepatic gastrinoma causing ZES, the patient was conducted **Radiofrequency ablation** of the liver tumor and treated with Proton pump inhibitors to reduce gastric acid secretion.

After 01 month of treatment, the serum gastrin level decreased to 126 pg/ml, his health improved significantly and no longer being suffered from diarrhea.

An important experience from this rare case is that the patient was only focused on the gastric acid treatment, but he was not paid attention enough to the symptoms of frequent loose stools in patients with reflux and the endoscopic image of multifocal D2 duodenal ulcer which is characteristic of ZES.

Abstract Submission No. 100094

P-0735

Ethanol ablation for intrahepatic bile duct dilatation in an elderly Patient

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Introduction: Surgical resection of the intrahepatic bile duct dilatation (IHBD) has traditionally been considered the only effective approach in symptomatic patients. We present a successful ethanol ablation of the IHBD in an 82-year-old patient.

Case report: An 82-year-old female sent to the hospital with fever, and right upper abdominal pain. Abdominal CT revealed the presence of common bile duct (CBD) stones, along with stones in liver segment 2 and 3, accompanied by left IHBD dilatation.

Endoscopic retrograde cholangiopancreatography was performed to remove the CBD stones and place an endoscopic retrograde biliary drainage. Surgical intervention for left lobe of the liver was declined due to the patient's advanced age. A percutaneous transhepatic cholangial drainage (PTCD) was placed in the left IHBD. Cholangiogram conducted via PTCD revealed a filling defect in the IHBD, with the contrast medium confined to the dilated IHBD, unable to flow downstream into the CBD.

Subsequently, we utilized PTCD to administer 95% ethanol into the left IHBD. The initial injection was 45ml, which was left in place for 30 minutes. Three days later, we administered an 80ml ethanol injection, following the same procedure. The daily drainage volume through PTCD was less than 10 ml. Afterward, we removed the PTCD, and the patient did not experience a recurrence of abdominal pain or fever during the subsequent three-month follow-up.

Conclusion: Ethanol ablation in IHBD can effectively treat patients with IHBD dilatation. It may serve as an alternative therapeutic approach for patients who are not suitable candidates for surgery.

Abstract Submission No. 100100

P-0736

A rare case of giant hepatic angiomyolipoma with malignant behavior

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Angiomyolipoma (AML) is usually a benign mesenchymal neoplasm located in the kidney, followed by the liver. First reported in 1976, today this rare tumor belongs to the family of perivascular epithelioid cell tumors and is typically composed of variable proportions of blood vessels, smooth muscle cells, and adipose tissue. It may be misdiagnosed as other diseases easily (e.g., hepatic cell carcinoma, IgG-4 disease) if it presents aggressive behaviors like large size (>5 cm), rapid growth rate, atypical liver biopsy results, and multiple organ involvement. We present a rare case of a 64-year-old man having complained of abdominal pain for months. He had a history of renal AML two years ago and underwent a right radical nephrectomy due to tumor rupture. There were not any liver tumors seen on abdominal computed tomography (CT) then. However, two years later, the abdominal CT showed multiple liver masses; the largest was 17.8 cm in the S4. The liver biopsy result revealed the diagnosis of hepatic AML (HAML). After multidisciplinary discussions, the patient refused the hepatectomy and only accepted transcatheter arterial chemoembolization (TACE). Unfortunately, active bleeding of the gastroduodenal artery happened after TACE. The patient then expired due to hypovolemic shock and multiple organ failure. Since 2000, only 17 cases of malignant HAML have been reported. The overall mortality rate associated

with typical HAML was 0.8%, but with malignant HAML was higher. Besides, it displays more aggressive behavior with a high recurrence and metastasis rate. Further research to predict this type of tumor is necessary.

Abstract Submission No. 100102
P-0737

A Case of Colonic Conduit Perforation in a patient with recurrent Gastroesophageal Adenocarcinoma

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Esophageal perforation is a life-threatening condition if not recognized promptly. Iatrogenic causes account for 73% of these perforations and may include NGT insertion. The mortality rate is 60% if intervention is delayed beyond 48 hours.

A 51-year-old male with GEJ carcinoma underwent radical subtotal gastrectomy, esophagectomy with gastric pull-up and chemotherapy. On annual PET scan, an enhancing soft tissue was noted and a gastroscopy was done showing an antral ulcer where biopsy revealed adenocarcinoma. Due to recurrence, he underwent takedown of gastric pull-up, colon interposition, cervical end-to-end esophago-colonic anastomosis, Braun jejunostomy, and feeding jejunostomy insertion. NGT was inserted blindly after the procedure. Days after, he developed pneumonia with pleural effusion and was started on antibiotics. He underwent VATS for deloculation and noted bile from the chest tube. Repeat VATS with intraoperative endoscopy was done showing an opening at the neoesophagus, 2 cm from the anastomotic site with connection to the pleural cavity confirmed by dye injection. Two resolution clips were deployed with no egress of air or dye afterwards. Blind NGT insertion is a bedside procedure that is done for feeding and decompression purposes. However, it can result to a serious complication when rigid type is used that can cause pressure leading to perforation. Common site of perforation is from previous anastomotic site. Management includes antibiotics, and prevention of further contamination. The decision to do a surgical or endoscopic therapeutic procedures depends on the clinical situation. Endoscopic therapy can be effective if performed for early perforation by means of clips.

Abstract Submission No. 100117
P-0738

Intestinal Lymphangiomatosis: A rare of cause of chronic diarrhea in young patient

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Introduction: Lymphangiomatosis is an exceedingly rare disorder primarily affecting the lymphatic system, commonly manifesting in head and neck regions, axillary and inguinal areas. Notably, colonic involvement is exceptionally rare, with no prior cases reported in Pakistan. Advances in diagnostic modalities have allowed for the detection of even uncommon gastrointestinal pathologies. This study reports a unique case of sigmoid lymphangiomatosis presenting as chronic diarrhea, diagnosed through MR enterography and subsequently treated via diagnostic laparotomy and sigmoid colon resection.

Case Report: An 18-year-old female presented with an 8-year history of chronic watery diarrhea, unresponsive to various treatments. The diarrhea, characterized by nocturnal awakening and significant weight loss, had persisted despite consultations with multiple specialists. Initial investigations, including blood tests and endoscopic evaluations, yielded no conclusive findings. However, MR enterography revealed substantial sigmoid wall thickening, interloop ascites, and lymphadenopathy. Following consultation with a colorectal surgeon, she underwent laparotomy, revealing a thickened sigmoid colon. Histopathology confirmed colonic lymphangiomatosis with dilated cystic spaces, cuboidal epithelium, congested blood vessels, and inflammation.

Discussion: Lymphangiomatosis, primarily affecting extra-colonic regions, is exceedingly rare in the colon, with a previously unreported case from Pakistan. Advances in diagnostic tools, including MR enterography, have enhanced the detection of such cases. The etiology of lymphangiomatosis remains uncertain, with congenital lymphatic malformations being a leading hypothesis. Colonic lymphangiomas typically present with diverse symptoms, and diagnostic methods like endoscopic ultrasound and MR enterography are instrumental. Management depends on symptomatology, ranging from conservative approaches to surgical resection for complications.

Abstract Submission No. 100140
P-0739

A successfully treated syphilis hepatitis in HIV infected patient

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Background: Liver involvement related to secondary syphilis is an unusual presentation. We present the case of an HIV infection patient with cholestasis hepatitis who was found with syphilitic hepatitis.

Methods: Case study reviewed a patient's medical record at Bhumibol Adulyadej Hospital, Thailand, in March 2022

Results: A 37-year-old man with HIV infection presented with fatigue and weight loss. Physical examination was remarkable for the multiple discrete, well-defined annular papules with excoriation and scale crusts with central atrophy on his face. The investigation showed abnormal liver function test: total bilirubin 2.62 mg/dL, direct bilirubin 2.11 mg/dL, aspartate aminotransferase (AST) 136 U/L, alanine aminotransferase (ALT) 235 U/L, and alkaline phosphatase (ALP) 1199 U/L. The abdominal ultrasonography revealed normal liver parenchyma without a space-occupying lesion. Liver histopathology found a focal aggregation of foamy macrophages in the hepatic lobule without significant necrosis and which negative staining for *Treponema pallidum*. The CD4 level was 544 cells/mm³. The blood test for Rapid Plasma Reagin (RPR) titer was 1:64 and the *Treponema pallidum* hemagglutination test was positive. Syphilis hepatitis was considered. The patient was given intramuscular benzathine penicillin 2.4 million units per week for three weeks. Six hours after the first dose of benzathine penicillin, the Jarisch-Herxheimer reaction was observed. All patient's symptoms and liver function tests were normal after 4 weeks of treatment.

Conclusion: Even though in HIV patients with normal CD4 levels, syphilitic hepatitis should be considered in markedly elevated alkaline phosphate and well-response to antibiotics may provide clues for the diagnosis.

Abstract Submission No. 100154
P-0740

A case of primary esophageal malignant melanoma with disseminated metastasis.

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Primary esophageal malignant melanoma is a rare condition which mainly affects males in the sixth to seventh decades of life. It is also a highly lethal disease, with a 5-year survival rate of less than 5% mainly due to its undetermined presentation and consequent late diagnosis. It is usually characterized by dysphagia and weight loss, which makes it difficult to differentiate from other types of esophageal malignancies. Immunohistochemical markers, such as S-100, HMB-45, and Melan-A are often required to confirm the diagnosis. A histopathologically proven case of primary esophageal malignant melanoma is described.

Abstract Submission No. 100172
P-0741

ACUTE PANCREATITIS COMPLICATING ACUTE HEPATITIS A AND E COINFECTION

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Introduction: Acute Hepatitis A and Acute Hepatitis E are common causes of jaundice in Asia Pacific region; We report a young boy, who had both hepatitis A (IGM) and hepatitis E (IGM) positive, and also was diagnosed to have Acute Pancreatitis; previously Acute Hepatitis E leading to pancreatitis has been reported (1)

Case: A 12 years old boy presented with history of fever, pain abdomen and jaundice of 3 days duration; He was evaluated, Liver function test was done, that revealed Increased bilirubin and transaminitis; SGOT/SGPT 4534 IU/7854;IU; Serum Bilirubin 6.2mg/dl; IgM HAV and IGM HEV both were positive; his pain abdomen persisted; Serum Lipase and Amylase were done: reported: 2304 IU and 1800 IU, respectively; USG abdomen, CECT abdomen and MRCP were done; which revealed Acute Edematous Pancreatitis with fluid collections; no necrosis was seen; No Gall stones seen; CBD was normal; serum PTH, lipids and triglycerides were normal; Patient was managed with IV fluids, supportive care, He improved gradually

Conclusion: The significance of this case report is to make clinicians aware about the fact that Acute Hepatitis A and E Coinfection can cause Acute Hepatitis in endemic region and can further lead to Acute Pancreatitis. Necrotizing pancreatitis can be prevented by timely fluid therapy.

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Abstract Submission No. 100201
P-0742

Hepatocellular carcinoma in patients with Polycystic liver disease: Three Cases Report

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Introduction: Polycystic liver disease (PLD) is a genetic condition characterized by multiple cystic formations in the liver. Modern diagnostics, using ultrasonography, CT scans, or MRI, identify PLD by the presence of over 20 liver cysts. In contrast, Hepatocellular carcinoma (HCC) is a primary liver cancer. HCC majorly affects those with chronic liver diseases. Despite their distinct natures, the coexistence of HCC and PLD presents unique challenges, mainly due to the lack of established surveillance guidelines for HCC in PLD patients. Here, we reported three patients HCC in PLD.

Case reports: Three notable cases depict this relationship: a 56-year-old female with hepatitis C and breast cancer history, a 71-year-old male with HCV and liver cirrhosis, and a 57-year-old male with alcohol, type 2 diabetes mellitus and HBV-related liver cirrhosis. All presented with non-specific symptoms. HCC diagnosis was triggered by rising AFP levels and unclear ultrasound results. Despite numerous treatments, their survival post-diagnosis spanned 9, 3, and 6 years respectively.

Discussion and conclusion: The diagnosis of PLD coexisting with hepatoma is complex, as PLD can potentially obscure typical hepatoma imaging markers. While ultrasound remains the primary diagnostic tool with 90% accuracy, its limitations in pronounced PLD cases make advanced imaging crucial. Treatment strategies are complicated due to the patients' multiple health conditions, requiring a mix of standard and customized approaches. As PLD patients' lifespan increases, more such overlapping cases are anticipated, emphasizing the need for ongoing research and knowledge-sharing in the medical community.

Abstract Submission No. 100267
P-0743

Septic thrombophlebitis of inferior vena cava after hepatocellular carcinoma treatment: A case report

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Septic thrombophlebitis of the inferior vena cava (IVC) is a rare but serious disease. We present a case of hepatitis C virus (HCV) related hepatocellular carcinoma (HCC) post radiofrequency ablation (RFA). The complication of IVC septic thrombophlebitis with persistent *Pseudomonas aeruginosa* and *Enterococcus gallinarum* bacteremia happened after procedure and successfully treated by antibiotics combination therapy.

Abstract Submission No. 100330
P-0744

Rare PKD1 mutations in an adult female with congenital hepatic fibrosis and ADPKD: a case report.

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Introduction: Congenital hepatic fibrosis (CHF) is a rare genetic fibrocystic liver disease that primarily affects children. However, CHF in adults, especially when occurring with autosomal dominant polycystic kidney disease (ADPKD), is extremely rare.

Case presentation: This study reports on a case of a 31-year-old female patient hospitalized for bleeding from esophagogastric varices. Physical examination revealed significant splenomegaly, biochemical tests indicated a slight elevation in liver enzymes, and a decrease in platelet count. The imaging examination showed significant dilation of the common bile duct and intrahepatic bile ducts, as well as multiple renal cysts. Liver biopsy revealed enlarged portal areas, bridging fibrosis, and numerous variably shaped small bile ducts. Genetic testing identified two unique mutations in the PKD1 gene, identified as compound heterozygous mutations composed of a mutation inherited from the father (c.8296T>C) and one from the mother (c.9653G>C). Based on the patient's multiple test results, she was diagnosed with mixed-type CHF in association with ADPKD. During her initial hospital stay, the patient underwent endoscopic treatment for gastrointestinal bleeding. This treatment showed beneficial short-term outcomes and no complications were observed. Moreover, a significant reduction in varices was observed in a gastroscopy examination 18 months later.

Conclusions: CHF is a rare genetic disease, and its co-occurrence with ADPKD is even rarer. Due to the nonspecific clinical symptoms of CHF, it is susceptible to misdiagnosis or oversight. For patients with unexplained cirrhosis, biliary dilatation and malformation, and polycystic kidneys, the possibility of CHF should be considered.

Abstract Submission No. 100345
P-0745

Progression of hepatic epithelioid haemangioendothelioma to noncirrhotic portal hypertension

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BACKGROUND:

Hepatic epithelioid haemangioendothelioma (HEHE) is a very rare liver tumour that is prone to missed diagnosis and misdiagnosis. Very few cases progress to noncirrhotic portal hypertension.

CASE SUMMARY:

The patient was a 32-year-old male who sought treatment 16 months prior due to abdominal pain. Multiple imaging examinations revealed multiple space-occupying lesions in the liver and lungs, and liver biopsy suggested inflammatory lesions. Sixteen months later, the patient presented with portal hypertension. Transjugular liver biopsy was performed. The results (Ki-67, approximately 10%; CD31 (+) and CD34 (+)) suggested HEHE, and the hepatic venous pressure gradient was 13 mmHg. Nocardia was detected in liver tissue. The patient was treated with sorafenib. However, treatment was terminated due to adverse reactions; the oesophagogastric varices then ruptured, with subsequent bleeding. After oesophageal variceal sclerotherapy and treatment of the gastric varices using tissue glue under gastroscopy, the patient's condition stabilized, and no further bleeding occurred.

CONCLUSION:

The diagnosis of HEHE requires multidisciplinary and experienced pathologists for confirmation. Bacterial infection may be one of the pathogenic mechanisms. For patients who do not have the option of

liver transplantation, treatment for noncirrhotic portal hypertension can improve quality of life.

Abstract Submission No. 100348
P-0746

Case Report of Simultaneous Treatment of Tuberculosis and Chronic Hepatitis C in 10 Patients

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Background: The efficacy and safety of simultaneous treatment of tuberculosis (TB) and hepatitis C virus (HCV) infection are limited. We aim to provide more evidence on this.

Methods: Clinical data were retrospectively collected and analyzed from adult patients with TB/HCV coinfection undergoing simultaneous treatment for both diseases at Jiangmen Central Hospital,

Results: From January 2010 to June 2023, a total of 181 adult patients with TB/HCV coinfection were admitted to our hospital. Among them, 10 cases met the inclusion criteria for simultaneous treatment. In these patients, Rifampicin free regimen (avoid drug-drug interaction) and sofosbuvir/velpatasvir were used. The 10 patients were all males aged 41-54 years. After simultaneous treatment, chest CT showed improvement in TB in 8 patients, similar findings in 1 patient, and pending follow-up in 1 patient. Currently, 4 patients are still undergoing tuberculosis treatment. Among the 10 patients, 9 received a 12-week course of sofosbuvir/velpatasvir, and 1 received a 24-week course, all achieved sustained virologic response at 12 weeks (SVR12). No adjustments to the anti-TB drug regimen were required during simultaneous treatment. Prior to treatment, 7 patients had elevated ALT levels above the upper limit of normal (ULN), and 9 patients had elevated AST levels above ULN. After treatment, all patients had ALT levels below ULN while 9 patients had AST levels below ULN. Albumin, APRI scores, and Fib-4 scores showed improvement after treatment. (Tables 1-4).

Conclusions: These 10 cases preliminarily suggest simultaneous treatment of TB/HCV coinfection is effective and safe.

Abstract Submission No. 100383
P-0747

Successful Endovascular Management of Pseudoaneurysm Following TACE: A Case Report

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Background: Transarterial Chemoembolization (TACE) is a widely accepted treatment for hepatic tumors, especially unresectable hepatocellular carcinoma (HCC). While generally safe, TACE can lead to severe complications, including liver abscess, liver failure, and non-target embolization. Arterial injuries like hepatic artery spasm or dissection can also occur, although pseudoaneurysms are rare. In this report, we describe a case of a successfully treated pseudoaneurysm following TACE using N-Butyl-cyanoacrylate (NBCA) glue embolization.

Methods: A 78-year-old man presented to the emergency department with melena lasting for 5 days. He had been receiving TACE for hepatocellular carcinoma in liver segment 8 for the past 5 years, with his most recent TACE procedure performed approximately a month ago. Computed tomography (CT) revealed hemobilia in the anterior branch of the right intrahepatic duct (IHD), common bile duct (CBD), and gallbladder (GB). Additionally, a pseudoaneurysm in the S8 hepatic artery was detected. The patient underwent NBGA glue embolization to treat the pseudoaneurysm.

Results: On CT, the pseudoaneurysm was successfully embolized, and the hemobilia resolved.

Conclusions: In patients undergoing TACE who present with melena, it is crucial to consider the possibility of iatrogenic arterial injury. Such cases can be safely and effectively managed through endovascular procedures.

Abstract Submission No. 100393

P-0748

Unusual AIH- Post renal transplant progressing to liver disease despite adequate immunosuppression

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Background: Recurrence of autoimmune hepatitis in known phenomenon and occurs in 17-33% of transplanted patients of liver. Risk factors implicated in recurrence include the susceptibility alleles HLA-DRB1*0301 or DRB1*0401 in the transplant recipient. HLA-DR locus mismatching, incomplete suppression of disease activity before transplantation are some of the mechanisms for rAIH. The other pupil is de-novo AIH with likely mechanism of autoimmunity against neo or self-antigen. This is very unusual case of auto immune hepatitis in post renal transplant patient despite immunosuppressive regimen with good adherence.

Case Report: The 50-year-old male, post renal transplant recipient (2013) on immunosuppression with tacrolimus and mycophenolate mofetil presented with complaints of abdominal distention and reduced urine output. On evaluation, USG abdomen showed changes of CLD with gross ascites. Ascitic fluid analysis showed high SAAG, low protein with SBP (cell count- 3359, N-70%). Upper GI endoscopy showed grade 1 varices with PHG. Transient elastography showed median of 75 KPA. On etiological front, non-alcoholic, non-diabetic, ANA 2+, speckled pattern, total Ig G levels 2130, normal 2D echo and hepatic vein doppler. Liver Biopsy showed mild to moderate lymphoplasmacytic inflammatory cell infiltrates in portal tracts with mild interface activity. Modified ISHAK HAI score 5/18, Fibrosis stage- 4-5/6. Steroids trial was given once SBP subsided, no improvement was seen. Patient advised Simultaneous Liver Kidney Transplant as further treatment modality.

Conclusion: AIH should be considered in all new onset liver disease patients. Patients may progress to end stage liver disease despite long term immunosuppression indicated for other condition.

Abstract Submission No. 100443

P-0749

Successful Autoimmune Hepatitis Management with Conventional Therapy in an Elderly Indonesian Man

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Introduction: Autoimmune hepatitis (AIH), epidemiologically had age peaks at 10-30 and 40-60 years. But some study reports incidence above 60 years old. As a specific population, diagnostic and management of AIH in elderly seems challenging. Notes should be made regarding atypical features, comorbidities, and tolerability of drugs when manage this specific population.

Case report: A 65 years old male with no past specific medical history was admitted with 1 month of jaundice. From laboratory, AMA was negative, ALT/AST were 591/793 U/L, IgG was 2004 (above normal) and ANA was 1:1000. Biopsy of the liver shown moderate lobular and portal inflammation, acute and chronic inflammatory cells (plasma cell and eosinophil) with periportal necrosis diffuse. Patient had history of hypertension.

This patient being managed by azathioprine and prednisone with evaluation of blood pressure intensively. After 2 month there was a significant improvement of jaundice, level of bilirubin (normal limit) and liver function (normal limit). No severe adverse effect were observed during therapy. There is no report of relapse up to 6 month during maintenance therapy.

Discussion: AIH is a rare condition, especially in elderly Asian males. Diagnostic and management AIH in elderly remain challenging. Intensive monitoring during treatment with tapering steroid as soon as possible became the key for management on this specific population.

Conclusion: This present case showing efficacy and safety of conventional therapy with a steroid and azathioprine for AIH in the elderly.

Abstract Submission No. 100509

P-0750

A Case of Clostridium difficile Detected on Rifaximin in a Patient with Alcoholic Liver Cirrhosis

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Case: Male, 40s.

Past History: Alcoholic liver cirrhosis, esophageal varices

April 2022: Infectious enteritis, Campylobacter bacteremia

Streptococcus bacteremia, hepatic encephalopathy (with multiple hospitalizations)

Clinical course: Patient has been in our hospital for alcoholic cirrhosis since March 2021. Liver function did not improve after abstinence from alcohol.

After abstinence from alcohol, his liver function did not improve, and he was hospitalized for repeated bacteremia and hepatic encephalopathy, so rifaximin was introduced on January 11, 2023.

On June 9, 2023, he was admitted to the hospital with frequent watery diarrhea and fever, and was diagnosed with infectious enteritis by CT scan.

On admission, both CD antigen and toxin were confirmed negative by fecal immunochromatography, and other stool culture tests were submitted. Rifaximin was continued. On the fourth day of admission, Clostridium Difficile was detected in a stool culture taken at the time of admission, and AZM was discontinued. Lower gastrointestinal endoscopy was performed the next day and showed only slight pseudomembrane formation. Since the antibiotic used at the time of submission of the stool culture test was rifaximin, it was discontinued and the patient is now under outpatient observation.

Discussion and Conclusion: We have experienced a case of Clostridium difficile caused by long-term oral use of rifaximin.

Abstract Submission No. 100594
P-0751

CASE OF ADVANCED LIVER FIBROSIS DUE TO HBV-INFECTION AND CONCOMITANT AUTOIMMUNE LIVER DISEASE

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Background: Non-organ specific autoantibodies particularly antinuclear antibodies (ANA) and anti-smooth muscle antibodies (SMA) have been reported frequently in HBV- and HCV-infected patients. In most of these cases autoantibodies are detected in lower titers compared to those found in autoimmune hepatitis (AIH), usually lack F-actin specificity of SMA. Chronic viral hepatitis concomitant with AIH often very difficult to be recognized given the heterogeneity of liver diseases, the absence of specific markers for the diagnosis.

Case report Patient A.S., female, 58 years old, BMI=32 kg/m², HBV-infection was diagnosed in April 2022. Patient was complained on fatigue, weight loss, subfebrile temperature, arthralgia, numbness of lower extremities. Comorbidities: Diabetes, diabetic nephropathy, polyneuropathy, angiopathy. Palmar erythema, in anamnesis 30 years age ectopic pregnancy. Abdomen US: hepatosplenomegaly, parapancreatic lymphatic nodes, minimal ascites. Fibrotest F3/A3, esophageal varix, 3rd degree. Quantitative PCR HBV DNA (*Abbott Real-Time™*) - **9.373.938** IU/mL, 7.0 Log; quantitative HBsAg (*ARCHITECT, Abbott*) - **4588.87** IU/mL AFP - **13.08** ng/mL IgG - **29.08** g/L (5.52-16.31 g/L). ASMA 1:100, F-actin 1:100 positive. Treatment with tenofovir alafenamide (TAF) and UDCA started in April 2022 with subsequent improvement of clinical manifestations, HBV DNA suppression, improvement of biochemical tests, AFP and IgG (Tab 1.).

Conclusion: In a few patients' chronic viral hepatitis B and AIH may co-exist. In countries with a high prevalence of viral hepatitis, diagnosis of concomitant AIH may be entirely overlooked in viral hepatitis infected patients. Management and follow up of patient with advanced fibrosis due to chronic HBV-infection and autoimmune is required combined approach.

Abstract Submission No. 100620
P-0752

A Rare, Benign Etiology of Isolated Elevation of AST in an Asymptomatic Individual: Macro-AST

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Introduction: Macro-aspartate aminotransferase (AST) is a high molecular mass complex of AST bound with immunoglobulins. It is a rare cause of isolated elevation of serum AST. We present a case of macro-AST in an asymptomatic patient without evidence of chronic liver disease.

Case: A 55 year old man was seen in the hepatology clinic for isolated elevation of AST for the past 3 years ranging from 106-181 U/L (reference range [RR] 8-48 U/L). Liver ultrasound demonstrated normal liver morphology. FibroScan calculated normal medial liver stiffness (4 kPa [RR <7 = no significant fibrosis]) and a Controlled Attenuation Parameter Score of 207 [RR S0 <248]). Serologic workup for etiologies of chronic liver disease including iron studies, ceruloplasmin, alpha-1-antitrypsin, anti-mitochondrial antibody, and hepatitis A, B and C were negative. Anti-smooth muscle antibody was positive with a 1:320 titer and ANA was negative. Liver enzymes were normal (total bilirubin 0.5 mg/dL [RR ≤1.2 mg/dL], direct bilirubin 0.1 mg/dL [RR

0.0-0.3 mg/dL], alanine aminotransferase 21 [RR 7-55 U/L], alkaline phosphatase 74 [RR 40-129 U/L]) apart from an elevated AST (95 U/L). The serum sample was stored at 4°C for 5 days and measured again. There was an observed 10.5% decrease in AST from 95 U/L to 85 U/L, indicating macro-AST.

Discussion: The method of measuring AST activity from a serum sample assayed at day 0 and day 5 is a cost-effective and reliable screening methodology for detecting macro-AST in the absence of other technologies. Identification of macro-AST as the etiology of serum elevation of AST can help avoid more invasive testing such as liver biopsy and unnecessary treatments.

Abstract Submission No. 100632
P-0753

Atezolizumab/bevacizumab followed by lenvatinib in a HCC patient with portal vein tumor thrombosis

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Introduction: Development of portal vein tumor thrombosis (PVTT) is associated with disease progression and poor prognosis in patients with hepatocellular carcinoma (HCC). Recent reports suggested that sequential systemic therapy improved prognosis in advanced HCC patients.

Case Presentation: A 70-year-old woman with cirrhosis due to hepatitis B virus infection showed tumor markers elevation during follow-up after treatment for HCC. She underwent RFA seven years before and underwent liver resection 4 years before. Contrast enhanced computed tomography and magnetic resonance imaging showed 13mm nodule in segment 8 and tumor in the portal vein. She was diagnosed as recurrence of HCC with PVTT. The extent of PVTT was classified as Vp2. She refused surgical treatment, and underwent treatment with atezolizumab plus bevacizumab. After second course of atezolizumab plus bevacizumab, she developed an anaphylactic reaction. She underwent lenvatinib therapy as second line systemic treatment. Three weeks after initiating lenvatinib, she developed pretibial edema and proteinuria (urine protein:creatinine ratio was 7.58 g/gCr). Her proteinuria was improved 2 weeks after the discontinuation of lenvatinib. We reevaluated HCC. Her tumor markers were decreased within normal range. Contrast enhanced ultrasonography did not detect blood flow in HCC and PVTT.

Conclusions: In this case, patient could not continue systemic therapy due to development of complications. However, the patient showed a remarkable response to a treatment with atezolizumab/bevacizumab followed by lenvatinib. Sequential therapy may be a useful treatment option for HCC patients with PVTT.

Abstract Submission No. 100667
P-0754

Hepatic sinusoidal obstruction syndrome: a rare complication of Paroxysmal Nocturnal Hemoglobinuria.

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A 20-year-old young man admitted to our institution presented with intravascular hemolytic anemia, symptomatic hepatomegaly, ascites, elevated liver enzymes and overt jaundice. He had a history of severe AA (SAA) treated by antilymphocyte globulin (ALG) and

combination of Cyclosporine A(CsA) and androgen successively. Abdominal enhanced computer tomography (CT) showed hepatic vein narrowing and patchy signal enhancement. The peripheral blood flow cytometry (FCM) showed that PNH clone increased up to 95.7%, which significantly indicated disease evolve to PNH (AA/PNH syndrome). Pathology of liver biopsy revealed microvascular thrombosis originating in the central lobule vein, accompanied with sinusoidal dilatation and mild centrilobular hepatocellular necrosis, indicated SOS. The patient was treated with anticoagulation by warfarin, keeping international normalized ratio (INR) between 2-3. The ascites and jaundice disappeared completely and liver function improved significantly. Hemoglobinuria was observed once during clinical course, regarded as acute attack of PNH. So he was started on methylprednisolone intravenous injection 40mg/day for 3 days then transitioned to oral prednisolone 50mg/day, with the stabilization of hemoglobin, the dose of corticoid decreased quickly. Eventually the patient's ascites and jaundice disappeared and liver function improved, the reexamined abdominal enhanced CT showed the injured hepatocyte vanished. He was followed up in clinic. The patient withdraw of corticoid himself, and hemoglobinuria relapsed, the patient didn't detect INR outpatient. The ascites recurrence 1 month ago.

Abstract Submission No. 100678
P-0755

AN ATYPICAL CAUSE OF MASSIVE HEMOBILIA IN A 66-YEAR-OLD FILIPINO MALE: A CASE REPORT

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Hemobilia is an unusual cause of upper gastrointestinal bleeding. It presents as a triad of jaundice, melena and abdominal pain. Half of these cases are secondary to trauma from invasive procedures done in the hepatobiliary tree. However, we present to you a case of hemobilia in the absence of an iatrogenic cause or a medical history of a hepatobiliary disease.

A sixty-six year old Filipino male presented with diffuse abdominal pain, melena, hematochezia and jaundice during the course of his admission. CT scan with angiogram revealed a heterogenous hepatic mass and intrahepatic biliary duct dilation probably secondary to tumor compression. UGIE and Colonoscopy showed no source of active bleeding and the scope was only passed until the transverse colon due to presence of blood clots. Successful Trans-arterial Embolization of the Hepatic Artery Pseudoaneurysm by Interventional radiology was done leading to resolution of the bleeding. Definitive management with surgery noted presence of multiple hepatolithiasis causing erosion of the left hepatic artery and left portal vein, leading to the hemobilia of this patient. Biopsy revealed Schistosomiasis with cirrhosis and chronic cholecystitis. Post operatively, there was no recurrence of the symptoms and the patient was discharged improved.

This report illustrates a classic case of hemobilia with an atypical cause, and highlights the roles of history, physical examination and radiologic workup in determining the diagnoses. High index of suspicion plus the use of an algorithm resulted to a prompt interdepartmental referral and appropriate management of the patient.

Abstract Submission No. 100737
P-0756

Non-Cirrhotic Portal Hypertension As An Unusual Manifestation of Hepatic Sarcoidosis

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Introduction: Sarcoidosis is an idiopathic systemic granulomatous disease, characterized by aberrant development of non-caseating granulomas in multiple organs. In Asia, the incidence of sarcoidosis is quite scarce (1-2 patients in 10,000 populations). In 50-65% of patients with sarcoidosis, hepatic granulomas can be observed, in which, only 5-15% will demonstrate clinical manifestation, including portal hypertension.

Case Illustration: A 23-year-old male arrived with recurrent abdominal discomfort and progressive dyspnea. He had a history of hematemesis and melena with esophagogastroduodenoscopy (EGD) examination revealed grade 1 esophageal varices and portal hypertensive gastropathy. His physical findings showed malnourished (underweight) nutritional status, anemic conjunctivae, decreased breath sounds on the basal and middle fields of left lung, and moderate abdominal distension. Laboratory examinations showed decreased hemoglobin (6.3 g/dl) with an increase of erythrocyte sedimentation rate (ESR) (109 mm/hour). A Computed Tomography (CT)-scan demonstrated left-sided pleural effusion; hepatomegaly; dilated intrahepatic biliary system; dilated intra-hepatic and extra-hepatic portal veins; accompanied with dilated superior mesenteric vein, splenic vein, and collateral formation towards left gastric vein. There was also a presence of loculated ascites and thickening of gastric and intestinal walls. An exploratory laparotomy procedure was performed, displaying frail liver with ongoing bleeding and perforated small intestine. Exteriorization and ileostomy procedure was performed on the perforated ileum. Histopathological findings from liver and peritoneum demonstrated non-necrotizing granulomas with dilated multiple vessels.

Conclusion: Sarcoidosis is an extremely rare condition; thus, making it potentially very difficult to diagnose. This case demonstrated a challenging process from clinical presentation to myriad diagnostic procedures to confirm sarcoidosis.

Keywords: sarcoidosis, non-cirrhotic portal hypertension, perforated intestine, unilateral pleural effusion

Abstract Submission No. 100773
P-0757

A case report on a 42-year-old male clinically diagnosed with Cowden syndrome

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Objective: To discuss a rare case of clinically diagnosed Cowden's Syndrome.

Introduction: Cowden syndrome is part of PTEN hamartoma tumor syndromes (PHTS) characterized by autosomal dominant mutations of the PTEN tumor suppressor gene. The presence of hamartomas is the defining clinical feature. PHTS have increased risk of both benign and malignant tumors, including colon cancers. However, some patients with mutations do not show clinical signs and symptoms, while patients with the clinical syndrome may not have detectable PTEN mutations.

Case Presentation: A 42-year-old man with macrocephaly and multiple trichilemmomas was diagnosed with benign nasopharyngeal mass, presenting as recurrent epistaxis. The patient was suspected to have PHTS hence referred for endoscopy to evaluate presence of gastrointestinal hamartomas. EGD revealed multiple esophageal glycogenic acanthosis. Colonoscopy showed innumerable polyps in the cecum, ascending and sigmoid colon. Biopsies of the polyps yielded juvenile

polyps, tubular adenoma and tubulovillous adenoma. No family member is suspected or confirmed to have PHTS. Based on the current National Comprehensive Cancer Network (NCCN) operational diagnosis of PHTS, patient satisfied three major criteria: macrocephaly, multiple trichilemmomas, and multiple juvenile polyps. Patient was then advised for colonoscopy every 2 years due to increased risk of developing colorectal cancer approximately 9 to 20%. Genetic counseling was advised for both the patient and family members.

Conclusion: PTEN gene mutations have poor penetrance. Even if PHTS is an autosomal dominant genetic condition, it may not be reliably detected in their family history. Screening colonoscopy is recommended because of increased risk of developing colorectal cancer.

Abstract Submission No. 100787
P-0758

Recanalization of portal veins by anticoagulation therapy in combination with embolization of SPSS

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Background: Studies have shown that the spontaneous portosystemic shunts (SPSS) may increase the risk of portal vein thrombosis (PVT). Anticoagulation therapy is the main treatment for portal vein thrombosis in patients with liver cirrhosis. However, the efficacy of anticoagulation maybe impaired when portal perfusion was diverted due to the presence of SPSS. Here we present a case of PVT treated by the anticoagulation therapy in combination with embolization of SPSS.

Case Report: A 53-year-old female patient was diagnosed with hepatitis B-related liver cirrhosis accompanied by portal vein thrombosis. The presence of large SPSS was found on CT scan. She had no previous history of hepatic encephalopathy. A plug was inserted into the shunt via the transfemoral access. Rivaroxaban was given at a dose of 10mg daily after the surgery. A CT examination 5 months later revealed the complete recanalization of portal veins and the disappearance of the SPSS.

Discussion: The presence of SPSS may be the potential reason of the PVT in the present case. Redirect the blood flow by the embolization of the SPSS may improve the efficacy of the anticoagulation therapy. Proper management of the SPSS should be taken into consideration in cirrhotic patient with PVT and large SPSS.

Abstract Submission No. 100801
P-0759

Primary biliary cholangitis in pregnant woman

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Background: Primary biliary cholangitis (PBC) is a rare immune-mediated, progressive chronic cholestatic liver disease, resulting in end-stage liver disease and its associated complications. PBC predominantly affects women, it is diagnosed at childbearing age in up to 25% of cases. Severity range from asymptomatic biochemical signs of cholestasis, through symptomatic disease presenting with fatigue, pruritus, sicca syndrome. Biochemical feature of PBC is increased serum ALP, immunoglobulin, particularly IgM, AST and ALT. Up to 70% of women with PBC had stable or improved serum liver tests during pregnancy, but increased liver disease activity was reported in 60-70% postpartum. Fetal outcome in PBC pregnancies is impaired, rates of

live births 58–76%, increased rates of preterm delivery of 6–33% and other neonatal complications. EASL recommends life-long ursodeoxycholic acid (UDCA) at 13–15 mg/kg/day as the first-line pharmacotherapy, should be continued during pregnancy as it is safe in pregnancy and breastfeeding.

Case report: 34 years old female, PBS diagnosed in 2021 (positive ANA, AMA, PCA, AP 547, GGT 241, AST 61 IU/ml) with UDCA prescription. In anamnesis complain on fatigue, nausea, anemia from 2012, splenomegaly from 2013, sicca syndrome diagnosed in 2017, first pregnancy interruption. Patient lost of follow up to March 2023, with 12 week of pregnancy. UDCA re-started with close monitoring of biochemical analysis and US. Delivery with Cesarean Section in 27.09.2023. with biochemical analysis in post-partum period.

Conclusions: PBC-specific experience in pregnancy is limited to case-series. Described case is interesting due to benign duration of pregnancy with UDCA therapy and fetal outcome.

Abstract Submission No. 100902
P-0760

Adult-Onset Still's Disease Mimicking Hemochromatosis: A Masquerade

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Background: Adult-onset Still's disease (AOSD) and hemochromatosis are two distinct disorders with some overlapping characteristics. Both are characterized by hyperferritinemia and abnormal liver function tests. While AOSD is distinguished by systemic inflammation, hemochromatosis mainly involves excessive iron absorption and deposition. Liver biopsies of patients with AOSD typically exhibit non-specific characteristics. However, no studies have reported the presence of iron deposition in liver biopsies of AOSD patients.

Case Presentation: This documents a case of a 58-year-old male with fever, arthralgia, and lymphadenopathy, whose initial clinical presentation did not fulfill the diagnostic criteria for AOSD. Diagnostic investigation revealed significantly elevated ferritin levels and hyperbilirubinemia, prompting consideration of both AOSD and hemochromatosis. Despite the consideration of hemochromatosis indicated by the findings from the liver biopsy, the negative HFE gene mutation testing further supported the diagnosis of AOSD. Treatment with corticosteroids led to a notable improvement in both clinical symptoms and biochemical markers.

Conclusion: The accurate diagnosis of AOSD poses challenges due to its nonspecific presentation. This case highlights the challenges involved in distinguishing AOSD from hemochromatosis, underscoring the need for comprehensive clinical, genetic, and histopathological examination. A multidisciplinary approach is imperative for the precise diagnosis and effective management of such intricate systemic conditions.

Keywords: Adult-Onset Still's Disease, Hemochromatosis, Ferritin, Liver Biopsy

Abstract Submission No. 100934
P-0761

Characteristics of Caroli's Disease Comorbid with Chronic Hepatitis B: A Case Series

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Background: Caroli's disease (CD) is a rare congenital condition characterized by multifocal, segmental, and non-obstructive dilatation of the intrahepatic bile ducts. As they can present some similar clinical manifestation, such as aminophosphatase elevation and fibrosis, when CD comorbid with chronic hepatitis B (CHB), it is often ignored.

Methods: Here we present a case series, and comprehensively demonstrate the characteristics of CD comorbid with CHB from several aspects, including clinical symptoms, imaging findings, pathological features, and genetic features.

Results: All seven patients in our series suffered intermittent upper abdominal discomfort, fatigue, and recurrent liver function abnormalities in the past (7/7). No specific characteristics was observed in the laboratory testing (elevated aminotransferase [2/7], elevated γ -glutamyl transpeptidase [3/7], slightly elevated bilirubin [1/7]). Ultrasound identified multiple hepatic cysts in all patients (7/7) and renal cysts in most patients (5/7). Radiological examination showed characteristic manifestation (central dots or tadpole sign) in all patients (7/7). The pathological examination showed saccular dilatation of bile ducts in 4/7 of patients, and slight to moderate fibrosis in 6/7 of them. 5 patients received whole exome sequencing, 3 of them carry suspecting pathogenic PKHD1 mutation (3/5).

Conclusion: No special clinical manifestation is found in CD comorbid with CHB, and the prevalence might be underestimated. Further data regarding long-term outcomes of CD comorbid with CHB is needed to tell us whether identifying CD in CHB patients is necessary.

Abstract Submission No. 100935

P-0762

Bleeding Rectal Varices Refractory to Endoscopic Treatment in Non-Cirrhotic Portal Hypertension

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A 71-year-old lady with previous chemotherapy for metastatic breast cancer developed massive haematochezia from bleeding large rectal varices (Figure 1), which was banded. CT mesenteric angiogram showed large peri-rectal varices with portosystemic collaterals without cirrhosis or splenomegaly. HVPg was 8.7mmHg. Due to recurrent bleeding with large residual varices and portosystemic collaterals, EUS-coiling of rectal varices was performed with 2x 10x14mm Nestor coils. This led to pressure re-distribution with post-procedure occurrence of 2 new but smaller rectal varices which bled and were treated with banding and clip (Figure 2).

Transhepatic portal venography showed terminal inferior mesenteric vein bifurcation into medial and lateral (right) branches, which respectively supplied the 2 new rectal varices. The rectal varices all drained rapidly into the left internal iliac vein (Figure 3). Embolization with a combination of coils and lipiodol/histoacryl mixture was performed. Portal pressure was 15mmHg pre-embolization and 17mmHg post-intervention. There was no further bleeding after. The recurrent bleeding post EUS-coiling was likely due to increased pressure in the proximal portosystemic shunt branches, not visible from EUS.

Liver biopsy revealed moderate steatosis with stage 1C pericellular fibrosis, consistent with porto-sinusoidal vascular disorder.

We report a patient with refractory bleeding of rectal varices with portosystemic shunt refractory to endoscopic interventions including EUS-coiling but was successfully treated with transhepatic venography and embolization. There is no consensus on the treatment of ectopic variceal bleeding. Embolization may be the preferred treatment

for bleeding ectopic varices with extensive portosystemic shunts as venography enables a more complete assessment of the portosystemic circulation.

Abstract Submission No. 100936

P-0763

Endoscopic Treatment Refractory Bleeding of Rectal Varices from Porto-Sinusoid Vascular Disorder.

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A 71-year-old lady with previous chemotherapy for metastatic breast cancer developed massive haematochezia from bleeding large rectal varices (Figure 1), which was banded. CT mesenteric angiogram showed large peri-rectal varices with portosystemic collaterals without cirrhosis or splenomegaly. HVPg was 8.7mmHg. Due to recurrent bleeding with large residual varices and portosystemic collaterals, EUS-coiling of rectal varices was performed with 2x 10x14mm Nestor coils. This led to pressure re-distribution with post-procedure occurrence of 2 new but smaller rectal varices which bled and were treated with banding and clip (Figure 2).

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We report a patient with refractory bleeding of rectal varices with portosystemic shunt refractory to endoscopic interventions including EUS-coiling but was successfully treated with transhepatic venography and embolization. There is no consensus on the treatment of ectopic variceal bleeding. Embolization may be the preferred treatment for bleeding ectopic varices with extensive portosystemic shunts as venography enables a more complete assessment of the portosystemic circulation.

Abstract Submission No. 100940

P-0764

Recurrent HCC with infiltration to inferior vena cava and portal vein: a case report

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Introduction: HCC is the most common form of primary liver cancer, accounting for 75%-85% of cases. Despite the approach of potentially curative treatments, up to 50-70% of individuals may experience a relapse in 5 years. HCC recurrence within 2 years of treatment is defined as "early", after 2 years is defined as "late". Early recurrence has a significantly poorer prognosis and outcome than late recurrence. Malignant vascular infiltration in HCC is usually an exclusion criterion for aggressive treatments like TACE and liver surgery or orthotopic

liver transplantation due to high recurrence and complication rates. The vascular infiltration is possibly associated with poor prognosis, and it is supposed to increase the risk of wide tumor transmission and the pressure of the portal vein.

Case Illustration: A 53-year-old male was admitted with a complaint of insufferable epigastric pain spreading to the right abdomen and the back. He had a history of HCC and had undergone a laparotomy liver resection and adhesiolysis 5 years ago. RFA was not recommended at the time considering the position of the nodule being near the gallbladder and portal vein. This time, liver biopsy showed a tissue resembling a moderately differentiated HCC in cirrhotic liver tissue and abdominal CT scan confirmed further infiltration of the HCC to inferior vena cava and portal vein.

Conclusion: The recurrence of HCC represents a relevant clinical issue, affecting 70% of patients undergoing curative treatment. This case demonstrated a challenging late recurrence of HCC with infiltration to inferior vena cava and portal vein.

Abstract Submission No. 101068
P-0765

A Successfully Resolved Case of Postoperative Bile Leakage with Biliary Ethanol Ablation Therapy

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Case Report: A man in his early 80's with a history of alcoholic cirrhosis, hypertension, and severe esophageal inflammation underwent a laparoscopic partial segmentectomy of segment (S) 4 for suspected carcinoma. Pathology revealed moderately differentiated hepatocellular carcinoma, pT3N0M0, pStage III, surrounded by Grade 3 fibrosis and burn-out non-alcoholic steatohepatitis. Postoperatively, a bile leakage was detected two months later via computed tomography. Initially, endoscopic internal drainage of the S4 bile duct was attempted but failed after two episodes of blood bacteremia from bile collection at the liver resection site, necessitating abscess drainage. Following an unsuccessful endoscopic internal drainage re-attempt, percutaneous transhepatic biliary drainage (PTBD) was performed twelve months postoperatively for the isolated S3 bile duct leakage site. About six months after PTBD, cholangiography showed persistent bile leakage. Subsequent attempts to penetrate the central obstruction of the S3 bile duct to the common bile duct via PTBD were unsuccessful. Eighteen months postoperatively, the patient underwent S3 intrahepatic biliary ethanol ablation therapy three times, with only minor complications, including fever and mild liver function test elevation. PTBD drainage volume decreased from 120 ml to 20 ml per day, enabling successful drainage tube removal after two weeks. There was no recurrence two months after the procedure. **Conclusions:** While the observation time after ethanol ablation remains short, we report a seemingly successful case of persistent postoperative bile leakage resolved through ethanol ablation of the responsible bile duct. For refractory cases of post-hepatectomy patients with bile leakage, ethanol ablation should be considered.

Abstract Submission No. 101069
P-0766

Steroid Treatment for Chronic Hepatitis B in Flare: A Case Report

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Background: Hepatitis B infection has diverse clinical manifestations including acute and chronic hepatitis B, liver cirrhosis, and hepatocellular carcinoma. To date, few cases have been reported about cholestatic hepatitis as a manifestation of chronic HBV infection in flare and here we present a case with improvement after prednisone.

Case Report: Patient is a 29 year-old male with Chronic Hepatitis B who presented with 1 month history of jaundice, icterisia, pruritus, easy fatigability, tea-colored urine, acholic stools. There was no history of drug ingestion and blood transfusions in the past. He has no family history of liver diseases. He is a non-smoker and occasional alcoholic drinker. Pertinent physical exam findings were icterisia, jaundice, non-distended abdomen with hepatosplenomegaly. Laboratory results showed transaminitis, hyperbilirubinemia, and elevated alkaline phosphatase; HBsAg, HBeAg, AntiHBc IgM, AntiHBc total reactive and HBV DNA 1385 copies/ml. Whole abdominal ultrasound and MRI of the upper abdomen were unremarkable. Liver biopsy showed subacute hepatitis with diffuse cholestasis (Fig. 1). Tenofovir standard dose and Prednisone 50 mg per day (15mg/kg/BW) tapering doses were given. Within a week, there was a dramatic reduction in pruritus and jaundice. At follow-up, the patient continues to be asymptomatic with HBV DNA undetectable; and has not shown any clinical or biochemical evidence of relapse.

Conclusion: Cholestasis due to Hepatitis B may be bothersome to patients. Steroids may be useful in patients with HBV infection and associated cholestasis. Prednisone 50 mg/day has shown to decrease bilirubins to <50% of its baseline levels.

Abstract Submission No. 101102
P-0767

Improvement of HCV-autoimmune hepatitis overlap syndrome with glecaprevir/pibrentasvir: Case report

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A 60-year-old man with type-2 diabetes and Chronic hepatitis C (HCV) was diagnosed with single hepatocellular carcinoma (HCC) of 67 mm in the hepatic posterior right lobe. We decided to multidisciplinary therapy, including molecular targeted drug. Lenvatinib 8 mg was initiated but discontinued because of grade 3 liver injury. The patient continued to have prolonged liver injury and persistently high immunoglobulin G levels of 2,632 mg/dL. Antinuclear antibody titer increased from 1:40 to 1:320. Histopathological examination of a liver biopsy specimen revealed interface hepatitis with lymphocyte and plasma cell infiltration, rosette formation, and emperipolesis, suggesting the possibility of autoimmune hepatitis (AIH). First, treatment with prednisolone was initiated; however, the response was poor. After starting glecaprevir/pibrentasvir (GLE/PIB) as direct-acting antivirals (DAAs), HCV RNA rapidly disappeared. The albumin-bilirubin grade was -1.94 (grade 2b) before DAAs and -3.04 (grade 1) at sustained virological response (SVR) 12, indicating liver function improvement.

After confirmation of SVR24, HCC recurrence was observed, and partial hepatectomy was performed. Background liver findings showed that liver parenchymal inflammation improved compared with that before DAAs treatment. There are few cases of DAAs treatment for HCV-AIH overlap syndrome. In the present case, we selected and treated GLE/PIB for DAAs. Liver function improved within a short treatment period of 8 weeks, as confirmed using serology and histology.

Abstract Submission No. 101116

P-0768

Primary Hepatic Neuroendocrine Tumor- A Case Report and Literature Review

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Primary hepatic neuroendocrine tumors (PHNETs) are rare neoplasms and challenging to distinguish from other tumors by imaging studies. A 43-year-old previously healthy female was referred for evaluation of a liver mass incidentally discovered on an abdominal ultrasound examination. A triphasic CT scan showed a hypodense lesion in the left lobe of the liver with early enhancement on the hepatic arterial phase and subsequent washout in delayed phases with a measurement of 2.0 cm. Upper endoscopy and colonoscopy yielded normal studies. The FDG-PET revealed an uptake only in the liver tumor. The patient underwent a laparoscopic left hepatectomy. Histopathological and immunohistochemical examination revealed a grade 1/2 neuroendocrine tumor. No other lesions were found one year after the surgery, making the diagnosis of PHNET highly probable. This case shows that diagnosing PHNET is a medical challenge, requiring differentiation of PHNETs and other hepatic masses and exclusion of occult primary neuroendocrine tumors. The excised tumor exhibited positive somatostatin receptor expression, and consideration of an octreotide scan is ongoing in the outpatient setting. This case emphasizes the importance of considering PHNETs in the differential diagnosis of a hepatic nodule.

Abstract Submission No. 101162

P-0769

A case of HCC with PSL-resistant irAE colitis after introduction of STRIDE followed by pneumonia

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Case: A 70-year-old man introduced STRIDE regimen in for hepatocellular carcinoma (HCC). After 10 days, he was admitted to the hospital with frequent diarrhea and abdominal pain. Sigmoidoscopy and biopsy revealed a diagnosis of irAE colitis. He was discharged on day 15, but symptoms flared up 2 days later. Increased PSL dose but no

improvement, he was considered to have PSL-resistant irAE colitis and started on IFX. He was discharged on day 33 but was readmitted and referred to pulmonary medicine because of decreased SpO₂ and ground glass opacity in both lobes. Suspected irAE pneumonia, PSL was increased. However, because of the high β -D-glucan levels, we could not rule out pneumocystis pneumonia(PCP) due to immunosuppression and started treatment at the same time. He was discharged home on day 89.

Discussion: Immune checkpoint inhibitors (ICIs) have become the mainstay of chemotherapy for HCC. STRIDE is the newest regimen and the most common irAE is diarrhea, but pneumonia can also occur. However, this patient was highly immunosuppressed prior to the onset of pneumonia and may have had an opportunistic infection. PCP in non-HIV patients has a high mortality rate of 30-50%, and 77.4% of patients have received steroids or chemotherapy. Having an appropriate response plan for both types of pneumonia is an important consideration in the future of cancer treatment.

Conclusion: It is important to be aware of irAEs associated with immunotherapy and to identify and manage opportunistic complications of immunotherapy in cancer treatment.

Abstract Submission No. 101186

P-0770

Early onset of ICI-colitis after STRIDE regimen in hepatocellular carcinoma

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Introduction: The HIMALAYA trial is the first chemotherapeutic trial to demonstrate the efficacy of combined immune checkpoint inhibitors (ICIs) for unresectable hepatocellular carcinoma (u-HCC). The regimen used in this trial is called the STRIDE regimen and consists of cytotoxic T-lymphocyte antigen-4 (CTLA-4) inhibitor, and programmed cell death ligand 1 (PD-L1) inhibitor. We herein report two cases of ICI-colitis, which occurred immediately after the start of the STRIDE regimen for u-HCC.

Case Presentation: A 73-year-old man and a 75-year-old man with u-HCC were treated with the STRIDE regimen. Both patients developed grade 3 diarrhea (Common Terminology Criteria for Adverse Events ver. 5.0) within 10 days of start of treatment. Colonoscopy revealed aphthous erosions and erythema extending from the terminal ileum to the rectum in one case, while the other showed aphthous ulcers in the terminal ileum and shallow ulcers in the colorectum. A histopathological examination of a biopsy specimen revealed epithelial cell apoptosis and neutrophil infiltration bodies, which were consistent with ICI-colitis. Prednisolone (0.5 mg/kg) was effective for both patients.

Conclusion: Our experience suggests the need for both the careful monitoring and early endoscopic examination of ICI colitis in patients with unresectable HCC treated with the STRIDE regimen.

Abstract Submission No. 101190

P-0771

INTRAHEPATIC CHOLANGIOCARCINOMA PRESENTING AS A LIVER AND ABDOMINAL WALL ABSCESS

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Background: Cholangiocarcinoma (CCA) is usually diagnosed late due to its silent clinical course, lack of specific radiologic findings, difficult-to-access location, and paucicellular nature. In rare cases, CCAs can present as a non-resolving liver abscess, leading to further delay in diagnosis and poor prognosis.

Case presentation: A 60-year-old female was admitted due to a recurrent abdominal wall abscess. She previously underwent percutaneous drainage via pigtail catheter insertion, which was eventually removed due to an apparent clinical improvement. She consulted at our institution due to recurrence of purulent discharge on the previous catheter insertion site. CT scan revealed a left hepatic lobe abscess with extension into the left rectus abdominis. Percutaneous drainage of the liver abscess was attempted but with only minimal fluid aspirated. Bacterial cultures were negative, while cytology was negative for malignant cells. Due to the non-resolution of symptoms after four weeks of antibiotics, a therapeutic trial of anti-tuberculosis (TB) medications was started. However, despite being on four months of TB treatment, she noted an enlarging epigastric mass associated with fatigue and progressive weight loss. Due to the progression of symptoms, malignancy was considered. A liver biopsy with immunohistochemical staining was performed and confirmed the diagnosis of cholangiocarcinoma. She was started on palliative chemotherapy with gemcitabine and capecitabine.

Conclusion: Intrahepatic CCAs mimicking an abscess pose a diagnostic challenge for clinicians. In patients with a non-resolving liver abscess without a clear etiology, malignancy should always be considered, with definitive confirmation through histologic examination and immunohistochemical staining.

Abstract Submission No. 101233
P-0772

Spinal Cord Ischemia After Transcatheter Artery Chemoembolization for Hepatocellular Carcinoma

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Case report: We report a case of 78-year-old male patient with chronic hepatitis B, diagnosed with HCC. He underwent the second TACE, and right after the procedure, the patient abruptly developed bilateral lower extremities motor weakness and sensory impairment below the T10 dermatome. Spinal magnetic resonance imaging showed T2-weighted scans showed increased intramedullary signal strength at the T1-T12 level. The patient received supportive care, ongoing rehabilitation, and steroid pulse therapy. The motor strength remained unchanged, but the sensory deficiencies practically disappeared.

Clinical discussion: The hepatic artery injury or decreased flow at the prior TACE site, which causes collateral recruitment, can explain why spinal cord injury following TACE typically happens after the second or third session. It can occasionally result from accidental embolized spinal branches originating from intercostal or lumbar collateral

arteries. In our case, we hypothesize the embolism caused the infarction to the spinal cord travel through the connection between the lateral branches of the right inferior phrenic artery and the intercostal arteries, which supply the spinal cord through the anterior spinal artery.

Conclusions: TACE in rare case can have severe complications. A tailored therapeutic strategy, including consideration of a shunt and selection of the vessels utilized for the Lipiodol infusion prior to TACE, is crucial to achieving an optimal end outcome to avert these significant consequences.

Abstract Submission No. 101237
P-0773

New laparoscopic approach for pancreatic duct stones

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Introduction: Chronic pancreatitis is characterized by irreversible structural damage, including fibrosis and compression of the pancreatic ducts, often leading to stones forming in the pancreatic duct and parenchyma. Surgery is indicated when severe obstruction with chronic pain is presented and conventionally drained by pancreatojejunostomy.

Method: A 56-year-old female patient with epigastric pain for many years. Computed tomography revealed an atrophic pancreas with a dilated pancreatic duct (18 mm) obstructed by a stone sized 1.3 cm. The patient underwent laparoscopic pancreatic duct exploration, used electrohydraulic lithotripsy for pancreatic duct stones, and then placed pancreaticoduodenal internal drainage with primary closure of the pancreatic duct. The operative time was 185 min, and the total blood loss was around 50 ml without intraoperative complication. The patient was discharged from the hospital on postoperative day 5 uneventfully. The epigastric pain symptoms dramatically decreased in the follow-up visit after one month.

Result: We combined several minimally invasive techniques to treat a chronic pancreatitis patient with a stone forming in the main duct in this patient. We used lithotripsy and internal drainage without the need for anastomosis. To our knowledge, this is the first report on this technique in literature. We found this technique is safe and applicable in selected patients to treat pancreatic stones with the dilated pancreatic duct.

Conclusion: In this case, we demonstrate a novel surgical treatment option for chronic pancreatitis with a simple and effective technique to manage pancreatic stones in chronic pancreatitis patients.

Abstract Submission No. 101299
P-0774

Unlocking the Hepatic Puzzle: A Case Report of Unraveling Autoimmune Hepatitis

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Autoimmune Hepatitis is an uncommon liver condition characterized by the immune system mistakenly attacks liver cells. This report contributes by detailing a specific case, emphasizing the patient's presentation, diagnostic journey, and successful therapeutic interventions. This case underscores the necessity of a multidisciplinary approach, involving, hepatologists, gastroenterologist, and immunologists. It

highlights the ongoing surveillance and adaptability in treatment plans and emphasizing the holistic care.

A 31y.o female who presented to the ER with a one-week history of profound fatigue. Over the past year, the patient reported persistent fatigue, joint pain, and stiffness. A six-month history of intermittent erythematous maculopapular rashes was also noted. Regular medication use was denied. No significant past medical history. Vital signs were within normal limits. BMI 22.3 kg/m². Physical examination revealed tenderness on palpation of the wrists, MCP joints, and right ankle. Laboratory investigations revealed an incidental elevation of SGOT(224 U/L), SGPT(201 U/L). Immunological testing revealed a positive ANA with a speckled pattern and negative AMA, dsDNA, and p-ANCA. Abdominal ultrasound demonstrated a bright liver with no intra and extrahepatic bile duct dilatation. Liver biopsy revealed lymphoplasmacytic infiltrates reaching the limiting plate and intralobular lymphocyte infiltration. Endoscopic examinations ruled out IBD. The patient was initiated on intravenous Glycyrrhizin, Omeprazole, and oral Silymarin. Prednisone was initiated at 40 mg/day, followed by a tapering regimen. Azathioprine was initiated at 50 mg/day one month later. The patient's liver function tests normalized, and clinical improvement was observed. Subsequent tapering of prednisone and escalation of azathioprine were performed, leading to sustained clinical improvement.

Abstract Submission No. 101301
P-0775

Paraneoplastic Jaundice and “double expressor” Diffuse Large B-Cell Non-Hodgkin's Lymphoma(DLBC-NHL)

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To our knowledge, only three cases on DLBC-NHL presenting with jaundice are reported. This case report will help elucidate further knowledge on the etiology of jaundice in patients with suspected malignancy.

A 63-year old male with no known co-morbidities with prior history of cholecystectomy presented with two-months of progressive painless jaundice (icteresia and tea-colored urine) and weight loss of 10kg. Work up revealed: ALT 229mg/dl, ALP 560U/L, GGT 528mg/dl, Total Bilirubin 15.86md/dl, Conjugated Bilirubin 15.38mg/dl, Normal CBC, PT INR, Crea and TSH[JC1] . ANA was negative. PIVKA II, AFP and CA 19-9 are normal. Negative for Hep A, B and C. MRI of the upper abdomen with IV contrast and MRCP was done revealing: Unremarkable Liver and Biliary Tree, Enlarged para-aortic Lymph nodes and blastic lesions at the left hemipelvis, T9-L1 vertebral bodies. Biopsy of the lymph node and pelvic lesion revealed a High Grade B-Cell NHL. Immunohistochemical staining done showed strong positivity to CD10, CD 20, Bcl-6(70-80%), Bcl-2(70-80%), c-Myc(60-70%), ki-67(80%). This concluded the diagnosis of a “double expressor” DLBC-NHL. He was given Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone chemotherapy for 6 cycles. After completion of chemotherapy his work revealed: Total Bilirubin 0.26mg/dl, Conjugated Bilirubin 0.16mg/dl.

Cholestasis as a paraneoplastic manifestation of NHL is not yet well recognized and fully understood. NHL can be a differential if work up fails to reveal a primary pancreaticohepatobiliary disease. Knowing other possible cause of jaundice can help in directing work up and prompt initiation of treatment

Abstract Submission No. 101344
P-0776

PSEUDO-DOMINANT INHERITANCE IN WILSON'S DISEASE: A CASE REPORT

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INTRODUCTION: Wilson's disease (WD) - monogenic disorder with autosomal-recessive transmission, but paradoxical and atypical inheritance cases have been reported. We describe a family in which WD was first diagnosed in a sister, and as a result of the screening, the brother and his 2 children were identified with WD.

CASE REPORT: Proband was diagnosed with WD at the age of 30 years when she was pregnant. As a result of the evaluation of the unexplained cytolytic, the diagnosis of WD in the phase of compensated liver cirrhosis was established. After examining her family, her 35-year-old brother and his 3- and 6-year-old boys were diagnosed with WD as well. They were clinically asymptomatic but had cytolytic, reduced ceruloplasmin, and elevated 24-hour urinary copper. On abdominal ultrasound, the father had hepatosplenomegaly without signs of portal hypertension, the older boy - hepatomegaly, and the youngest - without significant changes. They have not suffered from liver disease before. None presented neurological manifestations, the MRI was without specific changes and the Kayser-Fleischer ring was absent. In the proband and her brother, the same type of WD-causing mutations - c.2304dupC/c.2292C>T - was revealed in exon 8. In children, the pathogenic variant p.H1069Q was identified in a heterozygous state, but it was impossible to examine exon 8; the second mutation is currently unknown.

CONCLUSIONS: This case report shows how essential the family history is after registering a new WD patient. Thus, screening must be applied not only to parents and siblings but also to offspring.

Abstract Submission No. 101353
P-0777

A case of giant-tree-type gastroesophageal varices successfully treated with PTO.

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A 66-year-old woman, who had been treated with methotrexate and adalimumab for Rheumatoid arthritis, was transported to the emergency room due to blood vomiting. Contrast-enhanced CT failed to reveal active hemorrhage; however, a large variceal vein with a diameter of 6 mm was identified, extending from the gastric varices at the cardia to the lower esophagus. Emergency esophago-gastro-duodenoscopy (EGD) revealed consistent findings, confirming the presence of giant-tree-type varices in the patient. Since no bleeding spots or clots were observed, endoscopic hemostatic procedures, such as endoscopic variceal ligation (EVL), were not performed at that time. On the fourth day, percutaneous transhepatic variceal embolization (PTO) was performed, and the left gastric vein which was identified as the source of the blood supply was embolized. Follow-up EGD showed whitening of the varices. Subsequently, endoscopic injection sclerotherapy (EIS) was performed for the remaining esophageal varices and the patient was discharged on the 20th day. Although the etiology of liver cirrhosis in this case was unclear, there was a history of treatment with methotrexate for rheumatoid arthritis, and its involvement could

not be ruled out. For giant-tree-type esophageal varices, treatment with EIS or EVL is considered to be at high risk, and a combination of these, such as EISL or endovascular therapy, is usually employed. In this case, we successfully conducted percutaneous transhepatic variceal embolization for a giant tree-type esophageal varices.

Abstract Submission No. 101358

P-0778

Hepatic Artery Aneurysm: An unlikely cause of Obstructive Jaundice

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Introduction: Hepatic artery aneurysms (HAA) are uncommon and asymptomatic until it ruptures. Although they account for only 20% of visceral artery aneurysms, they carry a 30% mortality rate if they rupture. HAA presents as epigastric pain, jaundice and shock. The typical causes of HAA are atherosclerosis, mediointimal degeneration, trauma and infection.

Case presentation: A 40 year old woman presented with 1 month history of epigastric pain associated with occasional vomiting followed by pruritus and jaundice. Initial Ultrasound revealed an intrahepatic aneurysm of the portal vein. Follow up CT scan then revealed a hepatic artery aneurysm (2.97 cm X 3.69 cm) with associated biliary obstruction. ERCP with stent insertion was attempted however common bile duct access was not achieved despite pancreatic sphincterotomy due to long loop access. PTBD and Hepatic Arteriogram with embolization was offered however the family was not amenable. Surgical approach was done to relieve the biliary obstruction and repair the aneurysm at the same time. Intraoperative findings were a saccular aneurysm in the mid proper hepatic artery about 4 cm in diameter with a 1.5 cm defect, displacing the common bile duct (CBD) laterally. Repair of the proper hepatic aneurysm was achieved by vein patching followed by cholecystectomy then T - tube insertion in the CBD. The patient recovered well after the procedure with decrease in jaundice and no recurrence of abdominal pain.

Conclusion: This case highlights the approach and alternatives in managing hepatic arterial aneurysm presenting with obstructive jaundice and rupture in a resource – limited setting.

Abstract Submission No. 101363

P-0779

Hepatocellular carcinoma with PV invasion and L/N metastasis cured with multidisciplinary treatment

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Case: A female in her 70's with HCV, she had received TACE and RFA for HCC and no recurrence for last five years. This time, a hypovascular tumor appeared at S5/6 and invade into right posterior portal vein. She had received hepatectomy first, but PVTT could not be resected completely due to limitation of her hepatic reserve and progressed into origin of right portal vein rapidly. AFP increased to over 11,000 (ng/ml). For residual tumor and PVTT, HAIC with NewFP

regimen was introduced with temporarily implantable port and catheter system. After two courses of HAIC, CT revealed good *deposition* of lipiodol into residual tumor and PVTT, but two L/N metastases appeared behind pancreas newly and AFP re-increased, then irradiation with 30Gy/10fr was introduced. AFP remained still high (8,000 level), then Lenvatinib was administrated with 12 mg/day and AFP decreased to 3,000 level, but interrupted and reduced to 8mg/day due to thrombocytopenia, and interrupted again due to duodenal bleeding. CT revealed two L/N metastases reduced, but another metastasis appeared at para-aortic portion and AFP re-increased to 6,000 level. Instead, Sorafenib was administrated with the dosage of 800 mg/day, but interrupted due to high fever 10 days later. However, AFP decreased dramatically to normal range in two months and CT revealed L/N metastasis also reduced and disappeared finally. After that, she has been alive for five years.

Conclusion: Multidisciplinary treatment with combination of resection, HAIC, irradiation and systemic chemotherapy seemed to be effective in this advanced case with PV invasion and L/N metastasis.

Abstract Submission No. 101366

P-0780

A Serial Case Report: Successful Methylprednisolone Therapy for Biliary Atresia

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Introduction: Biliary atresia (BA) is the most common cause of obstructive cholestasis characterized by progressive intrahepatic and/or extrahepatic biliary fibrosis and destruction. In nearly 50% of patients, intrahepatic cholangiopathy remains unresolved after KPE. Based on the recent pathogenesis of BA, immune dysregulation plays an important role in fibrosis and biliary obstruction processes.

Case: First case, a 2-month-old girl with jaundice since birth, acholic stool, total bilirubin of 9.2 mg/dL and direct bilirubin of 6.4 mg/dL. Ultrasound revealed no visible gallbladder. Liver biopsy showed chronic hepatitis without fibrosis. Second case, a 3-month-old boy with jaundice since 2 weeks of age, urine-like tea, with a total bilirubin of 11.78 mg/dL and a direct bilirubin of 7.31 mg/dL. Ultrasound revealed a triangular cord sign, and liver biopsy showed extrahepatic cholestasis and mild fibrosis (F2). Third case, a 2-month-old boy with jaundice for 2 weeks, total bilirubin 10.7 mg/dL, direct bilirubin 7.5 mg/dL. Liver biopsy showed extrahepatic cholestasis and mild fibrosis (F1). All cases were treated with methylprednisolone 2 mg/kg/day. Clinical manifestation, bilirubin, liver function test, and abdominal ultrasonography improved following treatment. All patients had no jaundice, had pigmented stools, and yellow urine.

Results: This case series showed infants with BA who received oral methylprednisolone. In our three cases, all showed a good response to methylprednisolone treatment.

Conclusion: This case series provides evidence that steroids have potential effect on the suppression of bile duct inflammation and obliteration. Immunomodulatory treatment with steroids may stop the biliary inflammatory process.

Keyword: Biliary Atresia, Jaundice, Infant, Methylprednisolone

Abstract Submission No. 101427

P-0781

Gallstone ileus case report

An elderly patient presented with abdominal pain and vomiting for days

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A 81-year-old male had the underlying diseases poorly differentiated gastric adenocarcinoma status post wedge resection with recent recurrence at anastomosis. One 4.3 cm laminated gallstone had been documented on abdominal computed tomographic (CT) 5 months ago. This time, he presented to the Emergency Department with intermittent vomiting for 4 days and periumbilical pain for 1 day. Physical examination revealed soft but distended abdomen with periumbilical tenderness. The bowel sounds were decreased on abdominal auscultation. Lab testing revealed an elevated white blood cell count (19800/ μ L) and an elevated C-reactive protein (1.66 mg/dL). The abdominal CT revealed wall thickening of gallbladder with internal air density, and a gallstone impaction in the small bowel with proximal bowel loop dilatation. Upper gastrointestinal endoscopy showed a small hole at duodenal bulb, suspected fistula formation. Under the impression of cholecystoduodenal fistula related gallstone ileus, the patient underwent open enterolithotomy. A huge gallstone, locating at proximal jejunum was retrieved by enterolithotomy. He had an uneventful recovery thereafter.

Abstract Submission No. 101440

P-0786

Case of Hepatopulmonary Syndrome in Cirrhotic Patient with Primary Biliary Cholangitis

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Definition of Hepatopulmonary Syndrome (HPS) is reduced arterial oxygen saturation due to dilated pulmonary vasculature in the presence of advanced liver disease or portal hypertension. Currently there is no medication established as an effective therapy and only possible cure is liver transplantation. Therefore Cirrhotic patients complicated by HPS have poor prognosis. We herein report a case of HPS in cirrhotic patient with primary biliary cholangitis (PBC).

A woman in her early 60s who had been diagnosed with liver cirrhosis due to PBC before fourteen years, had experienced episodes of respiratory discomfort before two years in daily life and moreover easy fatigability and dyspnea to and from hospital before eight months.

She admitted at our hospital for treatment of portal venous thrombus and in addition we examined the cause of dyspnea. She was diagnosed with hypoxemia because her degree of oxygen saturation at rest was 80% level and that in exertion was 70% level. Because arterial blood gas analysis showed alveolar arterial oxygen difference (A-aDO₂) widen (86.1mmHg), we suspected HPS and examined 99mTc-MAA pulmonary perfusion scintigraphy (PPS) and contrast echocardiography. 99mTc-MAA PPS showed extrapulmonary accumulation (shunt fraction 14.2%). Contrast echocardiography Microbubbles were seen in the left atrium and left ventricle in 4 beats after the injection. Based on above, we diagnosed HPS.

Many of cirrhotic patients have been elderly people who have heart and pulmonary diseases. In case of cirrhotic patients who have dyspnea, We should exclude heart and pulmonary diseases and at the same time carefully observe to bear in mind that HPS might be latent.

Abstract Submission No. 101441

P-0787

Effect of Probiotic Supplementation in Neonatal Jaundice: an Evidence-Based Case Report

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Background: Neonatal jaundice (NJ) is one of the most common causes for neonatal readmission in the first weeks of life. Phototherapy as the main treatment for NJ often results in prolonged hospital stay and other unwanted side effects such as hyperthermia and dehydration. With underdeveloped normal intestinal flora, neonatal probiotic supplementation could assist to improve the recovery of NJ, through reducing enterohepatic circulation, suppressing beta glucuronidase enzyme activity, and improving intestinal pH.

This study aims at evaluating the use of probiotic supplementation in NJ patients who received phototherapy.

Method: A systematic search was conducted in Pubmed, Medline, and Scopus to retrieve primary studies published between 2013 and 2023. Quality and bias assessment were performed using Oxford tool. The main outcomes was the total serum bilirubin level and the duration of phototherapy or hospitalization.

Result: 2 RCTs with low risk of bias involving 166 neonatal with jaundice were included in this EBCR. Result showed total serum bilirubin levels were significantly reduced in both probiotic groups compared to both control groups. Probiotic supplementation also successfully reduced the duration of phototherapy or hospitalization in both studies.

Conclusion: Both of the studies agreed that probiotic supplementation had successfully reduce the duration of phototherapy as the main treatment for NJ. This can help minimize the risk of unwanted side effects from phototherapy.

Abstract Submission No. 101494

P-0788

WAUGH'S SYNDROME: CASE OF ADULT COLO-COLONIC INTUSSUSCEPTION WITH MALROTATION IN A 61-YEAR-OLD MALE

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Significance: The coexistence of gut malrotation and acute-onset intussusception is termed as Waugh syndrome. It is extremely rare in adults as most commonly presents in infants. We discuss the case of a male patient born with deformities of the extremities, diagnosed with malrotation with colo-colonic intussusception at a late age, and an ascending colon mass as a lead point.

Clinical Presentation: This is the case of a 61-year old male coming in due to a 1-week history of loose stools, cramping abdominal pain, and gradual abdominal enlargement which eventually led to difficulty passing of stool. Additional physical examination revealed

macrodonia, long extremities with oligodactyly of the fingers and polydactyly of the foot suspicious for a syndromic presentation.

Management: Abdominal CT scan revealed a long segment intussusception from the level of the ano-rectal area, which also involved the sigmoid colonic segment, left colon and parts of the transverse colonic segments. The rest of the evaluable colon was air distended. Hence, a total colectomy, reduction of colo-colonic intussusception, end ileostomy was done. Histopathology revealed a Mucinous adenocarcinoma of the transverse colon as the lead point.

Recommendation: The diagnosis of intussusception with malrotation requires a high index of suspicion. As malrotation itself can predispose to intussusception, an additional presence of intraluminal pathology would increase its risk. This necessitates appropriate surgical intervention because of the high incidence of underlying bowel malignancy. A good quality contrast-enhanced CT scan of abdomen can help to diagnose both these conditions and surgery remains the treatment of choice for managing these two conditions.

Abstract Submission No. 101531
P-0789

Primary biliary cholangitis masquerading as secondary hemochromatosis in a middle-aged male

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Background: Primary biliary cholangitis (PBC) is characterised by biliary epithelial injury, causing apoptosis and ductopenia. Earlier thought to be exclusively a disease of middle-aged women, with a gender skew of 10:1; current data shows that it is not as uncommon in male (4:6:1).

Methods: We report a 63 years old Indian male smoker presenting with itching and darkening of skin for 3 years and yellow discolouration of eyes for 1 year. General examination revealed icterus, pruritic nodules over bilateral arms, thighs and back with darkening and lichenification. Systemic examination unremarkable. LFT revealed direct hyperbilirubinemia with cholestatic pattern. HbA1C was 6.5%. Serum iron was increased, transferrin receptor saturation > 50% with normal ferritin. Ultrasound abdomen showed normal liver size, heterogeneous echotexture, no intrahepatic biliary radical dilatation or extrahepatic obstruction. Median liver stiffness was 14.6 kPa. Hepatitis B, C serologies were negative. IgG > 1.1X upper limit. ANA (immunofluorescence) negative. Autoimmune hepatitis serology negative; AMA positive. Liver biopsy showed medium sized bile duct injury with periportal fibrosis, CK7 staining demonstrated loss of bile ducts; Nakanuma stage 2. MRCP showed normal extrahepatic biliary tree.

Result: Based on raised Alkaline phosphatase, AMA positivity and liver biopsy, PBC was diagnosed and managed with UDCA. As pruritus did not improve, a trial of obeticholic acid and rifampicin was given, with good response.

Conclusion: Diagnosis of PBC should be considered in both sexes presenting with abnormal LFT, pruritus or fatigue in the susceptible age group. Early detection of PBC slows its progression to chronic liver disease.

Abstract Submission No. 101532
P-0790

A rare gastric tumor: mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN)

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Mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) is a rare neoplasm representing about the third of all poorly differentiated neuroendocrine carcinomas (PDNEC). MiNEN is composed of a neuroendocrine component, usually a PDNEC, and a non-neuroendocrine component, generally adenocarcinoma. Due to the lack of evidence, MiNENs are commonly treated according to the standard treatment for neuroendocrine carcinoma or adenocarcinoma from the same sites of origin. The prognosis is generally intermediate between the pure neuroendocrine and non-neuroendocrine carcinoma.

Mrs. Cao, a 40-year-old woman, who didn't have any systemic disease, visited for esophagogastroduodenoscopy. She mentioned sometimes epigastric fullness with dyspepsia, especially after meal, for about 3 months. However, the symptoms always subsided spontaneously and there was no vomiting, abdominal pain, black or bloody stool. While endoscopic exam, we found a huge tumor, around 6 centimeters, with thick stalk, growing from the great curvature side of gastric middle body. This tumor firstly stuck on the duodenum and distorted the stomach. After pulling it out from pyloric ring, we did polypectomy using single-use snare and retrieved the specimen. Afterward, the pathologist found the tumor was infiltrated both by neuroendocrine tumor (positive synaptophysin, chromogranin, CD56 in immunohistochemistry stain) and adenocarcinoma (loss synaptophysin, chromogranin and CD56) and the diagnosis of MiNEN was defined.

Here, we report accidentally found gastric MiNEN. Since there are no specific symptoms or definite risk factors of MiNEN, the diagnosis of MiNEN is usually accidental and late. MiNEN is still a wicked tumor that warranted more studies and attentions.

Abstract Submission No. 101583
P-0791

Progression of portal hypertension after atezolizumab plus bevacizumab for hepatocellular carcinoma

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Background: Immune checkpoint inhibitor becomes the first-line therapy for advanced hepatocellular carcinoma (HCC). Gastroesophageal varices should be monitored and managed due to the endothelial effect of bevacizumab. However, whether the progression of varices and portal hypertension during therapy is unclear.

Method: A case of portal hypertension progression (e.g., development of varices, ascites, and hepatic hydrothorax) during atezolizumab/bevacizumab therapy at National Taiwan University Hospital was reported, and the relevant literature from Pubmed were reviewed.

Results: We presented an 83-year-old male with resolved hepatitis B without cirrhosis. He had an 18cm HCC at BCLC stage C and received tri-weekly atezolizumab 1200mg/bevacizumab 500mg therapy for 34 cycles with sustained partial response. However, progressive ascites,

esophageal varices and left hepatic hydrothorax developed afterwards, even though his portal vein was patent and the tumor was under control. After the literature review, we found 3 case reports and one case series with 5 cases of HCC (BCLC B/C: n= 3/2). Among them, three had cirrhosis and all had small esophageal varices before treatment. One had a portal vein invasion. After 1~15 cycles of atezolizumab/bevacizumab therapy, progression of varices was found in 1 patient, and the other 4 patients developed variceal bleeding. None of these patients received beta blocker prophylaxis.

The association between atezolizumab/bevacizumab and portal hypertension was possible and multifactorial, which might involve VEGF pathway and immune-related adverse events with hepatic fibrosis.

Conclusion: Atezolizumab/bevacizumab treatment might be associated with exacerbation of portal hypertension. Monitoring signs and prophylaxis management of portal hypertension should be considered during treatment.

Abstract Submission No. 101595
P-0792

Case of PVT diagnosed and treated conservatively for hepatic mass with hepatolithiasis.

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We describe a case in which a postoperative patient with invasive intrahepatic papillary mucinous carcinoma (IPMC) developed a hepatic mass, which was diagnosed as portal vein thrombosis (PVT) and successfully treated conservatively by a combination of contrast-enhanced CT (eCT) and EOB-MRI. The patient was a 72-year-old man who had undergone pylorus preserving pancreatoduodenectomy for IPMC. He developed intrahepatic stone due to anastomotic stenosis and was treated endoscopically. He presented to one's previous doctor with nausea and anorexia as his main complaints and intrahepatic stones were found on CT. He was referred to our department and admitted for treatment of intrahepatic stones. eCT showed a 40 mm-sized hypodense mass in S8 of the liver, which initially suggested the possibility of a neoplastic lesion, and we decided to perform a thorough examination of this lesion and treatment of intrahepatic stones. On admission, eCT was performed again and revealed a mass in S8 of the liver, which was thought to be an ischemic change in the liver secondary to obstruction of P8. Three months later, when the patient was hospitalized for stone removal, eCT was performed, confirming that the lesion had decreased in size and the thrombus had also improved. Intrahepatic stones were also removed. This patient had a hepatic mass after IPMC surgery, and we had difficulty differentiating it from a metastatic liver tumor. When a hepatic mass is found in a patient with intrahepatic stones, it is important to differentiate secondary changes due to PVT and to perform imaging diagnosis.

Abstract Submission No. 101597
P-0793

A case of acute liver failure due to AIH complicated by APS type 3

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A 55-year-old woman, who had been diagnosed with type I diabetes mellitus, chronic thyroiditis, was transferred to our hospital because of severe acute hepatitis of unknown etiology. Blood tests revealed hepatic dysfunction with aminotransferase 503 U/L, total bilirubin 11.42 mg/dL, and abdominal ultrasound showed ascites and liver atrophy. She showed hypergammaglobulinemia, positive antinuclear antibodies, and was diagnosed with autoimmune hepatitis (AIH) with a score of 19 on the International Autoimmune Hepatitis Group diagnostic criteria. Methylprednisolone 500 mg/day was administered for 3 days, and prednisolone 45 mg/day was started thereafter. On the 9th day, hepatic encephalopathy appeared, which led to the diagnosis of subacute type acute liver failure. Her consciousness and liver function gradually improved with medical treatment such as lactulose enema and defecation control, and she was discharged from the hospital on the 64th day. She was finally diagnosed with autoimmune polyglandular syndrome (APS) type 3, complicated with three different autoimmune diseases. APS is defined as multiple endocrine gland disorders. In the present case, the patient had acute liver failure due to acute-onset AIH. Since patients with type 3 APS may present many manifestations over a long period of time, they should be carefully monitored.

Abstract Submission No. 101599
P-0794

Just Jelly Or Jelly Belly?: A case report on Pseudomyxoma Peritonei

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Pseudomyxoma peritonei is a rare disease characterized by intra-abdominal gelatinous ascites, commonly caused by a mucinous appendiceal neoplasm. Ten-year survival rate varies from 40-60% after CRS/HIPEC. This report can help highlight the features of this disease for early identification and treatment initiation as it can drastically affect patient's survival.

This is a 54 year old male, presenting with 7-months progressive abdominal enlargement accompanied by weight loss. Contrasted abdominal CT scan showed: Massive ascites with scalloping of the hepatic, splenic, and pancreatic margins as well as nodular densities in the omentum and mesentery. The intestinal tract is unremarkable including the cecal/appendiceal area. Ascitic fluid analysis revealed: brownish mucoid fluid. Rare histiocytes with no malignant cells were seen on cell block. The CEA: 357ng/ml and CA 19-9: 241U/ml are high. He underwent CRS showing: 16,250ml mucoid fluid. Cystic nodularities are seen in the area of the ileocecal valve. Omentum is solid and nodular. The resected terminal ileum to upper rectum, peritoneum and omentum were sent for histopathology. The patient had a sudden cardiac arrest at the end of the surgery leading to his demise despite ACLS. The histopathology revealed: a mucinous adenocarcinoma, moderately-differentiated, diffusely invading the appendix and cecum with intraperitoneal metastasis involving ileum, all colonic segments, rectum, omentum, and perisplenic tissues.

In patients found to have the following: mucoid ascites with histiocytes on cell block; scalloping on imaging, elevated CEA and CA 19-9 a diagnosis of Pseudomyxoma Peritonei can be strongly considered despite an unremarkable imaging of the appendix/cecum area

Abstract Submission No. 101641
P-0795

A case of hepatocellular carcinoma cured by drug therapy, microwave ablation, and c-TACE

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The case was an 84-year-old woman with liver cirrhosis due to HCV infection. She had a history of HBV infection and type 2 diabetes. Hepatocellular carcinoma first developed in 2013, and RFA and c-TACE were performed on the left lateral segment and S7 of the liver, respectively. She was cured of hepatitis C in 2014, but recurrence of hepatocellular carcinoma was observed in 2015 and 2018, and she underwent c-TACE and left hepatic lobectomy, respectively. When intermediate-stage hepatocellular carcinoma recurred in 2020, she was treated with lenvatinib, but treatment was discontinued due to fatigue and loss of appetite. Subsequently, treatment with atezolizumab plus bevacizumab was performed 15 times, which resulted in a marked reduction of the lesion and normalization of PIVKA-II. In 2022, microwave ablation therapy was performed on the residual disease in S6 of the liver, but PIVKA-II rose again and a recurrent lesion was found so c-TACE was performed. We experienced a case of intermediate-stage hepatocellular carcinoma in which ABC-Conversion (Atezolizumab plus Bevacizumab Curative Conversion) was performed. In the IMbrave150 study, the response rate for intermediate-stage hepatocellular carcinoma in the atezolizumab plus bevacizumab group was 44%, indicating that the treatment has a strong tumor shrinkage effect, and it is necessary to perform treatment while timing conversion.

Abstract Submission No. 101675
P-0796

Hepatitis B virus infection and the risk of developing gastrointestinal cancer - case report

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Hepatitis B virus (HBV), although considered a hepatotropic virus, can also exist in extrahepatic organs, playing a role in the development of gastrointestinal neoplasms through a mechanism similar to that involved in hepatocellular carcinoma (HCC) carcinogenesis. We present two cases associating chronic hepatitis B (CHB) with gastric cancer (GC) and colorectal cancer (CRC). Case 1: male, 65-year-old with family history of CHB and personal history of colon cancer operated and CHB under nucleoside analogue (NAs) treatment for the past 9 years. Clinically, he presented skin pallor, abdominal pain and intestinal transit disorders. Laboratory tests showed anemia and hepatocytolysis. Imaging evaluation excluded HCC but identified changes suggestive of colon neoplasia, confirmed as adenocarcinoma on biopsies obtained during colonoscopy. Case 2: male, 73-year-old, diagnosed with CHB under NAs for 2 years, reported epigastric pain, vomiting, and weight loss persisting for 4 months. Laboratory tests indicated anemia. Endoscopic examination revealed malignant gastric alterations, T3N0Mx stage by CT scan. HCC was excluded by imaging. In both cases, the virological status indicates undetectable HBV DNA, Ag HBs positive, HBe negative. In conclusion, evidence regarding the

mutagenic activity of HBV, demonstrated as an important factor in malignancy development, and the presence of HBV in the gastric and colonic mucosa, may support the risk of developing GC and CRC associated with HBV infection. This risk is highlighted even in patients with occult HBV infections and those receiving NAs. Regular screening for digestive cancers can be considered for these patient categories to prevent their development.

Abstract Submission No. 101702
P-0797

A case of lung abscess developing after corticosteroid treatment for severe alcoholic hepatitis

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Introduction: Opportunistic infection following corticosteroid treatment for severe alcoholic hepatitis is of great importance. Here we present a case of lung abscess developing after corticosteroid administration for severe alcoholic hepatitis.

Methods: A 51-year-old male with a history of excess alcohol intake presented with jaundice, and imaging revealed severe fatty liver. The coagulation profile and serum bilirubin level met the diagnostic criteria of severe alcoholic hepatitis, with an Maddrey's discriminant function score of 84.3. Corticosteroid was initiated at a dose of 40 mg/day. Serum bilirubin levels peaked at the initiation of corticosteroid and started to decrease following the treatment.

After a month of corticosteroid treatment, the patient's chest x-ray showed a cavitary lesion in the right upper lung with accompanying symptoms such as a tingling nature cough and chest discomfort. Chest CT revealed an ill-defined cavitary nodule of about 3.9x2.2cm in the right upper lobe, indicative of an abscess at an early stage of formation. The imaging did not exclude fungal infections, such as invasive aspergillosis or cryptococcosis. Bronchoscopy revealed no endobronchial lesion. Galactomannan from bronchoalveolar washing fluid came back positive, but was under the lower cut-off. As follow-up chest films showed regression of the initial cavitary lung mass using only antibiotics, it was concluded that the lesion was highly likely of bacterial origin. Therefore, no additional antifungal treatment was administered. **Conclusion:** As this case illustrates, lung abscess can develop after steroid treatment for severe alcoholic hepatitis and should be differentiated from aspergillosis, especially when presenting as a cavitary lesion.

Abstract Submission No. 101724
P-0798

An autopsy case of hepatic EBV positive DLBCL

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Introduction: Primary liver malignant lymphoma accounts for 0.41% of extranodal lymphoma, it is a rare disease that accounts for 0.07% of hepatic malignant tumors. Primary hepatic Epstein-Barr virus (EBV)

positive diffuse large B-cell lymphoma (DLBCL) is quite rare as primary liver malignant lymphoma.

Case: A 67 years old man was referred to our hospital for general malaise, and abdominal fullness. Computed tomography (CT) revealed multiple tumors in the liver and poor contrast effect with staining spreading from the margins to the center, and enlarged lymph nodes were observed around the aorta. We made the diagnosis of multiple metastatic liver tumor or cholangiocarcinoma. Blood examination showed that tumor marker was elevated only CEA. No abnormal finding was detected in the endoscopic examination of his stomach and large intestines. Ascites increased within a few days, and the patient and his family strongly desired treatment, so treatment for cholangiocarcinoma was started with UFT granules, but his general condition further deteriorated rapidly. The patient died 10 days after the decrease in oxygenation, and autopsy was performed.

Discussion: At autopsy, morphological change in the liver tumors were observed. Therefore, primary liver malignant lymphoma was suspected. His s-IL2R was measured in the remaining blood, it was found to be as high as 10,700U/ml. We finally diagnosed EBV positive DLBCL by immuno-histological examination.

Conclusion: In the case of liver tumors for which it is difficult to make a definitive diagnosis, diagnosis should be made by measuring s-IL2R or performing liver biopsy before treatment with malignant lymphoma in mind.

Abstract Submission No. 101725

P-0799

A case of rhabdomyolysis and acute renal failure due to atezolizumab plus bevacizumab therapy

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Combined immunotherapy for advanced hepatocellular carcinoma (HCC) has been widely implemented and effective. We experienced a case in which rhabdomyolysis due to atezolizumab plus bevacizumab therapy (Atez/Bev) and the patient died of acute renal failure. A man in his 50s. He developed HCC due to alcoholic cirrhosis. Before Atez/Bev, he had been treated with radiofrequency ablation (RFA), transcatheter chemoembolization (TACE) + RFA and Lenvatinib. Atez/Bev had been started for multiple HCCs 4 years after initial diagnosis. Background liver function at the time of introduction was Child-Pugh grade B. A total of 11 courses of Atez/Bev were administered, and the tumoral size and numbers decreased (PR on images) and tumor markers also decreased, evaluating effective. On the 7th day after completing the 11th course, the patient developed lower back pain and visited the emergency department. Influenza A infection and abnormally high levels of creatine phosphokinase (CPK) 65401 IU/L were observed, and severe rhabdomyolysis was diagnosed. Although the CPK decreased after hospitalization and treatment, the patient progressed to acute renal failure. Despite undergoing artificial dialysis, his general condition deteriorated, and also revealed infective endocarditis. The patient passed away 21 days after the onset of rhabdomyolysis. In this case, the patient had undergone the 10th course as an outpatient without any problems except for poor background liver function, but after the 11th course, the disease rapidly worsened with the sudden onset of Influenza A infection and rhabdomyolysis. Atez/Bev for patients with poor liver function requires careful judgment, including the indications.

Abstract Submission No. 101726

P-0800

Liver Histology and Cytokine Dynamics in a Case of Non-Severe COVID-19 with Hepatic Injury

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Background: The pathogenesis of liver dysfunction that complicates coronavirus disease 2019 (COVID-19) remains unclear, especially in mild to moderate severity cases.

Case report: A novel coronavirus infection was detected by polymerase chain reaction (PCR) in a 76-year-old woman hospitalized after presenting with fever. No other abnormal physical findings were observed, and oxygen administration was not required. Chest computed tomography (CT) showed a ground-glass-like and an infiltrative shadow in the right lung, and moderate COVID-19 was diagnosed. Initially, the fever resolved, and PCR turned negative; however, the fever reappeared on hospitalization day 14, and CT showed pneumonia exacerbation accompanied by new onset of fatty liver. Biochemical testing revealed marked liver dysfunction, accompanied by elevated serum interleukin (IL)-6, IL-10, and tumor necrosis factor- α levels. Physical findings and all laboratory parameters improved after conservative treatment, and she was discharged on day 22. A liver biopsy performed 44 days post-discharge showed T-cell-dominant inflammatory cell infiltration, mainly in the portal region. Some hepatocytes showed fatty degeneration. We report a case of moderate COVID-19 in which histological hepatitis persisted after a substantial period had passed since the initial infection had cleared and associated transaminase elevations had resolved, with a comparison of serum cytokine dynamics. In addition, we summarized the clinical features of non-severe COVID-19 cases with liver dysfunction at our institution.

Abstract Submission No. 101749

P-0801

A bleeding perianal mass - varix or haemorrhoid

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Despite the high prevalence of rectal varices, bleeding rates remain low and hence optimal treatment remains to be determined. In this report, we present a case of a middle aged man with an initial diagnostic dilemma of a bleeding varix versus haemorrhoid after presenting with hematochezia. He has a significant background of Child-Pugh B8 NASH cirrhosis complicated by gastro-oesophageal and rectal varices and untreated hepatocellular carcinoma (HCC).

Flexible sigmoidoscopy revealed external hemorrhoids and two columns of rectal varices. Towards the end of procedure, there was active spurting from the large mass protruding out of his rectum which was thought to be a haemorrhoid. Haemostasis was achieved with adrenaline packed gauze.

After discussion with the Colorectal surgeons, consensus was that the current degree of prolapse is unusual for a varix, however, it did not have typical features of haemorrhoids. MRI rectum suggested the bleeding perianal mass likely corresponded to varices. He eventually underwent successful percutaneous embolisation of varices. As he had an untreated HCC, he was not a candidate for transjugular intrahepatic

portosystemic shunt. Repeated flexible sigmoidoscopy post-embolisation showed smaller right rectal varices which was still soft and extended beyond dentate line and left varix was adequately treated with embolization.

In the literature, rectal varices have been established to be dilated veins that originate more than 4cm above the anal verge and not contiguous with the pectinate line. However, they can be difficult to distinguish from haemorrhoids and should be managed by a multi-disciplinary team involving Gastroenterology, Colorectal and Interventional Radiology.

Abstract Submission No. 101752
P-0802

A case of successful Lenvatinib for bone metastases from HCC complicated by psoriasiform dermatitis

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Effective treatment of hepatocellular carcinoma (HCC) with bone metastases has not been established. Herein, we report a case of anti-PD-L1 induced psoriasis-like dermatitis after atezolizumab plus bevacizumab combination therapy (Atz/Bev) for postoperative bone metastasis of HCC, and successfully achieved complete response to Lenvatinib (LEN) with sequential stereotactic radiotherapy (SRT). The patient underwent hepatic right lobectomy and cholecystectomy for 12 cm-sized HCC in the right lobe, and was diagnosed as pT3N0M0, Stage III (intermediate differentiated HCC). Subsequently, he had CT and MRI and FDG-PET noted osteolytic changes in the second lumbar vertebra, was diagnosed with recurrent bone metastasis and advanced HCC by CTNB. He was introduced to Atz/Bev as systemic chemotherapy, which was discontinued due to adverse effects of anti-PD-L1 induced psoriasis-like dermatitis. He started taking LEN after SRT (20Gy/1Fr), which still maintained complete response after 24 months, with a decrease from PIVKA 231.2 to 36.5 mAU/mL. The possibility that LEN, a broad-spectrum kinase inhibitor, may cause exacerbation of psoriasis has been pointed out. There is also a report that psoriasis induced by LEN was not worsened by Ramucirumab, which targets only VEGFR-2. On the other hand, anti-PD-L1 antibody-induced psoriasis-like dermatitis has been shown to be induced by blockade of PD-L1 signaling on Langerhans cells. Since multikinase inhibitors are different from these mechanisms, they may be introduced as a 2nd line therapy without psoriasis exacerbation.

Abstract Submission No. 101779
P-0803

Successful treatment of genotype 4 chronic hepatitis E virus infection after ribavirin failure

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Hepatitis E virus (HEV) is known to cause chronic HEV infection in immunosuppressed patients. Though ribavirin (RBV) is the recommended treatment, non-responders is not uncommon. We report a genotype 4 HEV (HEV-4) infected patient who relapsed after RBV treatment, achieved sustained viral response (SVR) after retreatment with RBV and sofosbuvir/velpatasvir (SOF/VPV).

A 54-year-old renal transplant recipient was diagnosed persistent HEV-4 infection 15 weeks post-transplantation. She received a 12-week course of RBV (400mg daily for 4 weeks then 400mg twice daily for 8 weeks). Alanine aminotransferase (ALT) returned to normal after 4 weeks and HEV RNA became undetectable at the end of 8 weeks. Shortly after treatment completion, rebound viraemia occurred (Figure 1). She received a second course of RBV (800mg-1000mg daily). However, viraemia persisted and ALT rose to 124 U/L. After 8 months of RBV treatment, SOF/VPV 400/100mg daily was added for another 6 months. Although it had no effect on the viral load, ALT returned to normal (Figure 2). As hepatitis recurred after the treatment was stopped, we retreated her with the same regimen for indefinite period. Unexpectedly, viraemia was cleared at week 18 of treatment (Figure 3). After 18 months of treatment, the patient requested to cease treatment. Till now, SVR is still maintained 20 months off-treatment.

Conclusion: This is the first report of successful treatment of RBV-refractory HEV-4 infection by a prolonged course of SOF/VPV and RBV therapy in a renal transplant recipient.

Abstract Submission No. 101802
P-0804

Sympathy, intentional, acetaminophen overdose: a cautionary tale with a unique presentation

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A 59-year-old female with a past medical history of polysubstance use disorder, major depression, gastric ulcer, and thoracic spinal stenosis, using daily naproxen, was admitted to the hospital after an overdose of acetaminophen 162,500mg. This event was in sympathy with her stepson's own acetaminophen overdose which occurred on the same day. He had a history of poorly treated depression and schizophrenia. Both the patient and stepson were obtunded on presentation; therefore, they were intubated. Treatment included N-acetylcysteine, fomepizole, and hemodialysis. AST (U/L), ALT (U/L), INR and acetaminophen (ug/mL) peaked at 107/168/1.9/537 (her) and 249/1072/2.5/163.9 (him). Three days later, the patient had an episode of hematemesis with a hemoglobin drop concerning for upper gastrointestinal bleeding. Upper endoscopy showed large duodenal bulb ulcers with an adherent clot, and fistulization to the antrum, consistent with double pylorus. The area of the ulcer close to the greater curvature of the antrum was noted to be pulsatile in the face of active bleeding; therefore, the patient underwent gastroduodenal artery embolization. The patient was stabilized and started on proton pump inhibitors with a plan to repeat upper endoscopy in three months. The patient was transferred to an inpatient psychiatry hospital upon discharge.

To our knowledge, this is the first reported case of sympathy, intentional, acetaminophen overdose complicated in one case by double pylorus and life-threatening NSAID-induced antral ulcer bleeding requiring GDA embolization. These cases highlight the psychosocial complexity associated with intentional drug overdose and the need to counsel households and family members at risk.

Abstract Submission No. 101806
P-0805

A case of imported infection with schistosomiasis japonica

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Background: Schistosomiasis japonica is a zoonotic infection caused by parasites that live in the portal vein of intermediate hosts such as the myriapod mussel and mammals. The parasite is said to cause cirrhosis and gastrointestinal mucosal damage by parasitizing the portal vein, where its eggs embolize the arterioles of major organs, forming inflammation and granulomas in the surrounding area. In this report, we describe a case of schistosomiasis japonica with typical imaging findings, with some discussion of the literature.

Case description: The 55-year-old man was from the Philippines and had been in Japan as a vocational trainee since 2020. After surgery for right hip osteoarthritis in 2022, a CT scan incidentally showed calcification in the liver and sigmoid colon, and he was referred to our department for close examination. Upper endoscopy showed yellowish changes in the mucosa of the descending duodenum, and lower endoscopy showed yellowish patches distributed in a band from the transverse colon to the sigmoid colon. Biopsies showed numerous insect eggs with eosinophil infiltration and calcification within the mucosa in both cases, and a diagnosis of schistosomiasis japonica was made. He was treated with praziquantel oral anthelmintic therapy, but then returned home because he wished to follow up in the Philippines.

Discussion: Although there are currently no new cases of schistosomiasis japonica in Japan, there have been scattered reports of imported cases and old cases. Prolonged disease can lead to complications such as cirrhosis and gastrointestinal mucosal damage. Then early detection is important.

Abstract Submission No. 101829

P-0806

An uncommon cause of ascites: POEMS syndrome

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Introduction: Ascites can be a manifestation of many diseases and cirrhosis is the most common cause. Here we reported an uncommon cause of ascites: POEMS syndrome.

Case report: A 52-year-old man was referred to our department complaint of ascites and edema for 4 months. The SAAG of 12g/L was suggestive of portal hypertension. Abdominal CT showed splenomegaly and multiple enlarged abdominal lymph nodes. PET-CT scan was performed to determine the FDG uptake of lymph nodes, and a needle biopsy of the axillary lymph node was performed. During hospitalization, he complained about toes numbness and limbs weakness one day. Meanwhile, we observed some overlooked skin changes: clubbing fingers, white nails, and scattered hemangioma on his trunk. POEMS syndrome was suspected. As expected, electromyography showed peripheral nerve damage. Immunofixation electrophoresis demonstrated positivity of monoclonal IgA/λ; light chain. Then lymph node biopsy reported Castleman disease. His VEGF level was 741 (range: 0-142) pg/ml. He also had papilledema, hypothyroidism, and pulmonary arterial hypertension. Finally, A POEMS syndrome was diagnosed since all the mandatory criteria were present (polyneuropathy, IgA/λ; monoclonal component), together with two major criteria (elevated VEGF, Castleman disease) and five minor criteria (splenomegaly, extravascular fluid overload, skin changes, papilledema, endocrinopathy). Then the patient was treated with lenalidomide and dexamethasone. The VEGF level decreased to 133.27 pg/ml after the first course of therapy. The ascites and edema disappeared during the follow-up of 0.5 year.

Conclusion: Uncommon causes of ascites need to be considered for hepatologist, when the common causes including liver cirrhosis were excluded.

Abstract Submission No. 101880

P-0807

Complications of RFA: Challenges to Treatment with the collective efforts of the Gastroenterology.

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Background: Local ablation plays an important role in the treatment of liver cancer. Especially in HCC, the results of the SURF trial showed that local ablation was comparable to resection in terms of recurrence-free survival and overall survival. Furthermore, in Japan, local ablation, which is relatively less invasive, is often chosen due to the aging of patients and complications. On the other hand, local ablation has unique complications, and countermeasures against them are of paramount importance for safe treatment.

Case: 73 years old female with chronic hepatitis C. 2009 Peg-IFN + Ribavirin. December 2012 first S6 2.5cm single RFA. April 2015 S6 2.5cm, S6 1.0cm RFA. October 2015 SOF + LDV started and SVR. February 2016 S8, S3, S3, S6. RFA with recurrence; August 2019 RFA with recurrence; January 2020 MWA with recurrence; February 2022 hospitalized for bile duct stenosis after RFA. Hilar bile duct stenosis Bismuth IV was observed; PTCd was inserted from B2 and then the drainage area was extended to B2+B6. The patient is now under observation with sodium correction.

Discussion: Complications requiring Interventional drainage, such as the present case, correspond to Major complication: in a review of 15,744 patients (RFA 13,044 MWA 2,700), the incidence of Major complication was 4.1% for RFA and MWA 4.6% with no statistically significant difference.

Conclusion: The prognosis for complications of local ablation therapy can be improved by the concerted efforts of the gastroenterology department. Further efforts to prevent complications and avoid serious complications through early detection are necessary.

Abstract Submission No. 101916

P-0808

Polymyalgia rheumatica caused by the combination therapy of durvalumab and tremelimumab for HCC.

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Back ground: Polymyalgia rheumatica (PMR) is an inflammatory rheumatologic condition characterized by aching and morning stiffness about the shoulders, hip girdle, neck, and torso. In recent years, PMR-like syndrome has been reported as one of the most frequent

rheumatologic immune-related adverse events (irAEs) in cancer patients with immune checkpoint inhibitors (ICIs). We report a case of PMR-like syndrome that occurred following the combination therapy of durvalumab and tremelimumab for advanced hepatocellular carcinoma (HCC).

Case Report: A 74-year-old male was diagnosed with HCC 4 years ago and had been treated with RFA and TACE, but multiple intrahepatic metastases were found. He started on the combination therapy of durvalumab and tremelimumab for HCC. 6 weeks later, he visited our department due to a myalgia. He had difficulty in raising right upper extremity and proximal muscle weakness. Blood tests showed signs of inflammation, elevated CRP, erythrocyte sedimentation rate and matrix metalloproteinase-3 (MMP-3), while CPK was low. Neurological examination was no abnormal findings. We diagnosed PMR-like syndrome from irAEs with ICIs and initiated treatment with 15mg/day of oral steroid. His symptoms improved immediately after oral administration of steroids and he was discharged on the 10th day of hospitalization.

Conclusion: PMR-like syndrome from irAEs with the combination therapy of durvalumab and tremelimumab is rare, early recognition and treatment of PMR-like syndrome will be important in combination therapy for HCC.

Abstract Submission No. 101919

P-0809

A case of rapid deterioration of general condition after discontinuation of sequential treatment.

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Background: Treatment of advanced hepatocellular carcinoma has become more diverse with the addition of IO+IO. There is much discussion about the timing of switching from primary to secondary treatment and drug selection. We look back on the process of caring for an elderly patient with advanced hepatocellular carcinoma.

Case: 79-year-old male with type 2 diabetes mellitus and hypertension. Right costal pain since June 2022, weight loss of 3 kg/6 months. Initial visit to our hospital on 07/23/2022 revealed a 16 cm hyper vascular tumor centered in the right posterior lobe with invasion of hepatic vein and portal vein. Biopsy revealed a diagnosis of hepatocellular carcinoma. Atezolizumab + bevacizumab (ATZ+BEV) started 08/03/2022. After 4 courses with no adverse events on 11/10/2022, the patient was determined to be PD. On 11/24/2022, TACE performed, then after 3 courses of ATZ+BEV resumed. On 1/24/2023 PD determined again. Lenvatinib started, but discontinued on 03/10/2023 due to fatigue. Thereafter, he was treated symptomatically, and his HCC ruptured on 06/21/2023 and he died on 06/22/2023.

Discussion: A multicenter study was conducted on post-treatment of ATZ+BEV therapy, including our institution. Post-treatment was possible in 59% of the cases. Patients who were able to receive post-treatment were those with preserved liver function and PS.

Conclusion: Reflecting on the course of treatment for elderly patients with advanced HCC, we reaffirmed the importance of maintaining liver function and PS.

Abstract Submission No. 101923

P-0810

Watch out for the chameleon sign in cases of breast cancer liver metastasis.

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BACKGROUND: We report a case of liver metastasis from breast cancer with unique CT findings.

CASE: A 49-year-old woman, who became aware of a lump in her right breast and a mass in her axilla in the summer of 20XX. Suspecting breast cancer, she was referred to our hospital. ER+, PgR+, HER2 (1+). Initial treatment consisted of chemotherapy and mastectomy + axillary lymph node dissection at 20XX+1 October. ypT2N2aM0 Stage 3A postoperative chemotherapy with capecitabine. In January 20XX+2, she visited a cancer center, and in March 20XX+3, she was referred to a local doctor, who recommended endocrine therapy. In February 20XX+4, bone scintigraphy and PET-CT showed multiple liver metastases, multiple thoracic spine metastases, rib metastases, supraclavicular lymph node metastases, and multiple lung metastases, and the patient returned to our hospital in March 20XX+4. Ultrasonography revealed multiple hypoechoic masses. Non-enhanced CT depicted it as multiple low-density areas, but contrast-enhanced CT obscured the multiple masses. Tumor biopsy was performed uneventfully under ultrasound and was positive for adenocarcinoma, GATA-3, consistent with breast cancer liver metastasis.

DISCUSSION: Contrast-enhanced CT is generally considered to have the best ability to delineate metastatic liver cancer. Some breast cancer liver metastases are oligometastatic and are low density on simple CT and slightly stained on contrast with iso density similar to that of the surrounding liver parenchyma (Radiol Oncol. 2021 19;55(4):418-425).

CONCLUSION: In cases of liver metastases from breast cancer, not only contrast-enhanced but also simple CT should be performed.

Abstract Submission No. 101927

P-0811

Cirrhodomimetic Hepatocellular Carcinoma - a mimic of sclerosing cholangitis

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A 61-year-old Chinese man with Child-Pugh A5 liver cirrhosis secondary to chronic Hepatitis B was admitted for abdominal pain and scleral icterus. He was lost to followup for the past three years. On examination, he was jaundiced and cachectic. There was no ascites clinically. His liver function test showed raised total bilirubin (162 µmol/L) and transaminases. Magnetic Resonance Cholangiopancreatography (MRCP) revealed multiple areas of stenosis and dilatation of the biliary tree. This "beaded appearance" raised the suspicion for sclerosing cholangitis. The main portal vein (PV) and its branches was expanded and showed high T2 signal, raising the possibility of a thrombus. Given his cachexia and raised serum alpha-fetoprotein (10.1 ng/dl, normal was <7.1ng/dl), there were suspicions of malignancy even though

hepatocellular carcinoma (HCC) was not reported on MRCP. He underwent ultrasound-guided fine needle aspiration cytology of the PV thrombus which showed HCC. He was diagnosed with diffuse/cirrhoto-mimetic HCC with tumour thrombus in PV.

Diffuse/cirrhoto-mimetic HCC is a rare diagnosis and diagnosis is often challenging. It is frequently associated with PV tumour thrombus. While chronic PV thrombus may cause portal biliopathy changes (ie strictures in the biliary tree due to extrinsic compression of the bile ducts by cavernous collaterals), this is distinct from the true beaded biliary tree appearance classical of sclerosing cholangitis. The difficulty detecting diffuse/cirrhoto-mimetic HCC in a cirrhotic liver as well as imaging findings classical of sclerosing cholangitis resulted in delayed diagnosis. Greater awareness on diffuse/cirrhoto-mimetic HCC is needed so that prompt diagnosis and appropriate treatment can be achieved.

Abstract Submission No. 101963
P-0812

The elusive diagnosis of myelofibrosis presenting as noncirrhotic portal hypertension: a case report

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Prehepatic causes of noncirrhotic portal hypertension (NCPH) are an infrequently encountered but important category of disorders to consider in patients presenting with esophageal variceal bleeding without objective evidence of liver synthetic dysfunction or cirrhosis. One key prehepatic cause to evaluate for is extrahepatic portal vein obstruction (EHPVO), which is commonly secondary to portal vein thrombosis (PVT). Once PVT is diagnosed, further evaluation should then be undertaken to identify underlying etiological factors. We present a rare case of a 37-year-old female with no past medical history who presented with esophageal variceal bleeding, and was found to have underlying NCPH secondary to chronic PVT, but with no apparent etiological factors identified for her PVT such as Protein S deficiency. She was not on any anticoagulation. In view of persistent remnant varices and progressively increasing splenomegaly, she subsequently underwent a splenectomy and splenorenal shunt. However, after the operation, a sharp rise in total white blood cell count from $9 \times 10^9/L$ to $23 \times 10^9/L$ was noted. Subsequently, JAK2 mutation studies were positive, and histology of the spleen was consistent with a myeloproliferative neoplasm (MPN), likely myelofibrosis (MF). Postoperatively, the patient developed mesenteric venous thrombosis complicated by small bowel ischemia with perforation and abscess formation, and underwent an open small bowel resection with terminal ileostomy and de-functioning cecostomy. She later developed short bowel syndrome. This case report highlights the importance of considering rare and sometimes elusive etiologies of NCPH such as MF, when a patient develops NCPH.

Abstract Submission No. 102020
P-0813

LIVER CIRRHOSIS TURNS TO BE WILSON DISEASE-DELAYED DIAGNOSIS

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BACKGROUND: Wilson's Disease (WD) is a genetic mutation that disturbs copper metabolism in the body leading to accumulation of copper in various tissues causing damage and dysfunction of the organ. Hepatic complications are the initial manifestation of the disease followed by neurological symptoms.

CASE REPORT: 28 years old Female in 2016, presented with ascites and jaundice that appeared during work (steward on the ship), acute viral hepatitis was excluded in New York, cirrhosis was established upon arrival in Moscow according to fibroscan data. Analysis control-ANA was detected, methylprednisolone therapy was initiated, azathioprine was refused, albumin was transfused for a long time, liver transplantation was discussed, after 2 years the condition stabilized, AST and ALT returned to normal. She returned to work in 2019. In 2021, against the background of vaccination against covid, fever, convulsive seizure occurred for the first time in her life. Head MRI scan showed "Face of a giant panda" lesion, Wilson's disease was suspected, which was confirmed by an analysis for ceruloplasmin levels - 0.06, and genetic analysis was conducted. Treatment with penicillamine, combined with methylprednisolone for a month was prescribed. Currently, her condition is stable with treatment on penicillamine.

CONCLUSION: Wilson Disease can be presented as an atypical form which is not to be dismissed but be suspected in case of liver cirrhosis of unknown etiology or sudden isolated neurological deficits such as seizures, tremors.

Abstract Submission No. 102021
P-0814

Gastric bronchogenic cyst mimicking pancreatic mucinous cyst

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Purpose: Bronchogenic cysts, benign congenital lesions resulting from abnormal foregut budding, are typically found in the posterior mediastinum but can occasionally be associated with cervical, thoracic, and abdominal structures. We present a case initially diagnosed as a pancreatic mucinous cyst on imaging but confirmed as a bronchogenic cyst after surgical resection.

Method: Retrospective, case-based case report

Results: A 59-year-old female presented to the gastroenterology clinic with abdominal pain. She had a normal physical exam, no systemic diseases, and used no regular medications. Laboratory results, including hemogram and biochemistry, were normal. An abdominal ultrasound revealed a pancreatic lesion, leading to dynamic pancreatic MRI, which identified a 47x44 mm cystic lesion in the pancreas tail and a 40x20 mm cyst nearby. Endoscopic ultrasonography, a dense echo measuring 37.5x30.1 mm was observed in the pancreatic tail localization, positioned in front of the spleen. Additionally, a cystic lesion with anechoic, homogeneous characteristics and a diameter of approximately 38x35 mm was noted in the distal part. Fine needle aspiration showed elevated CEA (30.6 ng/ml), CA19-9 (>700 U/ml), and amylase (766 U/L). Suspected mucinous cystic neoplasia led to cyst excision, but during the operation, cysts were found in the gastric mesa, unrelated to the pancreas. The final pathology reported gastric bronchogenic cysts.

Conclusion: CT, MRI/MRCP, and EUS aid in differentiating pancreatic cysts, yet challenges may require surgical resection for diagnosis and treatment. Notably rare, as in our case, bronchogenic cysts can mimic mucinous cysts, underscoring the need for consideration in the differential diagnosis.

Abstract Submission No. 102057

P-0815

A case of hepatic inflammatory pseudotumor with atypical image findings

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A 70-year-old man with a history of HBV infection and slight liver dysfunction was admitted for further examination of a 3.8 cm tumor in segment 5: ultrasound (US) revealed a hypo-iso-hypo pattern and computed tomography (CT) revealed a low-iso-low density pattern (double-target-sign). While CE US revealed slight hypovascularity, early washout in the portal phase, and defect in the Kupffer phase, contrast-enhanced (CE) CT and ethoxybenzyl diethylenetriamine penta-acetic acid-enhanced magnetic resonance imaging (EOB MRI) revealed slight hypervascularity and slight hypointensity at the hepatobiliary phase. Echo planar imaging of MRI revealed remarkable hypointensity. The aforementioned imaging modalities raised suspicions of inflammatory pseudotumor (IPT), atypical hepatocellular carcinoma, cholangiocellular carcinoma, cholangiolocellular carcinoma, and metastatic liver cancer. US-guided biopsy, however, showed hepatic IPT, and histopathological analysis disclosed the proliferation of fibroblasts, lymphocytes, plasma cells, and macrophages with hemosiderin on a background of collagen fibers. Without receiving any kind of treatment, the tumor had shrunk from 3.8 to 2.6 cm three weeks after the diagnosis. IPT is generally defined as benign, non-malignant, non-metastasizing tumors featured by the presence of myofibroblastic spindle cells, heterogeneous populations of inflammatory cells, particularly plasma cells, lymphocytes and macrophages, as well as locations of fibrosis and necrosis without cellular anaplasia or atypical mitoses. Despite subsequent reports, hepatic IPT keeps difficult to diagnose, as it occasionally shows atypical image findings, compared with that of other various benign diseases and malignant hepatic tumors.

Abstract Submission No. 102065

P-0816

A case of unresectable HCC treated with durvalumab/tremelimumab followed by conversion surgery

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Case Presentation: A 52-year-old man with chronic hepatitis C (post-SVR) who had not been followed after SVR. He was referred to our hospital due to multiple liver tumors. We diagnosed multiple huge HCCs occupying the right lobe and had slightly poor liver reserve function [ALBI score -1.47 (mALBI grade 2b)]. At the time of initial diagnosis, his general condition was poor due to cachexia (PS 2). We introduced durvalumab/tremelimumab (Durva/Treme) therapy. Two weeks after initiation, he developed skin eruption (Grade 3), elevated T.Bil (Grade 3), and transaminase (Grade 3), and we started PSL, the skin eruption and transaminase improved. After that PSL was tapered off, and Durva/Treme could be continued. CT showed tumor necrosis (RECIST 1.1: PR) and the tumor shrank markedly, and tumor markers decreased (AFP:281900.0 to 14.1 ng/mL and PIVKA-II:34722.9 to 29.0 mAU/mL). After 4 treatment courses, hepatic reserve function improved to ALBI score -2.56. Durva/Treme showed a significant response, and his general condition improved with tumor shrinkage, therefore conversion surgery was performed. He had no recurrence in 2 months without post-operative chemotherapy. The resected specimen showed complete tumor necrosis and achieved TE4. A large number of lymphocytes infiltrated into the tumor and surrounding tissue, suggesting a favorable immune response. The patient's general condition improved with the super-response of Durva/Treme, and conversion surgery was successfully performed. We believe this case is valuable for developing treatment strategies using Durva/Treme.

Abstract Submission No. 102070

P-0817

Acute Hepatitis due to Fenugreek

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Fenugreek (Cakir) is a plant that belongs to the parsley family and has yellow flowers. It grows in Southeastern Anatolia, Eastern Anatolia and the Mediterranean region in our country. Gooseberry root; It is reported that it is used in the treatment of sexual problems such as impotence and infertility and increases sexual potency.

Case: A newly married patient (Male, 27 years old) came to us with nausea, vomiting, and darkening of the urine color after using chalk herb upon the advice of his friends. In the examinations carried out; ALT was 442 IU/ml, AST was 338 IU/ml, and bilirubin levels were slightly high. The liver and spleen appeared normal on USG. Acute hepatitis was considered in the patient. HBV, HCV, HAV, Alcohol and other viral markers were negative. He told the patient that whenever he used anything else, he used seaweed. After cutting this herb, a significant improvement in liver functions was detected.

Conclusion: It should be known that some herbs used unconsciously and without consulting a physician may cause liver toxicity and even death.

Abstract Submission No. 102071

P-0818

Eosinophilic Ascites

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Eosinophilic gastrointestinal diseases are a group of rare diseases that present with signs and symptoms due to eosinophil infiltration in gastrointestinal tissues. In this case, a case with intestinal involvement and characterized by eosinophilic acid is presented.

Case: A 28-year-old Chinese patient applied to us with complaints of abdominal pain, bloating and diarrhea. His diarrhea was watery and soft and did not contain blood. Ascites puncture was performed, SAAG was found to be 1.27 and no TB bacilli were detected. Mild eosinophilia was detected in the blood count. At the endoscopy, Hp negative gastritis was found, Peritoneal fluid, cytological examination and cell block: Benign inflammatory smear consisting of eosinophil leukocytes was detected. Eosinophil leukocytes were observed in numbers greater than 100 in 1 high-power field, There was no growth in ascitic fluid culture. Abdominal USG revealed long segment wall thickening in the small bowel loops and minimal pleural effusion, without detecting hepatosplenomegaly. In MRI enteroclysis, diffuse minimal wall thickness increase and minimally increased contrast material retention in the small bowel segments, minimal dilatation in some small bowel segments, and intraabdominal free fluid were reported. No pathology was detected in the stool examination. After excluding other more common conditions such as inflammatory bowel disease, malignancy, vasculitis, infectious enteritis, celiac disease, and angioedema, eosinophilic gastroenteritis and eosinophilic acid were considered in the differential diagnosis. Corticosteroid treatment was planned for the patient.

Conclusion: This case is rare because the stomach, duodenum, and colon are spared from eosinophilic involvement.

Abstract Submission No. 200002

P-0819

Successful Treatment of Diffuse Postoperative Recurrences of HCC with Atezolizumab plus Bevacizumab

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Atezolizumab plus bevacizumab (Atezo + Bev) is the first immunotherapy for hepatocellular carcinoma (HCC), and in the current guidelines, it is positioned as the first-line chemotherapy for unresectable cases. Herein, we report a case of postoperative multiple diffuse recurrence of HCC by a complete response to Atezo + Bev. Herein, we define diffuse recurrence as uncountable HCCs recur within 3 months after treatment.

A 72-year-old man previously underwent trans arterial chemo embolization (TACE) and received hepatectomies twice for metachronous solitary recurrent pStage II HCC, respectively. Three months after last surgery, multiple intrahepatic recurrences and marked elevation of tumor markers were observed. The patient was diagnosed with diffuse recurrences of HCC and received combination immunochemotherapy with Atezo (1,200 mg/body) + Bev (15 mg/kg). After the fourth administration of Atezo + Bev, serum levels of tumor markers decreased to the normal range. Contrast CT scan showed prominently reduced tumor size. After the ninth administration, the CT scan showed the disappearance of all the liver lesions, indicating a complete response (CR). At 36 months postoperatively, CR was maintained and tumor markers were in the normal range.

We report a case of multiple postoperative diffuse recurrences of HCC treated with Atezo + Bev. In our experience, average of postrecurrent survival of diffuse recurrent HCC cases before 2012 were 4.25±1.24 months. Immunochemotherapy with Atezo + Bev may be one of the effective treatments for diffusely recurrent HCC with poor prognosis.

Abstract Submission No. 200059

P-0820

Wilson's Disease Masquerading as Steatotic Liver Disease: A Case Report

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Wilson's disease is a rare metabolic disorder characterized by copper accumulation. It caused by mutations of the ATP7B gene on chromosome 13. Ceruloplasmin is a protein synthesized in the liver and low plasma level of ceruloplasmin is an indication for Wilson's disease. A 16-year-old female visited for abnormal liver function for one year. The elevated aspartate aminotransferase and alanine aminotransferase were found accidentally in health check and she received examinations in regularly endocrinologist visiting this year. Abdominal sonography found severe fatty liver and the metabolic dysfunction-associated steatohepatitis (MASH) was diagnosed. However, the liver function got worsen with alanine aminotransferase up to 200IU/L despite weight loss. So, she was transferred to hepatologist for further survey. She mentioned that she ate lots of mushrooms for weight reduction. Due to the high copper level in mushrooms, we took Wilson's disease into our consideration and checked plasma ceruloplasmin which revealed very low level (2.5mg/dL) later. The liver biopsy was done, and the pathologic findings were compatible with steatotic liver disease with copper accumulation in liver. Nevertheless, under the strong suspicion of Wilson's disease, we did the immunohistochemical stain for metallothionein and the stains showed strong positive at all.

Here, we report a case of Wilson's disease who was diagnosed and treated as MASH at first. The hepatic histology was also compatible with steatotic liver disease. In this case, it warranted the importance of immunochemical staining for metallothionein, in patients with highly suspected Wilson's disease, no matter whether copper accumulation in liver or not.

Abstract Submission No. 200080

P-0821

Silent pylephlebitis, as manifestations of *Klebsiella pneumoniae* invasive syndrome, a case report

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Introduction: Although *Klebsiella pneumoniae* invasive syndrome was a common disease entity in Asia, presenting with hepatosplenic microabscess and pylephlebitis was unusual. We aim to report a case of notable presentation of this organism.

Case presentation: A 66-year-old Thai male patient with recently diagnosis of type 2 diabetes mellitus came to the hospital with a high-grade fever and productive cough without abdominal pain for 2 weeks. Physical examination revealed left lower lung fine crepitation accompanied with hepatomegaly. Chest x-ray showed interstitial left lower lobe infiltration. After the patient had been admitted for 9 hr, the blood culture was identified as *Klebsiella pneumoniae*. Then he was treated with empirical antibiotics with Ceftriaxone. Due to hepatomegaly and

abnormal liver function test (isolated elevated ALP), an abdominal ultrasonography and abdominal computed tomography (CT) were obtained and revealed acute thrombosis within the right, left, and main portal vein downward to superior mesenteric vein and diffuse hepatomegaly with hepatosplenic microabscess size 6-8 mm (likely to be a pseudolesion more than abscess). The patient's fever subsided within the first week of intravenous antibiotics without anticoagulant. Ceftriaxone was continued for 2 weeks and the patient was discharged with oral amoxicillin-clavulanic acid.

Discussion and conclusion: Pylephlebitis (septic thrombophlebitis of portal vein) can occur as a complication of *Klebsiella pneumoniae* bacteremia with unclear pathogenesis, presumably triggered by inflammation during infection. It is also a challenge in diagnosis due to its silent symptom and should be a concern in case of patients with hepatomegaly and abnormal liver function test.

Abstract Submission No. 200084
P-0822

Gastrointestinal Tuberculosis Appearing as A Colon Mass: A Case Report

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Gastrointestinal tuberculosis presents with non-specific symptoms along with multiple various lesions on endoscopy. GI TB may be mistaken for malignancy in endoscopy which may lead to delay in diagnosis which can result in increase in morbidity or mortality.

This is a case of an asymptomatic 53 year-old Filipino male, no known comorbidities, with a strong family history of colon cancer who underwent screening colonoscopy which revealed an ulcerating, friable, granular mass at the ascending colon approximately 1-1.5cm in widest diameter. Magnified chromoendoscopy suggests non-neoplastic features. Multiple biopsies taken and showed negative TBgeneXpert as well as absence of acid-fast bacilli but showed chronic granulomatous inflammation with multinucleated Langhans type giant cells as well as acute-on-chronic colitis with mucosal erosion and architectural distortion; positive for crypt abscess. Patient was then started on empiric anti-tuberculosis treatment and advised repeat colonoscopy after 6 months treatment of anti-tuberculosis therapy.

Gastrointestinal tuberculosis may present differently in various cases and it may also mimic malignancy. High clinical suspicion, especially in endemic countries, along with combination of endoscopic findings should guide as in considering GI TB as part of our differential diagnosis in patients with non-specific GI symptoms with endoscopic findings resembling malignancy as this would reduce morbidity and mortality.

Abstract Submission No. 200094
P-0823

One case and literature review of adult primary haemophilic syndrome(FHL3)

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Hemophagocytic syndrome (HPS), also known as hemophagocytic lymphohistiocytosis (HLH), represents a severe inflammatory syndrome, either genetically inherited or acquired, characterized by

dysfunctional immune regulation. Primary HLH has a very low incidence and high fatality, mainly in infants and young children. This case is a rare adult disease, and this report is about the onset and diagnosis of the patient and literature related to HLH.

Abstract Submission No. 200156
P-0824

PFIC -3 MASQUERADING AS WILSON DISEASE - FALLACY OF LEIPZIG SCORE

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Introduction: Progressive Familial Intrahepatic Cholestasis -3 is a rare autosomal recessive disorder characterized by mutation in the ABCB4 gene clinically manifesting as progressive or recurrent cholestasis.

Case: A 23 year old female, first presented at 6 years of age with jaundice and ascites and was diagnosed as Wilson disease(WD) based on Leipzig score of 4 (24 hours urinary copper excretion - 162mcg/dl; liver copper - 1692mcg/gm of dry weight and a positive penicillamine challenge test). She maintained stable liver function for few years on treatment with D-penicillamine and zinc however, since the age of 17 years gradual worsening of her liver functions was seen with development of ascites at the age of 22 years. Autoimmune and viral etiology was negative. On revisiting her diagnosis, she had persistently elevated gamma glutamyl transpeptidase levels with history of intermittent mild itching. Her modified Leipzig score was 2 at time of diagnosis (>4 - diagnostic). Whole exome sequencing revealed mutation in the ABCB4 gene.

Discussion: Chronic cholestasis is known to increase the hepatic copper content and may even result in false positive diagnostic tests for WD. Our case validates the modified leipzig score (Nagral A et al; J Clin Exp Hepatol 9 (2019) 74-98) which has excluded hepatic copper content and penicillamine challenge test from the scoring system.

Conclusion: PFIC-3 is a clinical mimic of WD. Diagnostic tests for WD should be cautiously interpreted in presence of cholestasis. Failure of improvement of liver function with effective chelation should prompt evaluation for alternative diagnosis.

Abstract Submission No. 200159
P-0825

WINDOW TO PORTAL VEIN VIA LUNGS (ABERNATHY MALFORMATION) - A MULTIDISCIPLINARY TEAM MANAGEMENT

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Introduction: Abernathy malformation (AM) is characterized by an abnormal congenital porto-systemic communication with resultant diversion of the portal inflow to systemic veins leading to numerous clinical manifestations including pulmonary hypertension (PH). The mainstay of treatment of PH includes endovascular or surgical closure of the shunt.

Case: A 23 year old female presented with hemoptysis and mild dyspnea secondary to moderate PH. Her workup did not reveal any cardiac, pulmonary and rheumatological etiology for PH. MR angiography of abdomen revealed a large venous sac of diameter 2.5cm draining the splanchnic circulation into left renal vein. A portomesentric venogram with balloon occlusion test revealed hypoplastic right PV with portal venous pressure of 23 mm Hg after shunt occlusion. She underwent surgical ligation as shorter length of the shunt precluded endovascular intervention. Propanolol was started a month prior to surgery to prevent acute rise in portal pressure after shunt occlusion. Intraoperatively, temporary clamping of shunt resulted in rapid reversal of flow in the hypoplastic right PV without any evidence of bowel ischemia. 24 hours post ligation, there was further improvement in the portal inflow. Six months postoperatively there is no worsening of PH.

Discussion: A single stage surgical closure of the shunt can be done if the portal pressures are < 30mmHg on shunt occlusion and does not result in acute portal hypertension if the main PV is visible (McLin VA et al; JHEP Reports. 2023 Oct).

Conclusion: Hypoplastic branch PV does not preclude successful AM closure in appropriately selected cases.

Abstract Submission No. 200170
P-0826

Extrahepatic Portal Vein Obstruction in a Filipino Male with VACTERL: A case report

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Introduction: The incidence of both extra hepatic portal vein obstruction (EHPVO) and VACTERL spectrum has not been reported yet in the literature. This case report illustrated a rare case of VACTERL (vertebral anomalies, imperforate anus or anal atresia, cardiac anomalies, tracheoesophageal fistula, renal and limb defect) spectrum associated with extra hepatic portal vein obstruction. Authors investigated if there was any interrelation between extra hepatic portal vein obstruction and VACTERL spectrum.

Case Presentation: A 19-year-old Filipino male presented with no any symptoms and admitted for follow-up surgery of his Imperforate Anus. Incidentally, Whole Abdominal CT scan showed a dilated portal vein with several tortuous enhancing vessels at the region of porta hepatis with multiple tortuous vessels at the splenic vein, parametrial vein and at the perigastric and lower paraesophageal region,

Conclusion: The authors proposed that the EHPVO found in the patient was caused by another anatomical aberration of patients with VACTERL association, resulting in portal hypertension. Considering there have been no research on the correlation of VACTERL spectrum and EHPVO yet, and this may be the first case reported, it would be challenging to draw any conclusions but future studies of VACTERL spectrum patients are worth considering. Hence further data is needed to support this unusual association.

Abstract Submission No. 200210
P-0827

PFIC - 2 RECURRENCE POST LIVER TRANSPLANT - LEARNING FROM MISTAKES

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Introduction: Progressive Familial Intrahepatic Cholestasis -2 is characterised by mutation in the ABCB11 gene encoding the BSEP resulting in end stage liver disease for which Liver transplantation (LT) is considered curative. Discerning the etiology of recurrent cholestasis post LT can be challenging.

Case: A 6 six year old boy with genetically proven PFIC-2 underwent living donor LT for decompensated cirrhosis. A year after LT, he developed cholestasis due to biliary stricture requiring percutaneous biliary drainage followed by hepaticojejunostomy with relief of symptoms. Cholestasis recurred a year later due to presumed hepaticojejunostomy stricture and was managed with balloon stricturoplasty. However, due to persistent itching and low GGTP, liver biopsy was done which revealed features of PFIC, portal fibrosis and no evidence of rejection. An internal biliary diversion was performed for recurrent PFIC-2 which reduced the itching for few months following which it recurred. Estimation of Anti BSEP antibody in his serum revealed a titre of 1:3200. He was treated with rituximab but died due to decompensated liver disease.

Discussion: PFIC - 2 recurrence post LT occurs due to development of antibodies against BSEP presenting as low GGT cholestasis. Diagnosis is by immunofluorescence of liver biopsy specimen or serum testing for Anti BSEP antibodies. Treatment options include plasmapheresis, high dose human immunoglobulin and rituximab. Re-transplantation is done for intractable pruritus and decompensated cirrhosis but results in recurrent PFIC-2.

Conclusion: Low GGT cholestasis post LT should prompt workup for recurrent PFIC -2 after exclusion of rejection and managed with measures for antibody reduction.

Abstract Submission No. 200214
P-0828

Liver transplantation in atypical Hemolytic uremic syndrome (aHUS - Complement Factor H mutation)

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Introduction: We describe successful short term outcome of LT in a child with aHUS with CFH mutation.

Case description 4 -year old girl born of 3rd degree consanguineous marriage presented with aHUS & acute kidney injury at 3.5 months age. Genetic testing revealed homozygous missense CFH mutation on exon 22. Anti factor H antibody and ADAMTS 13 levels were normal. In the acute phase she was managed with peritoneal dialysis followed by plasma infusion for next 2 years. She then received fortnightly eculizumab due to development of anaphylaxis to plasma. Her renal function, growth and development remained normal. She underwent a successful living donor LT with her paternal grandfather being donor who was genetically negative for the mutation. Four weeks post LT and her last Eculizumab, CBC, serum LDH and renal function remain normal.

Discussion: Genetic aHUS secondary to CFH mutation can be treated with plasma therapy, Eculizumab and LT. Difficult vascular access with intolerance to plasma therapy and high cost of eculizumab (300 mg costs US \$ 1900) precludes their longterm use. LT permanently cures the disease by providing CFH synthesized by the transplanted liver. Reported literature on LT in aHUS have described variable

perioperative morbidity due to complement activation which can be managed by pretransplant plasma exchange or eculizumab administration as was done in our case.

Conclusion: Liver Transplant is safe and effective treatment modality for aHUS and may prevent the need of simultaneous renal transplant if done before development of renal failure.

Abstract Submission No. 200254
P-0829

A decade of management of post-living donor liver transplant complications: A case report.

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Background: Bile duct anastomotic stenosis and intrahepatic stones after liver transplantation are complications that can cause cholangitis and graft liver failure. Endoscopic stenting is the primary treatment, but managing these complications, particularly in living donor liver transplant (LDLT) cases, can be challenging and often requires long-term stenting or percutaneous approaches.

Case presentation: A 64-year-old woman underwent left LDLT for hepatocellular carcinoma due to type C cirrhosis in year X. Four months post-operation, she developed cholangitis from anastomotic stenosis. Despite balloon dilation via ERCP, recurrence led to placement of an inside stent (IS) in B3. Subsequent cholangitis in B2 necessitated another IS placement, but inflammation remained uncontrolled. Uncovered self-expandable metallic stents (UCSEMS) were placed in B2 and B3. Following immediate cholangitis, PTBD was performed in B4. She remained cholangitis free for over three years.

In year X+4, cholangitis recurred. ERCP showed stone-filled SEMSs in B2 and B3. Due to severe biliary angulation, PTBD was performed in B3. Percutaneous cholangioscopy with electronichydraulic lithotripsy (EHL) was used to remove stones in B3.

In year X+5, recurrent stones in B3 were managed with percutaneous cholangioscopic stone removal. However, cholangitis due to stones in B2 occurred one month later, necessitating PTBD. Transpapillary stone removal using rendezvous technique was successful.

The patient has not had the PTBD tube removed due to recurrent cholangitis but has avoided liver failure for 12 years post-surgery.

Conclusion: This case demonstrates the management of post LDLT complications over a decade using various approaches.

Abstract Submission No. 200255
P-0830

The therapeutic hierarchy strategy or the treatment migration

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BCLC staging system is the most commonly used staging system of hepatocellular carcinoma. This prognostic classification coincides with the treatment algorithm. Since 2015, other proposals from Hong Kong, China, South Korea, also Italy have incorporated a stage hierarchy approach.

A 72 -year-old Caucasian male started his oncologic story in April 2019 when an hepatocellular carcinoma at the segment V with

pathologic lymphadenopathy at the hilar and celiac tripod level was diagnosed, he had a mixed steatotic liver disease (diabetes; et-OH). For the lymph node metastasis involvement (Stage IVA BCLC C), in multidisciplinary meeting we decided to involve the patient in a new clinical trial, a phase III LEAP-002 (First-line Lenvatinib Plus Pembrolizumab / Placebo in Advanced HCC). He started the chemotherapy at August 2019, he stopped Pembrolizumab/Placebo at May 2021 for suspected immunorelated pneumonia. In these years the disease was always in partial response or stability. He continued only Lenvatinib in reduced doses until May 2022, when the TC scan showed a progression epatic disease without pathologic lymphadenopathy. In multidisciplinary meeting we discussed the possibility of RFA, but it was impossible for the shape and size of the HCC nodule. We agreed to stop Lenvatinib and to do surgery. In October 2022 he was subjected to atypical partial hepatectomy enbloc. The last follow-up was in November 2023 with TC scan which was complete response.

The therapeutic hierarchy strategy or the treatment migration are particularly important in intermediate and advanced stages of hepatocellular carcinoma, when initially curative therapies are usually excluded.

Abstract Submission No. 200257
P-0831

M.B., a complex case of unsuccessful TACE: a case report

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This case report aims to focus on the concepts of TACE refractoriness and unsuitability, pointing out the need of a complete evaluation of all the patients affected by HCC, especially those who are candidate to TACE, as we currently cannot foresee how the patient will respond to the specific treatment. Further studies are needed in order to better understand this difference.

M.B. is a 84 years old caucasian male with many comorbidities. His most recent oncological history began in July 2020 when, after a traumatic event, the patient underwent a TC scan which showed a 7.7cm nodule in the right hepatic lobe and two smaller hepatic nodules. An hepatic US was performed, along with a fibroscan analysis, with no evidence of cirrhosis. A liver biopsy confirmed the radiological suspect of Hepatocellular cell carcinoma. The case was discussed in the multidisciplinary meeting, and a first TACE was performed. Two more TACEs were performed after incomplete responses, but the subsequent TC scan showed the appearance of at least 23 new hepatic nodules. A systemic treatment with Lenvatinib 8mg/die was then started (April 2021), after endoscopic and cardiological studies. A nutritional counseling was also needed as the patient lost about 5% of his weight during the first month. The first radiological evaluation during Lenvatinib showed an important partial response of the multiple hepatic nodules. The systemic treatment was continued for two years without major toxicities, and the TC scan performed at January 2023 showed a complete radiological response. The treatment was then stopped.

Abstract Submission No. 200273
P-0832

Endoscopic Ultrasound-guided RFA followed by Immunotherapy in A Patient with Cholangiocarcinoma

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Cholangiocarcinoma is a rare hepatobiliary malignancy, and it is difficult to manage due to its aggressiveness and poor disease prognosis. Surgery is still the main treatment for curing the disease, however, most patients have come in the late stage of the disease. Endoscopic management is the main biliary drainage procedure, whereas chemotherapy is the standard treatment for prolonged survival. Recently, there has been innovation in endoscopic ultrasound (EUS) procedure for radiofrequency ablation (RFA) as an option for loco-regional therapy. Another new development in controlling the cancer cells through immunotherapy. Herewith, we presented a case of 80 years old female with past history of breast cancer and was referred due to liver mass which caused bile duct obstruction. No jaundice was found during clinical examination, and the bilirubin level was normal. The hepatitis virus markers were negative. Based on tumor markers evaluation, the AFP level was 2.66 ng/mL, and CA 19-9 was 125.60 U/mL. The patient has been suggested for liver biopsy, followed by bile duct stenting, and possible for EUS-guided RFA. The liver biopsy was done using 22G FNB needle. All the procedures were performed in the same session, and it was technically successful without any adverse events or complications, such as bleeding, infection, or perforation. One week after, the patient underwent the first single immunotherapy using Durvalumab. The patient's condition is always stable with stable liver function test.

Abstract Submission No. 100647
P-0833

Barriers to patient adherence to longitudinal stool collection for microbiome research: pilot study

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Background: To date, most microbiome studies in cancer patients involve patients from Western countries, China or Japan, and baseline samples. We performed a pilot study to assess the feasibility of longitudinal stool collection for microbiome research in cancer patients in Singapore.

Methods: 22 patients with hepatobiliary cancer planned for immunotherapy initiation were recruited. Stool samples were collected at baseline and 6-weekly till 1 year, patient refusal or disease progression. Patients could mail back samples or return them at their next appointment. Patients had to answer a Food Frequency Questionnaire (FFQ), and an Environmental questionnaire (EQ), the latter reporting stool appearance and over-the-counter medication usage. EQ was also resubmitted with each sample.

Results: 20 patients provided at least one sample. Only 38/83 (45.8%) of potential samples were collected. The commonest reason was patient refusal, citing inconvenience or discomfort with sample handling. 38/42 (90.5%) kits dispensed were returned. 37/38 (97.3%) returned kits passed quality control. Mean samples collected per patient was 1.53 (median 1, range 0 - 4).

19/20 (95.0%) FFQ questionnaires were returned and 12/19 (63.1%) were completed. Missing responses were mainly for questions with a multi-choice response format. Questions requiring yes/no or numerical responses were mostly completed. 35/39 (89.7%) of EQ questionnaires were returned and 30/35 (85.7%) were completed. The commonest omission was on stool consistency grading by the Bristol scale.

Conclusions: Stool collection for microbiome studies remains challenging, particularly longitudinal sampling and questionnaire completion. Physician encouragement, improved collection processes, and better questionnaire design are key in improving patient participation.

Abstract Submission No. 100649
P-0834

Gut microbiota predicts response in patients with hepatobiliary cancer on immunotherapy

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Immune checkpoint inhibitors (ICIs) changed the treatment landscape of advanced hepatocellular/cholangiocarcinoma (HCC/CCA) but only 15 - 20% of patients respond to monotherapy. We conducted a pilot study to assess the stool microbiome profile as a predictive biomarker for disease control (DC) to HCC/CCA patients on ICI.

Methods: 18 HCC and 4 CCA patients were recruited. 21 started ICI and 20 provided at least 1 stool sample. Samples were collected at baseline and 6 weekly till 1 year, patient refusal or disease progression. 11 patients had primary progressive disease (PD) to ICI (all HCC) while 9 had DC (HCC: 4 stable disease (SD), 1 partial response; CCA: 4 SD).

Stool metagenomic taxonomic and functional profiles generated using the bioBakery meta'omics workflow yielded 392 microbial species and 2234 annotated Enzyme Commission features for analysis. We identified putative differential abundance analysis of all microbial omic measurements types using linear models. Each feature was modelled as a function of treatment response, whilst adjusting for age, body mass index, and cancer type.

Results: We identified distinct microbial signatures at baseline (Fig1A). 9 microbial species ($p < 0.05$), and 32 microbial enzymes ($FDR < 0.05$) (Fig1B) were significantly associated with DC. DC was associated with increased abundances of *Olsenella scatoligenes* and *Megamonas funiformis*, and increased aminodeoxyfutasoline synthase (menaquinone biosynthesis pathway). A microbial dysbiosis score developed using the 9 species (Fig1C) discriminated those with DC from those with PD to ICI ($p < 0.01$).

Conclusions: Our microbial dysbiosis score based on baseline gut microbiota profile is a promising predictive biomarker to ICI response for HCC/CCA.

Abstract Submission No. 100880
P-0835

Gut microbiota in patients with NAFLD without type 2 diabetes: Stratified by body mass index.

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Background: The relationship between gut dysbiosis and body mass index (BMI) in non-diabetic patients with nonalcoholic fatty liver disease (NAFLD) is not well characterized. This study aimed to assess gut microbiota's signature in non-diabetic individuals with NAFLD stratified by BMI.

Methods: The 16S ribosomal RNA sequencing was performed for gut microbiota composition in 100 patients with NAFLD and 16 healthy individuals. Bioinformatic analysis was determined by the DADA2 pipeline in the R program. Significantly different genera from the top 50 relative abundance were applied to classify between subgroups of NAFLD by the Random Forest algorithm.

Results: The alpha diversity (Chao1, Shannon, and observed feature) and beta diversity of gut microbiota significantly differed between patients with NAFLD and healthy controls. However, significant differences in their diversities were not observed among subgroups of NAFLD. At the phylum level, there was no trend of elevated *Firmicutes-to-Bacteroidetes* ratio according to BMI. At the genus level, patients with lean NAFLD displayed significant enrichment of *Escherichia-Shigella*, and the depletion of *Lachnospira*, and *Subdoligranulum*, compared to the non-lean subgroups. Combining these bacterial genera could discriminate lean from non-lean NAFLD with high diagnostic accuracy (AUC of 0.82).

Conclusion: Non-diabetic patients with lean NAFLD had a significant difference in bacterial composition compared with non-lean individuals. Our results might provide evidence regarding gut microbiota signatures associated with the pathogenesis of lean NAFLD.

Abstract Submission No. 200150

P-0836

Gut Dysbiosis in Chinese Patients with Antituberculosis Drug-induced Liver Injury

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Whether anti-TB drug-induced liver injury (ATDILI) affects the gut microbiota remains unclear. We assessed characteristic changes in the faecal microbiota, faecal metabolic profiles and short-chain fatty acids in samples of subjects at different clinical stages via 16S rRNA gene sequencing technology and gas chromatography-mass spectrometry. Compared with patients with naïve anti-TB drug treatment (TB0), those receiving long-term anti-TB drug therapy showed faecal microbiome imbalance, generally due to alterations in the relative abundance of bacteria such as *Roseburia*, *Butyrivibrio* and *Romboutsia*. The relative abundance of *Roseburia* was remarkably lower in ATDILI patients ($p < 0.05$). The relative abundance of *Bifidobacterium* and the levels of alanine aminotransferase and alkaline phosphatase were negatively correlated. Metabolite profiling of the ATDILI group distinguished it from the other three groups, characterized by an increase in lipids and lipid-like molecules such as sebacic acid and a decrease in butyric acid. Anti-TB treatment and ATDILI led to dysbiosis of the faecal microbiota and metabolic profile. The gut microbiota may have a key influence on ATDILI progression.

Abstract Submission No. 100058

P-0837

Sarcopenia and Covert Hepatic Encephalopathy in the Latency Period of Abnormal Ammonia Metabolism

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Objective: Early diagnosis is important for patients with Covert Hepatic Encephalopathy (CHE). We investigated the factors contributing to the development of sarcopenia and CHE in LAM.

Subjects and Methods: Subjects were 369 patients with clinically diagnosed cirrhosis between May 2022 and April 2023, who could undergo grip strength, abdominal CT, and neuropsychiatric tests at the same time, without a history of overt hepatic encephalopathy. 227 (62%) males, median age 69 (42-79) years, Child-pugh classification A/B/C: 209/133/27 cases, causative liver disease B/C/alcohol/NAFLD/Others: 46/55/156/76/36 cases.

As previously reported, patients were divided into 4 groups: Stage 0 with normal liver disease, Stage 1a with only decreased BTR, Stage 1b with low Alb, and Stage 3 with high NH₃ (161/28/93/87 patients). In addition, sarcopenia was diagnosed by grip strength and L3-PMI, and abnormalities in two or more of the NCT-A, B, Stroop-test, and Digit symbol test were defined as CHE using NP-test iPad ver. and factors related to CHE were examined by logistic regression analysis and ROC analysis. The factors associated with CHE were examined by logistic regression analysis and ROC analysis.

Results: CHE was observed in 42%, 28/29/53/59(%) in Stage 0/1a/1b/2, decreased grip strength in 33%, 23/18/46/43(%), and sarcopenia in 15%, 6/7/26/23(%), significantly increasing after Stage 1b ($P=0.002$, $P<0.0001$, $P<0.0001$).

When examining factors associated with the development of CHE during LAM (Stage 1a+1b), sarcopenia-related factors were not significant factors, while NH₃ (OR 1.040, 95% C.I. 1.010-1.060, $P=0.009$) and zinc (OR 0.956, 95% C.I. 0.934-0.979, $P=0.0002$) were extracted, and the cutoff values of ROC curves were NH₃ 47 (95% CI: 0.5639-0.7568, AUC: 0.6604) and zinc 71 (95% CI: 0.6641-0.8447, AUC: 0.7544).

Conclusion: NH₃ and zinc level were suggested to be possible predictors of CHE in LAM.

Abstract Submission No. 100089

P-0838

Prevalence of Osteosarcopenia and Liver Frailty Index (LFI) in patients with Cirrhosis

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Introduction: Chronic Liver Disease (CLD) can have a significant impact on the nutritional status of patients. Malnutrition is an under-recognized condition in patients with cirrhosis. Malnutrition increases the incidence and severity of decompensation, increase the risk of infections, and increases mortality.

Objectives: The present study aimed to assess osteosarcopenia and frailty in patients with cirrhosis.

Methods: Total 141 patients have been enrolled during the months of November 2022 to June 2023 at Dr. Ziauddin Hospital Clifton Campus, Karachi. This prospective cross-sectional study included cases of cirrhosis, aged between 18 to 85 years. Anthropometric measurements were performed. Sarcopenia was assessed by hand-grip strength using a hand-held Dynamometer. Bone mineral density was measured with the help of an office-based DEXA scan (Osteosys). Liver Frailty Index (LFI) is assessed by performance-based tests.

Results: The total number of patients included in this study were 141, male 98 (69.5%) with mean age 51.8 ± 13.83 . The prevalence of presarcopenia 66.7% and sarcopenia was 29.1%. The prevalence of osteopenia was 51.1 % and osteoporosis 14.9%. The patients who had osteopenia and osteoporosis were associated with high liver frailty index (p -value<0.001). Most of patients with Osteosarcopenia belonged to Child Pugh score C (p -value<0.001).

Conclusions: There is a high prevalence of pre-sarcopenia, sarcopenia, osteopenia, and osteoporosis, and high frailty in our patients with cirrhosis. Early detection and timely intervention of these conditions are important to reduce the associated consequences. All patients with cirrhosis should be assessed for Osteosarcopenia and frailty both at baseline and longitudinally.

Abstract Submission No. 100162
P-0839

A Diagnostic Marker for Portal Vein Thrombosis in Patients with Cirrhosis

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Background and Aims: Portal vein thrombosis (PVT) is one of the most common hepatic vascular disorders associated significant morbidity and mortality. A disintegrin-like and metalloproteinase with thrombospondin type-1 motifs 13 (ADAMTS13) specifically cleaves multimeric von Willebrand factor (VWF) thereby controls VWF-mediated platelet thrombus formation. An imbalance between ADAMTS13 and VWF is responsible for hypercoagulability, including spontaneous thrombus formation in blood vessels. We aimed to identify diagnostic markers for PVT in patients with cirrhosis.

Methods: 66 patients with cirrhosis were split into two group: PVT groups ($n=33$) and non PVT (NPVT) group ($n=33$). Plasma ADAMTS13 activity (ADAMTS13:AC) and VWF antigen (VWF:Ag) were measured using enzyme-linked immunosorbent assays at diagnosis of PVT in PVT group.

Results: Plasma ADAMTS13:AC was significantly higher in NPVT group than in PVT group, whereas no significant differences in plasma VWF:Ag were observed in patients with cirrhosis. ADAMTS13:AC was an independent risk factor for developing PVT on multivariate (Odds ratio [OR] = 0.00694, 95% confidence interval [95%CI]: 0.000786-0.0613, $p < 0.001$) as a risk factor of PVT. The Receiver operating characteristic analysis for PVT revealed a good classifying capability, with an AUC of 0.913. Patients having ADAMTS13:AC of greater than or equal to 20 had a higher incidence of PVT versus ADAMTS13:AC below 20.0.

Conclusion: Serum ADAMTS13:AC can serve as diagnostic marker for PVT in patients with cirrhosis

Abstract Submission No. 100170
P-0840

The characteristics and metabonomics of gut microbiota in liver cirrhosis patients

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Background/Aims: To investigate the characteristics and relationship of gut microbiota and metabolites in liver cirrhosis patients and explore the effect of *Saccharomyces Boulardii* on liver cirrhosis.

Methods: The characteristics of the gut microbiota in liver cirrhosis patients and healthy subjects from January 2019 to December 2020 were analyzed using 16S rRNA sequencing technology, and the correlation between microorganisms and liver, ROC and function prediction was analyzed. The metabolites in the fecal samples were analyzed using metabonomics, and the network and KEGG was analyzed. The effect of *Saccharomyces boulardii* on gut microbiota and phenotype of 16 liver cirrhosis patients from January 2021 to August 2021 was analyzed.

Results: There was a low similarity and diversity of gut microbiota in cirrhosis compared with normal group and a correlation between significant altered microorganism and liver function, the their diagnostic efficiency for cirrhosis. The function prediction show that abnormal amino acid biosynthesis and metabolism may play an important role in gut microbiota affect liver cirrhosis, meanwhile, the metabolomics certified this hypothesis by KEGG analysis. *Saccharomyces boulardii* was used to association with conventional treatment for liver cirrhosis and there was a rectification of abnormal intestinal microorganism and serum ammonia compared with single conventional treatment.

Conclusions: We considered that the gut microbiota disorder induced to abnormal amino acid metabolism and serum ammonia in liver cirrhosis patients and probiotics could rectified them.

Abstract Submission No. 100185
P-0841

Predictive modelling of liver disease-related mortality in cirrhotic patients using LFI nomogram

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Objective: This study aimed to develop a predictive model for assessing the risk of mortality related to liver disease in patient with cirrhosis utilizing the Liver Frailty Index (LFI) nomogram.

Methods: Inpatients diagnosed with liver cirrhosis at the Traditional Chinese Medicine Hospital Affiliated to Xinjiang Medical University from November 2021 to July 2022, were selected for predicting liver disease-related deaths based on the LFI.

Results: A total of 195 patients were ultimately included in the study, of which 28 (14.3%) experienced liver disease-related deaths. A multifactorial Cox proportional risk regression model was employed, revealing that LFI [HR=1.83, 95% CI (1.23, 2.72), $P=0.003$] and Child-Turcotte-Pugh (CTP) score [HR=1.26, 95% CI (1.03, 1.55), $P=0.028$] were independent risk factors for predicting liver disease-related deaths. The patients were randomly divided into a training set (136 patients) and a validation set (59 patients) in a 7:3 ratio. A nomogram

was constructed based on the aforementioned two variables, providing a robust prognostic assessment of liver disease-related deaths over an 18-month period. The training set exhibited an area under the curve (AUC) of 0.896 (0.732, 1.060), while the internal validation set had an AUC of 0.916 (0.747, 1.085). The C-index for the entire cohort was 0.875 and 0.821 for the training set and validation set respectively. The model calibration curves demonstrated a close fit to the ideal curve.

Conclusion: The nomogram based on LFI and CTP scores demonstrates a high level of accuracy in predicting the risk of liver disease-related mortality among cirrhotic patients.

Abstract Submission No. 100236
P-0842

Risk Factors Leading to Hepatorenal Syndrome in Patients with Cirrhosis

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Aims: Patients with hepatorenal syndrome (HRS) are usually poor prognosis. For better improving prognosis of patients, It requires a comprehensive analysis of the risk factors associated with HRS and clarify its predictive role for HRS.

Methods: 51 cases of inpatients from Central Hospital of Thai Nguyen were selected from January 2023 to July 2023. Their clinical data, including general information, clinical features, and blood biochemical indexes were analyzed as risk factors. They were further divided into two groups: (1) control group: patients received intravenous sodium supplement and oral liver-protective drugs treatment. (2) treatment group: patients received a series of therapies including intravenous supplement of sodium, albumin and Terlipressin, oral administration of liver-protective drugs. We then compared the incidence of HRS development during the hospitalization between the two groups.

Results: we discovered that the factors including gastrointestinal hemorrhage, bacterial peritonitis, long-term use of diuretics and releasing ascites in large quantities, lower plasma sodium and albumin level were risk factors for prediction of HRS. Our results showed that the incidence rate of HRS was significantly lower in patients received therapies, which indicated a significantly better prognosis of patients with cirrhosis after reducing the risk.

Conclusion: The analysis of HRS associated risk factors benefits to predict HRS and cirrhosis patient's prognosis.

Keywords: Risk Factors, Hepatorenal Syndrome, Cirrhosis

Abstract Submission No. 100315
P-0843

Acute gastrointestinal injury for the prediction of progression in acute decompensation of cirrhosis

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Background and Aims: This prospective, observational study evaluated the role of acute gastrointestinal injury (AGI) in the 28-day and 90-day prognosis of cirrhotic patients with acute decompensation (AD).

Methods: The baseline clinical characteristics of AD patients ($N = 231$) were recorded, and gastrointestinal function (GIF) was assessed. The patients were divided into three AGI groups based on their AGI grade (according to the European Society of Intensive Care Medicine guidelines), and they were followed for 90 days or until either death or liver transplantation.

Results: Follow up to 90 days, 63 patients (22.27%) died and 2 (0.87%) underwent liver transplantation. Cox regression analysis identified age, endotoxin, creatinine, international normalized (INR), and the occurrence of AGI as independent predictors of 28-day and 90-day death or transplantation. These five predictors were identified in the final Cox regression model, and 28-day (the AGIM28 model) and 90-day (the AGIM90 model) predictive models and their corresponding nomograms were constructed. Of five prognostic models, the AGIM models had the highest prediction efficiency. In the Kaplan-Meier survival curve analysis, the 90-day cumulative survival rate of the three AGI groups (no-AGI, AGI 1, and AGI 2) decreased gradually ($P < 0.001$). Multivariate logistic analysis showed that d-lactate, bilirubin, INR, and bowel sounds were independent predictors of AGI progression.

Conclusion: Our novel prediction models, the AGIM28 and AGIM90, can effectively predict the 28-day and 90-day death or transplantation risk of cirrhotic patients with AD. The presence of AGI plays an undeniable role in the poor prognosis of AD patients.

Abstract Submission No. 100388
P-0844

Endoscopic variceal ligation versus propranolol as prophylaxis of first variceal bleeding

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Introduction: Both endoscopic variceal ligation and propranolol are known to be effective methods for preventing variceal bleeding, but there are still few published data for comparing efficacy and safety. We analysed the efficacy and safety of endoscopic variceal ligation (EVL) and propranolol in terms of prophylaxis for the first bleeding rate.

Method: A retrospective cohort study was conducted in 1,052 cirrhotic patients with no history of previous esophageal bleeding with F2 or F3 esophageal varices from a university hospital between September 2008 and October 2022. 697 patients received EVL and 355 patients used propranolol. The primary end-point of the study was bleeding rate and secondary end-point was overall survival.

Results: Life-time table curves indicated that prophylactic EVL and propranolol were similarly effective for primary prophylaxis of variceal bleeding (147/697 [21%] vs 82/355 [23%], $P=0.72$) and overall mortality (279/697 [40%] vs 128/355 [36%], $p=0.46$). The 2-year cumulative mortality rate was 31%(217/697) in the EVL group and 27%(97/355) in the propranolol group. Comparison of Kaplan-Meier curves of the time to death of both groups showed no significant difference in mortality in both groups ($P=0.78$). Patients undergoing EVL died mainly of hepatic failure and propranolol group died mainly from infection.

Conclusion: Both prophylactic EVL and propranolol are effective and safe methods for reducing the incidence rate of first variceal bleeding and mortality.

Abstract Submission No. 100424
P-0845

Change in the Child-Pugh score after albumin infusion in decompensated cirrhosis

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Background and Aims: As albumin is quantitatively and qualitatively deficient in cirrhosis, it is hypothesized that albumin supplementation could prevent the decompensation of cirrhosis. This randomized unblinded pilot study compared the effect of albumin and the standard medical treatment on cirrhotic complications and survival in patients with decompensated cirrhosis.

Methods: Forty cirrhotic patients with Child-Pugh score 7-10 were randomized to receive the standard medical treatment (SMT) or SMT plus human albumin 40 grams at the initiation and 25 grams every two weeks for 12 weeks. Patients were followed up to 12 months.

Results: There were no significant differences between both groups in the one-year mortality ($p = 0.78$). However, patients treated with albumin showed a reduction in the progression of ascites and an improvement of liver function verified by Child-Pugh score ($p = 0.019$). No difference was found in the probability of developing complications of cirrhosis including spontaneous bacterial infections, hepatic encephalopathy, hepatorenal syndrome, and hyponatremia in the two patient groups.

Conclusion: In patients with decompensated cirrhosis, albumin infusion might act as a disease-modifying treatment and affect the improvement in liver function.

Abstract Submission No. 100459
P-0846

Hypoalbuminemia and zinc supplementation in patients with chronic liver disease.

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Background: Hypoalbuminemia has been reported to be a frequent complication in patients with cirrhosis. The purpose of this study was to clarify the relationship between serum zinc levels and the symptoms and disease progression of chronic liver disease.

Methods: 184 patients with chronic liver disease who visited our institution were subjected to measurement of fasting serum zinc levels in the morning. The presence of symptoms related to hypoalbuminemia was confirmed by a questionnaire. 48 patients with zinc deficiency were treated with zinc replacement therapy with zinc acetate or polyprezinc.

Results: In 94 patients with cirrhosis, the median zinc level was 63 µg/dL (22-94), with <60 in 43% (39 patients). In 90 patients with chronic hepatitis, the median zinc level was 77 µg/dL (38-114), with <60 in 14.4% (13 patients). The most common symptoms associated with hypoalbuminemia were dermatitis (23%), poor wound healing (18%), and aphthous stomatitis (14%). A significant increase in serum zinc (54.5→71µg/dL) was observed 3 months after zinc replacement therapy in 48 cases. There was no significant difference in improvement rate between patients with and without cirrhosis. A significant decrease in ammonia level (44→39µg/dL) was observed in patients with elevated zinc.

Conclusion: At our institution in Japan, there were many cases of hypoalbuminemia not only in patients with cirrhosis but also in patients with chronic liver disease. A significant decrease in ammonia levels was observed in patients with elevated zinc levels due to zinc supplementation.

Abstract Submission No. 100093
P-0847

Role of Endoscopic Ultrasound in diagnosis of unexplained distal Common Bile Duct stricture

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Background: Determining the etiology of a distal biliary stricture without an identifiable mass on imaging is crucial to the provision of appropriate therapy.

Aim of the work: To assess the ability of Endoscopic Ultrasound (EUS) to diagnose distal biliary strictures for which cross-sectional imaging modalities such as Computed Tomography (CT) scan and Magnetic Resonance Imaging (MRI) could not detect a causative mass or bile duct thickening.

Patients and Methods: Prospective study on 80 patients with unexplained distal biliary stricture diagnosed by Magnetic Resonance Cholangiopancreatography (MRCP), Endoscopic Retrograde Cholangiopancreatography (ERCP), CT or MRI underwent EUS.

Results: 80 patients (50 male; mean age 57.9 ± 9.8 years) were studied. Based on EUS findings; 51 patients were diagnosed with malignant strictures 63.75% (21 distal cholangiocarcinoma, 17 pancreatic head mass, 11 ampullary mass lesion and 2 intraductal papillary mucinous neoplasm) and rest of patients were diagnosed with benign strictures 36.25%. Mean distal CBD wall thickness in benign strictures (2.87 ± 0.76 mm) while in malignant strictures (4.49 ± 1.4 mm) with very high statistical significant difference (P -value <0.001). ROC analysis between malignant and benign strictures for distal CBD wall thickness has shown a cutoff value >3.2 (Sensitivity 80.39%, Specificity 89.66%, Positive predictive value (PPV) 93.2, Negative predictive value (NPV) 72.2 and accuracy 85.7%).

Conclusion: EUS is a useful investigational modality for patients with unexplained distal CBD stricture.

Keywords: Endoscopic ultrasound, Distal biliary stricture.

Abstract Submission No. 100415
P-0848

Endoscopic ultrasound for ampullary cancer: a case report

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Primary ampullary carcinoma is a rare type of periampullary tumor, with an incidence of about 4-10/1 million, accounting for about 6% of periampullary lesions, and leading to 20% of tumor-associated bile duct obstruction. For jaundice patients with suspected malignant biliary obstruction, Endoscopic retrograde cholangiopancreatography (ERCP) is the preferred initial endoscopic examination Because of its flexibility and practicality though it cannot figure out the extent of

local invasion of ampulla carcinoma. While endoscopic ultrasonography (EUS) to small ampulla carcinoma is as sensitive as ERCP, and it can find out the depth of tumor invasion and the degree of tumor expansion, which is conducive to preoperative staging. Some new endoscopic ultrasound techniques are used in the treatment. Here is a case: male, 73-year-old, chief complaint: skin and urine have been yellow for more than 20 days. In 2023.08, The Upper abdominal CT and PET-CT indicated his possibility of periampullary malignant tumor. PTCD was performed to relieve his obstructive jaundice with little success. Then EUS-FNB was performed. Endoscopic ultrasonography showed a hypoechoic space at the conjunctures of the bile pancreatic duct, the section was about 22×19mm large, and multiple lymph node enlargement in the abdomen. Pathological biopsy of the ampulla agreed with adenocarcinoma (pT2N1M0). On 9.18, the patient was performed with EUS-BD-CDS, then jaundice relieved. Endoscopic ultrasonography played an important role in this case, indicating that endoscopic ultrasonography has certain value in the diagnosis and treatment of ampulla carcinoma.

Abstract Submission No. 100540
P-0849

Longitudinal analysis of repeated variceal ligation in acute EV bleeding: a 5-year perspective

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Background: In acute esophageal variceal bleeding (EVB), initial treatment combines pharmacology and endoscopy, especially endoscopic variceal ligation (EVL). For rebleeding, transjugular intrahepatic portosystemic shunt (TIPS) is recommended, but in settings with limited TIPS access, repeated endoscopic therapy is common. This study assesses EVL outcomes on rebleeding and mortality in resource-limited contexts.

Methods: Patients experiencing acute EVB and undergoing EVL were monitored for up to five years or until their demise. These patients received treatment involving vasoactive drugs and EVL until variceal eradication was achieved. The primary endpoints were the effectiveness of bleeding control and the necessity for a second EVL session to manage EVB. Mortality rates at both 6 weeks and 5 years were analyzed. Logistic regression analysis was employed to identify risk factors associated with mortality.

Results: Among the 118 patients with acute EVB who underwent EVL, no treatment failures occurred within five days. 83% were successfully controlled with one EVL session, while 17% required at least two sessions for recurrent bleeding. There was no significant difference in 6-week mortality between rebleeding (15%) and non-rebleeding (18%) groups ($p=0.72$). Factors associated with 6-week mortality included age, hepatocellular carcinoma, post-bleeding beta-blocker use, creatinine, bilirubin, albumin, Child-Pugh class, and MELD score (Table). Over five years, rebleeding group had a higher mortality trend (90%) compared to non-rebleeding group (68.8%), although it wasn't statistically significant ($p=0.06$).

Conclusion: In resource-limited settings, multiple attempts of EVL demonstrates success in controlling rebleeding. The long-term trends showed higher mortality in rebleeding cases, though not statistically significant.

Abstract Submission No. 101203
P-0850

Self-expanding metal stent as therapy for refractory variceal bleeding: a single centre experience

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Refractory oesophageal variceal bleeding (OVV) is associated with high mortality rate. Balloon tamponade (BT) is a bridge to definitive therapy. Novel SEMS such as SX-ELLA Danis are alternatives to BT for refractory OVB. We report our centre's experience of two such cases which necessitated deployment of SEMS focusing on technical success, immediate haemostasis control, stent-related complications and mortality.

Case 1: A 43-year old male with Child-Turcotte-Pugh score (CTP) B8 alcoholic liver cirrhosis, MELD 18 presented with haemorrhagic shock from refractory oesophageal VB despite standard of care (SOC) and endoscopic variceal ligation (EVL). Although immediate haemostasis was achieved with SEMS insertion, he demised from multiorgan failure (MOF) shortly after.

Case 2: A 49-year old female with CTP A6 alcoholic liver cirrhosis, MELD 20 presented with OVB. Despite SOC, she had rebleeding and haemorrhagic shock requiring stabilisation with BT. Despite this, refractory bleeding was seen on removal of BT and EVL was unsuccessful, requiring SEMS deployment, after which haemostasis was achieved. Transjugular intrahepatic portosystemic shunt (TIPS) was performed 24 hours after with SEMS removal done 1 week later. In both cases, technical success and immediate haemostasis were 100% after SEMS insertion. There were no stent-related complications. In conclusion, SEMS insertion is safe, has good technical success and effective in achieving temporary haemostasis in refractory oesophageal VB. Timely insertion of oesophageal SEMS before development of MOF may be a determining factor for clinical success. Larger studies are required to evaluate early timing of SEMS insertion and cost-effectiveness.

Abstract Submission No. 101232
P-0851

NEW TUNNEL TECHNIQUE IN LAPAROSCOPIC-CHOLANGIOSCOPIC COOPERATIVE SURGERY FOR HEPATOLITHIASIS

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Introduction: Laparoscopic common bile duct (CBD) exploration using the cholangioscope has become a standardized technique within the last years. However, the using of the cholangioscope remove intrahepatic and bile stones often becomes a time-consuming and difficult part of the operation. Our newly design instrument, is a tube placed through the skin into CBD, the cholangioscope will be inserted through this tunnel to remove the stones.

Method: We describe the step-by-step technique using the new instrument under laparoscopic guidance, in patients with hepatolithiasis combined with choledocholithiasis. Main outcomes were complete stone clearance rate, single-session stone clearance rate, number of endoscopic sessions needed for stone clearance, and adverse events.

Result: Among 31 patients with hepatolithiasis and choledocholithiasis underwent laparoscopic CBD exploration to remove stones using cholangioscopy through the tube from June 2019 to June 2022. 32,2% of patients had a history of laparotomy, in which 22,5% had a history of CBD exploration. The complete stone clearance rate was 83,8%. Single-session stone clearance was achieved in 70,9%. Two cases of postoperative complication of minor bile leakage, no treatment were necessary. The average operative time and tube insertion time were 126 ± 36 minutes and 5 ± 2 minutes, respectively. Postoperative hospital stay was 8.5 ± 2.6 (days).

Conclusion: The combination of laparoscopic CBD exploration using the cholangioscope and the new instrument is a effective and safety technique, and may be considered as a standard approach of the treatment for hepatolithiasis combined with choledocholithiasis.

Abstract Submission No. 200101

P-0852

Feasibility of EUS-BD in the initial drainage for unresectable malignant hilar biliary obstruction

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Background: The efficacy and safety of EUS-guided biliary drainage (EUS-BD) in the initial drainage for unresectable malignant hilar biliary obstruction (MHBO) have not been well evaluated.

Methods: We retrospectively analyzed 42 patients who underwent EUS-BD in the initial drainage for unresectable MHBO with Bismuth II or higher.

Results: Characteristics of the study patients were as follows: age, median 72 years (range: 42-86); sex, 50% male; Bismuth classification, II (9)/IIIa (13)/IIIb (1)/IV (19); primary cancer site, pancreas (9)/colorectal (8)/gallbladder (7)/bile duct (6)/ICC (5)/others (7); reason for EUS-BD, severe stricture (16)/surgical altered anatomy (15)/duodenal invasion (5)/tumor characteristics (5)/failed cannulation (1). Drainage methods included EUS-BD alone in 28 and EUS-BD combined with ERC-BD in 14 cases. EUS-BD procedures included hepaticogastrotomy (HGS) in 25, HGS with bridging in 10, hepaticoduodenostomy (HDS) in 4, and HGS with HDS in 3 cases. Median procedure time, technical success rate, and functional success rate were 40.5 min (16-130), 100% (bridging success rate: 67%), and 86%, respectively. Early adverse events developed in 8 (19%), which included biliary peritonitis in 4, abdominal pain in 2, fever in 1, and cholangitis in 1 case. Recurrent biliary obstruction (RBO) developed in 8 (19%) with the median time to RBO of 126 days (95%CI: 75-NA). Median overall survival was 69 days (95%CI: 41-115).

Conclusion: Applying EUS-BD in the initial drainage for unresectable MHBO might be safe and feasible.

Abstract Submission No. 100515

P-0853

Post Transjugular Intrahepatic Portosystemic Shunt Cardiac Failure in patients with cirrhosis

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BACKGROUND: Transjugular intrahepatic portosystemic shunt (TIPS) is effective in alleviating the complications of portal

hypertension. However, post-TIPS cardiac failure has become one of the main concerns recently. The previous study has found that post-TIPS cardiac failure occurred in 20% of patients.

AIMS: This study was designed to evaluate the incidence of post-TIPS cardiac failure and predisposing factors in patients with cirrhosis.

METHODS: Between September 2022 and August 2023, consecutive cirrhotic patients who underwent elective TIPS were prospectively screened for inclusion. Symptomatic heart failure and organ failure that affect circulation before TIPS were excluded. A systematic cardiac assessment was conducted in each patient including biological parameters, BNP, and transthoracic echocardiography. The primary endpoint was the incidence of cardiac failure.

RESULTS: 138 patients underwent TIPS during the study period and 122 met inclusion criteria [aged 53.7 ± 10.5 years, 63.9% man]. Baseline echocardiography showed 59 (48.4%) patients had diastolic dysfunction, and the ejection fraction was 67.4 ± 6.4 . Before TIPS, the mean Child and MELD scores were 7.3 ± 1.5 , and 10.8 ± 2.4 respectively. 67.4% of the patients had virus-related cirrhosis. TIPS indication was variceal bleeding in 87.5% of the patients. During a median of 6 months of follow-up, none of the patients experienced cardiac failure. However, 87(71.3%) patients had lower limb edema.

CONCLUSION: Post-TIPS cardiac failure is rare in the current cohort. The effect of lower limb edema on the long-term outcome of cirrhotic patients following TIPS requires further investigation.

Abstract Submission No. 100533

P-0854

Liver and spleen volume are not a predictor of hepatic encephalopathy(HE) in post -TIPS cirrhosis

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Abstract

Background: BACKGROUND: Residual liver volume was closely related to liver function after hepatectomy. Hepatic encephalopathy is a common complication in cirrhosis after transjugular intrahepatic portosystemic shunt(TIPS). The purpose of this study is to assess the effect of liver and spleen volume on post-TIPS HE.

Methods: This was a retrospective study consisting of 737 patients who had undergone TIPS from January 2012 to December 2019. The baseline characteristics were collected. The univariate and multivariate cox regression analyses were used to identify the risk factors for hepatic encephalopathy after TIPS.

RESULTS: Of the 737 patients included in this study, 545(74.3%) were male, the mean age was 49.5 ± 10.7 years, and the etiology was mostly hepatitis cirrhosis(85.7%). Before the surgery, the mean MELD and CP scores were 11.2 ± 3.5 , 7.9 ± 2.6 , the mean liver and spleen volume $\pm$ standard deviation respectively were 9.6 ± 2.3 and 6.0 ± 2.7 at baseline. After a median follow-up of 49 (31-79) months, 306(41.5%) patients occurred hepatic encephalopathy. In the multivariate cox regression analyses, liver volume (HR 0.98, 95% CI 0.94 -1.0, P = 0.21) and spleen volume (HR 0.99, 95% CI 0.96-1.0 P = 0.43) was not a significant predictor for HE post-TIPS.

Conclusion: The liver and spleen volume before the placement of stent were not associated with HE in Post -TIPS cirrhosis.

Abstract Submission No. 100534

P-0855

Sleep disturbance in patients with cirrhosis and transjugular intrahepatic portosystemic shunt

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Background: Sleep disturbance (SD) is common in patients with cirrhosis and may lead to poor quality of life. Data regarding post-TIPS SD is scarce. The present study was designed to investigate the incidence and outcomes of post-TIPS SD.

Methods: From August 2018 to November 2019, 73 patients treated with TIPS were prospectively enrolled. The Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep quality, and the presence of hepatic encephalopathy was evaluated using the West Haven criteria before and after TIPS. The primary outcome was the incidence of SD after TIPS.

Results: 19 patients (26%) were the new onset of SD after TIPS and the median time from TIPS creation to the occurrence was 67 (40-98) days. Minimal hepatic encephalopathy (MHE) after TIPS (OR =3;95% CI 1.8;78; P=0.046) was demonstrated as an independent risk factor for SD. Five of six (83%) patients with SD improved after treatment with eszopiclone. Ten of thirteen (77%) patients with SD improved spontaneously without treatment. The incidence of MHE in patients with SD was higher than that in patients without SD (58% vs 31%, P=0.04).

Conclusions: The incidence of SD is not uncommon in patients who underwent TIPS. MHE is an independent risk factor associated with post-TIPS SD. Eszopiclone may be effective and safe for patients with SD after TIPS.

Abstract Submission No. 100616
P-0856

CART in patients with liver cirrhosis is useful not only albumin retention but also zinc retention

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Background: Liver cirrhosis causes zinc deficiency. If ascites cannot be controlled with diuretics, Ascites drainage alone or Cell-free and concentrated Ascites Reinfusion Therapy (CART) is necessary. CART is effective in albumin retention, but if CART is effective in Zinc retention or not.

Methods: We investigated zinc concentration of ascites who underwent CART (2018.4-2023.10). Asahikasei Medical's AHF-MO/AHF-UP were used.

Results: 13 cases were registered. but 2 were excluded due to insufficient filtration. Age68±12y.o, M/F 8/3, ALD/NAFLD/HBV/HCV 3/3/3/2, HCC/CCC 7/1, Diuretics use 11, and 10 cases use zinc preparations. TB 1.5±2.0mg/dL, PT 62±36%, Alb 2.7±0.4 g/dL, Zinc 56±21µg/dL. Zinc of ascites was 12±7µg/dL. Zinc in the filtered and concentrated ascites was 99±81µg/dL. The amount of zinc in ascites was calculated by checking the scale value on the collection bag, 490 ± 249 µg. The zinc recovery rate is calculated by assuming that the specific gravity of the ascites and the filtered concentrate are almost similar, and calculating Zinc of the filtered and concentrated (µg/dL) x the weight of the filtered and concentrate (kg) / Ascites zinc (µg/dL) x Ascites weight (kg), it was 84 ± 22%.

Conclusion: The daily zinc intake of Japanese people is said to be 11 mg(average),but the absorption rate of zinc is about 20-40%, although it depends on comorbidities, concomitant medications, and status of zinc transporters at small intestinal epithelial cells. Zinc deficiency in patients with liver cirrhosis results from malabsorption, loss of zinc

due to diuretics, etc. Simple ascites drainage causes zinc loss, on the other hand, CART is useful in zinc retention.

Abstract Submission No. 100637
P-0857

Frailty Based on LFI as predictor of Mortality in Liver Cirrhosis Patients: A Systematic Review

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Background: Frailty is a biologic syndrome that can lead to susceptibility to poorer outcomes. Frailty assessment is currently developing in the population of patients with liver cirrhosis, one of which is Liver Frailty Index (LFI). The prevalence of liver cirrhosis patients who experience frail is high that will increase the risk of mortality.

Aims: To assess frailty based on the Liver Frailty Index as a predictor of mortality in patients with liver cirrhosis

Methods and Material: Literature search was conducted through online databases: PubMed/MEDLINE, EMBASE, ProQuest, and EBSCOhost using the keywords "cirrhosis of the liver" and "liver frailty index". The studies included were prospective and retrospective cohort studies that included patients with liver cirrhosis and reported patient mortality based on frailty status.

Results: A total of 7 articles were included in this systematic review, 3 of which were included in a meta-analysis to assess the association with mortality and 2 studies assessed the association with the incidence of decompensation. There was a higher risk of mortality in cirrhotic patients with frailty (HR 1.68; 95% CI 1.36-2.08; p<0.00001). In addition, frailty was found to be associated with the incidence of ascites (OR 1.84 95% CI 1.41-2.40; p<0.00001). However, there was no association between frailty and the incidence of HE in patients with liver cirrhosis (OR 1.57 95% CI 0.65-3.80; p=0.31).

Conclusions: Frailty is a predictor of mortality in patients with liver cirrhosis. Frail liver cirrhosis patients have a greater risk of death than non-frail.

Abstract Submission No. 100668
P-0858

Contrast-induced Nephropathy in Patients with Cirrhosis: A Systematic Review and Meta-Analysis

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Background: Cirrhotic patients are frequently subjected to imaging procedures involving contrast agents, and may have additional risk factors that predispose them to contrast-induced nephropathy (CIN). The nephrotoxic potential of contrast agents among cirrhotic patients is still a debated issue due to limited and conflicting evidence.

Objective: To determine if the use of contrast agents for imaging procedures among cirrhotic patients is associated with the development of CIN.

Methodology: A comprehensive search for databases of randomized controlled trials (RCTs) and observational studies comparing contrast-enhanced studies versus without contrast for occurrence of CIN among adult patients with cirrhosis was done. PubMed, EMBASE, Cochrane library, and ClinicalTrials.gov were searched using relevant terms including cirrhosis, CIN or contrast associated acute kidney injury (AKI)

until October 2023. Data extraction was performed using a standardized data form, and any discrepancies were resolved by consensus among the authors. Data were pooled using Review Manager Software version 5.4.

Results: A total of nine studies were included in the systematic review, with reported incidence of CIN ranging from 2.5-5%. Two prospective (n=385) and two retrospective (n=604) observational studies were included in the meta-analysis. The contrast group was associated with an increased risk for CIN, OR 2.52, 95%CI: 1.52-4.16. Risk factors predisposing cirrhotic patients to CIN include ascites and presence of infection (OR 2.796, 95%CI: 1.109-7.052; OR 22.18, 95%CI: 2.87-171.22, $p=0.003$ respectively).

Conclusion: Available evidence suggests that the risk of AKI among cirrhotic patients exposed to contrast agents is increased, and thus post-contrast renal function should be closely followed.

Abstract Submission No. 100672

P-0859

Multi-target drug discovery for TGF β -mediated liver cirrhosis/HCC: *in silico* and *in vitro* approaches

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Background: It is well known that decompensated liver cirrhosis (LC), regardless of etiology, eventually develops hepatocellular carcinoma (HCC). Transforming growth factor beta (TGF- β) activates multiple kinases in the pathogenesis of LC/HCC. Multi-target drug discovery is the preferred approach in chronic disease therapy. Therefore, we used this approach involving *in silico* and *in vitro* techniques.

Methods: We conducted virtual high-throughput screening (VHTS) of the Korea Chemical Bank (KCB) natural products library against TGF- β receptor type-1 (TGF- β RI), focal adhesion kinase (FAK), and phosphoinositide 3-kinase (PI3K) using AutoDock Vina software. We used VMD and NAMD software for dynamics simulation. We predicted the drug-likeness and pharmacokinetics profiles of the hit compounds using free webtools, SwissADME and ADMETlab 2.0. We examined the anticancer effects of diosmetin and luteolin on HepG2 cell lines using MTS and q-PCR techniques.

Results: Docking and dynamics simulation results revealed potential TGF- β inhibitors with better binding affinities (ranging from -11.2 to -10.4 kcal/mol) than galunisertib (-10.0 kcal/mol). Dihydrosanguinarine (DHS) and eriocitrin showed the best docking scores against the key targets of LC. Matrix metalloproteinase 2 (MMP2) and MMP13 were identified as potential targets related to alcoholic LC through bioinformatics. Moreover, the drug-likeness and pharmacokinetic profiles demonstrated that DHS, trisindoline, and alpha-naphthoflavone could be acceptable oral drug candidates. Luteolin exhibited dose-dependent, multi-target inhibitory effects. However, diosmetin upregulated the gene expressions dose-dependently.

Conclusions: VHTS revealed promising multi-target hit compounds in comparison with reference inhibitors. However, validation of the anti-fibrotic effects in an *in vivo* LC model is needed.

Abstract Submission No. 100702

P-0860

Nutritional Status is Associated with Cognitive Function in Chronic Liver Disease

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Background: Nutritional status and cognitive function are important factors that affect the morbidity and mortality in chronic liver disease patients. The aim of this study is to find out whether the nutritional status of chronic liver disease patients could affect patients' cognitive function.

Methods: Among chronic liver disease patients admitted to the tertiary hospital, department of Hepatology from 2018 to 2021, who underwent a number connection test (NCT) before performing diagnostic endoscopy were retrospectively analyzed. Nutritional status was evaluated by the Psoas Muscle Index (PMI), which was calculated using psoas muscle area at the L3 level adjusted by height (cm^2/m^2).

Results: A total of 134 patients had NCT results. The mean age was 56.93 (± 9.598) years, and 99 (73.9%) were males. HBs Ag was positive in 43 patients (32.1%), and Anti-HCV was positive in 21 patients (15.7%). Hepatocellular carcinoma was diagnosed in 49 patients (26.6%) and liver cirrhosis in 85 patients (63.4%). The baseline NCT was 47.12 (± 18.241), the MELD score was 7.74 (± 6.579), and the PMI was 3.57 (± 1.075). The baseline NCT was associated with age ($r=0.514$, $P<0.0001$), MELD ($r=0.230$, $P=0.007$), and PMI ($r=-0.272$, $P=0.002$), respectively. PMI was statistically associated with NCT in both LC ($r=-0.230$, $P=0.034$) and HCC ($r=-0.432$, $P=0.002$) patients. As a result of multiple regression analysis, the regression coefficients were revealed as age: 0.964 ($P<0.0001$), MELD: 0.519 ($P=0.010$), and PMI: -2.780 ($P=0.026$), respectively.

Conclusion: The nutritional status of chronic liver disease was significantly associated with cognitive function.

Abstract Submission No. 100734

P-0861

The Comparison of PEG 3350 and Lactulose Use for Hepatic Encephalopathy Management: an EBCR

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A 68-year-old male patient with liver cirrhosis was admitted to the ER with altered consciousness and diagnosed with hepatic encephalopathy (HE). The lactulose was given. Hepatic encephalopathy is caused by the increase of ammonia levels and neurotransmitters. Inhibiting ammonia absorption with lactulose is the current management for hepatic encephalopathy. However, PEG (Polyethylene Glycol) 3350 is considered to have a role in HE management. The article search from five sources of articles was done with the keywords: “((((hepatic encephalopathy) AND polyethylene glycol 3350) OR PEG 3350) AND lactulose) AND hepatic encephalopathy scoring algorithm) OR HESA”. A study that compared the use of PEG 3350 and lactulose in HE management showed that the HESA (hepatic encephalopathy scoring algorithm) score improved more rapidly in the PEG 3350 group with a relative risk (RR) of 1.61, absolute relative risk (ARR) of 0.32, relative risk reduction (RRR) of 0.615, and number needed to treat (NNT) of 3.125. The PEG 3350 can increase the fecal excretion of ammonia compared to lactulose. In addition, the mild metabolic acidosis effect from PEG 3350 can increase the level of NH_4^+ and lower the level of NH_3 , a compound that can bypass the blood-brain barrier. However, because of the high amount of PEG that needed to be given (4 liters of PEG in 4 hours), lactulose use (only 20-30 grams or 30-45 mL) is more

feasible. In conclusion, the use of PEG 3350 for improving HESA in HE patients is more potent than lactulose, but it lacks of practical feasibility.

Abstract Submission No. 100791
P-0862

A novel tool for the treatment of liver cirrhosis and hypertension: wearable technologies

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Introduction: A common and significant cause of death in India is liver cirrhosis, along with hypertension. Heart rate monitoring, cardiovascular identification and liver problems, and access to health-related data are all features of modern wearable smartwatches. The present study examine that patients would wear and keep wearable smart watches on a regular basis, as well as would effectively collect and transmit sensor data, we conducted a feasibility study in this study.

Method: About 135 individuals with liver cirrhosis and hypertension participated for the current study. Every patient was given a set of wearable technology, and information was collected via questionnaires, audio recordings, physical activity, acceleration, and heart rate. A variety of methods were employed to collect data on relevant adherence factors, including life questionnaires on quality health-related aspects,, examinations of cardiovascular health, and the Scale Compliance on Hypertensive.

Result: Of the 135 patients with liver cirrhosis and hypertension, 110 underwent the research, used the wearable watches on a regular basis and successful. Reduced adherence to lifestyle changes and prescription regimens, and increased overall adherence are significant predictors of compliance, according to the binary logistic regression models. Direct data extraction from the devices yielded the heart rate and accelerometer values. An average day of 60.2, 61.3, and 58.2 was reported for secondary findings such as heart rate, physical activity, and questionnaire survey.

Conclusion: According to our hypothesis, people who have liver cirrhosis and hypertension wear and utilize the wearable device on a regular basis and provide this technology positive feedback

Abstract Submission No. 100809
P-0863

Specialist nurse-led 'stable cirrhosis' clinics in a UK hospital – enabling service development

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Background: In our unit, patients with stable cirrhosis are seen in a specialist nurse-led clinic if they have Child-Pugh A disease, no hospital admissions in the preceding year and have had a senior medical review.

Methods: This was a retrospective analysis of patients reviewed in the clinic from January 2017 to December 2017. Medical notes and blood tests were reviewed for the three-year period from the point of referral.

Results: Over 3 years, 56 patients were referred to the clinic. Alcohol-related liver disease (ARLD) (34%) and NAFLD (34%) were the most

common aetiologies. Over the 3-year period, 37 patients (66%) remained in the clinic whilst 19 patients (34%) left. Reasons included death (11%), repeated non-attendance (37%) and decompensation of liver disease (32%). The mean time for departing from clinic was 17 months and median time was 21 months. Overall, 11% of patients referred to the clinic decompensated (requiring hospitalisation/consultant-led care). Rate of decompensation has previously been shown to be 11.8% per year in a UK cohort study (1).

Of non-attenders, 71% had ARLD, whilst 67% of decompensations had a background of ARLD. 50% of patients who decompensated required hospital admission. Mean time from referral to decompensation was 16 months.

Conclusions: This analysis demonstrates the effectiveness of a specialist nurse-led clinic in managing compensated cirrhosis patients. Patients can be seen in a timely fashion, and the clinic facilitates increased capacity in medical-led clinics. The strategy is likely to be cost-effective. We also demonstrated a lower rate of decompensation than previously seen.

Abstract Submission No. 100888
P-0864

Simvastatin in Treatment and Reducing Events of Decompensation in Liver Cirrhosis: A Meta-Analysis

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Background: Liver cirrhosis represents a late stage of progressive hepatic fibrosis with most deaths being secondary to decompensation and evolution of portal hypertension. Since disease progression reversal is hardly attainable, it is essential to intervene early with a therapeutic agent that could reduce disease evolution. There are studies coming out about statins being beneficial in patients with liver cirrhosis, in which they are showed to have modest direct effect in lowering portal vein blood pressure from vasodilatory properties. This will be explored in our study.

Methods: A systematic review and meta-analysis was done using randomized control trials who applied patients aged 18-75 years old with known liver cirrhosis with portal hypertension using Simvastatin as therapy. Decrease in levels of HVPG post treatment was used as marker for improvement.

Results: There was significant difference in HVPG levels and liver function among patients with liver cirrhosis who had adjunct use of simvastatin vs. standard treatment. Visual inspection of the forest plot appears to favor use of simvastatin in improving liver function in patients with liver cirrhosis. A moderate heterogeneity was also observed using the fixed effect model.

Conclusion: While earlier data depict statins to have harmful effects in the liver, evidence, as shown in this paper, suggest that there is positive impact in reducing events of decompensation and portal hypertension. Combining this knowledge with our long track-record of safety and tolerability of statins, we might soon rely on statins to achieve better outcomes in patients with liver cirrhosis without significant additional costs.

Abstract Submission No. 100953
P-0865

Impact of the growth hormone-insulin like growth factor on complications and prognosis in cirrhosis

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Background: This study evaluated the impact of growth hormone-In-sulin-like growth factor (GH-IGF1) axis on sarcopenia, frailty, autonomic neuropathy, and the prognosis in decompensated cirrhosis patients.

Methods: Adult stable decompensated cirrhosis out-patients recruited at a tertiary care institute between 2021-2023 were subjected to the estimations of serum GH-IGF1, sarcopenia, frailty, autonomic dysfunction, clinical decompensations, and survival.

Results: 150 patients, 95% males with a mean age of 45.5±9.86 years, with ascites (grade-I: 30%, grade-II: 47.3%, grade-III: 19.3%), HE (grade-I: 5.4%, grade-II: 2%), MELD-Na of 15.4(IQR:11.9-18.6), and CTP of 8(7-9) [CTP A-11.3%, CTP B-64.7%, CTP C-24%] were recruited. Sarcopenia, frailty, and autonomic neuropathy were noted in 64.7%, 25%, and 29% patients.

IGF1 levels were significantly reduced in patients with sarcopenia (OR:0.15; p=0.021), negatively associated with liver frailty index (β =0.453), severity of autonomic neuropathy (β =0.11), MELD (β =-4.74), and CTP (β =-1.92) (p<0.05, each). Three-month survival was significantly lower in patients with low IGF-1 levels (79%; with IGF-1<28.1ng/ml) than those with intermediate (93%; IGF-28.1-58.7ng/ml) and high (97%; IGF-1>58.7ng/ml) IGF-1 levels (p<0.001). Both IGF-1 and MELD predicted 3-month mortality with an AUC of 0.687; p=0.018 and 0.686; p=0.008. Adding IGF-1 with MELD further improved the discrimination of MELD for mortality prediction with an AUC of 0.732 (p<0.001). GH levels were not associated with sarcopenia, frailty, autonomic dysfunction, MELD and survival.

Conclusion: Reduced IGF-1 levels are associated with sarcopenia, frailty, autonomic dysfunction, increased severity, and mortality in stable decompensated cirrhosis. Modulation of GH-IGF1 axis is a potentially disease modifying target in cirrhosis.

Abstract Submission No. 100961
P-0866

Cirrhosis prognosis: Neutrophil-to-Lymphocyte, Lymphocyte-to-Monocyte, Platelet-to-Lymphocyte Ratios

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Background: Previous studies have showed high neutrophil-to-lymphocyte ratio (NLR), low lymphocyte-to-monocyte ratio (LMR), and high platelet-to-lymphocyte ratio (PLR) as significant prognostic indicators in patients with decompensated cirrhosis. However, there is paucity of data in stable outpatient cirrhotics. Our aim was to explore prognostic value of these indices for 3-month decompensation event and mortality in this group.

Methods: Total 196 patients were recruited, of whom 10 met predefined outcome of unscheduled hospital admission for decompensating events. Cox regression and Kaplan Meier analysis for 3-month outcome was performed with these cutoffs: NLR > 5, LMR < 3, PLR > 90. Receiver operating characteristic (ROC) curve was constructed for

above indices and the area under the curve (AUC) was estimated for 3-month outcome.

Results: Mean Child Pugh score and MELD in patients with 3-month outcome were significantly higher at 7.9 and 11.6 respectively. In univariate logistic regression, MELD, NLR, LMR, and PLR were independent predictors of 3-month outcome (p = 0.029, 0.002, 0.007, and 0.044 respectively). Kaplan Meier analysis showed significantly higher cumulative 3-month outcome for NLR > 5 (p < 0.001), LMR < 3 (p = 0.005), and PLR > 90 (p=0.034). AUC for these indices were 0.707 (0.511-0.903) p= 0.039, 0.765 (0.668-0.861) p = 0.000, and 0.673 (0.516-0.830) p= 0.030 respectively (AUC for MELD was 0.745 with p = 0.000).

Conclusion: High NLR, low LMR, and high PLR can predict 3-month unscheduled hospital admissions and liver related mortality in stable outpatients with cirrhosis, with low LMR being the best predictor.

Abstract Submission No. 101026
P-0867

Recurrence of portosystemic encephalopathy in cirrhotic patients and its risk factors

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Objectives: Recurrent episodes of Portal Systemic Encephalopathy (PSE), poses a significant burden of illness on the patients and healthcare system. The objective of this study was to assess the recurrence of PSE in cirrhotic patients after index episode of PSE and to identify various risk factors associated with it.

Methods: A retrospective, single-centre study was conducted at Aga Khan University Hospital over a span of one year. Patients who were admitted first time with PSE and admitted within three months of index PSE were enrolled in the study. Variables assessed were demographic data, associated comorbid conditions, aetiology of cirrhosis, ChildTurcotte-Pugh (CTP) score, Model of End-Stage Liver Disease (MELD) score, PSE grade, laboratory tests, ascites with spontaneous bacterial peritonitis (SBP), variceal bleeding. Statistical analysis was done and variables of those who developed recurrence were compared with those who did not.

Results: Fifty one patients were recruited. Thirty three (64.7%) were readmitted with PSE. On comparative analysis of both groups; infection, Meld score, low albumin, and raised total bilirubin showed significant P-value (<0.05)

Conclusion: Identification of risk factors during assessment can reduce the recurrence of PSE. We would recommend to validate result of our study on a large scale prospectively.

KEYWORDS: Portosystemic Encephalopathy, Risk Factors, Recurrence

Abstract Submission No. 101029
P-0868

Impaired endothelial integrity and density of mucosal vessels in the small intestine of cirrhotics

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Background/Aim: Disruption of endothelial integrity in small intestinal mucosal vessels is possibly correlated with the translocation of antigens to the portal circulation. Decreased ZO-1 expression may contribute to the impaired endothelial integrity.

We assessed changes in epithelial vessel density and endothelium integrity of intestinal vessels in cirrhotics by assessing the expression of ZO-1 in biopsy samples.

Methods: We enrolled 63 cirrhotics (M/F:35/28, mean age $\pm$ SD:62 $\pm$ 13). Nine non-cirrhotics served as controls. Small intestine biopsy samples were taken during endoscopy and endothelial ZO-1 expression was assessed by indirect streptavidin biotin peroxidase method.

Results: Thirty-four (54%) had compensated and 29 (46%) decompensated cirrhosis. Child-Turcotte-Pugh (CTP) classification was A:46/B:14/C:3. Mean $\pm$ SD MELD score was 10.5 $\pm$ 3.7. CTP-A patients had increased number of mucosal vessels per x20 optical field compared to controls (3.8 $\pm$ 1.1 vs 3.2 $\pm$ 0.9, $p=0.048$) as also compared to CTP-B (3.8 $\pm$ 1.1 vs 3.2 $\pm$ 0.7, $p=0.045$). A negative correlation was observed between the number of mucosal vessels and CTP score ($r: -0.428$, $p=0.016$). Loss of endothelial ZO-1 staining in more than 50% of vessel perimeter or total loss of ZO-1 staining across vessel perimeter, in more than 50% of vessels was observed more frequently in cirrhotic samples (42/63, 66.6%) compared to controls (1/9, 11.1%, $p=0.001$).

Discussion: Increased loss of endothelial ZO-1 expression was found in the small intestine of cirrhotic patients. We also observed an increase of vessel numbers in patients with CTP-A compared to controls and to CTP-B patients. We believe that bacterial translocation mechanisms in cirrhosis are not confined to the intestinal lumen and merit further investigation.

Abstract Submission No. 101084
P-0869

Carnitine deficiency and improvement of symptoms by administration of carnitine in patients with LC

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Context: In recent years, there are reports that L-carnitine is useful in improvement of hyperammonemia and cognitive function in patients with liver cirrhosis, and of muscle symptoms in dialysis patients. We measured carnitine levels in patients with liver cirrhosis including dialysis patients, and examined whether administration of L-carnitine improved muscle symptoms.

Methods: We measured carnitine levels in 27 patients with liver cirrhosis (Child-pugh classification A/B/C=14/9/4) who were receiving treatment in our hospital, and administered L-carnitine (600 mg - 1,800 mg) to patients having muscle cramps for approximately one month and examined the presence/absence of the symptom.

We measured carnitine concentration before and after dialysis, before dialysis after the administration to eight dialysis patients, before and after the administration to 19 nondialytic patients. In addition, we examined the presence/absence of symptom after the administration of L-carnitine in symptomatic patients.

Results: The total carnitine levels before the dialysis of dialysis patients were low, with the mean of 42.2 μ mol/L that was significantly decreased to 17.7 μ mol/L after the dialysis ($p=0.011$). It was increased

to 155 μ mol/L after the administration of L-carnitine. In the nondialytic patients, the total carnitine levels were significantly increased from 71.7 μ mol/L to 101.7 μ mol/L after the administration of L-carnitine ($p<0.05$). In a total of 27 patients, muscle cramps existed in 18 patients (67%), consisting of four (50%) out of 8 dialytic patients and 14 (74%) out of 19 nondialysis patients. For symptomatic patients, significant improvement of muscle cramps was observed in the L-carnitine administered group when compared with the non-administrated group ($p=0.0002$).

Conclusions: Total carnitine levels were low even before dialysis in the dialysis patients with liver cirrhosis in particular and they further decreased after the dialysis.

Administration of L-carnitine increased the total carnitine levels and improved the symptom. Based on these results, we conclude that L-carnitine is useful for carnitine deficiency in patients with liver cirrhosis

Abstract Submission No. 101085
P-0870

Carnitine deficiency and improvement of muscle cramp by administration of carnitine in patients with liver LC

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Context: In recent years, there are reports that L-carnitine is useful in improvement of hyperammonemia and cognitive function in patients with liver cirrhosis, and of muscle symptoms in dialysis patients. We measured carnitine levels in patients with liver cirrhosis including dialysis patients, and examined whether administration of L-carnitine improved muscle symptoms.

Methods: We measured carnitine levels in 19 patients with liver cirrhosis (Child-pugh classification A/B/C=10/5/4) who were receiving treatment in our hospital, and administered L-carnitine (600 mg - 1,800 mg) to patients having muscle cramps for approximately one month and examined the presence/absence of the symptom.

We measured carnitine concentration before and after the administration to 12 patients. In addition, we examined the presence/absence of symptom after the administration of L-carnitine in symptomatic patients.

Results: Patients, the total carnitine levels were significantly increased from 71.7 μ mol/L to 101.7 μ mol/L after the administration of L-carnitine ($p<0.05$). In a total of 19 patients, muscle cramps existed in 14 patients (74%). For symptomatic patients, significant improvement of muscle cramps was observed in the L-carnitine administered group when compared with the non-administrated group ($p=0.0002$).

Conclusions: Administration of L-carnitine increased the total carnitine levels and improved the symptom. Based on these results, we conclude that L-carnitine is useful for carnitine deficiency in patients with liver cirrhosis

Abstract Submission No. 101087
P-0871

Carnitine before and after in patients with ascites and LC and improvement by intravenous

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Introduction: Recently, carnitine has been reported to be useful for improving blood ammonia and cognitive function in cirrhotic patients with subclinical hepatic encephalopathy In Japan

Method: Total carnitine concentration was measured in 5 cirrhotic patients undergoing ascites drainage during our hospital ambulatory, and after ascites drainage, intravenous administration of carnitine was conducted to examine whether or not the symptoms improved. drainage.

Case presentation: In a patient with liver cirrhosis, improvement of hepatic encephalopathy associated with decreased carnitine level and decreased ammonia were reported, and deterioration of muscle symptoms associated with carnitine deficiency in a dialysis patient was also reported. Therefore, Carnitine concentration and acylcarnitine/free carnitine ratio were measured in this patient, and administration of carnitine preparation was started. Carnitine concentration 1 month after administration of carnitine was increased in all cases, and the ratio of acylcarnitine/free carnitine was also decreased (0.388 to 0.253). one patient is currently hospitalized and discharged from the hospital after drainage of ascites. Ascites drainage was performed once or twice a week. Carnitine administration after ascites drainage increased the carnitine level without cramping or general malaise .

Result: The total carnitine concentration was within the normal range in the non-dialysis patients, and the concentration of carnitine decreased in the dialysis patients before and after dialysis.

Conclusion: The case in which the muscle cramp disappeared in the liver cirrhosis patient with the carnitine administration was experienced.

Abstract Submission No. 101103

P-0872

Network pharmacology analysis of Ginkgo biloba extract in treating liver cirrhosis

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Background: Liver cirrhosis (LC) has been a seriously threaten the public health. Ginkgo biloba extract (GBE), a long-standing and well-used medicine, has been widely used to treat cirrhosis diseases. Here, we aimed to explore the mechanism of GBE in the treating LC.

Methods: We first obtained target genes of GBE and LC from public databases. Then we constructed a protein-protein interaction network of the key targets and screened out the hub genes. The LC rat model was constructed by intraperitoneal injection of diethylnitrosamine. The hub genes' expression was further verified in the LC rats' liver tissues with RNA-sequencing approach. Finally, we performed the pathway enrichment analysis of the key targets and hub genes.

Results: After database mining, we obtained 368 overlapped genes between GBE's targets and LC's targets. These overlapped genes were further used to construct PPI network and screen the hub genes. With the rat LC mode, we next detected the mRNA expression of the hub genes in the liver tissues. And the results showed that compared with the control, the expression of MAPK14, EGFR, and NR3C1 was significantly down regulated in LC; while the expression of AR, CASP3, and CCND1 was just the reverse. In the last, the KEGG pathway enrichment analysis results showed that the key targets and hub genes were significantly correlated to the PI3-AKT and MAPK signaling pathways.

Conclusions: We obtained the hub genes of GBE in treating LC. And GBE might exert anti-LC effect by regulating the PI3-AKT and MAPK signaling pathways.

Abstract Submission No. 101113

P-0873

Impact of endoplasmic reticulum stress on neutrophil extracellular traps in liver cirrhosis

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Backgrounds: The present study aims to investigate the impact of endoplasmic reticulum stress (ERS) on the phagocytic activity and neutrophil extracellular traps (NETs) in patients with liver cirrhosis and acute-on-chronic liver failure (ACLF).

Methods: The correlation between ERS and NETs, phagocytic activity in patients with liver cirrhosis and ACLF were studied by in vivo and vitro study.

Results: The mRNA and protein of XBP1S, GRP78, ATF4, ATF6 α , and CHOP in neutrophils of patients with liver cirrhosis and ACLF were significantly elevated compared to those in the normal control (NC). The level of double-stranded DNA (dsDNA) in neutrophils were significantly elevated in patients with liver cirrhosis and ACLF compared to those in NC ($P<0.05$). The levels of neutrophil elastase (NE) in neutrophils of ACLF were significantly increased compared to those in NC ($P<0.05$). The phagocytic activity in patients with liver cirrhosis and ACLF were significantly decreased compared to that in NC ($P<0.05$). In vitro studies demonstrated that 4-PBA significantly inhibited the expression of XBP1S, GRP78, ATF4, CHOP, and ATF6 α in neutrophils of NC induced by TG ($P<0.05$). Moreover, 4-PBA significantly inhibited the expression of NE and CitH3 induced by TG ($P<0.05$) and increased the phagocytic activity of neutrophils ($P<0.05$).

Conclusion: In patients with liver cirrhosis and ACLF, neutrophils had significant ERS, reduced phagocytic function and increased NETs. The ERS is involved in increased release of NETs and decreased phagocytic function in neutrophils in patients with liver cirrhosis and ACLF.

Abstract Submission No. 101138

P-0874

Association between gut microbiota and <str

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Background: The purpose of this study was to explore the association between gut microbiota and glucose metabolism disorders in patients with liver cirrhosis (LC) .

Methods: The gut microbiota were detected by 16s rRNA gene sequencing in 80 patients with LC. Oral glucose tolerance test (OGTT) was performed to evaluate glucose metabolism disorders. The association of gut microbiota with glucose metabolism disorders was analyzed.

Results: The richness of gut microbiota was significantly lower in patients with impaired glucose tolerance (IGT) as compared with that in patients with normal glucose tolerance (NGT). The bacterial community composition in patients with IGT and HD was significantly lower than that in patients with NGT ($P<0.05$). At the phylum level, the abundance of Firmicutes obviously decreased and the abundance of Bacteroides remarkably increased in patients with IGT and HD. Firmicutes/Bacteroidetes (F/B) ratio in patients with NGT, IGT and HD were

3.286, 2.225 and 2.232, respectively. At the genus level, compared with those in NGT, patients with HD had a significantly lower abundance of *Faecalibacterium*, *Lactococcus* and *Roseburia* and a significantly higher abundance of *Enterobacter*, *Megasphaera* and *Enterococcus* ($P<0.05$). *Roseburia*, *Clostridium* and *Faecalibacterium* negatively correlated with 2-hour post OGTT plasma glucose, Child-pugh class, international standardized ratio and model for end-stage liver disease score. *Enterococcus*, *Enterobacter*, *Ruminococcus*, *Faecalibacterium* and *Roseburia* had predictive values for HD in patients with LC.

Conclusion: Different gut microbiota composition in patients with LC is associated with development of glucose metabolism disorders.

Abstract Submission No. 101139
P-0875

Association of hepatogenous diabetes with minimal hepatic encephalopathy in liver cirrhosis

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Objective: Hepatogenous diabetes (HD) and minimal hepatic encephalopathy (MHE) are common complications in patients with liver cirrhosis. The purpose of this study is to study the association of HD with MHE in patients with liver cirrhosis.

Methods: 134 patients were prospectively included. Oral glucose tolerance test (OGTT) was used to diagnose HD. Traditional neuropsychological tests and new neuropsychological tests and animal naming tests were used to diagnose MHE.

Result: 1. Among 134 patients with liver cirrhosis, 36 (26.9%) patients had HD and 65 (48.5%) patients had MHE. Patients with HD had significantly higher levels of total bilirubin, MELD score, total bile acid, international standardized ratio, and Child-push grade than those without HD ($P<0.05$); Patients with MHE had significantly older age and higher levels of fasting insulin, aspartate aminotransferase/alanine aminotransferase (AAR) ratio, liver fibrosis score 4 (FIB-4) index, and significantly lower level of hemoglobin (Hb) than those without MHE ($P<0.05$); Among 36 patients with HD, 23 patients (63.9%) had MHE, which was significantly higher than that (42.9%) of 98 patients without HD ($P<0.05$). Multivariate logistic analysis showed that HD ($OR=2.388$, 95% CI : 1.021~5.586), AAR ratio ($OR=2.09$, 95% CI : 1.053~3.832), and Hb ($OR=0.981$, 95% CI : 0.966~0.996) were independent risk factors for MHE.

Conclusion: The incidence of HD and MHE in patients with liver cirrhosis increases with the severity of liver injury. HD, higher AAR ratio and lower Hb are independent risk factors for MHE in patients with liver cirrhosis.

Abstract Submission No. 101152
P-0876

OUTCOMES OF PATIENTS WITH LIVER CIRRHOSIS ADMITTED WITH SBP: A RETROSPECTIVE COHORT STUDY

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Spontaneous bacterial peritonitis (SBP) carries a mortality rate as high as 70%. To date, there are no published local data on the incidence of SBP, antimicrobial profile, and survival among patients with SBP.

This study aims to determine the 30-day in-hospital outcomes of patients with liver cirrhosis admitted with SBP, to determine the antimicrobial profile and susceptibility, to determine the incidence of concurrent decompensating events, and to correlate Child-Pugh scores and MELD scores during admission to mortality.

In this study, viral hepatitis was the most prevalent cause of liver cirrhosis (48.83%). This study revealed that 42.76% of patients treated satisfied the diagnostic criteria for SBP. Subgroup analysis shows no mortality among patients with liver cirrhosis treated for SBP with ascitic fluid ANC of < 250 cells/uL. The majority of patients received empiric antimicrobials within 24 hours at 67%. Subgroup analysis shows that 212 from 287 of patients given antibiotics within 24 hours were discharged. *Enterococcus faecalis*, *Escherichia coli*, and *Staphylococcus aureus* are the most prevalent isolates. A mortality rate of 37.38% within the 30-day observation period was noted.

A significant proportion of patients had favorable outcomes. Majority received empiric antimicrobials within 24 hours of SBP suspicion contributing to improved outcomes. With the antimicrobial profile of isolates in this study, a third-generation cephalosporin is a reasonable choice as an empiric antimicrobial for patients with suspected SBP.

Abstract Submission No. 101156
P-0877

Developing a Multidisciplinary Palliative Care Model for Patients with Liver Cirrhosis

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Despite its high symptom burden and increased mortality risk, palliative care utilization in patients with liver cirrhosis remain low and variable. Specialist palliative care involvement also often occurs very late in the disease trajectory.

We sought to develop a palliative care model for patients with liver cirrhosis in our institution. A literature review was performed, focusing on the palliative care needs of these patients. These were discussed at multidisciplinary meetings comprising of healthcare professionals from both Hepatology and Palliative Care departments.

A multi-pronged, multidisciplinary, evidence-based approach will be implemented. This comprises of 1. Identifying patients with cirrhosis with palliative care needs using the Supportive and Palliative Care Indicators Tool. 2. Ensuring early access to specialist palliative care, particularly in patients with complex needs. 3. Ensuring good physical, psychoemotional and spiritual symptom control with multidisciplinary input. 4. Addressing comorbidities and multimorbidity from frailty and sarcopenia. 5. Setting up appropriate community and outpatient services, including a multidisciplinary cirrhotic clinic, and facilities to perform outpatient abdominal paracentesis. 6. Patient empowerment through early patient engagement and education, goals of care discussions and advance care planning. 7. Supporting caregivers. 8. Optimising end-of-life care and addressing anticipated symptoms and physical care needs in the patients' preferred place of care, either in their homes or an institution such as an inpatient hospice.

A multidisciplinary palliative care model will address the physical, psychoemotional, social and spiritual domains of our patients with liver cirrhosis. More studies will be required to review the impact of this shared model of care.

Abstract Submission No. 101157

P-0878

Improving the Uptake of Advance Care Planning in Patients with Decompensated Liver Cirrhosis

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Advance care planning (ACP) is essential in the care of patients with liver cirrhosis. However, its uptake remains low and variable. A Quality Improvement Project was performed, targeting patients with decompensated liver cirrhosis presenting for their regular abdominal paracentesis and/or intravenous albumin infusion. A two-step intervention was implemented. The first step involved administration of a brochure containing information on ACP to the patient at registration, with a brief explanation on what ACP is and instructions to read the brochure during therapy. The second step involved a Hepatology nurse educating the patient on cirrhosis with simple pictorial aids, while the patient was undergoing therapy. This was followed by the showcase of a short video depicting an interview of an actual ACP participant, and verbal counselling on its importance. The study was performed over three months. The "Plan-Do-Study-Act" methodology was used to refine the intervention.

In the preceding three months pre-intervention, 3 out of 18 patients had prior ACPs. After the intervention, 12 out of 19 patients agreed to participating in the ACP discussion, while 3 patients had prior ACPs. This increased the percentage of eligible patients with ACPs from 17% to 78% in 3 months. Patients interviewed after shared that the intervention was effective, and the order of the interventions was logical. As of August 2023, 26 out of 37 eligible patients have agreed to ACP discussion.

Our two-step intervention is effective in increasing ACP uptake amongst patients with decompensated cirrhosis, and may be considered for adoption on a larger scale.

Abstract Submission No. 101169

P-0879

NLR and LMR for the Prediction of Prognosis and severity of Liver Cirrhosis Patients

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Background: Cirrhosis is scarring of the liver caused by long-term liver damage. Neutrophil to lymphocyte ratio (NLR) is an essential as well as a simple method that reflects the severity of inflammation and can be used to predict severity of decompensated cirrhosis. Lymphocyte to Monocyte ratio (LMR) is widely followed as it is cost-effective, simple to calculate and interpret the severity of cirrhotic patient. The study aimed to evaluate the neutrophil-to-lymphocyte ratio and lymphocyte to monocyte ratio for the prediction of prognosis of liver cirrhosis patients.

Methodology: The cross-sectional study was done from July 2020 to December 2020 in the Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. A total of 80 patients were selected from the diagnosed cases of cirrhosis of liver patients for this study. The study population was divided into two groups. Group A consisted of patients who had compensated cirrhosis, and group B consisted of patients who had decompensated cirrhosis. Data were collected using a preformed data collection sheet (questionnaire). Informed written consent was obtained from each

participant. Data were analyzed by SPSS 20. $p < .05$ was considered as a level of significance.

Results: The average age of patients was 47.55 ± 13.25 years where the majority 26(32.5%) belonged to the age group 41 – 50 years. The mean value of NLR was significantly higher in decompensated cirrhosis patients than that of compensated ones and LMR was significantly higher in compensated cirrhosis patients ($p < .001$). NLR had a significant strong positive correlation with CPS scores ($r = 0.774$, $p < .05$) whereas LMR had a significant negative correlation with CPS scores ($r = -0.732$, $p < .05$). At a cut-off value ≥ 5.61 NLR had 80% sensitivity and specificity & LMR had 64% sensitivity & 79% specificity, cut-off value was found ≤ 2.45 . CPS score at a cut-off value ≥ 12.5 showed 100% sensitivity and 96% more specificity than LMR, NLR & MELD. A cut-off value of MELD score ≥ 26.5 was 100% sensitive but 80% specific in the prediction of death among patients with cirrhosis. AUC of NLR, LMR, CPS, MELD was 0.849, 0.096, 0.992 & 0.957 respectively.

Conclusion: Routine assessment of these parameters may provide valuable information for assessing disease conditions in patients with liver cirrhosis in outdoor patient management.

Keywords: NLR, LMR, Liver cirrhosis, Child-Pugh Score, MELD

Abstract Submission No. 101192

P-0880

Clinical Performance of Serum ELF levels on Predicting LC in Patients with CHB

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Background/Aim: The Enhanced liver fibrosis (ELF) is known as a serological biomarker for predicting liver fibrosis. However, there was lack of data to evaluate the clinical performance of the serum ELF levels on predicting liver cirrhosis (LC) in Korean patients with chronic hepatitis B (CHB).

Methods: We reviewed medical records for 312 patients with CHB who were performed serum ELF levels in Kosin University Gospel Hospital from September 2020 to August 2022. Exclusion criteria were co-infection with chronic hepatitis C, significant alcohol intake, malignancy except hepatocellular carcinoma, and inadequate data. Multivariate logistic regression analysis was performed to identify independent predictors for diagnosing LC. The diagnostic accuracy of serum ELF levels for predicting LC was compared to that of other fibrosis markers, FIB-4 and APR) using ROC.

Results: The mean ($\pm$ SD) of age of study patients was $62.1 (\pm 10.9)$ years and the proportion of male was 73.4%. 209 (67.0%) patients were diagnosed with LC. The mean ($\pm$ SD) of serum ELF levels showed significant differences between LC group (11.3 ± 1.51) and non-LC group (10.2 ± 1.63) ($P < 0.001$). (Table 1) Adjusting for age, gender, platelet count, albumin, INR, and sodium, serum ELF levels was an independent predictor of LC [adjusted odds ratio (OR): 1.40, 95% confidence interval (CI) 1.17-1.68, $P < 0.001$]. The area under the curve of serum ELF level for prediction of LC (0.700) was comparable to that of FIB-4 (0.763) and APRI (0.708), respectively. ($P < 0.001$) (Fig. 1) The cut-off value of serum ELF that maximized the sum of sensitivity (73.2%) and specificity (62.1%) was 10.2.

Conclusion: Serum ELF levels would be a reliable non-invasive marker for diagnosing LC in Korean patients with CHB.

Abstract Submission No. 101196

P-0881

Serum C-Reactive Protein Predicts Early Mortality in Patients with Decompensated Cirrhosis

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Background: Serum C-reactive protein is a marker of systemic inflammation, which has been studied to predict mortality in cirrhosis

Objectives: To evaluate the role of serum C-reactive protein as a predictor of early mortality in patients with decompensated cirrhosis.

Materials and methods: This was a prospective observational study, carried out in the Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka. Patients were compared of CRP level, CTP score, MELD score and cirrhosis related complications. Receiver-operator characteristic curve was used to detect serum CRP level for prediction of mortality within 30 days.

Results: Total WBC count, serum CRP, serum sodium, bilirubin, CTP score & MELD score were statistically significant ($p < 0.05$) between the groups. In multivariate analysis, only serum CRP level (OR 1.075, 95% CI, 1.027-1.122, $p = 0.001$) was found significantly associated with mortality within 30 days. Receiver-operator characteristic (ROC) was constructed, using serum CRP level, which gave a cut off value of 31 mg/L, with 78% sensitivity and 90% specificity for prediction of mortality within 30 days.

Conclusion: Elevated serum CRP level is an independent predictor of early mortality in patients with decompensated cirrhosis of liver.

Abstract Submission No. 101297

P-0882

The long term efficacy of Rifaximin for overt and non-overt hepatic encephalopathy.

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¹Fukui Prefectural Hospital Fukui Japan

Background:

Rifaximin (RFX) improve on overt hepatic encephalopathy.

However, the efficacy of long-term RFX administration for non-overt hepatic encephalopathy and have remain unclear. In this study, we compared the clinical outcomes of RFX for overt and non-overt hepatic encephalopathy.

Methods:

We enrolled 72 patients with hepatic encephalopathy for whom RFX was newly introduced between January 2018 and December 2022.

We retrospectively examined (1) patient backgrounds, (2) concomitant drugs, (3) opportunities for administration of RFX, and (4) early and long-term (4/12 weeks) efficacy of RFX.

Results:

Of the 72 patients, 60 patients who could take RFX for more than one month were included in this analysis. Background liver diseases were nutritional in 33, viral in 10, autoimmune in 7, and other in 10 cases.

Regarding the opportunities for RFX administration, 37 cases had overt encephalopathy. On the other hand, the opportunities for administration in non-overt encephalopathy was hyperammonemia alone in 12, amnesia in 5, intolerance diarrhea due to disaccharides in 4, respectively. The number of taken tablets before/after administration of RFX were 15.5 ± 5.2 / 21.1 ± 5.2 tablets/day, and the patients were advanced polypharmacy states.

The ammonia levels were significantly reduced after 4 and 12 weeks ($P < 0.001$). Comparing between overt and non-overt encephalopathy cases, after the administration of RFX, the period until readmission due to encephalopathy tended to be prolonged in the non-overt encephalopathy group ($P = 0.051$).

Conclusion:

RFX significantly reduced ammonia levels even with long-term administration. The early administration of RFX for non-overt hepatic encephalopathy could prolong the period until readmission.

Abstract Submission No. 101376

P-0883

Enhancing Bioavailability of Furosemide for the Management of Liver Cirrhosis

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Objective: The objective of this study was to enhance the bioavailability of furosemide (FURO), an antihypertensive loop diuretic used in the management of liver cirrhosis, by improving its water solubility, permeability, and absorption after oral administration. To achieve this aim, a novel drug delivery system, Self Nano Emulsifying Drug Delivery System (SNEDDS), was employed.

Methods: Various oils, surfactants, and co-surfactants were tested to determine their ability to improve the solubility of FURO. The self-emulsification region was identified using pseudoternary diagrams, and SNEDDS formulations were developed accordingly. The formulations were characterized using zeta potential determination, droplet size analysis, dilution test, viscosity determination, in vitro dissolution studies, and in vivo pharmacodynamic evaluation.

Results: Mean droplet size of the optimized formulation was found to be 26.8 nm. In vitro performance of the optimized preparation was satisfactory as observed by various analyses such as dilution test, emulsification time, and precipitation assessment. In vitro dissolution studies exhibited that the optimized SNEDDS formulation F3 exhibited a 1.7 fold increase in dissolution efficiency as compared to plain FURO and marketed formulations. In vivo studies showed enhanced bioavailability of F3 in terms of diuretic efficacy.

Conclusion: The study confirms the potential use of SNEDDS formulation as an alternative to traditional oral formulations of FURO to enhance its bioavailability in the management of liver cirrhosis.

Abstract Submission No. 101464

P-0884

The prognostic value of high-density lipoprotein cholesterol in patients with hepatic encephalopathy

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Background: Overt hepatic encephalopathy (OHE) is a serious complication of liver cirrhosis that impacts lipid and lipoprotein metabolism. We aimed to determine the relationship between high-density lipoprotein cholesterol (HDL-C) and transplant-free (TF) mortality in patients with OHE.

Methods: We identified 821 patients with OHE at Beijing Ditan Hospital between January 2010 and August 2016. A multivariate regression analysis was performed to identify the independent risk factors associated with TF-mortality, and the area under the receiver operating characteristic curve (AUC) was used to assess the prognostic values of

these factors. One-year TF mortality was analyzed using the Kaplan-Meier method and compared using the log-rank test. All the results were confirmed in a prospective cohort ($n=480$).

Results: Patients with OHE who died were more likely to have lower HDL-C levels than those who survived. The prognostic value of HDL-C was good (AUC at 1 year: 0.745) and was similar to the Model for End-Stage Liver Disease (MELD) score (AUC at 1 year: 0.788). In the validation set, the HDL-C showed AUC values similar to those of MELD at 1 year (0.724 vs. 0.724). The optimal cutoff value of HDL-C and MELD were 0.5 mmol/L and 17, respectively. The 1-year TF mortality rates in the low-risk (HDL-C $\geq$ 0.5 mmol/L and MELD $<$ 17) and high-risk (HDL-C $<$ 0.5 mmol/L and MELD $\geq$ 17) groups were 7.5 and 51.5% in the training set, and 10.1 and 48.2% in the validation set, respectively.

Conclusions: HDL-C is closely linked with 1-year TF mortality in patients with OHE. HDL-C $<$ 0.5 mmol/L and MELD $>$ 17 can facilitate identification of high-risk patients and therefore provide timely treatment and care.

Abstract Submission No. 101471
P-0885

Study of sleep patterns in patients with liver cirrhosis/ chronic liver disease.

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BACKGROUND: Chronic liver disease is an important cause of morbidity and mortality in general population across our country. Sleep disturbances have been reported in patients with hepatic cirrhosis. Therefore this study aimed to investigate sleep patterns in these patients to help optimize their overall health outcomes.

METHOD: A descriptive cross sectional study was conducted in a tertiary health care hospital. A total of 50 patients diagnosed with CLD were included in the study and their sleep patterns were carefully analysed. Demographic profile was documented, structured questionnaire and Pittsburgh Sleep Quality Index Scale (PSQI) were used for sleep pattern and quality assessment.

RESULTS: Findings revealed distinct sleep disturbances among these patients, with varying prevalence rates. Among the participants 12% reported experiencing constant drowsiness indicating a significant level of day time sleepiness and fatigue. Moreover 26% of the patients exhibited sleep reversal, leading to sleep during day time hours and wakefulness at night. Furthermore, a substantial portion of participants, 42% reported experiencing insomnia.

CONCLUSION: According to the PSQI scale, 96% of the patients experienced poor sleep (score $>$ 5) and only 4% of the patients had good sleep (score $<$ 5). These results confirm that majority of patients with DCLD experience sleep disturbances. Insomnia being the dominant pattern of disturbed sleep. Further research is warranted to explore the underlying mechanisms of sleep disturbances in DCLD and to develop tailored approaches to address this significant aspect of patient care.

Abstract Submission No. 101507
P-0886

VWF/ADAMTS13 ratio is a useful marker for ACLF onset and prognosis in patients with liver cirrhosis

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Aim: Acute-on-chronic liver failure (ACLF) is associated with a high risk of short-term mortality after progression to multiple organ failure. A disintegrin-like and metalloproteinase with thrombospondin type-1 motifs 13 (ADAMTS13) is a metalloproteinase that specifically cleaves multimeric von Willebrand factor (VWF). An imbalance between ADAMTS13 enzyme and VWF substrate is associated with liver cirrhosis progression that induces ACLF. This study examined the relationship between ADAMTS13 and VWF and ACLF development to determine whether ADAMTS13 and VWF are useful predictive biomarkers for ACLF development and prognosis of patients with liver cirrhosis.

Methods: The study enrolled 67 patients with Child-Pugh class A and B liver cirrhosis. ADAMTS13 activity (ADAMTS13:AC) and VWF antigen (VWF:Ag) were measured using enzyme-linked immunosorbent assays. The ratio of VWF:Ag to ADAMTS13:AC (VWF:Ag/ADAMTS13:AC) was used to divide patients into two groups according to the classification and regression tree based on Gray model survival analysis.

Results: Compared with patients with Child-Pugh class A liver cirrhosis, class B patients had a higher VWF:Ag/ADAMTS13:AC and a higher risk of ACLF development.

Cumulative incidence of ACLF was significantly higher in patients with high ($>$ 7.9) versus low ($\leq$ 7.9) VWF:Ag/ADAMTS13:AC (hazard ratio [HR], 6.50; 95% CI, 2.31–18.29; $p <$ 0.001). Cumulative survival was significantly lower in cirrhotic patients with high versus low VWF:Ag/ADAMTS13:AC (HR 5.11; 95% CI, 1.85–14.14; $p =$ 0.002).

Abstract Submission No. 101510
P-0887

Validation of MELD scores in patients with acute decompensation in alcoholic liver cirrhosis

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The Model for End-Stage Liver Disease (MELD) has long served as a dependable prognostic tool for short-term outcome prediction in patients with end-stage liver disease. Recently, MELD 3.0 was introduced to enhance the accuracy of its predecessors. This study sought to assess the performance of MELD 3.0 in comparison to MELD and MELD-Na in patients with alcoholic liver cirrhosis.

This study utilized a multicenter prospective cohort comprising patients with alcoholic cirrhosis who were admitted due to acute deterioration of liver function in the Republic of Korea between 2015 and 2019. The study compared the predictive abilities of MELD, MELD-Na, and MELD 3.0 for 30- and 90-day outcomes, specifically death or liver transplantation. Additionally, the study explored the factors influencing these outcomes.

This study utilized a multicenter prospective cohort comprising patients with alcoholic cirrhosis who were admitted due to acute deterioration of liver function in the Republic of Korea between 2015 and 2019. The study compared the predictive abilities of MELD, MELD-Na, and MELD 3.0 for 30- and 90-day outcomes, specifically death or liver transplantation. Additionally, the study explored the factors influencing these outcomes.

All MELD models exhibited strong predictive power for short-term outcomes in patients with alcoholic liver cirrhosis. While MELD 3.0

demonstrated improved performance compared to previous models, the differences were not statistically significant.

Abstract Submission No. 101514
P-0888

Causal role of immunophenotypes in non-autoimmune related cirrhosis: a Mendelian randomization study

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Abstract

Background: Complex immune-liver interactions is closely linked to liver disease development. While observational studies have reported positive associations between immune-mediated inflammatory and autoimmune liver disease, the genetic association between these immune cells and non-immune mediated cirrhosis is still divergent.

Methods: Summary Genome Wide Association Study (GWAS) data of non-autoimmune liver disease related cirrhosis and 731 immune cell signatures were obtained from the GWAS Cataloga. Bidirectional Mendelian randomization was performed to determine the causal relationship between immune cells and non-autoimmune liver disease related cirrhosis.

Results: According to inverse variance weighted method, a total of 29 immune cells ($p < 0.05$) were associated with non-immune mediated cirrhosis. Among them, significantly protective causal associations were identified for CD38 on CD20-, BAFF-R on IgD+ CD38dim and BAFF-R on naive-mature B cell, CM CD8br %T cell, CD28 on CD4+, CD28-CD25++, CD20- %B cell. Furthermore, the expression of CD38 on CD20-, Unsw Mem %lymphocyte, activated Treg %CD4 Treg, secreting Treg %CD4, and SSC-A on DC plasmacytoid were associated with an increased risk of non-immune mediated cirrhosis. In addition, genetically predicted non-immune mediated cirrhosis did not affect the expression of immunophenotypes.

Conclusions: Our findings do support a genetic association between immune cells and non-autoimmune liver disease induced cirrhosis. Immunosuppression and immune escape related immunophenotypes are associated with the liver cirrhosis development. However, larger-scale GWAS summary data and more genetic instruments are needed to confirm these findings.

Abstract Submission No. 101515
P-0889

Deciphering the Novel Functions of Aurora Kinase A in Chronic Liver Disease

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Aurora Kinase A (AURKA) is an important regulator of cell division and often linked to tumor development and progression. Its functions are described to be tissue- and disease-specific, and its underexplored mechanism of action in various diseases may be attributed to its kinase activity able to regulate multiple targets. Although its oncogenic role in hepatocellular carcinoma (HCC) has been described, its precise role in chronic liver disease (CLD) remains poorly understood. This study aims to elucidate the nuanced role of AURKA in modulating the activities of Yes-associated protein (YAP) and the Glycogen synthase kinase 3 beta (GSK-3 β) in the context of CLD. YAP and GSK-3 β are reported substrates of AURKA-mediated phosphorylation and are key components of Hippo and WNT signaling, two pathways heavily involved in liver repair and regeneration. Our data showed an upregulated AURKA expression ($p < 0.001$) within the paired, non-tumoral tissues ($n = 54$) liver tissues in contrast to the paired neoplastic tissues ($n = 54$) excised from HCC-resected livers, suggestive of a distinctive role for AURKA in a cirrhotic liver. Consequently, we probed for mRNA and protein levels of YAP and GSK-3 β using RT-qPCR and Western blot, respectively. Our results revealed an elevated YAP protein expression ($p < 0.01$) in the non-tumoral tissues relative to the nodules from these HCC tumors, while GSK-3 β protein ($p < 0.0001$) displayed an inverse trend. As anticipated, YAP mRNA showed no significant difference in the two tissue groups, supporting our hypothesis that AURKA predominantly influences YAP protein, while GSK-3 β mRNA ($p < 0.01$) showed significantly lower levels in the distal tissues.

Abstract Submission No. 101536
P-0890

Oral branched-chain amino acids as a cost-effective option for managing hepatic encephalopathy

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Background: Oral branched-chain amino acids (BCAAs) may benefit patients with cirrhosis, especially those with hepatic encephalopathy (HE). We aimed to analyze the cost-effectiveness of BCAAs in improving the prognosis of patients with HE.

Methods: We compared the total costs and effectiveness of oral BCAA treatment (Scenario 1) versus no BCAA supplementation (Scenario 2) in a virtual cohort of 10,000 patients who had experienced HE over a 5-year period. A nested Markov model consisting of four health states (remission, recurrence, stabilization after recurrence, and death) for decompensated cirrhosis was used. Effectiveness was estimated as the cumulative number of HE recurrences and deaths. Additionally, the number of life-years and quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratio (ICER) were analyzed. Deterministic and probabilistic sensitivity analyses were also performed.

Results: Oral BCAA treatment prevented 34% of HE recurrences and reduced the number of HE-related deaths by 18%. Although the patients in the BCAA-treated group had spent an additional 4,086 USD on average compared with their counterparts in the non-treated group (\$27,088 vs. \$23,003), they experienced 0.34 more QALYs (2.77 vs. 2.43) during the 5-year period. The ICER for BCAA treatment was 12,017 USD/QALY, indicating the high cost-effectiveness of the therapeutic option. Moreover, the sensitivity analyses showed that its economic feasibility was robust. With the willingness-to-pay threshold set at 1 GDP per capita, the probability of cost-effectiveness of BCAA treatment exceeded 80%.

Conclusions: Oral BCAAs for HE prevention may contribute positively to both the clinical status of the patient and the national healthcare budget.

Abstract Submission No. 101540
P-0891

Impact of Vitamin K On International Normalized Ratio In Chronic Liver Disease

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The use of vitamin K to correct deranged INR in cirrhotic patients is still questionable. This single-center observational cross-sectional study aimed to determine the effect of intravenous vitamin K on deranged INR in chronic liver disease (CLD). Hospitalized CLD patients ≥ 18 yrs of age, baseline INR > 1.3 and received vitamin K were included. The primary and secondary outcomes were the change in INR after 1st and 3rd doses of vitamin K and comparing dosing frequency (single vs multiple doses) and Child-Pugh Classification (CTP) respectively. Eighty patients included with 58.8% males and 41.3% females of which CTP A, B and C was 5%, 15% and 80% respectively. The mean change in INR after 1st and 3rd doses was 0.078 ± 0.265 ; $P = 0.01$ and 0.1403 ± 0.382 ; $P = 0.002$ respectively. The mean change in INR between single vs three doses was -0.056 ± 0.33 ; $P = 0.049$. The mean change in INR after 1st and 3rd doses in CTP A was 0.195 ± 0.404 ; $P = 0.001$ and 0.0250 ± 0.635 ; $P = 0.005$ respectively. The mean change in INR after 1st and 3rd doses in CTP B was 0.0825 ± 0.449 ; $P = < 0.001$ and 0.0717 ± 0.15 ; $P = < 0.001$ respectively. The mean change in INR after 1st and 3rd doses in CTP C was 0.077 ± 0.299 ; $P = < 0.001$ and 0.160 ± 0.420 ; $P = < 0.001$ respectively. Overall majority of CLD patients showed improvement in INR after three doses of vitamin K primarily CTP C.

Abstract Submission No. 101560
P-0892

Paracentesis in Cirrhotic Patients: Conventional Angiocatheter vs. New Anchoring Device (KARAHOC)

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Background: In cirrhotic patients with intractable ascites, paracentesis is commonly performed using an 18G angiocatheter. However, catheter is unstable and frequently falls out during percutaneous drainage. KARAHOC (KH) is a new anchoring device designed to compensate for this instability. This study compares the success rates and complications of paracentesis using conventional angiocatheters and KARAHOC. (NCT05578573)

Methods: Eighty-seven cirrhotic patients with intractable ascites were randomized between Jan 2022 and Jan 2023. Regardless of the order, paracentesis using KARAHOC and conventional angiocatheter were performed once in all patients at intervals of 7 days or more. Successful paracentesis (≥ 3 L ascites drainage) was assessed, along with patient satisfaction using a visual analogue scale.

Results: Thirteen out of 87 patients were excluded from the paired analysis because they did not receive the second paracentesis. The success rate of paracentesis was significantly better in KARAHOC (70/80, 87.5%) than angiocatheter (58/81, 71.6%) (odds ratio:2.78, p-value=0.021). There was also a significant difference in the time taken for paracentesis and total drainage time ($p=0.024$), but not different in

the number of repeated punctures ($p=0.997$). The patient's satisfaction score was also higher in KARAHOC group. 30 minutes after paracentesis, KARAHOC patients had lower systolic blood pressure and slightly higher pulse rates. Serious adverse events occurred in 3 cases, with no significant difference between groups.

Conclusion: KARAHOC is an effective and safe device for cirrhotic patients requiring frequent paracentesis.

Abstract Submission No. 101662
P-0893

Changes in the gut microbiome associated with disease severity in hepatitis B-related cirrhosis

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Background: Hepatitis B-related cirrhosis has high mortality and morbidity in Asia. However, the characteristic of gut microbiota and its correlation with cirrhosis severity remains elusive. The study aim to relate the intestinal flora characteristics to the disease severity in hepatitis B-related cirrhosis patients.

Methods: The study consist of 40 healthy controls (HC) and 83 patients with hepatitis B-related liver cirrhosis (LC). Gut microbiota composition the two groups was compared using 16S rRNA gene sequencing. The relative abundance of gut bacterial on genus level was associated with clinical and laboratory parameters. Gut microbiota different depending on the cirrhosis severity were compared.

Results: Bacterial diversity and relative abundance was significantly decreased in the LC group. The correlation analysis revealed beneficial genus negatively correlated with the model for end-stage liver disease (MELD) and Child-turcotte-Pugh (CTP) scores. Patients with MELD ≥ 21 showed an increased abundance of *Escherichia-Shigella* and a reduced abundance of *Alistipes* and *Roseburia*. Patients with ascites or hepatic encephalopathy had significantly increased relative abundances of *Fusobacterium* while the relative abundance of *Lachnospira* was decreased. We also observed a reduction in the *Roseburia* abundance and an increase in *Fusobacterium* abundance in patients with high international normalized ratio and low albumin levels.

Conclusion: Changes in gut microbiome characteristics in patients with hepatitis-B related cirrhosis were associated with adverse disease severity. The gut bacterial microbiota may be a therapeutic target for preventing and treating cirrhosis.

Abstract Submission No. 101801
P-0894

Comparision of methods that evaluate the prognosis of liver cirrhosis

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OOjective: To compare the new method that evaluate prognosis of liver failure with the traditional method.

Materials and Methods: 322 patients with liver cirrhosis who had been in the Third State Central hospital were evaluated. Before treatment we took the sample of hematology, biochemistry and coagulation. Laboratory examination performed by Sysmex-KX 21, Biochemistry

by Humalizer 2000, for the coagulation we used Humaclot apparatus. All statistical analysis were conducted with the SPSS 21.0.

Results: Among all cases 39.3% of patients were in group A, 50.8% in group B, 9.8% in group C according to the Child Pugh classification. For the MELD score 10.9% of patients were in up to 10 score, 73.2% were in 10-19, 13.7 % were in 20-29, 2.2% were in 30-39 score and there was no patients who had over 40 score. In the MELD classification total bilirubin or liver functional test indicate jaundice, INR point to coagulation, creatinine shows renal function thus it is more sensitive than the Child Pugh. Therefore we have some idea other researchers. PLT was 119.2 ± 6.2 in A group according to the Child Pugh whereas PLT was $132.3 \pm 16.7 \times 10^9/l$ in 0-9 score group in the MELD, PLT% was 26.9 ± 1.3 in A group and 26.7 ± 2.3 in 0-9 score of MELD, prothrombin time was 17.3 ± 0.4 in A group and 16.4 ± 0.9 in 0-9 score of MELD. The splenic length was 12.1 ± 0.2 in A group whereas 11.8 ± 0.5 in 0-9 score of MELD.

Conclusion: The MELD score more sensitively than CTPscore. 13.7% of studied patients requires urgent liver transplantation.

Abstract Submission No. 101929
P-0895

Albumin in Decompensated Cirrhosis: A Cost-Effectiveness Breakthrough in Low-Resource Settings

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Background: In the treatment of decompensated cirrhosis, Human Albumin (HA) is highly effective for managing complications like spontaneous bacterial peritonitis (SBP), hepatorenal syndrome (HRS), and large-volume paracentesis (LVP). However, its cost poses a significant barrier, particularly in low-resource settings.

Objective: This study aims to assess the cost-effectiveness of HA in treating SBP, HRS, and LVP in such environments, using Indonesia's healthcare system as a model.

Methods: We constructed three decision-tree models to evaluate: 1) antibiotics with and without HA for SBP, 2) terlipressin with and without HA for HRS, and 3) LVP with HA vs. gelatins for ascites. The analysis integrated clinical, utility, and economic data over a three-month period, presenting outcomes as incremental cost-effectiveness ratios (ICER) in 2021 IDR per quality-adjusted life year (QALY).

Results: Our findings reveal that HA addition significantly enhances cost-effectiveness across all scenarios: ICER for SBP was 64,505,960 IDR/QALY (3,741 EUR/QALY), for HRS 15,665,600 IDR/QALY (908 EUR/QALY), and for LVP 16,374,871 IDR/QALY (949 EUR/QALY) - all well below the determined willingness-to-pay thresholds.

Conclusion: This groundbreaking study demonstrates HA's cost-effectiveness in SBP, HRS, and LVP treatments in resource-limited settings, offering a viable, economical solution for healthcare systems like Indonesia's. This approach could be revolutionary for similar

settings globally, indicating a significant shift in managing decompensated cirrhosis cost-effectively.

Keywords: Human Albumin, Decompensated Cirrhosis, Cost-Effectiveness, Resource-Limited Settings, SBP, HRS, LVP, Indonesia

Abstract Submission No. 101950
P-0896

Outcome of PARTO(vascular plug assisted retrograde transvenous obliteration) for Gastric varix

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The purpose of this study was to determine the effectiveness of PARTO for gastric varices.

A retrospective study was conducted on 49 patients who underwent PARTO for gastric varices from January 1, 2018, to January 2023.

The PARTO procedure was performed on 26 patients who were hospitalized due to bleeding from gastric varices, and 23 patients who did not have gastric variceal bleeding but underwent the procedure prophylactically due to the high possibility of future bleeding.

Of the 26 patients hospitalized with gastric variceal bleeding, PARTO succeeded in hemostasis in 21 (80.8%), hemostasis failed in 5 patients, 4 patients died from gastric variceal bleeding.

One patient had rebleeding 2 days after the PARTO procedure, so an additional histoacryl injection was administered for gastric varices, which successfully achieved hemostasis, and the patient survived. Two patients died due to liver failure, not gastric variceal bleeding.

All 23 patients who underwent PARTO prophylactically because they did not have gastric variceal bleeding but had a high risk of future bleeding had successful procedures, and there was no gastric variceal bleeding during follow-up.

In 2 of the 23 patients, esophageal variceal bleeding occurred 73 and 537 days after the PARTO procedure, respectively. Hemostasis was successfully achieved with endoscopic variceal ligation. All 26 patients who underwent PARTO prophylactically were alive.

In conclusion, this study showed that PARTO was relatively very safe and effective as a primary or secondary preventive treatment for gastric variceal bleeding.

Abstract Submission No. 101995
P-0897

EFFICACY OF HOME-BASED EXERCISE AND BRANCHED-CHAIN AMINO ACIDS FOR TREATMENT SARCOPENIA IN CIRRHOSIS

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Background and Aim: Sarcopenia is associated with an increase in morbidity and mortality in cirrhosis. This study aimed to evaluate the

efficacy of 12-week supervised home-based exercise and branched-chain amino acids (BCAAs) supplementation in cirrhotic patients with sarcopenia.

Methods: This prospective pilot study enrolled compensated cirrhotic patients with sarcopenia defined by gender specific L3 skeletal muscle index (SMI) cut-offs (<42 for men and <38 for women). All participants received a tailored 12-week home-based exercise program supervised by sport scientists included: (1) aerobic walking exercise (>5,000 steps/day monitored by personal activity tracker), and (2) progressive full-body resistance training (30 minutes/day, at least 5 sessions/week). After the first 1:1 face-to-face training session, participants were provided with training videos and monitored for compliance by mobile calls/applications at least 3 times/week throughout the study period. Individualized dietary counselling by nutritionists and once-daily BCAAs supplementation (210 kcal, protein 13.5 g, BCAA 2.03 g) were given to all patients. The primary outcome was changes in SMI and psoas muscle index (PMI) at L3 evaluated by CT. Secondary outcomes were aerobic fitness evaluated by six-minute walk test (6MWT), cardiopulmonary exercise test (CPET), and functional capacity evaluated by liver frailty index (LFI).

Results: 15 patients were enrolled and 12 patients who had >80% adherence rate to the study protocol were included for final analysis (age 63.3±4.2 years, female 58%, HCV/alcohol 33%/33%, BMI 30.7±20.3 kg/m², MELD 8.5±1.6, Child A 91.7%). At week 12, there was a significant increase in SMI at L3 level (37.6±2.2 vs. 44.5±3 cm²/m², P<0.001); PMI at L3 level (4.6±1.7 vs. 6.1±1.8 cm²/m², P=0.002). Notably, 11/12 (91.7%) of participants had sarcopenia resolution. In addition, there were a significant increase in 6MWT distance (372.5±58.2 vs. 442.5±78.7 m., P=0.002), LFI (4.16±0.4 vs. 3.71±0.4, P<0.001) and hand-grip strength (23.07 ± 8.1 vs. 26.23 ± 7.9 kg., P=0.047). No significant changes in CPET parameters, MELD and MELD-Na were observed. There was no major intervention-related adverse event was found.

Conclusion: A 12-week supervised home-based exercise program and BCAA supplementation was effective for the treatment of sarcopenia in cirrhotic patients. This intervention also resulted in an improvement in functional capacity in these patients.

Abstract Submission No. 102004
P-0898

LIVER STIFFNESS ACROSS AGES: A STRATIFIED ANALYSIS OF VIRAL ETIOLOGIES USING ELASTOGRAPHY

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INTRODUCTION: Chronic HBV and HCV infections account for 57% of cirrhosis cases worldwide. Given the tendency of viral hepatitis-induced cirrhosis to progress to liver cancer, understanding liver disease subtleties across demographic age groups is imperative for effective health strategies.

METHOD: This study involved the selection of 1,631 participants aged 30 to 90, diagnosed with cirrhosis, from the results of 11,696 individuals who underwent the elastography (FibroTouch) test at Happy Veritas Hospital between 2015 and 2023.

RESULT: Participants were stratified into three cohorts based on virus detection: those without, those with HBV alone, and those with combined HBV and HDV. Examining liver cirrhosis across age groups revealed a consistent lower prevalence in the group without viral

hepatitis. However, in the HBV only group, notable peaks in liver cirrhosis were observed in the 30-35 years old cohort and the 41-45 years old group.

Among participants with viral infections, a positive correlation was observed between viral presence and liver stiffness, indicating that increased number of viral presence was associated with increased liver stiffness, implying a potential synergistic effect in co-infection scenarios. The odds of liver cirrhosis were 2.71 times higher in participants with HBV and HCV co-infection. Delving into age-specific dynamics, the 41-60 age group exhibited a heightened prevalence of co-infection compared to single virus infection and non-viral groups.

Abstract Submission No. 200032
P-0899

Antibiotic prophylaxis: does it protect against recurrence of spontaneous bacterial peritonitis?

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Background: Spontaneous bacterial peritonitis (SBP) is associated with significant short-term mortality. Antibiotic-prophylaxis is the main method of prevention.

Our aim was to determine the prevalence of SBP recurrence in cirrhotic-patients receiving antibiotic-prophylaxis and to identify predictive factors.

Patients and methods:

We conducted a retrospective and analytical study including all cirrhotic patients hospitalized for a recurrence of SBP who were undergoing fluoroquinolone-based antibiotic-prophylaxis.

Results: Of the 73 patients with SBP, only 8 patients had recurrent SBP, with a prevalence of 10.95%.

The mean age was 60±21 years and the sex-ratio (F/M) was 1.6.

The etiology of cirrhosis was dominated by viral origin in 50% of cases. All patients had a C Child-Pugh-score and a mean MELD-score of 20. The mean time between the first and second episodes was 6 months. Antibiotic-prophylaxis had been in place for at least 8 months on average. The mean time between the last esophageal-variceal ligation session and the episode of SBP was 5 months.

The mean value of biological data was: CRP 94.9mg/L, total-bilirubin 95.92mg/L, creatinemia 14.9mg/L, albumin 18g/L and ascites fluid protein level at 10.

The predictive factors for recurrence in the univariate study were: age>60 years (p=0.04), viral etiology of cirrhosis (p=0.03), C Child-Pugh-score (p=0.02), occurrence of digestive hemorrhage during hospitalization (p=0.042), and a history of esophageal-variceal ligation<5 months (p=0.029). No independent factors were found in the multivariate analysis.

Conclusion: In our study, recurrence of SBP in cirrhotic patients undergoing antibiotic-prophylaxis was noted in 10.95% of cases, which is a difficult infection to anticipate because there are few predictive factors.

Abstract Submission No. 200070
P-0900

Association between controlled attenuation parameters and clinical outcomes in cirrhotic patients

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Background and aims: Advanced liver fibrosis in steatotic liver disease is often accompanied by loss of hepatic fat.

We aimed to elucidate the association between controlled attenuation parameters and clinical outcomes in cirrhotic patients.

Material and Methods: Between January 2022 and December 2022, a total of 167 consecutive patients with LSM greater than 13kPa were included. Liver stiffness and CAP were measured by Fibroscan (Echosens, Paris).

Results: The mean age was 63.5 ± 12.3 , with 102 males and 65 females. The median values (25th- 75th percentiles) of liver stiffness and CAP were 19.6 kPa (16-29.6) and 250 dB/m (207-305), respectively. The mean follow-up period was 506 days and ten patients died during the observation period. A total of 10 patients had been lost to follow-up and censored at the time of last visit. The survival rates differed significantly in CAP (250 vs. CAP > 250 ($P < 0.01$ by the Log-rank test). CAP > 250 was a significant factor for survival in univariate analysis (Hazard ratio, 0.10; 95% confidential interval, 0.012-0.784 $P=0.028$).

Conclusions: Decreased CAP was a significant risk factor for survival in cirrhotic patients. Overtime change of CAP and with a larger cohort should be evaluated in further study.

Abstract Submission No. 200102
P-0901

Utility of ultrasonography shear wave for esophageal varices in patient with chronic liver disease

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Background and aim: Esophageal varices (EV) are one of the serious complications in liver cirrhosis. The guideline of cirrhosis/chronic disease does not specify a follow-up period or the need for esophagogastroduodenoscopy (EGD) in patients with chronic liver disease. On the other hand, follow-up with periodic abdominal ultrasonography (AUS) is recommended. If EV are assessed by AUS, minimally invasive and effective EGD can be performed for close examination. We investigated whether AUS shear wave elastography (Vs and F-index) could predict the presence and morphology of EV.

Methods: Between April 2018 and October 2022, we retrospectively collected data in 181 patients who underwent elastography and EGD for liver disease. Elastography was measured at liver segment 7 with intercostal manipulation. Endoscopic evaluation of EV were assessed with EV guideline. Vs and F-index were evaluated by presence and morphological of EV. The cut-off values of diagnosis and treatment indication for EV were investigated.

Result: Vs and F-index were significantly higher in patients with EV ($n=109$) than without EV ($n=72$) ($p<0.0001$), and positively correlated with the morphological grade of EV. The cut-off values of Vs and F-index were 1.63 and 1.86, with sensitivity (86.5%, 85.1%), specificity (45.8%, 49.2%) and AUC (0.70, 0.69), respectively, for the presence of EV, and 1.68 and 1.92, with sensitivity (91.4%, 88.6%), specificity

(40.8%, 41.8%) and AUC (0.68, 0.65), respectively, for treatment indication.

Conclusion: AUS elastography may provides objective assessment and can thus be a non-invasive screening tool for diagnosis and treatment indication of EV.

Abstract Submission No. 200130
P-0902

Changing Trend in Etiology of Liver Cirrhosis Among Hospital Admitted Cirrhotic Patients Bangladesh

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Background: Cirrhosis is a leading cause of morbidity and mortality among patients suffering from chronic liver disease. But etiology of cirrhosis is not same all over the world. Moreover, the etiology trend changes over the period of time.

Aim: To know the etiology of cirrhosis of liver in Bangladesh and compare with global and neighbouring countries.

Materials and methods: The study was an observational one conducted at the Department of Hepatology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh. Cirrhosis of liver patients admitted in the Hepatology ward in this hospital from July 2022 to June 2023 were included in the study. Their etiology were determined and recorded. Total 114 patient's data were recorded.

Results: Among 114 patients median age was 44.9 ± 12.9 . Male were 67.54% and female were 32.46%. Regarding the etiology, 37 (32.46%) patients had HBV infection, 25 (21.93%) patients had NAFLD, 19 (16.67%) patients had HCV infection, 11 (9.65%) patients had alcoholic liver disease, 7 (6.14%) patients had Wilson disease, 5 (4.39%) patients had Budd Chiari Syndrome, 4 (3.50%) patients had Autoimmune hepatitis and 6 (5.26%) patients had cryptogenic cirrhosis. Among 19 (16.67%) Hepatitis C infected decompensated cirrhosis patients 12 (10.52%) were female above the age of 45 years. Here female patients are more than male.

Conclusion: HBV infection is the leading cause of cirrhosis of liver followed by NAFLD and HCV infection in Bangladesh. Why female suffers from decompensated Hepatitis C more than male it should be needed to investigate.

Abstract Submission No. 200157
P-0903

CHIBA score -novel model for predicting 3-month mortality in a cohort of Decompensated Liver Disease

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Background: Decompensated liver disease (DCLD) has high mortality, and is important to prognosticate and prioritize for liver transplantation. MELD, MELD variants, and CTP were tested for this with drawbacks. The aim of study is to propose new prognostic model for DCLD.

Materials and methods: Retrospective study with 321 DCLD patients were enrolled. Patient relatives were contacted regarding date of death, and mortality at 3 months was assessed. After Logistic regression, coefficient of beta of independent variables were found out, and new CHIBA score was proposed.

CHIBA score = creatinine $\times$ 0.6 + HE $\times$ 0.4+ INR $\times$ 0.8 + bilirubin $\times$ 0.125 + ascites $\times$ 1.2) where C creatinine, H hepatic encephalopathy, I INR, B bilirubin, and A ascites.

Results: CHIBA score has AUROC of 0.793 (at a cutoff of > 5.5 , it has a sensitivity of 66% and specificity of 76%) compared to MELD-Na of 0.735 (cutoff > 25 , sensitivity 65%, and specificity 72%); MELD of 0.727 (cutoff > 17 sensitivity of 80.37% and specificity of 55.14%); I-MELD of 0.72; MESO index of 0.72; and UKELD of 0.686. For validation, 214 patients were selected, and AUROC of CHIBA score in the validation cohort was 0.77. At a cutoff of > 5.5 , it has a sensitivity of 60% and specificity of 77%.

Conclusion: CHIBA score is superior to MELD and variants in predicting 3 month mortality and is validated in external cohort. It can be calculated at bedside as it is simple score with no logarithmic variables

Abstract Submission No. 200169

P-0904

Self-Care of Japanese Patients with Decompensated Cirrhosis

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Background: Patients with decompensated cirrhosis (P-DC) have various physical symptoms and are repeatedly hospitalized and discharged before gradually transitioning to the end-of-life phase. The aim of this study was to identify the self-care experiences of P-DC in order to provide implications of the support needed by P-DC.

Methods: Semi-constructive interviews with six P-DC. Data were analyzed using qualitative integration methods (KJ method).

Results: Self-care of P-DC included “management they had done” in their own way and “management buried in life” due to being busy and other reasons. These were based on two aspects of their relationship with other people around them: “management supported by the connection with the people around them” or “management at a distance from the people around them.” Furthermore, as P-DC gradually realized the progression of their illnesses, they began “coming to terms with their declining bodies” while still being “anxious about the future.” Overall, these self-care experiences were influenced by an “elusive body” experience as P-DC were not well aware of the conditions of their own livers or the need for treatment.

Conclusion: This study showed that P-DC live with “anxiety about the future” and “elusive bodies.” Our results suggest the need for end-

of-life care from early stages and from a long-term perspective, as this is a complex disease with various physical symptoms.

Abstract Submission No. 200216

P-0905

The efficacy and safety of NOACs in cirrhosis and portal vein thrombosis patients: a meta-analysis

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Background: The imbalance of pro- and anticoagulant factors increases the risk for both bleeding and thrombosis in patients with cirrhosis. This study was to identify the efficacy and safety of novel oral anticoagulants (NOACs) in portal venous thrombosis (PVT).

Methods: We performed searches in PubMed, Embase, CNKI, Wanfang data, and CQVIP, up to Nov, 2023, using the key words “liver cirrhosis”, “cirrhotic”, “Portal Vein Thrombosis”, “New oral anticoagulants”, “anticoagulants” in English or Chinese. The meta-analysis was performed by Revman 5.4.1.

Results: We enrolled 11 studies, 2 RCT and 9 cohort studies, with a total of 899 PVT patients. The PV recanalization rate after NOACs anticoagulation therapy was better than that in the traditional therapy group. [RR=2.59, 95%CI(1.33,5.01),Z=2.81, P=0.005]. Meanwhile, the risk of bleeding was lower in the NOACs group than that of traditional group. [RR=0.47, 95%CI(0.31,0.72),Z= 3.52, P=0.0004].

Conclusions: Anticoagulant therapy is necessary for patients with cirrhosis complicated with portal vein thrombosis, and it is safe and effective to use new oral anticoagulant. due to the lack of large sample randomized controlled trials, the accuracy of the results needs to be further verified.

Abstract Submission No. 200217

P-0906

FB-1603: a potential therapeutic agent for liver injury_ preclinical and ongoing clinical studies

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Background: In our previous study, given the *Arthrospira* FEM-102 strain as a supplement to hepatocellular carcinoma patients undergoing liver resection or transarterial chemoembolization for 30 weeks was found to improve the total bilirubin (T-Bil), ALT, and AST post-surgery, and also albumin, liver stiffness relief significantly. Therefore, the active pharmaceutical ingredient, FB-1603, isolated from the FEM-102 was for further development.

Methods: The anti-oxidant efficacy of FB-1603 in-vitro is by co-culture with H₂O₂ and then measured by OxiRed staining. We also treat the TGF-beta activated Hepatic Stellate cell (HSC) with FB-1603 to evaluate the anti-stiffness activity. Finally, DEN-induced liver cirrhosis rat model was administrated with FB-1603 in chow diet, and were sacrificed in 12th week for liver tumor burden, hydroxyproline, AST, ALT, γ -glutamyl transpeptidase (γ -GT), T-bil, and oxidative stress.

Results: First, the FB-1603 showed the H₂O₂ scavenging activity in 400 µg/ml. We also found the specific cytotoxicity in TGF-beta activated HSC cell (EC₅₀= 22.6µg/ml). Given the FB-1603 to DEN treated liver cirrhosis rats displayed reduced hepatic hydroxyproline levels upon administration of 0.4~2 g/kg/day of FB-1603 and also mitigated the AST, ALT, γ-GT, T-bil, and oxidative stress in liver tissue.

Discussion: The FB-1603, can decrease hepatic impairment, oxidative stress, and liver stiffness in DEN induced rat model, and also no toxicity in acute, sub-acute toxicity, or genetic mutation assay. A Phase I/II randomized, double-blinded study of FB-1603 to evaluate the safety and efficacy in hepatocellular carcinoma patients receiving transarterial chemoembolization (FECHT trial) is exciting in Taiwan since Feb., 2024.

Abstract Submission No. 200243

P-0907

SII is used to evaluate the degree of fibrosis and the severity of liver cirrhosis

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Objective: To the role of SII in the assessment of fibrosis and disease severity in patients with liver cirrhosis.

Methods: A total of 185 patients with liver cirrhosis diagnosed in the Second Affiliated Hospital of Nanchang University from January 2019 to December 2021 were randomly selected. The transient elastography was used to detect the liver stiffness of the patients. According to the degree of fibrosis, the patients were divided into group A (E < 13.450, n=77) and group B (E > 13.450, n=108). The differences of serological indicators in different groups were compared. Multivariate logistic regression was used to analyze the independent risk factors of decompensated cirrhosis, and a prediction probability model was constructed. At the same time, the correlation between independent risk factors and the prediction probability model and the degree of liver fibrosis was analyzed.

Results: Univariate analysis showed that there were no significant differences in age, height, weight, BMI, admission temperature, heart rate, and mean arterial pressure between group A and group B (p>0.05); The RBC, HGB, PLT, PLR, Child-Pugh score, CHO, CHE, NE, LYM, SII and ALB in group A were significantly higher than those in group B (p<0.05); The HA, LN, III, IV, TBA, MELD score, FIB-4, APRI, PT, ALP, AST and INR of group A were significantly lower than those of group B (p<0.05). Multivariate logistic regression analysis showed that ALB, SII, CHO and HA were independent risk factors for group B (p<0.001). According to the combination of SII and ALB, the prediction probability model was $\text{logit}(P) = 8.714 - 0.181 \times \text{ALB} - 0.003 \times \text{SII}$. SII and ALB were negatively correlated with Fibroscan-E(kPa) ($r = -0.30$, -0.54 , $p < 0.001$, $p < 0.001$), and the prediction model was positively correlated with Fibroscan-E(kPa) ($r = 0.554$, $p < 0.001$).

Conclusions: SII is an independent risk factor for decompensation cirrhosis. The lower the SII, the higher the degree of liver fibrosis and the more severe the disease.

Key words: SII, liver stiffness, prediction model

Abstract Submission No. 200259

P-0908

Long-term CARTO results in a patient with cirrhosis of the liver. the experience of Kazakhstan.

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A 60-year-old patient with cirrhosis of the liver with portal hypertension, VRS 2-3 degrees.

2 SAE courses were conducted. Initially, PLT - 20.00 10E9/L; after 2 courses of SAE, the level of PLT - 41.00 10E9/L. Ultrasound - varicose veins of the esophagus and stomach, 3 cases of bleeding, computed tomography with contrast revealed a gastrointestinal shunt with a diameter from 15 to 18 mm. CARTO embolization was performed using 3 removable Azur CX 0.18 coils (Terumo Europe NV) and 2 removable PC400 coils (Penumbra) through the femoral vein (Fig.1,2).

After the coils were implanted through a 2,4 Fr coaxial microcatheter (Terumo Europe N.V.), an adhesive suspension with complete occlusion of blood flow in the shunt was introduced (Fig.3-5).

Control angiography showed complete occlusion of the gastrointestinal shunt.

Control CT scan 3 days after the CARTO procedure: the gastrointestinal shunt is still working, but the varicose veins are partially thrombosed - since the shunt is so huge/large, a second CARTO procedure or a combination with another technique (BARTO) may be required in the future (Fig.6-8).

A control CT scan with contrast after 12 months.

A decrease in the volume and number of varicose-dilated shunts, the shunts disappeared, and the varicose veins of the esophagus decreased to 0-1 degrees.

Reduction of clinical signs of portal hypertension and encephalopathy. (Fig. 9-10).

Transvenous obliteration is currently a recognized minimally invasive endovascular method that is effective and durable in the treatment of varicose bleeding from the stomach caused by portal hypertension.

Abstract Submission No. 200270

P-0909

Development and validation of the Adult cirrhosis Knowledge Questionnaire (ASK-Q)

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Background: Assessing a patient's liver cirrhosis knowledge is important in improving patient outcomes. To date, no questionnaire has been developed to assess patients' knowledge regarding multiple aspects of liver cirrhosis. This study aimed to develop and validate the Adult cirrhosis Knowledge Questionnaire (ASK-Q).

Methods: The ASK-Q was developed based on literature review and input from an expert panel. Five English-speaking cirrhotic patients who participated in a pilot study commented that the font size was too small. Hence, the font was enlarged and the final version of the ASK-Q [which consists of 24 items with 4 domains: self-understanding (5 items), aetiology (5 items), complications (5 items), and management (9 items) of liver cirrhosis] was then administered to English-speaking cirrhotic patients, aged ≥18 years, with or without decompensation at a tertiary centre, from September 2020 to November 2021, at baseline and a fortnight later. Patients with hepatic encephalopathy were excluded.

Results: A total of 120/135 patients agreed to participate (response rate=88.9%). The overall median score was 59.1[45.6-68.2]. A total of 7/22(31.8%) items were “easy”, 14/22(63.6%) items were “moderately easy” and 1/22(4.5%) items were “difficult”. Exploratory factor analysis extracted nine factors and two items were omitted. The ASK-Q was able to discriminate the knowledge level of patients with and without tertiary education (59.1[50.0-72.7] vs 54.5 [36.4-63.6], $p<0.05$). The overall Kuder-Richardson(KR) coefficient was 0.760 indicating adequate internal consistency. At retest, 77/120 patients participated (response rate=64.2%) and 15/22 items were not statistically significant, indicating adequate reliability.

Conclusions: The ASK-Q was found to be a valid and reliable questionnaire for evaluating the knowledge of liver cirrhosis amongst English-speaking adult patients.

Abstract Submission No. 200282

P-0910

Clinical characteristics of patients with decompensated cirrhosis with sepsis

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Objective: To investigate the clinical features and prognosis of patients with decompensated cirrhosis with sepsis.

Methods: A total of 120 patients with decompensated cirrhosis from October 2018 to October 2022 were enrolled and divided into sepsis group (n=56) and No-sepsis group (n=64) according to whether there was sepsis during hospitalization. There was no difference in age, gender and etiology between the two groups. The general condition and laboratory parameters of patients were collected. Patients with sepsis were treated with empirical antibiotic therapy to observe the short-term prognosis of patients.

Results: There were differences between the two groups in SBP, antibiotic exposure within 30 days, Child-Pugh grade, MELD score, gastrointestinal bleeding within 30 days, HGB and PCT. Logistic regression analysis showed that MELD score (OR=2.310, 95%CI: 1.586-5.145), Child-Pugh grade (OR=3.217, 95%CI: 1.236-7.159), gastrointestinal bleeding within 30 days (OR=5.596, 95%CI: 1.798-17.322), antibiotic exposure within 30 days (OR=3.358, 95%CI: 2.519-11.198) were independent risk factors for sepsis. In sepsis group, 23 (41.1%) patients were blood culture-positive, of which 18 (78.2%) were Gram-negative and 5 (21.8%) were Gram-positive. The main Gram-negative bacteria were *Escherichia Coli* (n=12, 66.7%), *Pseudomonas Aeruginosa* (n=4, 22.2%) and *Klebsiella Pneumoniae* (n=2, 11.1%). The main Gram-positive bacteria were *Staphylococcus Aureus* (n=3, 60.0%), *Staphylococcus Epidermidis* (n=1, 20.0%) and *Streptococcus Viridis* (n=1, 20.0%).

Conclusion: Recent gastrointestinal bleeding and antibiotic exposure may increase the susceptibility of patients. Gram-negative bacteria are still the most common cause of sepsis in patients with decompensated cirrhosis, which is helpful to guide the use of empirical antibiotics.

Abstract Submission No. 100079

P-0911

Mindin promotes macrophage-driven liver fibrosis resolution and tissue remodeling

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Background and Aims: Liver disease accounts for approximately 2 million deaths per year worldwide and the half was due to complications of cirrhosis. The secretory protein Mindin has been demonstrated to have important functional roles in the immune responses, but its role on maintaining liver homeostasis is largely unknown. This study aimed to investigate the role of Mindin in the regulation of liver fibrosis.

Methods and Results: Mindin was up-regulated in CCl₄ and TAA-induced liver fibrosis mouse models. Expression of Mindin was mostly expressed in hepatocytes but not in nonparenchymal liver cells. By constructing global Mindin knockout mice, we found that Mindin protected against CCl₄ and TAA-induced liver fibrosis. Further results revealed that Mindin fail to directly act hepatic stellate cells, but rather influenced the progression of liver fibrosis by orchestrating the immune status, particularly macrophages recruitment. Mindin recruited more macrophages to promote deposited extracellular matrix degradation by releasing matrix metalloproteinases, which in turn remodeled fibrosis. Meanwhile, liver fibrosis aggravated after macrophage clearance. Liver fibrosis was induced in parallel in Mindin and its acceptor CD11b^{-/-} mice, Mindin^{-/-}/CD11b^{-/-} mice, and their corresponding controls. Results revealed that either Mindin or CD11b^{-/-} individually would increase liver fibrosis, and when both genes knocked out simultaneously, liver fibrosis exacerbated dramatically. The Mindin/CD11b axis promoted the phenotypic switch of restorative macrophages by promoting phagocytosis, which facilitated collagen degradation via up-regulation of MMP-9. In turn, liver fibrosis resolved.

Conclusions: Mindin promotes liver fibrosis resolution and may provide a rationale for therapeutic strategies in chronic liver disease.

Abstract Submission No. 100120

P-0912

KDM4C represses liver fibrosis regulating H3K9me3 methylation

of ALKBH5 and m6A of snail1 mRNA

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Object: Snail1 is involved in liver fibrosis by mediating epithelial-mesenchymal transition. This present study hence probed into the molecular mechanism of snail1 in liver fibrosis.

Methods: The mouse model of liver fibrosis was induced by CCl₄. Serum levels of ALT and AST were determined, and liver pathological alternations were assessed utilizing hematoxylin-eosin and Masson stainings. Rat hepatic stellate cells (HSC-T6) were activated by TGF-β1, followed by assessment of cell viability and migration using MTT and scratch tests. Snail1, ALKBH5, and KDM4C levels were determined by means of immunohistochemistry, Western blot, or RT-qPCR.

The levels of α-SMA, Colla1, vimentin, and E-cadherin were also measured. m6A modification of snail1 was detected by Me-RIP. PAR-CLIP and RNA stability analysis were performed to assess the relationship between ALKBH5 and snail1. ChIP was processed to determine the level of KDM4C-bound ALKBH5 promoter and enrichment of H3K9me3 at the ALKBH5 promoter.

Results: Snail1 was upregulated but ALKBH5 and KDM4C were downregulated in liver fibrosis mice. KDM4C overexpression reduced

serum ALT/AST levels, liver injury, and α -SMA/Col1a1/vimentin levels, and increased E-cadherin. However, the above trends were counteracted by simultaneous overexpression of snail1. In TGF- β 1-activated HSC-T6 cells, ALKBH5 overexpression weakened cell viability and migration, downregulated α -SMA/Col1a1/vimentin, upregulated E-cadherin, and decreased m6A modification of snail1 and its mRNA stability. KDM4C promoted ALKBH5 expression by reducing the level of H3K9me3.

KDM4C inhibited HSC-T6 activation by regulating the ALKBH5/snail1 axis.

Conclusion: KDM4C decreases H3K9me3 methylation to upregulate ALKBH5 and subsequently represses snail1, ultimately impeding liver fibrosis.

Keywords: KDM4C; ALKBH5; Snail1; Hepatic stellate cell; Liver fibrosis; m6A

Abstract Submission No. 100135
P-0913

Preventive Effect of Angiotensin II Receptor and Neprilysin Inhibitor on hepatic fibrosis in mice

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The renin-angiotensin-aldosterone system has gained attention due to its role as a mediator of liver fibrosis and hepatic stellate cell (HSC) activation. Meanwhile, the natriuretic peptide (NP) system, including atrial NP (ANP) and C-type NP (CNP), is a counter-regulatory hormone regulated by neprilysin. Although the combination of an angiotensin receptor and a neprilysin inhibitor (sacubitril/valsartan: SAC/VAL) has shown clinical efficacy in patients with heart failure, its potential effects on hepatic fibrosis have not been clarified. This study assessed the effects of SAC/VAL in carbon tetrachloride (CCl₄)-induced murine liver fibrosis as well as the in vitro phenotypes of HSCs. Treatment with SAC and VAL markedly attenuated CCl₄-induced liver fibrosis while reducing α -SMA⁺-HSC expansion and decreasing hepatic hydroxyproline and mRNA levels of pro-fibrogenic markers. Treatment with SAC increased plasma ANP and CNP levels in CCl₄-treated mice, and ANP effectively suppressed cell proliferation and TGF- β -stimulated *MMP2* and *TIMP2* expression in LX-2 cells by activating guanylate cyclase-A/cGMP/protein kinase G signaling. Meanwhile, CNP did not affect the pro-fibrogenic activity of LX-2 cells. Moreover, VAL directly inhibited angiotensin II (AT-II)-stimulated cell proliferation and the expression of *TIMP1* and *CTGF* through the blockade of the AT-II type 1 receptor/protein kinase C pathway. Collectively, SAC/VAL may be a novel therapeutic treatment for liver fibrosis.

Abstract Submission No. 100141
P-0914

Liver fibrosis and association factors in blood-transfused thalassemia patients

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Background: Iron accumulation in liver is an important cause of liver fibrosis in thalassemia patients. Therefore, early detection with a reliable and non-invasive approach is crucial.

Method: A cross-sectional study of 74 blood-transfused intermediate thalassemia patients at Bhumibol-Adulyadej Hospital from October 2018 to 2019. We evaluated the correlation between significant liver fibrosis by using transient elastography (TE) and association factors (patient history, laboratory test).

Result: Significant liver fibrosis was found in 26 (35.13%) patients, which 4 (15.4%) were TDT (Transfusion-Dependent-Thalassemia) and 22 (84.6%) were NTDT (Non-Transfusion-Dependent-Thalassemia). The mean value of TE was 13.65 $\pm$ 5.71 kPa. Higher level of direct bilirubin (DB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), iron and ferritin were found in the significant liver fibrosis group comparing to the nonsignificant liver fibrosis group as the following data; DB 0.68 $\pm$ 0.28 mg/dL vs 0.51 $\pm$ 0.16 mg/dL (p-value=0.008), AST 43.04 $\pm$ 26.7 U/L vs 27.98 $\pm$ 12.16 U/L (p-value=0.01), ALT 36.35 $\pm$ 29.27 U/L vs 21.27 $\pm$ 11.98 U/L (p-value=0.018), iron 190.42 $\pm$ 102.14 μ g/dL vs 145.02 $\pm$ 55.02 μ g/dL (p-value 0.043) and ferritin 2381.35 $\pm$ 1937.92 ng/ml vs 1633.31 $\pm$ 1624.98 ng/ml (p-value=0.082), but the chelating agents initiation rate was lower as 6/26 (23.07%) vs 25/48 (52.08%). The APRI and FIB-4 scores elevated in the significant liver fibrosis group 7/26 (26.9%) and 2/26 (7.7%) respectively.

Conclusion: The ferritin level may not be an adequate indicator for iron-chelating therapy, but DB, AST, ALT and iron level should necessary be considered. APRI and FIB-4 scores were not correlated to significant liver fibrosis by TE in thalassemia patients.

Abstract Submission No. 100218
P-0915

Fibroscan 402 in the Management of Chronic Viral Hepatitis in Armenia

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Background: Chronic viral hepatitis represents a significant public health challenge in Armenia. Early diagnosis and effective management of infections are crucial to reduce disease burden. Fibroscan402, a non-invasive elastography-based tool, has emerged as a valuable diagnostic and monitoring tool for assessing liver fibrosis in chronic liver diseases patients.

Material and methods: 18 months we conducted liver stiffness measurements (LSM) on 458 patients diagnosed with HBV (273 patients) and HCV (185 patients). Unfortunately in 3 patients reliable LSM results were not attainable. The remaining 455 patients were included in study.

For hepatitis B treatment was indicated if LSM results showed significant fibrosis (>F2) along with a significant viral load (>2000 IU/mL). In the case of hepatitis C genotypes 2 or 3 antiviral treatment was advised irrespective of LSM results. For genotypes 1 and 4 treatment was recommended if the fibrosis stage exceeded F2. Patients with fibrosis stage > F3 were advised to further observation for HCC.

Results: Fibroscan402 LSM findings revealed that patients 240 (52.7%) had F0-F1, 85 patients (18.5%) were at F2, 130 patients (28.8%) were at F3 and F4. 102 patients underwent liver biopsies within one year of LSM.

Notably, LSM results led to a change in clinical management for 32% of the patients (147 cases). Specifically, 215 patients were recommended antiviral treatment, 130 patients were advised to further

observation for HCC and 26 patients with successfully treated hepatitis C were able to be discharged from clinical follow-up due to the absence of severe fibrosis or cirrhosis

Conclusion: Based on the experiences it is evident that the incorporation of liver stiffness measurement via Fibroscan402 represents a significant non-invasive enhancement to clinical care for individuals afflicted by chronic viral hepatitis B and C.

Abstract Submission No. 100426

P-0916

Discordance between transient elastography and liver biopsy for assessing fibrosis in HBV and HCV

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Introduction: The objective of this study was to determine the frequency of major discrepancies and identify the clinical variables associated with these differences.

Methods: The data of 391 patients with chronic HBV infection (CHB) and 453 patients with chronic HCV infection (CHC) who accepted VCTE, liver biopsy, clinical, and biological examination were collected retrospectively. Liver fibrosis was evaluated using the METAVIR scoring system.

Results: The optimal diagnostic values of liver stiffness measurement (LSM) for significant fibrosis ($\geq F2$), severe fibrosis ($\geq F3$), cirrhosis (F4) were 6.85, 8.85, 11.65 kPa in CHB cohort and 7.85, 9.40, 11.15 kPa in CHC cohort, respectively. Among the CHB patients, 240 (61.3%) exhibited discrepant results for the diagnosis of fibrosis. Of these, 111 patients (28.3%) had an overestimation, while 129 patients (32.9%) had an underestimation. Also, a total of 304 (67.1 %) [overestimation, 105 (23.1 %); underestimation, 199 (43.9 %)] patients showed discrepant results in CHC cohort. We found that an association between host factors and measurement factors like BMI, gender, interquartile range/median LSM values with underestimation, while AST and ALT, reflecting inflammation, was associated with overestimation.

Conclusions: Our findings demonstrate that overestimation or underestimation of fibrosis by VCTE is common, particularly in patients with high levels of clinical inflammatory activity. While VCTE is highly sensitive in detecting liver fibrosis, its specificity is not as reliable.

Abstract Submission No. 100554

P-0917

Diagnostic Accuracy of FIB-4 compared to Liver Elastography in Assessing Liver Fibrosis in Filipinos

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Background: The Philippines has the third highest mortality growth worldwide from cirrhosis. The Fibrosis-4 (FIB-4) index is a non-invasive scoring uses age, platelet count, and liver transaminase levels generally used to estimate the degree of hepatic fibrosis. No previous study has looked into the applicability of this tool in Filipino patients.

Objectives: The aim of this study is to determine the diagnostic accuracy of the FIB-4 index compared to liver elastography for assessment of liver fibrosis in Filipinos.

Methodology: This cross-sectional study collected clinical data, laboratory results, and liver elastography findings. Data was analyzed using an area under the receiver operating characteristic (AUROC) curve.

Results: In 459 patients (57.1 percent male, mean age 53.1 years, mean BMI 28.79 kg/m²), the FIB-4 has an AUC of 0.698 (95% CI 0.653-0.739). Using the best cut-off score through Youden's index 1.21, FIB-4 showed sensitivity of 63.3% (95% CI 56-70.2) and specificity of 73.1% (95% CI 67.4 to 78.3) in detecting the presence of fibrosis on liver elastography.

In the subset of non-obese Filipinos, FIB-4 has an AUC of 0.778 (95% CI 0.695-0.847). The best cut-off score through Youden's index is 1.37, sensitivity of 69.8% (95% CI 53.9-82.8), and specificity of 82.9% (95% CI 73-90.3).

Conclusion: FIB-4 still has a low sensitivity and low to moderate specificity in predicting hepatic fibrosis in Filipinos. Thus, we recommend further research on other feasible and accessible non-invasive modalities to assess liver fibrosis.

Abstract Submission No. 100638

P-0918

Corylin attenuated CCl₄-induced liver fibrosis in mice by regulating the GAS6/AXL signaling pathway

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Liver fibrosis can be reversed when treated in its early stages and the factors that cause liver inflammation are inhibited. No studies have investigated the therapeutic effects of corylin, a flavonoid extracted from *Psoralea corylifolia* L. (Fabaceae), on liver fibrosis. Therefore, we evaluated the anti-inflammatory activity of corylin and investigated its efficacy and mechanism of action in ameliorating liver fibrosis. Corylin significantly inhibited the activation of MAPK signaling pathways and expression of interleukin (IL)-1 β , IL-6, and tumor necrosis factor- α in human THP-1 and mouse RAW264.7 macrophages, thereby inhibiting inflammatory responses. Furthermore, corylin inhibited the expression of growth arrest-specific gene 6 (Gas6) in human hepatic stellate cells (HSCs) and the activation of downstream phosphatidylinositol 3-kinase (PI3K)/Akt pathway, thereby inhibiting the activation of HSCs and the expression of extracellular matrix proteins, including α -smooth muscle actin and type I collagen. Additionally, corylin induced caspase 9 and caspase 3 activation, which promoted apoptosis in HSCs. Further, in vivo experiments confirmed the regulatory effects of corylin on these proteins, and corylin alleviated the symptoms of carbon tetrachloride-induced liver fibrosis in mice. These findings revealed that corylin has anti-inflammatory activity and inhibits HSC activation; thus, it represents a potential adjuvant in the treatment of liver fibrosis.

Abstract Submission No. 100657

P-0919

Serum CHI3L1 combined with GP73 helps evaluate liver fibrosis in CHB patients

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Background: Early identification of fibrosis in chronic hepatitis B(CHB) patients can reduce liver-related adverse events. Though numbers of predicting models have been reported, there is still a need of more effective, practicable non-invasive serological diagnosis modes. Previous studies indicated that both chitinase-3-like protein 1 (CHI3L1) and serum Golgi protein 73(GP73) were associated with liver fibrosis.

Methods: Our study enrolled 324 CHB patients with biopsy and 167 had completed liver stiffness measurement (LSM). Serum CHI3L1 and GP73 level, LSM, fibrosis-4(FIB4), and aspartate aminotransferase-to-platelet ratio index (APRI) were determined to analyze the correlation between these non-invasive tests and liver fibrosis by logistic regression analysis. The area under receiver operating characteristic (AUROC) was calculated to evaluate the diagnostic accuracy of each model.

Results: Multivariate logistic regression analysis indicated that CHI3L1 and GP73 were independent risk factors for significant fibrosis (S2-4) and advanced fibrosis (S3-4). We combined the two markers and developed our prediction model. The AUROC of our prediction model for identifying significant fibrosis was 0.757 (95 CI 0.685-0.828), significantly higher than the model with FIB-4(0.636, 95CI 0.553-0.719, $p=0.022$), comparable to LSM(0.743, 95CI 0.668-0.819, $p=0.790$) and APRI(0.717, 95CI 0.638-0.795, $p=0.431$) models. The AUROC of the prediction model for identifying advanced fibrosis was 0.735 (95CI 0.652-0.818), comparable to LSM (0.832, 95CI 0.766-0.898, $p=0.051$), FIB-4(0.653, 95CI 0.560-0.746, $p=0.185$) and APRI(0.724, 95CI 0.637-0.811, $p=0.845$) model.

Conclusion: CHI3L1 and GP73 were positively correlated with liver fibrosis. The diagnostic model constructed by CHI3L1 and GP73 can help identify the significant and advanced liver fibrosis in CHB patients.

Abstract Submission No. 100680
P-0920

Liver regeneration after resection: progressive versus regressive fibrosis of cirrhosis

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Background: Hepatocellular carcinoma (HCC) occurs in chronic hepatitis/cirrhosis. The aim of this study is to investigate pathological features of non-neoplastic liver, which are related to hepatic regeneration after HCC resection.

Methods: We evaluated pathological features of 97 non-neoplastic liver of resected HCCs. Pathological features including inflammation grade, fibrosis stage (regressive and progressive/indeterminate), small and large liver cell change were evaluated and immunohistochemical stains for the markers of senescence (p21), DNA damage (γ H2AX), and progenitor cell (EpCAM) were performed. Liver volume (LV) was measured using VoxelPlus® 2 program of Mevisys company with computed tomography of preoperative and 7th and 90th postoperative day. The liver regeneration ratio (LRE) was calculated as follows: LRE = LV90 days post-op /LV7 days post-op.

Results: LRE and p21 expression showed no significant difference among stages of 2, 3, and 4 regressive, and there were significant decrease of LRE, and increase of p21 between stage 4 regressive and stage 4 progressive/indeterminate ($p<0.05$ for both). When dividing into two groups according to the median LRE (1.38), low-LRE group showed higher expression of p21 and γ -H2AX, and lower expression of EpCAM compared to high-LRE group ($p<0.05$ for all). Inflammation grade, and small and large liver cell change showed no significant difference between two groups.

Conclusions: LRE is considered to be inefficient in liver with high senescence and DNA damage of hepatocytes, and low progenitor cell activation. Liver regeneration capacity is considered to be preserved upto fibrosis stage 4 regressive, and significantly impaired in stage 4 progressive/indeterminate.

Abstract Submission No. 100721
P-0921

Factors contributing to liver stiffness in the acute phase of acute hepatitis

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Background: The factors involved in liver stiffness in acute hepatitis still need to be investigated. This study performed to clarify factors affected to liver stiffness in patients with acute phase of acute hepatitis.

Subjects and methods: Blood samples were collected, abdominal ultrasound examination and liver stiffness measurement were performed early in the morning the day after admission. Previous reports on chronic liver disease have defined a Vs value ≥ 1.63 as F4. Patients were divided to two groups according to liver stiffness, follow as normal stiffness (N group) and high stiffness (H group). Patients with a Vs value of 1.63 or higher were included in the H group. Various parameter of blood sample and length of hospital stay were compared between the N group and the H group.

Results: A total of 43 adult Japanese patients with acute hepatitis except for chronic liver diseases. Twenty-seven patients had virus related acute hepatitis and 16 patients had drug induced liver injury. Serum levels of total bilirubin (T-Bil) and direct Bil (D-Bil) in the H group were significantly higher than those of the N group. The average of length of hospital stay in the H group was significantly higher than those of the N group, also. In univariate analysis, collapsed gallbladder, T-Bil, and D-Bil were related to the liver stiffness. But serum levels of transaminase and hepatomegaly were not related to it.

Abstract Submission No. 100893
P-0922

Loss of SREBP-1c Ameliorates Hepatic Steatosis and Liver injury in NASH through Lipocalin-2

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Roles of sterol regulatory element-binding proteins (SREBPs) have been established as lipid synthetic transcription factors especially for cholesterol and fatty acid synthesis. SREBP-1c isoform, which constitutes more than 90% of the in vivo SREBP-1, is a key regulator of early events in the liver's response to insulin and is a major determinant of lipogenic gene transcription. In this study, we explored the role of SREBP-1c on NASH and LCN2 gene expression regulation.

Wild-type and SREBP-1c knockout (KO) mice fed with a high-fat/high-sucrose diet, carbon tetrachloride (CCl₄)-treated, and with lipocalin-2 (LCN2) overexpression. LCN2 gene expression and secretion increased in CCl₄-induced liver fibrosis mice models, and SREBP-1c regulated LCN2 gene transcription. Moreover, treatment with holo-LCN2 stimulated intracellular iron accumulation and fibrosis gene expression in mouse HSCs, but this effect was not observed in SREBP-1cKO HSCs, indicating that SREBP-1c-induced LCN2 expression and secretion stimulate HSCs activation through iron accumulation. Further, LCN2 expression was strongly correlated with inflammation and fibrosis in patients with NASH. Our findings indicate that SREBP-1c regulates Lcn2 gene expression, contributing to diet-induced NASH. Reduced Lcn2 expression in SREBP-1cKO mice protects against NASH development. Therefore, the activation of Lcn2 by SREBP-1c establishes new connection between iron and lipid metabolism, affecting inflammation. These findings may lead to new therapeutic strategies for NASH.

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Abstract Submission No. 101088
P-0923

Noninvasive Assessment of Liver Diseases — Hepatic Fibrosis Using Shear Wave Elastography (SWE)

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1. Introduction

Recently, number of studies on the noninvasive assessment of hepatic fibrosis . SWE was performed

2. Purpose

The usefulness of SWE in assessing the degree of hepatic fibrosis was evaluated.

3. Materials

SWE was performed in a total of 31 subjects: 8 in the normal adult group 17 in the chronic hepatitis group , and 6 in the cirrhosis group . The diagnosis was confirmed by liver biopsy in 7 subjects in the chronic hepatitis group and 2 subjects in the cirrhosis group. For the remaining 10 subjects in the chronic hepatitis group and the remaining 2 subjects in the cirrhosis group, the diagnosis was confirmed based on the findings obtained by diagnostic imaging studies , clinical evaluation, and clinical laboratory tests. The subjects in the normal adult group were con Written informed consent to participate in the study was obtained from each subject.

4. Subjects

A diagnostic ultrasound system (Aplio™, Toshiba Medical Systems Corporation, Tochigi, Japan) and convex probe was employed in this study.

5. Results

The SWE values were 1.5 m/s in the normal adult group 2.73 m/s in the chronic hepatitis group 2.71 m/s in the cirrhosis group and 9.43 m/s for patients with cirrhosis and ascites In the ascites patients, we measured before and after ascetic drainage.

7. Conclusion

The results of the present study suggest that noninvasive SWE may become the method of choice for assessing hepatic fibrosis in routine clinical practice.

Abstract Submission No. 101114
P-0924

Predictive value of AIMS65 score and carvedilol in cirrhotic patients with acute variceal bleeding.

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Background: Acute variceal bleeding (AVB) remains a common and life-threatening complication in patients with liver cirrhosis. We evaluated the ability of various bleeding risk stratification scores including AIMS65 and compared with liver severity as predictors of mortality and rebleeding.

Methods: We retrospectively enrolled 122 patients with liver cirrhosis and AVB at the Daejeon St. Mary's hospital from April 2014 to March 2021. Patients were risk stratified using AIMS65, ABC, Child-Pugh, Model for End-stage Liver Disease (MELD) scores. Primary outcomes were overall survival and rebleeding.

Results: Liver function showed child A, B, and C (32.7%, 40.9%, and 26.2% respectively). 1-month mortality showed 12.2%. Child class, MELD grade, AIMS65, and carvedilol showed significant stratification of 1Month-Mortality except ABC score (P<0.001, 0.015, <0.001, and 0.007 but P=0.353). The mean OS of AIMS65 grade 1, grade 2, and grade 3 patients were 72.9, 40.3, and 28.9 months, respectively (P<0.001). The ABC, child class, and MELD also significantly showed survival difference (P=0.025, P=0.003, and P=0.000, respectively). However, AIMS65, ABC, child class, and MELD did not predict rebleeding risk (P=0.655, P=0.548, P=0.180, and P=0.160, respectively). On the other hand, treatment of carvedilol showed survival benefit and reduced rebleeding rates (P=0.001, 0.021, respectively). In a multivariate analysis, the AIMS65 and carvedilol treatment were significant predictive factors for OS (P=0.006, 0.000, respectively).

Conclusion: AIMS65 is superior to established AVB and liver disease severity risk stratification scores in predicting mortality of cirrhotic patients with AVB. In addition, carvedilol treatment reduced overall mortality and rebleeding. Therefore, application of AIMS65 score and treatment of carvedilol may show more favorable clinical outcome in patients with AVB.

Abstract Submission No. 101374
P-0925

Overexpression of MUDENG in liver enhances CCL₄-induced liver fibrosis

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Background and Aims: Transforming growth factor (TGF)- β plays an important role in the activation of hepatic stellate cells. AP5M1 is known to participate in cell death and has been reported to be involved in Golgi trafficking. In this study, we identified the physiological effects of AP5M1 in mouse liver with overexpression and suppression of IL11.

Method: Eight 8-weeks-old male human AP5M1 transgenic (hAP5M1-Tg) mice and eight C57BL/6N male mice were injected with carbon tetrachloride. Lenti:mIL11 and Lenti:mIL11 mutein viruses were injected intraperitoneally into 6-week-old mice and intranasally into the mice after a week. The difference in the percent collagen area was evaluated.

Results: The collagen proportionate area (CPA) in C57BL/6N mice infected with Lenti:mIL11 or Lenti:mIL11 mutein showed no difference in the absence of liver injury caused by CCl₄. However, CCl₄ injected Lenti:mIL11 mutein infected C57BL/6N mice demonstrated significantly reduced collagen accumulation in the liver tissue compared to Lenti:mIL11 infected C57BL/6N mice. In hAP5M1 transgenic mice, the infection of Lenti:mIL11 or Lenti:mIL11 mutein showed no significant difference in the CPA. The expression levels of collagen, α -SMA, and TGF- β were higher in the liver of hAP5M1-Tg mice challenged with CCl₄ than in the liver of C57BL/6 mice.

Conclusion: Overexpression of hAP5M1 enhances liver fibrosis caused by intraperitoneal injection of CCl₄. C57BL/6N mice injected with Lenti:mIL11 mutein showed significantly reduced collagen accumulation in the liver. The application of IL11 mutein may be considered as a potential treatment method for alleviating liver fibrosis.

Abstract Submission No. 101639

P-0926

NAFLD combined with HBV significantly worsens the clinical tests and degree of the liver fibrosis

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Background: Nonalcoholic fatty liver disease (NAFLD) and Hepatitis B virus infection (HBV) are increasingly prevalent with worldwide distribution and represent a growing challenge in terms of prevention and treatment. To determine whether body-mass index (BMI) is associated with liver-related enzyme elevation and liver tissue state among HBV carriers and other viral infections we prospectively reviewed to analyze the relationship between HBV infection and NAFLD.

Patients and Methods: Our study was performed on 51 patients who were treated in our hospital from May 2019 to June 2023, who were free of cancer and surgery. Main outcome measures included biochemical blood tests, Magnetic Resonance Imaging Proton Density Fat Fraction (MRI-PDFF), and imaging-based elastography.

Results: During the follow-up of four years, there was no case of hepatocellular carcinoma (HCC) or death. There is no association between gender or age with NAFLD. Excess BMI was significantly associated with the occurrence of liver steatosis ($p < 0.0001$), detected by MRI-PDFF as well as elevated ALT, AST, bilirubin, and triglycerides during follow-up (Table 1). Also, the association of BMI with liver fibrosis ($p < 0.009$), detected by elastography (Figure 1), was strong and together with elevated alpha-fetoprotein (AFP) levels might be the accurate predictors for incident HCC and liver-related death. In addition, HBV infection cases elevated, but not significantly ($p = 0.0674$) in NAFLD patients.

Conclusion: In conclusion, our study indicates that dysregulated fatty-acid metabolism and lipotoxicity in NAFLD seem to initiate liver-tissue inflammation, disrupt hepatocyte cell homeostasis, and promote

the progression to fibrosis, and HCC. HBV-NAFLD co-existence may further have an additional impact on liver disease progression.

Abstract Submission No. 101895

P-0927

Enhancing Diagnostic Precision in Advanced Liver Disease Detection Utilizing M2BPGi

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Background: Chronic liver disease is a major challenge in Thailand, requiring easily accessible biomarkers for identifying critical cases. Non-invasive testing, particularly using the novel serum marker Mac-2 binding protein glycosylation isomer (M2BPGi), is a promising method for remote support. The study aims to assess M2BPGi's accuracy in complementing existing protocols for detecting severe fibrosis and cirrhosis across diverse causes.

Methods: The study, approved by the institutional review board, involved 132 patients with varied liver fibrosis, stemming from hepatitis B and C, and non-alcoholic fatty liver disease. Utilizing residual serum samples, the accuracy of the novel serum marker M2BPGi was assessed against classical biomarkers, including APRI, FIB-4, transient elastography, and liver biopsy. Additionally, a sequential assessment aimed to determine diagnostic accuracy in profiling advanced liver disease (F3/4 cases), crucial for specialist center care.

Results: Our study found positive correlations between M2BPGi and classical liver disease markers (APRI, FIB-4, TE, and liver biopsy) using Pearson correlations. M2BPGi showed superior diagnostic accuracy compared to other non-invasive markers (AAR, PLT, APRI, and FIB-4) based on AUROC curve analysis. Combining M2BPGi with TE for fibrosis staging in advanced liver disease resulted in an AUROC of 0.83. Using a sequential diagnostic algorithm with FIB-4 as the initial parameter and subsequent M2BPGi testing (cutoff of 1.0) improved the ability to distinguish advanced disease, increasing patient referral accuracy from 59% (using FIB-4 alone) to 79%.

Conclusions: In conclusion, non-invasive liver disease testing using novel serum marker M2BPGi emerges as a promising method, particularly in supporting remote testing.

Abstract Submission No. 102034

P-0928

Serum DANCE levels in MASLD and significance of elastic fibers in fibrosis development

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Background and Purpose: There are two types of fibers that construct liver fibrosis: collagen fibers and elastic fibers, but in recent years there have been few reports on the differences and significance of the two types of fibers. However, elastic fibers have some useful findings, such as the absence of newly developed elastic fibers in acute hepatitis and the fact that those in the portal region reflect the actual degree of hepatic fibrosis. In particular, the involvement of elastic

fibers in fatty liver diseases such as alcohol-associated liver disease and MASLD has been considered less significant than in viral liver diseases. Recently, DANCE (developmental arteries and neural crest EGF-like), an index of elastic fiber content, has become available as a simple serum assay. Therefore, we measured serum DANCE levels in patients with MASLD and investigated its usefulness.

Methods: We measured serum DANCE concentrations in 60 NAFLD patients and 20 healthy subjects undergoing treatment at our units, and compared them with existing fibrosis markers such as M2BPGi, type IV collagen 7S, and FIB-4, as well as liver histology in patients who underwent liver biopsy, in addition to general blood data.

Results: Serum DANCE levels were higher in MAFLD patients than in healthy controls, especially in MASH patients (healthy vs. non-MASH vs. MASH: 122 vs. 151 vs. 213 ng/mL, $p < 0.0001$). This value correlated with the degree of fibrosis on liver biopsy histology ($p < 0.0001$) and with existing fibrosis markers such as M2BPGi ($p = 0.0002$), type IV collagen 7S ($p < 0.0001$) and FIB-4 ($p < 0.0001$). DANCE levels did not correlate with the degree of liver tissue inflammation or AST and ALT levels, suggesting that DANCE is a fibrosis marker independent of liver inflammation.

Conclusion: DANCE, also known as fibulin-5, is an essential protein for elastic fiber formation. In this study, DANCE levels increased with the progression of liver tissue regardless of the intensity of inflammation, suggesting that DANCE may be useful as a new fibrosis marker. On the other hand, elastic fibers are involved in the progression of MASLD, and their role in the progression of fibrosis should be investigated in the future.

Abstract Submission No. 200031

P-0929

Role of Spleen Stiffness Measurements with 2D-SWE for esophageal varices in patients with cACLD

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Background: Spleen stiffness measures (SSM) as a non-invasive diagnostic technique for esophageal varices (EV) have been studied, with the majority of the data collected by transient elastography (TE). Using 2D Shear-Wave Elastography (2D-SWE.PLUS) integrated into the Supersonic Imagine Aixplorer system.

Aim: We aimed to determine the diagnostic performance of SSM for the presence of EV in patients with compensated advanced chronic liver disease (cACLD).

Methods: We prospectively enrolled patients with cACLD (≥ 12.5 kPa by Transient Elastography) from January 2023 to November 2023 without history of liver decompensation. All patients included performed an esophago-gastro-duodenoscopy (EGD) for varices assessment and a complete abdominal multiparametric assessment of liver and spleen assessment using Aixplorer MACH 30 (Supersonic Imagine, Aix-en-Provence, France).

Results: There were 73 patients analyzed (78% were men, the mean age 60.3 ± 12.1 , BMI 23.1 ± 5.12 kg/m²). Eighteen (24.7%) had alcoholic liver disease, 29 (39.7%) had non-alcoholic fatty liver disease, 11 (15.1%) had chronic viral hepatitis, and 15 (20.5%) had various etiologies. The mean SSM was 38.6 ± 12.8 kPa whereas the mean liver 2D-SWE.PLUS was 17.4 ± 8.61 kPa. EV was detected in 37 (50.7%)

patients [grade I – 11 (29.7%); grade II – 10 (27%); grade III 16 (43.2%)]. High risk EV (grades II/III) were associated with higher spleen ($p < 0.001$) and liver ($p = 0.017$) 2D-SWE.PLUS, increased spleen volume ($p < 0.001$), portal vein ($p < 0.001$) and splenic vein diameter ($p = 0.008$). A cut-off of 31.3 kPa of SSM could predict any grades of EV (Ss 92%, Sp 54%, PPV 73.7%, NPV 90%, AUROC 0.807, $p < 0.001$), while a value of 44.3 kPa can predict EV grade 3 with red signs and white nipples of Sp of 92.1%, Sv of 73.1%, PPV of 37.3%, and NPV of 92.9%, AUC = 0.881, $P < 0.001$.

Conclusion: 2D-SWE SSM is a valid approach for ruling in or out EV in cACLD individuals. If bigger studies validate this results, up to 50% of endoscopies might be prevented in this patients.

Abstract Submission No. 200135

P-0930

Rosa rugosa Thunb. extract attenuates hepatic fibrosis via inhibition of TGF/Smad signaling pathway

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Rosa rugosa Thunb. has been used to treat hematemesis, dysmenorrhea, diarrhea, and dysentery. The present study investigated anti-fibrogenic effects of *Rosa rugosa* Thunb. extract (RRE) *in vivo* and *in vitro*. We evaluated the effects of RRE to inhibit transforming growth factor- β 1 (TGF- β 1)-induced LX-2 cells (a human hepatic stellate cell (HSC) line) using biochemical assays, reporter gene assays, and immunoblot analysis. Additionally, we conducted a model of carbon tetrachloride (CCl₄)-mediated liver fibrosis to examine the effects of RRE using serum biochemistry, histopathological analysis, and immunohistochemistry. Up to 100 μ g/mL RRE treatment showed no cytotoxicity on LX-2 cells. Treatment with RRE significantly blocked TGF- β 1-inducible Smad binding element-driven luciferase activity, Smad2 and Smad3 phosphorylations, and plasminogen activator inhibitor-1 expression in HSCs. Also, increases of matrix metalloproteinases-2 and -9 genes, and α -smooth muscle actin (α -SMA) expression by TGF- β 1 were diminished by RRE treatment. Moreover, administration of RRE significantly inhibited the alanine aminotransferase and aspartate aminotransferase activities mediated by CCl₄. RRE administration also prevented liver fibrosis, as showed by decreases in hepatocellular degeneration, inflammatory cell infiltrations, collagen fiber accumulation, and α -SMA immunoreactivity in mice. Therefore, RRE may be a promising candidate to attenuate hepatic fibrosis through inhibition of TGF/Smad signaling pathway.

Abstract Submission No. 200137

P-0931

A prospective validation study for the Baveno elastography criteria in shear wave elastography

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Background: The Baveno criteria for assessing advanced liver fibrosis were mainly determined by transient elastography (TE), and its pathology-based validation studies in two-dimensional shear-wave elastography (2D-SWE) remain limited.

Aim: To validate the Baveno criteria through use of 2D-SWE.

Method: Consecutive patients who underwent liver biopsies for various benign liver diseases were prospectively recruited. Liver stiffness measurement (LSM) was simultaneously evaluated by TE and 2D-SWE. The optimal cut-off value to predict advanced liver fibrosis was determined by the Youden Index, and the diagnostic performance was estimated using area under the receiver operating characteristic (AUROC) analysis.

Results: A total of 101 patients were enrolled having a median age of 55.0 (IQR: 46.0-63.5) years, with 53 (52.48%) of them being male. Using <9 and >14 kPa as the optimal dual cut-offs, the AUROC values in TE and 2D-SWE were 0.92 (95% CI: 0.83-0.97) and 0.93 (95% CI: 0.84-0.98), respectively ($P=0.61$). The sensitivity and specificity of LSM by TE/2D-SWE achieved rates of 94.44%/94.44% and 86.00%/88.00%, respectively. However, using the Baveno criteria, the AUROC values in TE and 2D-SWE could remain achieving 0.91 (95% CI: 0.82-0.97) and 0.93 (95% CI: 0.84-0.98), respectively ($P=0.36$). The sensitivity and specificity in TE/2D-SWE were 88.24%/88.24% and 86.79%/90.57%, respectively.

Conclusion: This study establishes the compatibility of the Baveno dual cut-off criteria with 2D-SWE, positioning it as an easily used criteria in clinical practice and research.

Abstract Submission No. 0

P-0932

Alviter-Raymundo Gustavo, Authors

G. Alviter-Raymundo, F. Bachinger, S. Ghimire, K. Saeb-Parsy & L. Vallier

¹

Abstract Submission No. 100188

P-0933

Impact of Employment Status on Mortality in CLD Patients: Insights from the NHIS (2005-2018)

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Chronic liver disease (CLD) is an important cause of morbidity and mortality globally. Socioeconomic factors of CLD patients such as employment status can potentially affect their prognosis. This study thus investigates the influence of employment status on mortality in CLD patients using data from the National Health Interview Survey (NHIS) from 2005 to 2018.

NHIS is a cross-sectional health survey representing the non-institutionalized U.S. population. Individuals aged ≥ 18 years with available parameters for CLD evaluation and employment status were included in the study. Mortality analysis utilized NHIS data linked to National Death Index (NDI) death certificates. Cox proportional hazards and Fine-Gray subdistribution hazard ratio models were applied to assess associations, adjusting for various factors, including comorbidities, lifestyle behaviors, and sociodemographic characteristics.

18,108 CLD patients, with 7,856 employed and 10,252 unemployed individuals were included in the study. Employed CLD patients were

younger, more likely to be male, and had fewer comorbidities. Univariate and multivariate analyses revealed that employment status was significantly associated with lower overall mortality (multivariate HR: 0.329, 95% CI: 0.194 to 0.557, $p<0.001$). Employed CLD patients also had lower rates of cardiovascular-related mortality (sHR: 0.297, 95% CI: 0.122 to 0.720, $p=0.007$) and cancer-related mortality (sHR: 0.228, 95% CI: 0.094 to 0.552, $p=0.001$).

Overall, employment status is a significant predictor of lower mortality in CLD patients, with employed individuals experiencing reduced overall, cardiovascular, and cancer-related mortality

Abstract Submission No. 100466

P-0934

Drug-related problems managed by pharmacists for cirrhotic patients in Singapore General Hospital

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Background: Pharmaceutical care service with the Liver Team was initiated in 2017 in Singapore General Hospital (SGH). The roles of the liver pharmacist include reviewing medications for patients admitted under the Liver team, identifying drug-related problems (DRP), discussing and optimising pharmacotherapy with hepatologists.

Aim: Describe types of DRP identified and managed by a Liver pharmacist for patients admitted under Liver team specialty in SGH.

Methods: DRP intervened by Liver pharmacists from 1 January to 31 December 2022 were retrospectively retrieved from SGH electronic medical records.

Results: A total of 484 patients were reviewed by Liver pharmacists. 261 DRP were identified and interventions made. The highest percentage of DRP was for inappropriate drug regimens (37.2%), followed by omission of drug therapy at 16.9%. 13.4% of DRP were to avoid adverse drug reactions, where recommendations include discontinuation of drug, dose reduction or switching to alternative drug choice. 11.5% of DRP were for drugs with no indication and thus discontinuation was recommended. Some commonly encountered DRP were renal dose adjustment of antibiotics, deprescribing proton-pump inhibitors and changing diluent of intravenous medications to reduce sodium load for ascitic patients. Vaccination in cirrhosis patients was initiated in July 2022. 17 patients (3.5%) had vaccinations prior to discharge.

Conclusion: The continual involvement of pharmacists in optimizing medication therapy has improved prescribing accuracy and safety, thereby improving patient quality of care. Moving forward, the analysis on DRP may guide designing of an effective education on pharmacotherapy in liver cirrhosis for our junior doctors, nurses and pharmacists.

Abstract Submission No. 100841

P-0935

Values of Nurse Practitioners in Managing Chronic Liver Disease Patients in an Acute Care Hospital

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Background: Literature has provided evidence the value of integrating nurse practitioners (NPs) into the health care system. NPs specialized in hepatology remain rare in Canada. This study aims to describe the clinical role and outcomes of the two hepatology NPs practicing in an acute care hospital in Toronto.

Methods: The Toronto Centre for Liver Disease has 2 full time NPs working collaboratively with hepatologists. Data presented were extracted from hospital EMR. Outcome measures include 90-days hospital readmission rate, safety of paracentesis performed, and size of HCC on detection.

Results: A total of 1,108 patients were under the direct care of the 2 NPs. Disease etiologies of their patients are largely hepatitis B and alcohol related liver disease. They performed 11 % of the total number of therapeutic paracenteses within a 6-month study period. No procedure complications were observed demonstrating NPs can perform the procedure as safely as their physician counterparts.

The NP-led post discharge transitional care program is effective in reducing 90-day readmission risk for patients with advanced liver disease. This is the result of a retrospective cohort study (Jan 2018 to Dec 2019) (Manuscript in preparation).

In patients with chronic hepatitis B being followed by the NP for > 2 years, the size of hepatocellular carcinoma at presentation is smaller (< 2.9 cm) if detected.

Conclusions: This study demonstrates the extended clinical role and the values of hepatology NPs. The NPs' specific role and scope of practice can be tailored to organization and departmental needs.

Abstract Submission No. 100955
P-0936

Kidney transplantation and the regeneration: From the past to the future

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According to the World Health Organization, 5 to 10 individuals die globally each year due to a lack of access to kidney disease treatment. Kidney disease continues to be a significant contributor to mortality and morbidity worldwide. The available treatment options for managing kidney disease involve medical or surgical intervention.

How will technology and science impact kidney transplants and drug usage currently and in the future?

Kidney transplant is crucial in treating end-stage kidney disease and can enhance patients' quality of life while extending their lifespan. Many issues can be prevented by correcting abnormalities found during preoperative evaluation. However, it's essential to avoid technical errors during all stages of the transplant process (donor nephrectomy, bench work preparation, and implant) and to conduct attentive postoperative monitoring, including a comprehensive examination by attending physicians.

Obesity is a growing problem worldwide. It puts kidney transplant recipients at risk both before and after surgery. Experts do not agree on the impact of obesity before and after a transplant. Further research is needed to fully understand this issue.

Finally, there exist two potential pathways for kidney regeneration through the utilization of stem cells: the development of a completely new kidney using stem cells (known as de novo whole kidney fabrication) or the application of stem cell therapy

The progress of knowledge and technology has positively affected kidney transplantation, and it has also lessened the impact on patients after the procedure. However, experts still need to conduct more research to decrease post-surgery mortality.

Abstract Submission No. 101217
P-0937

Bibliometric analysis of publications in Post hepatectomy live failure based on Web of Science

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Abstract

Aims The article about Post hepatectomy live failure(PHLF) in the Web of Science database was visualized and analyzed by bibliometrics method, so as to provide reference for future research in this field.

Methods: The PHLF-related studies in the Web of Science Core Collection (WoSCC) database were retrospectively collected, and bibliometrics were used to analyze the number of literatures, countries, journals, authors, keywords, etc.

Results: A total of 2150 English literatures were included in the analysis, and the annual publication volume showed an overall increasing trend. The country with the highest number of articles was Japan (488); The journal with the largest number of articles is HPB; The author with the most publications is Timothy M. Bowlik from the United States (30 articles); The research focuses on the mechanism of liver regeneration and liver transplantation in PHLF in the early stage, clinical research and prognosis in the middle stage, and prediction in the near future.

Conclusion: Based on the analysis of articles in the PHLF field by Vosviewer and Citespace, the prediction of PHLF is expected to become a research hotspot in the future.

Abstract Submission No. 101403
P-0938

Effect of branched-chain amino acids in increasing survival among hepatic encephalopathy patients

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Hepatic encephalopathy (HE) is a serious complication of cirrhosis and is associated with decreased branched-chain amino acid (BCAAs) levels. Recent meta-analyses have shown that oral BCAAs can help prevent HE development. However, there is conflicting evidence regarding their mortality benefit. A 2017 Cochrane review by Gluud et al. on the efficacy and safety of oral and intravenous BCAAs included 16 studies from 1984 to 2011, with a comprehensive search for articles until May 2017. Their review showed no significant difference in mortality rates between patients given BCAA and control, but there was a beneficial effect on the signs and symptoms of HE among patients who were not treated with lactulose or neomycin. Here, we aim to provide an updated meta-analysis by incorporating the latest available randomized controlled trials (RCTs) to re-assess the treatment and mortality benefit of BCAAs in patients with HE. Databases and existing meta-analyses were thoroughly searched until October 26, 2023. A total of 146 articles were thoroughly screened, with 126 articles excluded and 18 RCTs included based on set inclusion criteria. A total of 996 participants (473 treatment, 551 control) were included. Preliminary findings suggest that BCAAs, whether oral, intravenous, or given with active interventions do not have a significant effect on mortality (OR 0.84, 0.60 - 1.18 [95% CI]). Patients given BCAAs orally were shown to have HE improvement when compared against placebo (OR 0.24 (0.08-0.69 [95% CI]) but had no significant effect versus all combined control groups (BCAA OR 0.93, 0.69 - 1.25 [95% CI]).

Abstract Submission No. 101567
P-0939

Role of MR Enterography in assessment of small bowels diseases

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MR Enterography is a valuable tool in diagnosis and follow up of small bowel diseases. As a non-invasive, radiation-free method for visualizing small bowel and provide information about morphology and function of small bowel, despite small bowel imaging challenges related to its long and tortuous anatomy, continuous peristaltic movement, complex histology.

MRE is done using surface coil and both oral and intra-venous contrast with bowel preparation and antispasmodic agent, MRE has wide variety of sequences including; Echoplanar imaging, Rapid acquisition with relaxation enhancement, Single Shot RARE, Balanced steady-state free precession, Spoiled gradient echo, 3D T1W (Volumetric Interpolated Breath-hold Examination), Hydrographic Projection Imaging, Fat Suppression and Dixon technique, dynamic imaging, DWI and perfusion technique.

MRI enterography has been found to be particularly useful in diagnosis and follow up of Congenital disease, Inflammatory bowel disease, Autoimmune disease, Small bowel tumors. MR Enterography has a role in follow up of post chemo/radiotherapy changes. although CT is the main imaging for small bowel obstruction diagnosis, MRE is more valuable in detected of intermittent obstruction which can be missed on CT. MRE has found to be helpful in detected of small bowel vasculitis. MRE has a role like CT in correlated with laboratory test to diagnosis of infections diseases. While CT is the main imaging modality for acute GIT bleeding assessment, MRE is valuable in detection of occult or obscure GIT bleeding. MRE has a valuable role in investigating causes of abdominal pain in pregnancy.

Abstract Submission No. 101709
P-0940

Development of mannose receptor targeting mouse MSC-derived exosomes for liver fibrosis regeneration

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The prevalence of liver disease is increasing every year, and has a high mortality rate and its treatment process is notoriously complicated. In a healthy liver, blood circulation is facilitated by the exchange of substances between blood and liver tissue through the fenestrae of liver sinusoidal endothelial cells. However, if the perforation is closed and blood circulation is not possible due to liver damage, it can lead to fibrosis and chronic liver disease. Since there is no specific treatment after cirrhosis, it is important to address liver fibrosis in the early stages.

In recent studies, mesenchymal stem cell-derived materials have the potential to alleviate fibrosis, so an approach to treating fibrosis has been sought by replacing it with exosomes containing active ingredients for regeneration. Since exosomes inherently lack liver-targeting capabilities, the mannose receptor, which is a scavenger receptor specifically expressed in liver endothelial cells, was utilized as a liver target. In this study, exosomes were PEGylated to enhance their stability, and coupled with mannose molecules to facilitate effective delivery to liver cells. Subsequent in vitro transfection demonstrated specific binding to RAW 264.7 and LSEC cells, which highly express mannose receptors. Man-Exo also exhibited a more specific binding affinity for LSEC compared to RAW 264.7 cells in coculture. Furthermore, the biodistribution studies showed that the intravenously administered Man-Exo accumulated longer in the blood and localized higher compared to bare exosomes. These findings suggest the Man-Exo are clinically applicable as a novel targeted delivery system for the regeneration of liver fibrosis.

Abstract Submission No. 101782
P-0941

The ShuGanAnWei formula inhibited NSAIDs induced gastrointestinal inflammation and injury

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Background: This study aimed to observe the effect of ShuGanAnWei formula (SGAW) in the treatment of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) induced gastrointestinal inflammation and its potential mechanisms.

Methods: The 24 healthy male Sprague Dawley rats were categorized into control, model, SGAW, and rebamipide groups (6 rats/group). Over a 2-week period, the SGAW and rebamipide treatment groups received an clinical equivalent dose drug via gavage. To induce the rat model, 7.5mg/kg diclofenac sodium solution was administered twice a day for the final 5 days, except in the control group. We utilized BAT-MAN-TCM public databases, Cytoscape software and network pharmacology analysis methods to investigate the medicated mechanisms. **Results:** Network pharmacology analysis results suggested the mainly related to pathways of SGAW on NSAIDs induced gastrointestinal inflammation were IL-17 signaling pathway. Compared to the model group, SGAW-treated and rebamipide-treated groups rat showed lighter gastrointestinal injury based on the gross photograph observation of the stomach, intestines, and intestinal wall. However, the model group rats exhibited gastrointestinal perforation phenomenon, and the liver surface of the perforated rats were contaminated.

Conclusions: Our study suggested that the preventive treatment of SGAW is beneficial in reducing the occurrence of NSAIDs induced gastrointestinal injury, with efficacy similar to that of rebamipide.

Abstract Submission No. 101869
P-0942

Timing of Endoscopy and Outcomes in Filipino patients with Acute Upper Gastrointestinal Bleeding

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Background: Upper gastrointestinal bleeding (UGIB) is a common cause of hospitalizations in adult Filipinos. While guidelines recommend upper endoscopy within 24 hours, data on its optimal timing remains limited in the locality. Thus, this study investigated the clinical outcomes in relation to endoscopy timing.

Methods: A single-center retrospective analysis of adult patients diagnosed with UGIB who underwent endoscopy between 2019 and 2022. Patient demographics, clinical data, and endoscopy results were recorded. Patients were categorized based on the endoscopic timing from admission or diagnosis of UGIB: urgent (≤ 6 hours), early (>6 -24 hours), late (>24 -48 hours), and very late (>48 hours). Clinical outcomes compared were 30-day all-cause mortality, further bleeding, endoscopic treatment, average units of blood transfusion, intensive care unit (ICU) admission, and duration of hospitalization within 30 days.

Results: 142 patients were included with a mean age of 62 years, and 66.2% were male. The most common findings were non-variceal (53.7%), malignancy (8.45%), and varices (7.75%). The 30-day all-cause mortality ($p=0.26$), ICU admission ($p=0.747$), and number of blood transfusions ($p=0.246$) were not significantly different. Further bleeding occurred mostly from the late group (14.8%). Endoscopic treatment was performed in 18.3% of patients, with higher rates of intervention for variceal bleeding. A significant association in the duration of hospitalization was observed ($p=0.032$).

Conclusions: No differences in mortality and clinical outcomes were found in all four groups except for the duration of hospitalization. This study demonstrates endoscopy within 24 hours or until patient is stabilized can be safely performed in an acute setting.

Abstract Submission No. 101899
P-0943

Efficacy of Zinc Acetate in Patients with Chronic Liver Disease Complicated by Hypozincemia

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Background: Chronic liver disease is one of the known causes of hypozincemia and some studies suggest the effects of zinc acetate administration on liver function in patients with chronic liver disease complicated with hypozincemia.

Methods: Among 55 patients with chronic liver disease complicated with hypozincemia who received zinc acetate at our hospital between April 2017 and December 2021 and blood ammonia level, serum albumin level, Child-Pugh score, ALBI score, and Fib-4 Index were confirmed. The changes in the above laboratory parameters before and 3, 6, 9, and 12 months after zinc acetate administration were compared.

Results: Ammonia levels decreased significantly from 80.3 ± 41.6 $\mu\text{g/dL}$ before treatment to 65.9 ± 41.2 $\mu\text{g/dL}$ at 6 months ($p=0.006$) and 70.5 ± 39.4 $\mu\text{g/dL}$ at 9 months ($p=0.045$). Albumin levels increased significantly from 3.2 ± 0.6 g/mL before treatment to 3.31 ± 0.5 g/mL at 3 months ($p=0.015$) and 3.3 ± 0.5 g/mL at 6 months ($p=0.041$), Child Pugh score was improved significantly from 7.4 ± 1.8 before treatment to 7.0 ± 1.7 at 6 months compared ($p=0.047$). The ALBI score was

significantly improved from -1.8 ± 0.6 before treatment to -1.9 ± 0.6 at 3 months ($p=0.004$) and -1.9 ± 0.5 at 6 months ($p=0.018$). Fib-4 Index was significantly improved from 7.0 ± 4.8 before treatment to 5.8 ± 3.0 at 3 months ($p=0.042$).

Conclusion: Significant improvement in liver function was observed at 3 and 6 months after administration of zinc acetate. However, the improvement in hepatic function at 9 and 12 months was less pronounced.

Abstract Submission No. 102058
P-0944

Efficacy of MR imaging in clinical management of hepatic encephalopathy and Alzheimer's disease

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In the current aging society, the number of patients with liver cirrhosis demonstrating encephalopathy and/or Alzheimer's disease (AD) has been increasing; however, addressing the complex clinical diagnosis of hepatic encephalopathy and/or AD is challenging. Hepatic encephalopathy (HE) is defined as brain dysfunction caused by liver insufficiency and/or portosystemic shunting; it manifests as a wide spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma. AD is defined as progressively deteriorating dysfunction of various intellectual domains, memory, language, and executive function. Imaging findings through T1 weighted magnetic resonance imaging (MRI) have disclosed, bilateral symmetric high signal intensity at the globus pallidus, as described in the clinical diagnosis of HE. On the other hand, imaging findings of the Voxel-based specific regional analysis system (VSRAD) in the clinical diagnosis of AD have disclosed significant atrophy exceeding the threshold value of 2 and 1 on a scale of 5 in the target parahippocampal gyrus, revealing significant atrophy extending to the whole brain. The VSRAD system revealed that 12 of 32 (37.5%) elderly patients under treatment for hepatic encephalopathy displayed signs of brain atrophy. The presence or absence of brain atrophy under the VSRAD system has been closely associated with the degree of self-support ability in the activities of Daily Living (ADL) of the aged with HE. The VSRAD system could, thus, play an essential role in the management of the clinical course of patients with HE.

Abstract Submission No. 102067
P-0945

The predictors of the effect by lusutrombopag in patients with liver cirrhosis

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Objective: We examined the factors that predict the increase in platelet count in patients with chronic liver disease treated with lusutrombopag.

Methods: The subjects were 26 cases.

Background: Liver disease was 38/23/15/12/12 (%) for ALD/HCV/NASH/HBV/others, mean age 65.2 years, 20:6 for men and women, and 42/27/15/8/8 (%) for RFA/TACE/Liver biopsy/EIS/other invasive procedures. They were classified into three groups ($<40,000/40,000 \leq <50,000/50,000 \leq$) based on their platelet counts before administration.

Methods: We examined relationship between platelet increase and WBC/RBC/Hb/PT Activity/Alb/Total Bil/AST/ALT/NH3/ALBI Score/VCTE/CAP/Spleen Index (SI)/spleen volume/collateral path diameter.

Results: The pre-dose platelet count was $<40,000$ in 10 patients, 5 patients with $4-50,000$, and 11 patients with $50,000 \leq$, and the mean /Max/Min/Med before administration was $4.8 \pm 1.6/8.0/2.6/4.7$. On the day of treatment, the rate of platelet count of $50,000 \leq$ was 70% in the $<40,000$ group and 100% in the $4-50,000$ group. The time to reach the highest values was 13.4 ± 5.3 days and 12.0 ± 5.4 days. The cut-off value of the platelet count required to increase the platelet count to $50,000 \leq$ on the ROC curve was 37,000 ($P=0.037$), and 100% (3/3) for $37,000 \leq <40,000$ and 57.1% (4/7) for $<37,000$ increased to $50,000 \leq$.

Conclusion: In lusutrombopag treatment, if the platelet count is 37,000 or more, it increases to 50,000 or more, but if it is less than 37,000, it is a strategy to select a treatment drug based on the ALBI score and SI value.

Abstract Submission No. 200060
P-0946

Feasibility and Safety of Transjugular Liver Biopsy (TJLB) for Patients with Chronic Liver Diseases

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Back ground: TJLB is recognized as an alternative liver biopsy method in cases where percutaneous liver biopsy (PLB) is not applicable or where bleeding is at risk. The aim of this study to investigate the usefulness of TJLB.

Methods: This study is a retrospective cohort study conducted in a single institution. The patient who was requiring liver biopsy between 2014 and 2021 at our institution was enrolled. TJLB was performed on patients with accumulated ascites, coagulopathy, and bleeding tendency. The primary endpoint was the utility and safety of TJLB in patients who were not indicated for PLB. Secondary endpoints were technical success rate, the rate of appropriate sample collection for histology and adverse events.

Results: The detail of the 26 patients who underwent TJLB were as follows: 8 in acute immune hepatitis (AIH), 4 in drug-induced liver injury, 3 in alcoholic hepatopathy, and 2 in non-alcoholic steatohepatitis (NASH). Conversely, the 123 patients who underwent PLB as follows: AIH in 43, NASH in 13, drug-induced liver injury in 10, Primary biliary cholangitis in 9. Child Pugh score was 9.9 in the TJLB group and 6.4 in the PLB group ($P<0.001$). The technical success rate and the rate of appropriate sample collection for histology was 100% in both groups. No severe adverse events were recorded in either group.

Conclusions: TJLB can be performed safely even in patients for whom regular PLB is difficult, and can be an alternative to PLB.

Abstract Submission No. 200114
P-0947

causal relationship between mitochondria-associated proteins and chronic liver diseases

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Mitochondria-related proteins (MRPs) and chronic liver diseases have been linked in various studies, although their causal relationship has not been elucidated. In this study, we investigated the causal associations between MRPs and non-alcoholic fatty liver disease (NAFLD), liver cirrhosis and hepatocellular carcinoma (HCC) by two-sample bidirectional Mendelian randomisation (MR) analysis. The random-effect Inverse variance weighted (IVW) is the primary analysis for causality analysis while MR-Egger and Weighted Median (WM) as complementary analyses. Cochran Q test, MR-Egger intercept test, MR-PRESSO and leave-one-out analysis were used for sensitivity analyses. In addition, we performed bonferroni correction, multivariable MR analysis (MVMR), reverse causality detection and protein-protein interaction (PPI) network to enrich the results of this study. After rigorous genetic variant selection, IVW, sensitivity analysis, 3 genetically determined MRPs were significantly associated with NAFLD [MRPL33 (OR: 1.06, 95% CI: 1.00-1.11, $p=0.0284$), MRPL34 (OR: 0.88, 95% CI: 0.78-0.98, $p=0.0294$) and FARS2 (OR: 0.90, 95% CI: 0.84-0.97, $p=0.0120$)], 2 MRPs were significantly associated with liver cirrhosis [MICU1 (OR: 1.11, 95% CI: 1.00-1.22, $p=0.0337$) and NUDT8 (OR: 1.16, 95% CI: 1.03-1.30, $p=0.0096$)], and 4 MRPs were significantly correlated with HCC [MRPL32 (OR: 0.62, 95% CI: 0.39-0.99, $p=0.0492$), MRPL33 (OR: 1.29, 95% CI: 1.07-1.55, $p=0.0063$), SCO1 (OR: 0.56, 95% CI: 0.38-0.83, $p=0.0036$) and SIRT5 (OR: 0.71, 95% CI: 0.53-0.96, $p=0.0283$)]. Our findings provide a new perspective on the exploration of the underlying mechanisms of chronic liver diseases. However, further studies are still needed to explore the mechanisms of possible potential causal associations between MRPs and chronic liver diseases.

Abstract Submission No. 200116
P-0948

Mendelian randomization identifies 1400 metabolites that may be pathogenic candidates for NAFLD

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The observational association between circulating metabolites and non-alcoholic fatty liver disease (NAFLD) has been somewhat demonstrated. However, it is unclear whether there is a causal relationship for this association. In this study, we used a two-sample bidirectional MR analysis approach to assess the association between 1,400 blood metabolites and NAFLD. Causality was estimated using the inverse variance weighted (IVW) method, and sensitivity analyses were applied after performing false discovery rate (FDR) correction to assess heterogeneity and pleiotropy. In addition, we performed linkage disequilibrium regression (LDSC) analysis, confounder analysis and metabolic pathway analysis. Corrected for FDR, we identified seven metabolites suggestively associated with NAFLD, including imidazole lactate levels (OR = 0.90, 95% CI = 0.85-0.95, $P=0.0004$), cysteine-glutathione disulfide levels (OR = 0.80, 95% CI = 0.72-0.89, $P=0.0001$), 3-indoleglyoxylic acid levels (OR = 0.87, 95% CI = 0.80-0.94, $P=0.0009$), lithocholate sulfate (1) levels (OR = 1.18, 95% CI = 1.07-1.30, $P=$

0.006), bilirubin degradation product, C17H18N2O4 (2) levels (OR = 1.14, 95%CI = 1.07-1.21, $P = 4.02 \times 10^{-5}$), bilirubin degradation product, C17H18N2O4 (3) levels (OR = 1.13, 95%CI = 1.06-1.21, $P = 0.0001$), and biliverdin levels (OR = 1.12, 95%CI = 1.05-1.18, $P = 0.023$). This study provides evidence support for the causal effect of seven metabolites on NAFLD, and provides new perspectives for combining genomics and metabolomics to explore the biological mechanisms of NAFLD.

Abstract Submission No. 200134

P-0949

Sihosogan-tang has diverse pharmacological effects on liver disease

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Liver diseases, including hepatitis, fatty liver, liver fibrosis, liver cirrhosis and liver cancer, are occurred due to various causes such as damage of hepatocytes, activation of Kupffer cells and stellate cells. Therefore, we investigated diverse pharmacological effects of Sihosogan-tang (SST) on liver disease. To confirm the effects of SST, HepG2 cells were exposed to AA+iron to induce oxidative stress. RAW 264.7 cells were activated by LPS to induce inflammatory response. LX-2 cells were treated by TGF- β 1 to induce fibrosis. Cell viability was measured through MTT assay and the expression level of proteins was confirmed by immunoblot analysis. ROS production, GSH level, mitochondrial membrane potential, NO production and pro-inflammatory cytokines were measured using DCFH-DA, GSH assay kit, FACS analysis, Greiss reagent and ELISA kits, respectively. As a result of study, SST prevented AA+iron-induced cell death, in addition, SST inhibited the mitochondrial dysfunction and excessive ROS production and increased GSH level. Furthermore, SST increased the accumulation of Nrf2 in the nucleus and regulated Nrf2 target antioxidant genes. In LPS-activated RAW 264.7 cells, NO production, iNOS expression, and pro-inflammatory cytokines were inhibited by SST treatment. And SST suppressed the expression of phospho-I κ B α , NF- κ B and phospho-MAPK. In LX-2 cells, SST decreased the expression of α -SMA, phospho-Smad 2/3 and PAI-1 induced by TGF- β 1. On the whole, SST has diverse pharmacological effects such as hepato-protective effect via Nrf2 pathway, anti-inflammatory effect through the NF- κ B and MAPK pathway and anti-fibrotic effect by way of TGF- β 1/Smad signaling pathway.

Abstract Submission No. 200235

P-0950

Critically ill patients and identifying the results of enteral nutrition treatment

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Introduction: Malnutrition is prevalent among critically ill patients. Due to lack of nutrition, the mass of muscles and tissues decreases, the muscle becomes weak, and the movement capacity decreases and the decreased immune response increases the risk of infection, respiratory failure, prolongs recovery time and even can lead to death.

Material and method: A total of 60 patients were included in the study who were hospitalized in the Intensive Care Unit and Inpatient clinic of the Mongolia Japan Hospital of MNUMS. The study was conducted using a cross sectional and hospital based clinical trial design.

Result: In the current study, 43.3% of the respondents were male and 56.7% were female. 26 (43.3%) of them were malnourished, 32 (53.3%) were at risk of malnutrition, and 2 (3.3%) had normal nutritional status. In terms of quality of life, the average of the respondents was 59.32 points. After treatment, nutritional status in the trial group was changed from 17.48 $\pm$ 3.60 points to 19.19 $\pm$ 3.42 points ($p < 0.0000$); in the control group, it was changed from 16.55 $\pm$ 3.26 points to 15.53 $\pm$ 3.65 points ($p > 0.0000$) which were statistically significant. Furthermore, in the trial group after treatment, the average body weight was increased from 63.22 $\pm$ 16.17 kg to 64.07 $\pm$ 15.65 kg ($p < 0.0001$), BMI was 23.69 $\pm$ 5.36 kg/m² to 24.00 $\pm$ 5.21 kg/m² ($p < 0.0001$), arm circumference was increased from 24.81 $\pm$ 3.11 cm to 24.90 $\pm$ 3.04 cm ($p < 0.04$), and subcutaneous fat tissue was increased from 23.94 $\pm$ 6.61 cm to 24.20 $\pm$ 6.53 cm ($p < 0.04$) while in the control group, body weight was decreased from 68.48 $\pm$ 15.13 kg to 67.98 $\pm$ 14.89 kg ($p < 0.0066$), BMI decreased from 26.10 $\pm$ 6.29 kg/m² to 25.81 $\pm$ 6.22 kg/m² ($p < 0.0045$) and waist circumference decreased from 89.38 $\pm$ 13.48 cm to 88.71 $\pm$ 13.46 cm ($p < 0.0004$). Quality of life in the trial group was 55.65 $\pm$ 7.07 points before treatment and it improved to 62.59 $\pm$ 7.83 points after treatment ($p < 0.01$); in the control group, it was 62.90 $\pm$ 6.42 points before treatment and it changed to 60.92 $\pm$ 7.45 points after treatment ($p < 0.01$).

Conclusion: Enteral feeding treatment in malnourished and at-risk patients has improved nutritional status, anthropometric parameters, clinical symptoms, laboratory parameters, and quality of life.

Abstract Submission No. 200263

P-0951

Establishment of Ultrasonography Center for Effective Diagnostic Testing at Our Hospital

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Background: Our hospital's Ultrasonography Center was established in November 2021. Prior to its opening, abdominal, pelvic, and superficial ultrasonography examinations were conducted separately by each medical department. The centralization of these examinations has enabled the efficient operation of staff and ultrasound diagnostic equipment. By increasing the number of examinations, we contribute to the early detection and treatment of diseases. Additionally, collaborative discussions among examination staff regarding ultrasound findings have led to an improvement in technical proficiency.

Overview of the Ultrasonography Center: The Ultrasonography Center consists of 9 examination rooms, each equipped with medical information terminals and high-definition monitors. Examinations are conducted with reference to electronic medical records and images. There is a separate space for creating reports, enhancing the overall efficiency of the examination booths. The average monthly

examination count for the three years before the opening was 748, while for the two years after the opening, it increased to 1,022, marking a 1.37-fold increase. The number of JSUM Registered Medical Sonographers increased from 1 before opening to 5 after opening.

Conclusion: Our hospital's Ultrasonography Center, by consolidating ultrasound examinations within the hospital, has efficiently responded to unscheduled and emergency examination requests, leading to a significant increase in the number of examinations conducted. Moving forward, we will continue to collaborate with various medical departments to identify potential needs for ultrasonography examinations and strive to enhance the infrastructure for high-quality diagnostic testing.

Abstract Submission No. 101364

P-0952

The effectiveness of hepatitis A vaccine in liver transplanted children

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Objectives: The data in liver transplant (LT) children have been not established. The present study aims to evaluate the seroprevalence of HAV and the effectiveness of inactivated HAV vaccine in seronegative LT children.

Methods: Medical record, vaccination book and anti-HAV IgG were assessed. Seronegative LT children received inactivated HAV vaccine at 0 and 6 months. Blood sampling was collected for anti-HAV IgG at 0, 1, 6 and 7 months after the first dose (visit 1, 2, 3 and 4). Adverse effect was recorded within 3 days after immunization.

Results: Of 105 LT children, there were 85 (81%) children had vaccination record in which 6 (7.1%) and 14 (16.5%) of them received one dose and two doses of HAV vaccine. After LT, the prevalence of seropositive was 20.1% in which 9.5% of them was from immunization. The seropositive rate in 2-dose immunized children was 71.4%. Of 83 LT children (age 7.25 (4.40) years) had seronegative and received 2-doses HAV vaccination. The seropositive rate was significantly increased from 68.1% to 95.7% at visit 2 comparing to visit 4 ($P=0.035$). The were significantly increase of the titer of anti-HAV IgG at visit 2 comparing with visit 4 (0.24 (1.24 (0.53, 2.6) vs 12.81 (9.61, 14.42), ($P<0.001$)). No serious adverse effect was recorded. Serum albumin tended to be an associated factor for antibody response after vaccination (277.93 (0.66, 117656.1), $P=0.068$).

Conclusions: The seroprevalence of HAV in LT children was low. Two-dose inactivated HAV vaccination in LT children were significantly effective and safe.

Abstract Submission No. 101733

P-0953

A Prognosis Prediction Model for Pediatric Cholestatic Liver Disease Using Machine Learning Approach

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Objective: This study aims to build a machine-learning algorithm to predict the poor prognosis (liver transplantation or mortality) of infantile cholestatic liver disease.

Methods: We utilized National Taiwan University Hospital Integrated Medical Database (NTUH-iMD) and enrolled cases below one year of age who had been examined for liver function tests and abdominal ultrasonography from 2006 to 2018. Seventy percent of the data was used as the training data set, and the rest was taken as a testing data set. Furthermore, we used patient data from the Asian-Pacific multicentered consortium (ANGELD) study for external model validation.

Results: This study included 1008 cases with 52 variables for machine-learning training. We developed several models to predict the poor clinical outcome of infantile cholestatic liver diseases, defined as death or receiving liver transplantation. Model 1 was developed via random forest with 25 variables (from disease onset to one-year follow-up time), which showed an AUC of 0.9215 and a sensitivity of 0.8947. In model 2, using 23 variables in the random forest model, an AUC of 0.8766 and a sensitivity of 0.8947 was noticed. These twenty-three variables were within three months after jaundice onset. We validated Model 2 using the Asian-Pacific consortium data with an AUC of 0.8292 and a sensitivity of 0.9048. Model 2 may offer earlier decision-making information for clinical physicians.

Conclusions: We proposed machine-learning models to predict the poor prognosis of cholestatic infants. This may be beneficial for clinical practitioners to make clinical decisions, as well as to make prompt treatment strategies.

Abstract Submission No. 101961

P-0954

Psychosocial Programs for Pediatric Liver-Related Disease Treatment Approach: LMICs Analysis

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Objectives: The crucial role of psychosocial programs (PP) has risen in children with liver disease. This study aims to analyze the field of study in which treatment can be delivered to children in emerging countries by discovering research that may be beneficial for adopting the best treatment for pediatric liver disease.

Methods: This study used the review procedures with modifications, including co-word analysis, themes mapping. The articles to be reviewed were identified by entering the search keywords "Pediatric" AND "Liver" AND "Psychosocial Program" AND "Emerging Countries" in the Scopus. After applying the criteria, 34 articles were used in the subsequent analysis in Asia.

Results: Psychosocial programs focus on the treatment of care planning and Quality of Life (QoL) in the long term. Initiating the treatment in psychosocial assessment such as reducing anxiety or depression, and improving family and social support are the main goals. Pediatric autoimmune liver disease that requires life-long psychosocial programs reports children tend to have lower health-related QOL. Therefore, the parents as informal caregivers of pediatric liver transplantation have high anxiety (51.5 ± 4.8) which results in a lower of the children's QoL. Meanwhile, the satisfaction of both caregivers and

pediatric-related liver disease shows the satisfaction of education on the treatment by professional guidance.

Conclusions: The potential of this study is to be an initial guide for caregivers and practitioners for psychosocial programs in pediatric-related liver disease. However, it still many ways for emerging countries to fully apply psychosocial programs due to practitioner limitations and treatment access.

Abstract Submission No. 200003
P-0955

Clinicopathological Study of Intrahepatic IPNB Resection Cases at Our Hospital

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Background: Intraductal papillary neoplasm of the bile duct (IPNB) has been reported to be pathologically similar to intraductal papillary mucinous neoplasm of the pancreas (IPMN). However, to date, there have been few reports on the relationship between the two neoplasms, and many points remain poorly understood. In this study, we clarified the characteristics of IPNB using an autopsy case and investigated its relationship to IPMN.

Methods: We conducted a histopathological study of 14 cases of intrahepatic IPNB resected at our hospital between 2005 and 2021.

Results: The median patient age was 67.2 years. Cases could be classified into four subtypes according to the handling protocol. Mucus production was observed grossly in 7 cases and microscopically in all cases.

Histologically, papillary growth of mild to highly atypical adenoma or invasive carcinoma was observed, and the advanced part of the tumor showed intraepithelial extension along the bile duct mucosa. Recurrence was observed in four patients, with a median recurrence period of 35.1 months, and all recurrences occurred in the common bile duct distal from the site.

Conclusions: A variety of atypia characteristic of adenoma to intraepithelial carcinoma and invasive carcinoma was observed in IPNB, which was shown to be clinicopathologically similar to IPMN in terms of intraepithelial extension and atypical recurrence.

A comparatively more favorable prognosis is associated with IPNB compared with that of conventional cholangiocarcinoma, and in cases of recurrence, IPNB can be safely resected.

Abstract Submission No. 200212
P-0956

Correlation between monocytes and HBsAg clearance in children with chronic hepatitis B

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Objectives: To explore correlation between monocytes and HBsAg clearance in children with chronic hepatitis B(CHB).

Materials and Methods: 285 children with HBeAg-positive CHB aged 1 to 18 years, treated with interferon α (IFN α) 48 weeks follow up 24 weeks. The number of monocytes was detected at baseline, 24,

36, and 48 weeks of antiviral therapy. Based on the results of HBsAg clearance, the patients were divided into HBsAg clearance group and non HBsAg clearance group. The area under the receiver operating characteristic curve (AUROC) was used to assess the prediction for HBsAg loss.

Results: Patients with HBsAg loss showed a significantly high baseline monocyte levels in comparison to those patients without HBsAg loss ($p < 0.05$). Monocyte count at the 36 and 48 weeks of treatment in the HBsAg loss group was also significantly higher than that in the non HBsAg loss group. The baseline monocyte count is negatively correlated with HBsAg levels at 24, 36, and 48 weeks. ROC analysis showed that baseline monocyte count forecast HBsAg loss at the 48th week of antiviral treatment with an area under the curve of 0.69(95%CI: 0.628-0.752), the positive predictive value(PPV) and negative predictive value(NPV) for HBsAg loss were 59% and 75%, respectively, with a sensitivity of 75.4% and specificity of 58.5%.

Conclusions: The baseline monocyte count is closely related to HBsAg loss with interferon treatment in children with CHB. Children with high baseline monocyte count are more likely to occur HBsAg loss after antiviral treatment.

Abstract Submission No. 200222
P-0957

B cell transcriptional characteristics of children with chronic hepatitis B

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Objectives: To explore the transcriptional characteristics of children with chronic hepatitis B (CHB) undergoing IFN therapy with HBsAg loss based on single cell sequencing.

Methods: Establishing a patients study cohort for antiviral treatment of children with chronic hepatitis B(CHB), collecting peripheral blood to isolate B cells, carry out single cell RNA sequencing. After dimensionality reduction, clustering, and cell group naming, the expression levels and functional differences of transcripts in each cell subgroup were analyzed through expression enrichment score, gene expression differential analysis, and differential gene function enrichment analysis.

Results: Four B cell subsets were obtained by single cell sequencing cluster analysis. Compared with the non HBsAg loss group(HN), the expression enrichment score of HLA-I and HLA-II gene sets in the main subsets of antigen presenting cells in HBsAg loss(HL) group was significantly higher. HLA-DRB5 and FOS were significantly overexpressed in APCs of the HL group. KEGG enrichment analysis showed that the highly expressed genes of two types of APCs in the HL group were significantly enriched in the B cell receptor signaling pathway of Naive B cells; GO enrichment analysis also showed that the IFITM1 of differentially expressed genes in HL group were also significantly enriched in Naive B cells.

Conclusions: The increased expression of HLA-DRB5 in HL group is related to the antiviral treatment effect of children with CHB; Naive B cells may play a more important role in antiviral therapy in children with CHB, and IFITM1 may play a key role in it.

Abstract Submission No. 200230
P-0958

Immune characteristics of CHB children with poor treatment outcomes

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Objective: To explore the immune characteristics of chronic hepatitis B children with poor treatment outcomes.

Methods: Establishing antiviral treatment cohort for children with chronic hepatitis B. The qualified peripheral blood cell samples were obtained for cell sorting, and the selected B cell samples were sequenced by single cell 5' terminal transcriptome and immune bank, and the transcriptome data and BCR immune bank data were obtained for single cell sequencing, cell clustering analysis and labeling annotation.

Results: Plasma cells, naive B cells, memory B cells, activated memory B cells and other cell clusters were identified, and the proportion of naive B cells in the HBsAg loss group was higher than those with poor treatment outcomes, while memory B cells showed a lower proportion of cells in poor treatment outcomes group.

Conclusion: Naive B cell and memory cell populations may be associated with children with poor treatment outcomes.

Abstract Submission No. 100047

P-0959

IMPACT OF TIME TO ENDOSCOPY ON OUTCOMES OF VARICEAL BLEEDING IN A TERTIARY CENTER IN THE PHILIPPINES

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BACKGROUND: The evidence on the effects of performing endoscopy within 12 hours of presentation for variceal bleeding on outcomes is conflicting. Local data are also lacking.

AIM: This study aimed to determine if timing of endoscopy is associated with clinical outcomes.

METHODS: Adult cirrhotic patients admitted at a tertiary center for VB from January 2016 to September 2022 were retrospectively evaluated. The primary outcomes were in-hospital and 6-week mortality. Secondary outcomes included 5-day rebleeding, length of hospital stay (LOS) and blood transfusion requirements (BTR). The relationship between timing of endoscopy and outcomes was evaluated using regression analysis.

RESULTS: In 140 patients, 5.7% underwent urgent endoscopy (≤ 12 hours). The overall median door-to-endoscopy time was 39.4 hours (IQR 20.0-73.4). The overall in-hospital mortality, 6-week mortality, and 5-day rebleeding rates were 12.9%, 11.4%, and 8.6%, respectively, without significant variability at different time intervals to endoscopy ($p > 0.05$). Longer LOS was evident when endoscopy was delayed to > 12 hours from admission (3.5 [IQR 2.25-5.75] vs 6 days [IQR 4-9.75], $p = 0.021$). BTR was greater starting at endoscopies performed at > 24 hours (1 [0-2] vs 2 units [1-3], $p = 0.000$). Delayed endoscopy was significantly correlated with LOS (Beta 0.316, SE 0.011, $p = 0.000$) and BTR (Beta 0.214, SE 0.469, $p = 0.003$), but not with mortality and early rebleeding.

CONCLUSION: Timing of endoscopy may be independent of mortality and early rebleeding. Timely endoscopy may shorten hospitalization and decrease need for blood transfusion. Other factors affecting clinical outcomes may be at play.

Abstract Submission No. 100108

P-0960

Association between pancreatic congestion and exocrine pancreatic function in patients with LC

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Aim: In the liver cirrhosis (LC), pancreas exhibits congestion due to portal hypertension because pancreatic drainage blood flow drains to a portal system. We have clarified that portal hypertension induces pancreatic congestion and impaired insulin secretion in patients with liver cirrhosis (LC). However, it remains controversial whether pancreatic congestion results in exocrine pancreatic insufficiency (EPI). The present study focused on exocrine pancreatic function, as assessed by fecal elastase 1 (FE-1), and examined its association with portal hypertension.

Method: 82 patients were prospectively enrolled in the study. Relevant clinical data, shear wave elastography (SWE), shear wave dispersion (SWD) and FE-1 were examined and compared.

Result: 82 patients were divided into LC group ($n=41$) or control group ($n=41$). The baseline characteristics were similar between the LC and control group. FE-1 in the LC group was lower than in the control group ($312 \pm 89 \mu\text{g/g}$ vs $442 \pm 100 \mu\text{g/g}$, $p < 0.01$). The number of patients with EPI was higher in the LC group than in the control group (6 cases vs 0 case, $p=0.03$). Pancreatic SWE values and pancreatic SWD values were significantly higher in the LC group [$7.78 \pm 1.36 \text{ kPa}$ vs $5.41 \pm 0.93 \text{ kPa}$, $p < 0.01$, DS, $14.6 \pm 2.3 \text{ (m/s)/kHz}$ vs $10.4 \pm 1.6 \text{ (m/s)/kHz}$, $p < 0.01$, respectively]. FE-1 was significantly correlated with pancreatic SWE values ($R=0.62$) and pancreatic SWD values ($R=0.57$).

Conclusion: FE-1 in the LC group was lower than in the control group and FE-1 was significantly correlated with pancreatic congestion. Thus, in LC patients, portal hypertension may result in EPI.

Abstract Submission No. 100113

P-0961

Abdominal Tuberculosis Lymphadenopathy presenting as Portal Hypertension: A Case Report

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Gastrointestinal tuberculosis makes 1-3% of tuberculosis. This case presents a patient having extra pulmonary tuberculosis manifesting as portal hypertension. Upper abdominal CT scan shows lymphadenopathies in falciform ligament and peritoneal wall. Biopsy of these lymphadenopathies shows granulomatous inflammation with caseous necrosis suggestive of tuberculosis. Portal hypertension usually rises from compromised vascular resistance and blood flow in the liver, often associated with liver cirrhosis. However, in rare occasions, portal hypertension can be caused by non-cirrhotic factors, accounting for 16-25% of cases. Common non-cirrhotic causes include extrahepatic portal venous obstruction, idiopathic portal hypertension, schistosomiasis, biliary cirrhosis, congenital hepatic fibrosis, veno-occlusive disease, nodular transformation, hepatoportal sclerosis, and peliosis hepatitis. For patients presenting with non-cirrhotic portal hypertension, extra intestinal tuberculosis should be considered especially in our country where tuberculosis is endemic. This study aims to present a case of gastrointestinal tuberculosis presenting as portal hypertension. In the Philippines where case of TB was endemic, diagnosis of

gastrointestinal tuberculosis should be considered and managing such case, medical management will not suffice and surgical intervention should be considered in addressing the progression of portal hypertension and Gastrointestinal bleeding. Further, this case report highlights an uncommon incidence of abdominal tuberculosis lymphadenopathy causing portal hypertension which leads to compromised portal blood flow, underscoring the importance of recognizing and managing such unique clinical presentations in a clinical setting.

Abstract Submission No. 100169
P-0962

Duration of vasoconstrictors after endoscopic ligation in variceal bleeding: A network meta-analysis

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Background: Guidelines recommending continuation of vasoconstrictors for at least 3-5 days after endotherapy for acute variceal bleeding (AVB) are based primarily on old studies in which sclerotherapy was used. Hence, the present network meta-analysis was conducted to compare the outcome of vasoconstrictors after Endoscopic variceal ligation (EVL) based on the duration of therapy.

Methods: A comprehensive literature search from inception to March 2023 was done for randomized trials, comparing the outcome of continuing vasoconstrictors after EVL in AVB based on the duration (Group 1: 5 days, Group 2: 2 to 3 days, Group 3: Less than 24 hours). Both pairwise and network meta-analyses were performed to analyze the risk of rebleeding and mortality.

Results: A total of 9 studies (n = 816) were included in the final analysis. There was no difference in the risk of rebleeding in Group 2 (Risk ratio [RR]: 1.34, 95% confidence interval [CI]: 0.42 – 4.13) and Group 3 (RR: 1.12, 95% CI: 0.42 – 2.49), compared to Group 1. Similarly, there was no difference in the mortality risk between Group 2 (RR: 3.80, 95% confidence interval [CI]: 0.46 – 39.1) and Group 3 (RR: 0.36, 95% CI: 0.04 – 1.54) compared to Group 1. There was neither significant inconsistency nor publication bias.

Conclusion: The present network meta-analysis did not show any benefit of continuing vasoconstrictors after EVL.

Abstract Submission No. 100602
P-0963

Tracheal Intubation And Long Hospital

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Aim: Our aim was to determine endotracheal intubation practices for variceal bleeding and associated factors leading to worse outcomes.

Methods: All variceal bleeding events in cirrhotic patients between July 2018 and February 2023 at a tertiary hospital in Singapore were analyzed retrospectively. Patients were grouped into those that bled once and those that bled more than once within a six-month period.

Logistic regression analysis was conducted to determine the possible factors associated with recurrent bleeding or mortality at six months.

Results: 211 patients, with 326 bleeding events, were included in the study. Occurrence of variceal bleeding was highest in Non-Alcoholic Steatohepatitis (NASH) cirrhosis at 37%, while rebleeding was highest in alcoholic cirrhosis with a mean of 2.2 bleeds per patient.

9% (29/326) of endoscopies for variceal bleeding were done with intubation. 41% (12/29) of which were in patients with recurrent bleeding. Endotracheal intubation for endoscopy (OR 9.59 [2.84-32.35], p<0.01) and length of stay (OR 1.07 [1.02-1.13], p<0.05) had significant association with 6-month mortality.

Conclusion: Intubation for gastroscopy and increased length of stay were associated with higher mortality. Avoiding prophylactic intubations and actively reducing hospital stay could improve outcomes in cirrhotic patients with variceal bleeding.

Abstract Submission No. 100603
P-0964

Non-cirrhotic portal hypertension in Systemic Lupus Erythematosus, a 40-year-old Filipino Female

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Portal Hypertension results from the changes in portal resistance in combination with changes in the portal inflow. In noncirrhotic causes of portal hypertension especially those associated with autoimmune diseases such as SLE, vasculitis of the intrahepatic arteries from deposition of immune complexes in the intrahepatic vessels has been one of the accepted pathogeneses. We report a case of a 40-year-old female who is diagnosed with SLE since year 2022 by ANA-IF (+) 1:1280 coarse granular pattern and low C3. She presented with clinical symptoms such as joint pains, alopecia, rashes, anemia and currently admitted for massive ascites. She underwent paracentesis which revealed a serum ascites albumin gradient of 1.3g/dL with ascitic fluid total protein of 1g/dL. Abdominal CT scan with contrast showed hepatomegaly, smooth hepatic margins, splenomegaly, enlarged portal veins and splenic veins at 1.6 cm and 1.4 cm respectively. Serologic markers for Hepatitis A, B and C were all non-reactive. EGD done did not show esophageal and gastric varices. She was started with Methylprednisolone pulse therapy and carvedilol. Repeat Abdominal CT scan with contrast revealed regression of the portal and splenic veins, measuring 1.4 cm and 1.2 cm respectively. Non-cirrhotic portal hypertension from autoimmune diseases like SLE, is a rare condition with only a few cases reported

Abstract Submission No. 100716
P-0965

The effect of B-RTO on hepatic functional reserve and its volume in cirrhotic patients

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Aims: Balloon-occluded retrograde transvenous obliteration (B-RTO) has come to be reported to improve shunt encephalopathy. In this study, we aim to analyze the changes in hepatic functional reserve (HFR) and its volume before and after B-RTO, with related clinical parameters.

Methods: Nineteen cirrhotic patients (12 males and 7 females, median age 72 years) who underwent B-RTO for gastric varices in our institution in the last decade were included. Their HFRs were evaluated before and 1/6/12 months after B-RTO. Hepatic and splenic volumes were calculated by SYNAPSE VINCENT® software.

Results: In the 13 patients with F2/F3 gastric varices, twelve successfully had down-staged varices of F0/F1 within a month after B-RTO treatments, and all of the six patients with overt encephalopathy got a drastic improvement in the same period. The median pre-treatment Child-Pugh score of 6.9 [5.0-8.0] was significantly improved into 6.4 [5.0-10.0] at 6 months after treatment ($p<0.05$). Total hepatic volume as well as splenic one were not significantly changed in the comparison between before and after B-RTO treatments ($p=0.985$ and $p=0.127$, respectively). An increase in postoperative hepatic volume of more than 10% and the presence of overt encephalopathy before intervention contributed to the improvement of HFRs ($p<0.05$ and $p<0.01$, respectively). A case of esophageal varices rupture was derived.

Conclusion: B-RTO is effective not only for the size reduction and rupture risk of gastric varices but for hepatic encephalopathy and may also improve HFRs. Future studies are desired to predict which population would increase their total hepatic volume after B-RTO.

Abstract Submission No. 100786
P-0966

Portal hypertension in a non-cirrhotic liver: modified Sugiura's procedure and complications<!--
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We report a 34-year-old male, managed as a case of recurrent esophageal variceal bleed secondary to portal hypertension despite five sessions of esophageal variceal ligations. He also underwent endoscopic retrograde pancreatography (ERCP) with biliary stenting for obstructive jaundice secondary to biliary compression by pericholedochal varices which was confirmed by endoscopic ultrasound (EUS). The patient was advised for modified Sugiura's procedure instead of transjugular intrahepatic portal systemic shunt (TIPS), because of the high rate of hepatic encephalopathy nor of surgical shunts since the patient had portal cavernoma. Patient had a complicated course post operatively. This report highlights the choice of management for failed endoscopic therapy for bleeding esophageal varices, the choice of surgical management and associated complications. He underwent devascularization known as modified Sugiura's procedure but developed dyspnea post operatively. He was diagnosed with pneumothorax and was managed with chest tube thoracostomy. However, on feeding, he experienced abdominal pain and vomiting accompanied with bilious leak on his surgical drain placed adjacent to the transected esophagus. Jejunostomy tube was inserted and used for feeding until the healing of esophago-gastric anastomosis. The cause of portal hypertension in non-cirrhotic patients may be different from those with liver cirrhosis and the managements have overlapping similarities and differences. The choice of management including radiological (TIPS) or surgical shunt procedure or devascularization depends on the benefits and risks acceptable and appropriate to the patient.

Abstract Submission No. 100826
P-0967

An Unusual Cause of Massive Per-Vaginal Bleeding

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This clinical case report highlights an unusual cause of per-vaginal (PV) bleeding associated with ectopic uterine varix bleeding; an exceedingly rare manifestation of clinically significant portal hypertension secondary to liver cirrhosis.

A 60-year-old woman with previous history of caesarean section presented with massive PV bleed. Initial test revealed low haemoglobin (8g/dL), low platelet ($71 \times 10^9/L$), prolonged prothrombin time of 23.8 seconds and partial thromboplastin time of 53.4 seconds, and deranged liver function tests (bilirubin of $25 \mu\text{mol/L}$, albumin 15g/L , ALT 20U/L , AST 52U/L). CT angiography revealed incidental finding of liver cirrhosis, extensive portosystemic collaterals with shunting from splenic vein to the anterior uterine wall at the region of the caesarean scar. She was planned for early transjugular intrahepatic portosystemic shunt (TIPSS) procedure but this was held off due to presence of pulmonary hypertension during TIPSS workup. She eventually underwent angiographic embolization of the uterine varix and splenic vein shunt. She recovered well post-procedure and did not have a recurrence of PV bleeding in the following 6 months.

This case highlights the importance of considering ectopic uterine varices in cirrhotic patients with PV bleeding. Imaging techniques like bedside US Doppler and CT angiography aid in diagnosis. The role of NSBBs is debatable in the management of ectopic varix hence addressing portal hypertension through procedures like transjugular intrahepatic portosystemic shunt is necessary. Embolization of the uterine varix and its shunt can be a useful interim therapeutic option to reduce the risk of rebleeding.

Abstract Submission No. 101181
P-0968

Clinical outcomes of acute variceal bleeding in a tertiary asian hospital

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INTRODUCTION: Acute variceal bleeding (AVB) is a serious complication in patients with liver cirrhosis with significant morbidity and mortality. We aim to evaluate the clinical outcomes of patients who present with AVB in our cohort.

METHODS: A retrospective study of 199 patients who presented to National University Hospital between January 2015 to December 2021 with AVB was conducted. The main clinical outcomes assessed were ability to achieve haemostasis on endoscopy, rebleeding within 5 days as well as mortality within 6 weeks and 1 year.

RESULTS: The most common etiologies of cirrhosis were non-alcoholic fatty liver disease (24.1%), chronic hepatitis B (22.6%) and alcohol (12.6%). A fifth of the patients (20.6%) had hepatocellular carcinoma (HCC) and 17.6% had portal vein thrombosis (PVT). The patients who were child pugh A, B and C were 38.4%, 48.5% and 13.1% respectively. Most bleeding was from esophageal varices (84.4%) and 15.6% was from gastric varix. Endoscopic haemostasis was not achieved in 4.5% of the patients. The 5-day rebleeding rate was 8.5% and mortality rate at 6 week and 1 year was 8.5% and 29.6% respectively. A higher child pugh score (OR 7.86, $p=0.02$) and gastric varix (OR 7.21, $p=0.007$) were associated with a higher rebleeding rate at 5 days. A higher child pugh score (OR 12.1, $p=0.003$), PVT (OR 6.82,

$p=0.009$) and HCC (OR 19.2, $p<0.001$) were associated with increased mortality at 1 year.

CONCLUSIONS: Gastric varix bleeding is associated with a higher rebleeding rate compared to esophageal varices. The severity of underlying liver disease, HCC and PVT influenced mortality at 1 year after AVB.

Abstract Submission No. 101220

P-0969

The Role of Vasoactive Drugs in Acute Variceal bleeding in Child A Cirrhosis patients.

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Background: According to Baveno VII recommendations, the role of vasoactive drugs in CHILD A cirrhosis patients with acute variceal bleeding (AVB) is yet an unmet need.

Aim: To evaluate the role of vasoactive drugs (VAD) in Child A cirrhosis with AVB.

Method: A prospective study was conducted on 100 child cirrhotic patients with AVH who were double blindly randomized 1:1 to two groups. A group which was subjected to VAD (Octerotide 50 mcg IV bolus followed by 25 -50 mcg/hr up to 5 days) and a second non-VAD treated group. All patients were admitted to intensive care unit for resuscitation and management and upper endoscopy within 12 hours of hemodynamic stability.

Results: The 2 studied groups were predominantly males, (75%) in group I and (83%) in group II with mean age of (53.7 ± 10.5) years and (53.2 ± 7) years in group I and II, respectively. No significant difference between the studied groups as regards MELD score, type and size of varices and all laboratory results. VAD group had significantly ($p=0.001$) higher rate of control of AVB with significantly lower rate of early rebleeding ($p=0.001$), duration of hospitalization ($p<0.001$), and blood transfusion requirement ($p<0.001$) as well as significantly lower mortality rates ($p=0.001$). In multivariate analysis, age, total bilirubin, albumin, AST, and platelets count were the only risk factors for controlling AVB.

Conclusion: The role of vasoactive drugs in patients with Child A cirrhosis in controlling active variceal bleeding was substantially negated with recommended further larger size studies.

Abstract Submission No. 101291

P-0970

Proximal splenorenal shunt surgery for gastric bleeding in extrahepatic portal vein obstruction

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Introduction: Extrahepatic portal vein obstruction (EHPVO) is one of the clinically significant causes of gastrointestinal bleeding in children, a relatively rare disease but one of the most common causes of portal hypertension in pediatric patients. Risk factors include umbilical catheterization. Patients manifest with splenomegaly, thrombocytopenia and bleeding varices which may be life-threatening.

Objectives: This case illustrates the effectiveness of proximal splenorenal shunt surgery (PSRS) in resolving variceal bleeding from cavernous transformation in (EHPVO) in a non-cirrhotic pediatric patient.

Materials and Methods: We report a case of a 15 year old southeast asian female who presented with hematemesis and melena. Diagnosed as bleeding esophageal and gastric varices secondary to cavernous transformation of the portal vein due to EHPVO. Her multiple and recurrent episodes of massive gastrointestinal bleeding were managed endoscopically with histoacryl glue injections and repeated blood transfusions. Due to recurrent admissions for massive, frequent and shortened intervals of bleeding which led to hemorrhagic shock and complaints of debilitating pain with disruption to quality of life, she underwent splenectomy with proximal splenorenal shunt.

Results: There was noted resolution of portal cavernous transformation and collateral vessel formation on radiographic scans performed 3 weeks after surgery and symptomatic resolution of gastrointestinal bleeding with no recurrence.

Conclusion: Treatment for EHPVO is addressed by flow diversion. Creation of a portosystemic shunt (PSS) is reserved for patients presenting with life threatening and refractory bleeding. PSRS is an effective treatment for pediatric patients to address life threatening complications and improve quality of life as well.

Abstract Submission No. 101706

P-0971

Changes in liver/spleen volume and HVPG after DAA treatment for decompensated HCV-related cirrhosis

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Background: The relationship between changes in liver and spleen volume and hepatic venous pressure gradient (HVPG) after direct-acting antiviral (DAA) treatment in patients with hepatitis C virus (HCV)-related cirrhosis remains unclear.

Methods: This observational, single-centered study included 21 patients with decompensated HCV-related cirrhosis treated with sofosbuvir/velpatasvir and 19 patients with compensated cirrhosis treated with glecaprevir/pibrentasvir. All patients underwent laboratory tests, computed tomography, and transient elastography, and HVPG was measured in patients with decompensated cirrhosis. Changes in parameters after achieving sustained virological response (SVR) at 24 weeks after DAA treatment were evaluated.

Results: The level of Mac-2 binding protein glycan isomer ($p<0.001$, $p<0.001$) and the FIB-4 index ($p<0.001$, $p=0.012$) decreased in the compensated and decompensated groups. Spleen volume decreased in the compensated ($p=0.034$), but not in the decompensated group ($p=0.251$). Liver stiffness decreased in the compensated ($p=0.043$), but not in the decompensated group ($p=0.552$). HVPG declined in 67% of the decompensated group. Spleen volume before DAA treatment ($p=0.006$) and after SVR ($p=0.003$) were significantly smaller in patients with decreased HVPG than with increased HVPG. Spleen volume decreased in patients with decreased HVPG, while increased in those with increased HVPG (median, -21 vs. 43 mL; $p=0.039$).

Conclusions: Liver and spleen volumes changed after DAA treatment in patients with HCV-related cirrhosis. Spleen volume decreased in

compensated, but not in decompensated cirrhosis. Increased spleen volume after SVR might be an indicator of the “point of no return” in portal hypertension.

Abstract Submission No. 101723
P-0972

Analysis of the incidence of sarcopenia among cirrhotic patients with portal hypertension

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Background: Sarcopenia is a syndrome characterized by a decrease in skeletal muscle and strength, and has been reported to relate with the poor prognosis of patients with liver cirrhosis.

Aim: The incidence of the sarcopenia was analyzed in 182 cirrhotic patients complicated with portal hypertension which required invasive treatments.

Methods: All patients undergone therapeutic interventions for portal hypertension such as gastro-esophagogastric varices and were measured their grip strength and skeletal muscle mass using bio-impedance analysis (BIA) at the same time. Clinical factors related to the sarcopenia were retrospectively analyzed.

Results: The subjects included a median age of 69 years, a male to female ratio of 126:56, and major cause of the liver disease were viral hepatitis (40.7%) and alcohol (27.5%), and the main treatment for portal hypertension were endoscopic (69.8%). The median skeletal muscle index (SMI) was 7.17 kg/m², and the median grip strength was 26.9 kg. Thirty-two cases (17.6%) were diagnosed to have sarcopenia according to the standards of the Japan Society of Hepatology. Of the remaining cases, 31 cases (17.0%) had insufficient SMI diagnosed as pre-sarcopenia, 26 cases (14.3%) had a decrease in grip strength diagnosed as dynapenia. In multivariate analysis of factors contributing to sarcopenia, age (odds ratio 11.45), female (odds ratio 2.43), and non-obese (odds ratio 5.86) were significant independent factors (P<0.05).

Conclusion: In cirrhotic patients complicated with portal hypertension, the incidence of sarcopenia was thought to be relatively high in elderly woman without obesity, suggesting that muscle mass evaluation might be desirable.

Abstract Submission No. 101788
P-0973

Efficacy of partial splenic embolization on portal hypertensive gastropathy in cirrhotic patients

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Background: There are few reports regarding endoscopic findings before and after partial splenic embolization (PSE) in cirrhotic patients and the application of PSE for treatment of portal hypertensive gastropathy (PHG). The purpose of this study was to investigate the therapeutic effect of PSE for PHG in relation to portal hemodynamics.

Methods: We retrospectively analyzed endoscopic findings and the portal venous system of 32 cirrhotic patients with PHG. The improved

group was defined as amelioration of PHG findings using the McCormack classification.

Results: PHG was improved in 19 of 32 (59%) patients (improved group). Child–Pugh scores of the improved group were significantly lower compared with those of the non-improved group (p = 0.011). The changes in the diameters of the portal trunk and those of the spleno-portal junction and spleen hilum in the splenic vein of the improved group were significantly larger than those of the non-improved group (p = 0.004, p = 0.018, and p = 0.004, respectively). The changes in the diameters of the portal vein and splenic hilum of the splenic vein showed significant correlations with Child–Pugh score (r = 0.45, p = 0.013; r = 0.465, p = 0.008). In multivariate analysis of baseline factors related to the improved group, Child–Pugh grade A was significantly associated with the improvement of PHG by PSE (odds ratio 7.56, p = 0.024).

Conclusion: PSE could be useful for PHG, especially in patients with Child–Pugh grade A.

Abstract Submission No. 200043
P-0974

VALIDATION OF THE AIMS65 SCORE IN VARICEAL UPPER GASTROINTESTINAL HEMORRHAGE

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Objectives: Validation of the AIMS65 score to predict 30-day mortality and 30-day rebleeding in variceal upper gastrointestinal hemorrhage.

Study method: Descriptive and prospective study of 237 patients diagnosed with variceal upper gastrointestinal hemorrhage because of portal hypertension at Bach Mai Hospital and Hanoi Medical University hospital from 12/2018 to 6/2019. AIMS65 scores are evaluated to determine the predicted value. AIMS65 scores were calculated by allotting 1 point each for albumin (A) levels <30 g/L, INR (I) >1.5, alteration in mental status (M), systolic blood pressure (S) ≤90 mm Hg, and age >65 years.

Result: A total of 237 patients (mean age 52.86 ± 10.63 years), mostly diagnosed with alcoholic cirrhosis (180/75.9%), presented with variceal UGIH. Rebleeding occurred in 33 (13.9%) patients and 30-day mortality was 16 (6.8%). Initial hemostasis was achieved with endoscopic variceal ligation (181/76.4%), and N-butyl cyanoacrylate (23/9.7%). Median hospital stay was 5.28 ± 2.79 days. The mean AIMS65 scores were 1.32 ± 1. The predictive accuracy of AIMS65 scores ≥2 was high for blood transfusion (AUROC, 0.73), fresh frozen plasma transfusion (AUROC, 0.784), and 30-day mortality (AUROC, 0.757). The overall mortality was 6.8% (n=16), and was 0%, 4.1%, 9.2%, 22.2% and 0% for AIMS65 scores of 0, 1, 2, 3, and 4, respectively; these values were significantly higher in those with scores ≥2 (12.4%) than in those with scores <2 (2.3%, p=0.02).

Abstract Submission No. 200047
P-0975

Mortality and risk factors for elderly cirrhotic patients with acute upper gastrointestinal bleeding

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Background: Acute upper gastrointestinal bleeding (AUGIB) is a life-threatening complication of liver cirrhosis. Elderly patients with this condition has increased with the aging of population. Clinical characteristics and risk factors associated with short term mortality in elderly cirrhotic patients with AUGIB remain little known.

Methods: We retrospectively included cirrhotic patients with AUGIB admitted in Department of Emergency from April 1st 2021 to Dec 31st 2022 in Beijing You'an hospital. Clinical characteristics of the elderly patients were compared with younger ones. Risk factors for short term mortality were analyzed with adjusted multivariate logistic regression models.

Results: A total of 628 patients aged ≥ 60 years constituted the elderly group. Compared with the younger patients < 60 years old, the elderly ones were more likely to present with lower level of DBP, pulse and shock index, lower PT, higher BUN and Cr level. The elderly patients had a higher incidence of hypertension, diabetes, coronary heart disease, chronic kidney disease, HCC and simultaneous PVT/Diabetes. All-cause mortality in hospital and at 6-week of the elderly was 16.7% and 24.0%, respectively. Age and male were independent risk factors for both in-hospital mortality and 6-week mortality. Esophageal sclerotherapy, melena, obvious encephalopathy, hyperlipoidemia and Con PVT/Diabetes were independent risk factors for in-hospital mortality, whereas unknown source of AUGIB and HCC were independent risk factors for 6-week mortality.

Conclusion: Age and male increase in-hospital mortality and 6-week mortality in elderly cirrhotic patients with AUGIB. Esophageal sclerotherapy, control of diabetes, treatment of encephalopathy and PVT help to reduce in-hospital mortality.

Abstract Submission No. 200083
P-0976

Omeprazole plus sucralfate Vs omeprazole alone for prevent post EVL ulcer in cirrhotic CTPA or B

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Background: Post-endoscopic variceal ligation (EVL) ulcers represent a complication following EVL, with potential implications for mortality in cirrhotic patients. Prophylaxis against this complication typically involves either a proton pump inhibitor (PPI) or sucralfate. Limited studies have explored the combination of PPI with sucralfate suspension in the prevention of post-EVL ulcers. We aimed to assess the efficacy of the combination of omeprazole and sucralfate suspension in comparison to omeprazole alone for preventing post-EVL ulcers in cirrhotic patients.

Methods: From March 2019 to December 2022, A prospective, single-center, randomized controlled trial was conducted. We enrolled patients diagnosed liver cirrhosis CTPA or B with esophageal varices to receive either omeprazole plus sucralfate suspension or omeprazole alone and performed subsequent esophagogastroduodenoscopy at 2 weeks to evaluate EVL ulceration using Jamwal's classification and complications.

Results: 84 cirrhotic patients were enrolled. There were no significant differences between the combination of omeprazole plus sucralfate suspension and omeprazole alone groups in terms of EVL ulcer type, EVL ulcer numbers, and percent decreasing of EVL ulcer numbers. No

statistically significant variations in post-EVL complications were observed between the two treatment groups.

Conclusion: This study indicates no discernible differences in post-EVL ulcer type, EVL ulcer numbers, percentage reduction in EVL ulcer numbers, and complications between the combination of omeprazole plus sucralfate suspension and omeprazole alone. However, there is a trend towards reducing complications such as chest pain, dysphagia, nausea and vomiting, and diarrhea in the combination therapy group.

Abstract Submission No. 200249
P-0977

New ARFI-based ratio scores, identify cirrhotic patients with high-risk oesophageal varices.

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Introduction: Portal hypertension is a complication of liver cirrhosis. Acoustic Radiation Forced Impulse (ARFI) is an ultrasound integrated method, measuring tissues stiffness by point shear wave elastography. **Aims:** To evaluate the diagnostic performance of liver and spleen ARFI, combined with spleen dimension and platelet count in new ratio scores, in predicting clinical events related to portal hypertension.

Materials and methods: Between May 2016 and November 2020, a prospective and cross-sectional study was conducted, enrolling for the first six months all consecutive cirrhotic patients in ultrasound surveillance for hepatocellular carcinoma. The following ratio scores with ARFI measurements were performed at the enrollment: ALSDP (ARFI Liver-Spleen Diameter-to-Platelets ratio score), ASSDP (ARFI Spleen-Spleen Diameter-to-Platelets ratio score), ASSAP (ARFI Spleen-Spleen Area-to-Platelets ratio score), ALSAP (ARFI Liver-Spleen Area-to-Platelets ratio score).

Results: 100 subjects were enrolled. Spleen ARFI, ASSDP, ASSAP, were significantly associated with high-risk varices (HRVs) in the prospective short- and long-term follow-up and in the cross-sectional study ($p < 0.05$), while ALSDP and ALSAP were associated with HRVs only in the prospective long-term follow-up and cross-sectional study ($p < 0.05$). ASSAP was the ARFI-ratio score best performing for HRVs at the long-term follow-up [value of area under curve (AUC) = 0.88], although all the ARFI-ratio scores performed better than liver and spleen ARFI alone (AUC > 0.7) in detecting HRVs. Moreover, liver ARFI at the long-term follow-up ($p = 0.039$) and spleen ARFI, at the short-term follow-up ($p = 0.009$), identified only patients at risk of ascites.

Conclusions: ARFI-ratio scores can predict, in cirrhotic patients, the risk of developing HVRs in short and long-term period.

Abstract Submission No. 200258
P-0978

The role of interventional radiology methods in the treatment of portal hypertension in Kazakhstan.

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The aim of the study was to evaluate partial superselective spiral embolization of splenic artery branches in patients with splenomegaly. 146 cases of superselective spiral embolization in 71 patients from April 2021 to December 2022. The average age of the patients was 48±5.2 years, 51 (72%) women. The main causes of liver cirrhosis are hepatitis B - 33%, hepatitis C - 21%, hepatitis D - 14%, primary biliary cirrhosis and autoimmune hepatitis in 32% of patients. We used a microcatheter (Progreat, Terumo Corporation, Japan) and removable coils Azur CX (MicroVent, USA) and PC-400 (Penumbra, USA). Angiographically, the target artery, more often the branches of the inferior segmental artery, its diameter and the area of blood supply to the spleen were determined. The first course led to a decrease in blood flow by 10-20%, the second - by 20-30% and a further increase. The frequency of partial superselective spiral embolization averages 2.5±0.4 times. At the first observation from 6 to 12 months, the average volume of the spleen decreased by 23% according to computed tomography and ultrasound. The initial average platelet level ranged from 65±15x10⁹/l, after 1-2 courses of embolization, the platelet level reached 93±21x10⁹/l. Clinically, there was a decrease in the symptoms of portal hypertension.

Conclusions: step-by-step partial superselective spiral embolization of splenic artery branches in portal hypertension can be performed safely and gives positive results in the form of symptom relief and normalization of hematological parameters.

Abstract Submission No. 100081
P-0979

IMPLEMENTED RESPONSES OF VIRAL HEPATITIS ELIMINATION IN MONGOLIA

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Mongolia has some of the highest rates of viral hepatitis prevalence in the world with 9.3% for hepatitis C virus and 7.8% for HBsAg infections as of 2021, and following, the high burden prevalence of liver cirrhosis and liver cancer which most of them diagnosed at a late stage. To address these public health threats, the Healthy liver program (HLP) was implemented between 2017-2021 years to combat viral hepatitis and embarked on ambitious criteria as global goals. The HLP have successfully implemented aims to control hepatitis B virus and eliminate hepatitis C virus as a public health threat. Otherwise it is population based given opportunity mass screening the whole population to identify prevalence of these infections.

Therefore, the Ministry of Health has approved the HLP to continue with 34 different actions and 15 national criteria in four goals during 2022-2025 years.

Additionally, Mongolia has piloted a pre-assessment for validation of viral hepatitis elimination in 2022 to understand experience and gaps, and it was crucial to address the way forward.

For chronic surveillance, Mongolia has assessed the situation analysis on establishing hospital based sentinel surveillance of viral hepatitis sequelae including liver cirrhosis, cancer, and death and developing guidance on sequelae surveillance for liver cirrhosis and liver cancer caused by viral hepatitis.

Conclusion: Prevalence and incidence rate of viral hepatitis infection is decreasing year by year in Mongolia.

Abstract Submission No. 100145
P-0980

Prevalence of obesity among school-aged children in Vietnam: A systematic review and meta-analysis

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Aim: The global incidence of obesity is rising, posing a substantial public health threat. This meta-analysis aims to estimate the prevalence of obesity among school-aged children in Vietnam and to analyze the risk variables that have been linked to this problem.

Method: MEDLINE, PubMed, and Scopus were used to identify articles published up to May 2022. According to peer-reviewed literature, studies reported the proportion of obesity among Vietnamese school-aged children. The Scales of Newcastle-Ottawa Quality Assessment was used to evaluate the study quality for all qualifying research. The data was analyzed using R-Studio software, and the combined effects were estimated using a random-effects model.

Results: Eleven studies with 27,363 participants were suitable for inclusion in the final model after meeting the prerequisites. The proportion of obesity among Vietnamese school-aged children was 13.08% (95% CI, 7.04%– 23.01%) with higher heterogeneity through the observed prevalence estimates ($Q = 1,0339$, $p < 0.01$, $I^2 = 99\%$). A higher prevalence was observed in boys (17.5%) than in girls (8.07%). Male gender of the children: 2.42 (95%CI: 1.43–4.09), mothers have less education: 2.63 (95% CI 1.52–4.55) have shown a positive association with the development of obesity among children.

Conclusions: The recent pooled analysis of studies demonstrates that school-aged children in Vietnam have a high prevalence of obesity. The male gender and the low education status of the mother were found to be significantly associated with obesity. The findings provide evidence for prevention intervention strategies to reduce obesity in school-age children.

Abstract Submission No. 100152
P-0981

Mechanistic Underpinning And Weight Loss Effects Of Time-Restricted Eating Across Diverse Adult

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Time-restricted eating (TRE) is a promising and cost-effective dietary approach for weight management. This study aimed to evaluate the effects of TRE on weight loss in three adult populations using pre- and post-intervention analyses while also investigating its underlying mechanisms. A systematic search was conducted across four databases (PubMed, Web of Science, Scopus, and the Cochrane Library) up until April 20, 2023, specifically focusing on cohort studies that examined the efficacy of TRE in achieving weight loss. A random effects model was employed to conduct meta-analyses, while heterogeneity was assessed using the I² statistic. The study encompassed 36 selected studies involving 44 effect sizes and 914 participants. The effectiveness of the TRE diet was found to vary across health conditions, with modest weight loss observed in healthy individuals (pooled effect size -1.04 Kg, 95% CI: -1.42 to -0.65) and more significant weight reduction seen in participants with chronic diseases (pooled effect size -3.33 Kg, 95%

CI: -5.05 to -1.62) and overweight/obesity (pooled effect size -4.21 Kg, 95% CI: -5.23 to -3.10). The observed decrease in body weight could be partially attributed to factors influencing energy balance, as evidenced by the significantly lower mean calorie intake at the end of the intervention (1694.71 kcal/day, 95% CI: 1498.57-1890.85) compared to the baseline intake (2000.64 kcal/day, 95% CI: 1830-2172.98), despite the absence of intentional efforts to restrict energy intake by the participants. These findings support the efficacy of this lifestyle intervention for weight loss maintenance and guide the development of its clinical guidelines.

Abstract Submission No. 100246
P-0982

Prevalence of Vitamin C Deficiency and its Association with Stroke Risk in the U.S. Adult Population

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Background: Stroke is a major health concern, prompting the need for urgent public health measures. While Vitamin C shows potential against cardiovascular diseases, its role in stroke risk remains uncertain. This study aimed to assess Vitamin C deficiency prevalence in stroke patients and its correlation with stroke risk.

Methods: We examined data from 13,339 U.S. adults in the National Health and Nutrition Examination Survey between 2003-2018, excluding those with missing serum Vitamin C levels and self-reported stroke status. Using adjusted multivariate logistic regression models, we assessed the association between Vitamin C deficiency (<11.4 µmol/L) and stroke incidence, considering various factors.

Results: Stroke prevalence rates in the NHANES cycles 2003-2006 and 2017-2018 were 2.8% (95% CI: 2.3-3.4) and 3.3% (95% CI: 2.7-4.2), respectively. Vitamin C deficiency was more common in individuals with a history of stroke, with rates of 3.6% (95% CI: 2.2-5.8) and 5.3% (95% CI: 3.9-9.1) compared to 2.7% (95% CI: 2.3-3.3) and 3.2% (95% CI: 2.5-4.1) in the non-stroke cohorts. Nevertheless, vitamin C deficiency was distinctly prevalent across diverse demographic and health-related subgroups. Multivariate analyses invalidated any statistically significant correlation between Vitamin C deficiency and stroke risk across all employed analytical models within both time intervals.

Conclusions: Our study found no evidence linking Vitamin C deficiency to increased stroke risk in U.S. adults, despite higher deficiency rate among stroke patients. Further trials are needed to clarify its role in managing stroke-related oxidative stress, including optimal dosing and delivery methods. Healthcare providers should consider its prevalence in specific subgroups.

Abstract Submission No. 100292
P-0983

Hepatitis Free Mongolia, Phase 2 Rotary International and FIRE Projects

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The collaborative project, Hepatitis Free Mongolia, Phase 2 set the goal of eliminating hepatitis C (HCV) across Sukhbaatar province in rural Mongolia while creating a scalable project.

METHODS: To accomplish the elimination of HCV we developed a mobile screening model. These include:

1. The project adopted the best practice initiated by Saga University of Japan to train Hepatitis coordinators to assist every community member to be tested and treated for liver disease.
2. A database was created at www.hepatitisfreemongolia.com to record and track testing and treatment results.
3. Hepatitis and liver cancer screening to rural populations by the mobile clinic provides testing for HBV, HCV, ultrasound, fibroscan, examination by joint team of Mongolian and Japanese hepatologist, oncologist and referral to further specialized care and service.
4. The project provided financial support for those residents who are unable to afford anti-viral treatment.

RESULTS: 80% of the target population has been tested for hepatitis B, C and liver cancer. Out of these people, 12.3% chronically infected with HBV and 5.2% exposed to HCV. Those who were diagnosed with chronic viral hepatitis B, C and suspected with HCC have been referred to the specialized care and treatment.

CONCLUSIONS: The successful model created by Hepatitis Free Mongolia, proves elimination of HCV can be accomplished at the provincial level. To achieve the global goal of viral hepatitis elimination by 2030 it contributed to the WHO's framework and criteria for validation of hepatitis elimination. We hope to expand the model across Mongolia and other countries.

Abstract Submission No. 100461
P-0984

Impact of HCV on Health-Related Quality of Life and Work Productivity Loss in Pakistani Patients

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Background and aims: Pakistan has the highest hepatitis C virus burden. We examined health-related quality of life (HRQoL) and work productivity loss in screened individuals, emphasizing socio-demographic HRQoL influences.

Methods: A cross-sectional study with HRQoL assessment conducted mainly in Karachi and Gujranwala. Chronic hepatitis C (CHC) patients received 12- or 24-week treatments based on cirrhosis risk. HRQoL was assessed using the EuroQol-EQ-5D-3L, before revealing HCV antibody status. Work productivity loss was evaluated through the WPAI-GH questionnaires. EQ-5D-3L scores were converted to HRQoL weights from Pakistani general population value set. Tobit regression identified associations between HCV or cirrhosis status and HRQoL, controlling for socio-demographics.

Results: Among 5,468 participants, median age 39 (IQR: 30, 50), 59.14% males, 1,263 were CHC positive. CHC patients exhibited

lower HRQoL [0.952, 95%CI: 0.947-0.956] compared to HCV Ab-negative participants [0.979, 95%CI: 0.977-0.981, $p < 0.001$]. Tobit regression found significant associations. CHC was linked to lower HRQoL, as unemployed, and older age. Living in Karachi and being male were associated with positive HRQoL. Education showed diverse effects. Among CHC patients, older age, unemployment, and being widowed related to significantly lower HRQoL, while residing in Karachi had a significantly positive effect. Cirrhosis and 24-week treatment duration didn't significantly affect HRQoL. CHC was associated with increased absenteeism (29.14% vs. 13.56%, $p = 0.002$) and an annual indirect cost of USD440.

Conclusions: HCV infection may be reducing HRQoL in Pakistan, incurring a significant cost to individuals and the economy. Further research is needed to understand whether treatment of HCV can reduce these detrimental effects.

Abstract Submission No. 100477
P-0985

Role of Reimbursement in Survival of Sorafenib-eligible Advanced Hepatocellular Carcinoma Patients

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In 2008, sorafenib became the first approved systemic therapeutic agent for advanced HCC. Although its pharmacological efficacy has been established, reimbursement for such new, high-cost drug as well as physicians' awareness and prescription practice, likewise contribute to its clinical effectiveness. We therefore conducted a retrospective study using 38 sorafenib-eligible, advanced HCC patients when sorafenib was approved but not yet reimbursed, as control, and 216 patients during the reimbursed era. Study group showed longer survival at 8.2 months versus the control's 4.9 months ($p = 0.0063$ hazard ratio: 0.612 (0.431~0.868), $p = 0.0059$). Among the 42 (19.4%) patients who survived more than 2 years, 50% with tumor rupture and all 32 patients with portal vein tumor thrombus and/or extrahepatic metastasis, received sorafenib ($p = 0.003$). Furthermore, during their first 2 years of HCC management, sorafenib had been given in 29.1% of the treatment courses among survivors between 2 and 5 years, while it was prescribed in 55.8% among the more than 5 years survivor group ($p < 0.001$). In conclusion, survival of sorafenib-eligible HCC patients significantly improved after reimbursement. Patients who underwent longer sorafenib treatment had a survival advantage, except for those with tumor rupture. Reimbursement and awareness of prescription for a newly introduced medication therefore improve clinical effectiveness.

Abstract Submission No. 100496
P-0986

Including mpMRI in liver resection pathways reduces healthcare costs in a Japanese Healthcare system

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The reported societal cost of liver cancer in Japan is more than ¥600 billion and growing¹, therefore steps to reduce the economic burden are needed. Liver resection is a curative option however the per patient cost of liver cancer hepatectomy is up to ¥5 million² including surgery, hospitalisation, complications and drugs. Up to 16% of patients experience post-operative complications including infection, bleeding and organ failure³. Assessing liver tissue pre-surgery using non-invasive multiparametric MRI (proton density fat fraction (PDFF) and iron corrected T1 mapping (cT1)) may lead to changes in surgeon decision making, decreased complication rates, and better clinical outcomes⁴. Using a hypothetical cohort of 100 post-liver surgery patients, costs associated with experiencing post-operative complications were compared between 2 scenarios: 1. Standard care, and 2. After introducing mpMRI. The incidence and cost of post-operative complications were taken from literature^{3,4,5}. Costs were reported per 100 patients and per patient. Where complication costs were unavailable for a Japanese health care system, published costs were converted to Japanese Yen. Microsoft Excel was used for analysis.

16 patients experienced major complications post-surgery in scenario 1 compared to four patients in scenario 2. The total cost of complications in scenarios 1 and 2 were ¥121,389,197 and ¥23,048,582 respectively. The difference in total costs (complication and no complication) between scenarios was ¥55,931,532 per 100 patients. Per patient difference was ¥55,932.

The introduction of mpMRI to those undergoing liver resection due to liver tumours may lead to cost savings benefitting both patients and society and improve clinical outcomes.

Abstract Submission No. 100550
P-0987

The role for the hepatitis medical care coordinator training course proposed by a dental association

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Background: In 2018, the Aichi Dental Association (ADA) (Aichi, Japan) took the initiative to raise awareness of viral hepatitis among dentists. ADA has more developed a hepatitis project for dentists and started a hepatitis medical care coordinator (hepatitis-coordinator) training course in 2020. We propose a new role for the hepatitis-coordinator training course that became apparent from this training course.

Methods: In the training course, as well as hepatologists, dentists provided lecturers. The dentists gave lectures on the importance of standard precautions, the role of dentists as hepatitis-coordinators, and so on. After the training course, 159 participants were surveyed about their motivation for attending the training course and their plans for activities. Answers from 90 dentists and 49 participants working outside the dental field were compared (that from 20 participants other than dentists working in the dental field were excluded).

Results: According to the questionnaire (response rate 91.2% [145/159]) for participants, dentists have more opportunities to interact with the patients with hepatitis than the attendees from the non-dental field ($p = 0.001$). Dentists had expanded their knowledge of the role of hepatitis-coordinators ($p = 0.047$) and hope to recommend hepatitis B vaccination ($p < 0.001$). Because 94 dentists were certificated as

hepatitis-coordinators, the number of dentists became the largest in the number of hepatitis-coordinators by occupation in Aichi Prefecture.

Conclusion: The training courses by ADA serve to provide an opportunity to take a leading position on hepatitis for dentists. Because dentists play a major role in health management, improving their knowledge about viral hepatitis is important for infection control.

Abstract Submission No. 100671

P-0988

Evaluation of the attributable fraction of liver diseases due to hepatitis B and C in Hong Kong

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Background: A retrospective review of clinical and laboratory record of deaths from selected liver diseases was conducted to estimate their attributable fraction due to hepatitis B and C, and thus to measure the hepatitis-related mortality in Hong Kong.

Methods: All deceased Hong Kong residents registered in 2015 and 2020, whose ICD-10 code of their underlying cause of death was liver cancer (C22), cirrhosis (K74.3-K74.6) or other chronic liver diseases (CLD) (K72-K75, excluding K74.3-K74.6), were included. Those with history of hepatitis B and C diagnosis were identified by record tracing in the databases of local public hospitals, and evaluated by causes of death.

Results: A total of 1977 and 1915 persons died from the selected liver diseases in 2015 and 2020 respectively. Of hepatocellular carcinoma (HCC) deaths, 68.5% (2015) and 66.4% (2020) had HBV infection, and 13.4% (2015) and 11.1% (2020) had HCV infection. For deaths from non-HCC liver cancer, cirrhosis and other CLD, 31.9%-39.0% (2015) and 29.8%-36.8% (2020) had HBV infection, and 5.2%-12.6% (2015) and 4.4%-12.2% (2020) had HCV infection. In 2020, the estimated crude mortality due to hepatitis B and C was 12.71 and 2.25 per 100 000 population respectively. As compared with 2015, the relative reduction in mortality was 6.8% and 20.5% for hepatitis B and C respectively.

Conclusions: While elimination of HCV infection has been on track in Hong Kong, more actions are required to achieve the WHO goal of eliminating viral hepatitis as a public health threat by 2030, in particular to reduction of hepatitis B-related deaths.

Abstract Submission No. 100745

P-0989

SAGA MODEL OF HEPATITIS COORDINATORS IN MONGOLIA TO ELIMINATE VIRAL HEPATITIS

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BACKGROUND: Mongolia is with the highest prevalence of viral hepatitis B, C and liver cancer in the world. Approximately, 53% and 35% are respectively, of estimated people chronically infected with HBV and HCV are diagnosed through government-funded screening

program (Cumulative data for 2017-2020). Mainly, uninsured individuals, herders and mobile residents are not enrolled in the screening program. There is a greater challenge to reach out to those who live in the rural countryside, who do not know their liver disease status.

METHODS: "Hepatitis Coordinators" (HC) is a new model in Mongolia developed by Japanese all prefectures organized by the Ministry of health, including Saga prefecture and adopted by "Hepatitis Free Mongolia" project funded by the Rotary Foundation.

In coordination with local government authorities and primary health care providers, we select health care workers, social workers, and community members to be trained as HCs.

RESULTS: Since 2017, 500 health care workers, social workers, and community members have been trained as HCs in three different provinces. HCs were helpful during the screening to reach out to community members to invite them to the screening and disseminate information about liver disease.

CONCLUSIONS: Social worker HCs will contact every community member in their assigned community who needs to be tested and communicate until they are tested. The health care worker HCs will follow each person who is positive for viral hepatitis B or C until they are treated. HCs will work within this long-standing social system of Mongolia to locate individuals.

Abstract Submission No. 100988

P-0990

SAME compared to UDCA for intrahepatic cholestasis treatment in China: a cost-utility analysis

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Introduction: Intrahepatic cholestasis (IHC) is a disorder of bile formation, secretion, or excretion such that bile flow is impeded from entering the duodenum and bloodstream. Two main treatments are available in China for the treatment of IHC, namely S-Adenosylmethionine (SAME) and ursodeoxycholic acid (UDCA). The aim of this study is to assess the cost-utility of SAME and UDCA.

Methods: A 3-state Markov model (mild IHC, severe/moderate IHC, dead) was developed to analyze the cost-utility of each drug. Quality-adjusted life years (QALYs) and incremental cost-utility ratio (ICUR) were chosen as the primary endpoints. Clinical trial input data was obtained from the literature, and local costs and clinical practice input were sought from key Chinese clinical experts.

Results: SAME yielded additional 0.0349 QALYs at CNY2,634, resulting in a ICUR of CNY75,398 compared to placebo. The cost difference was driven by CNY3,438 in drug costs but offset with -CNY804 in health care costs. UDCA resulted in a gain of 0.0087 QALYs at an additional cost of CNY3,582 and an ICUR=CNY410,198. The costs were split into CNY3,784 in drug costs and -CNY201 in health care costs. This means that the extended cost-utility of SAME would be 0.0349-0.0087=0.0262 QALYs at a cost of CNY2,634-CNY3,582=-CNY948.

Conclusion: This study shows SAME leads to 0.0262 QALYs when compared to UDCA at -CNY948. While the drug costs were similar the SAME health care costs were four (-CNY804/-CNY201=4) times lower than UDCA. In conclusion, SAME is estimated to deliver improved health outcomes and savings for the treatment of IHC.

Abstract Submission No. 101210

P-0991

Nationwide survey of clinical indicators to assess quality of liver disease care in Japan

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Background: Since 2017, we have been developing clinical indicators for hepatitis and cirrhosis care at regional core centers for the management of liver disease in Japan. In this study, we have used these indicators to assess the changes in the quality of care for liver disease that is provided at the regional core centers across the country.

Methods: The survey regarding 29 clinical indicators ("hepatitis CIs") was conducted with 72 regional core centers from 2018 to 2022 (except for 2019). The hepatitis CIs consisted of 5 categories (general hepatitis and cirrhosis, hepatitis C, hepatitis B, cirrhosis and subsidy systems). Based on the results of our survey over the past four years, we evaluated the trends of each indicator over time.

Results: In this survey, most of CIs in five categories showed the rate of achievement more than 80% of the relevant target values. However, six indicators, including resistance-associated substitutions testing for HCV DAA failure and routine upper GI endoscopy for cirrhosis patients, failed to meet their goals. In 2021, the CIs showed the lowest values for all categories, except for the subsidized systems, due to the negative impact of COVID-19 pandemic. Most categories showed recovery in 2022, except for the CIs regarding the management of liver cirrhosis.

Conclusion: The annual survey using CIs is useful for the trend assessment of the achievement of clinical practice for hepatitis patients. In Japan, highly standardized treatment and care has been provided nationwide to the patients in need.

Abstract Submission No. 101296

P-0992

Level of immunity against HBV in of pre-and post-HBV vaccinated populations of Mongolia

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Background: Since 1991 newborns were partially or fully vaccinated with HBV vaccine. People who born before 1991 were not. We wanted to see the difference between those groups.

Methods: 492 patients have enrolled who were investigated with quantitative HBsAb (qHBsAb) using Sysmex HISCL -800 (full automated analyzer) at Happy Veritas hospital. The vaccination scheme consists of three doses. Vaccination is considered successful if the antibody-titer (qHBsAb) is higher than 10 mIU/L.

Results: In this study 492 patients have participated, 313 female (63%) and 179 male (37%), out of which 471 (96%) people born before 1991 and remaining 21 (4%) people born after 1991. Twelve people (57%) who were born after 1991 or vaccinated within 24 hours after birth had qHBsAb low titer (<10 mIU/L), remaining (43%) were qHBsAb titer

(>10 mIU/L), while 297 people (64%) who born before 1991 were qHBsAb titer (<10 mIU/L), and remaining 169 people or 36% had higher than cut-off value. The 99 people who born before 1991 have enrolled in HBV catch up vaccination voluntarily, while 372 people were not vaccinated at all.

Conclusion: Persistent immunity against HBV is developed not only in people who were vaccinated but also in persons who have had HBV infections. It was observed people aged 50-60, had the highest HBV non-immune population in Mongolia. Catch-up vaccinations need be advocated and implemented aggressively.

Abstract Submission No. 101410

P-0993

Cost-utility of novel biomarker-based strategies for HCC surveillance in Thailand

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Background: Hepatocellular carcinoma (HCC) represents the fifth leading cause of death in Thailand. Even though alpha-fetoprotein (AFP)+Ultrasound (US) has been suggested for HCC surveillance, most patients still lack access. Novel biomarker-based strategies are suggested to help overcome the limitations of current surveillance methods. This study assessed the cost-utility of different routine HCC surveillance methods in Thailand from a public-payer perspective.

Methods: A health-economic model was developed to simulate lifetime outcomes from bi-annual HCC surveillance strategies in patients with chronic hepatitis B or compensated liver cirrhosis (CLC) aged 40-60. US+AFP and 'no-surveillance' were the main comparators in patients with CLC and chronic hepatitis B, respectively. Further routine surveillance strategies and scenarios were analyzed. The model was based upon the best available local data and utilized a Markov-style microsimulation framework for simulating disease progression, screening outcomes, and subsequent treatments.

Results: The model found GAAD¹ to be the dominant strategy in CLC patients over US+AFP, mostly due to its better sensitivity and specificity which are associated with higher true positive and significantly lower false positive cases. This corresponds to better health (QALYs) and lower overall costs for the healthcare system. In HBV patients and compared to 'no-surveillance', GAAD is suggested to be cost-effective with an incremental cost-effectiveness ratio (ICER) of B168,115 per QALY.

Conclusions: This economic modeling analysis suggests that GAAD appears to be a cost-effective strategy for HCC surveillance in Thailand for both CLC and hepatitis B patients when compared to various surveillance strategies.

[1] Gender, Age, AFP, DCP (PIVKA-II)

Abstract Submission No. 101535

P-0994

Impact of the novel coronavirus disease 2019 on outpatient care of liver disease

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Against the global COVID-19 pandemic backdrop, physicians had altered outpatient care, postponing regular visits to curb infection spread. This study will clarify the clinical impact of the pandemic on liver disease by analyzing patients referred to the Department of Hepatology at Nagasaki University Hospital before and during the pandemic. Defined in four periods—pre-COVID-19 (March 2019 to February 2020), early pandemic (March 2020 to February 2021), mid-pandemic (March 2021 to February 2022), and late pandemic (March 2022 to February 2023)—the study examined 509 referred cases. Results revealed a decline from 140 to 114 cases in the early pandemic, a mid-pandemic increase to 147 cases, and a subsequent late pandemic decrease to 108 cases. Post-pandemic, referred patients skewed younger. Significant variations were observed in referrals for primary liver cancer: 36 cases pre-pandemic, 24 cases early pandemic, 44 cases mid-pandemic, and 25 cases late pandemic. Hepatocellular carcinoma diagnosis stages shifted, with UICC stage III/IV cases increasing from 30% pre-pandemic to 42%, 42%, and 48% during subsequent pandemic periods.

Over the three-year COVID-19 course, changes in hepatocellular carcinoma referral patterns aligned with societal responses to pandemic phases. Trends of younger referred patients and increased advanced hepatocellular carcinoma cases suggest reduced healthcare-seeking among the elderly and potential delays in cancer detection due to screening reductions. In conclusion, continuous screening of high-risk patients is crucial during pandemics to avert delays in hepatocellular carcinoma detection.

Abstract Submission No. 101581

P-0995

Does public health insurance in Indonesia help improve health? A Systematic Literature Review

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In the majority of low- and middle-income countries (LMICs), universal health coverage (UHC) is a major health policy concern (World Health Organization 2014). National health insurance programs are gaining traction again as a result of UHC's inclusion in the Sustainable Development Goals (SDGs) for health (United Nations 2018). In Indonesia itself, the Healthy Indonesia Card program called JKN-KIS (Jaminan Kesehatan Nasional -*Kartu Indonesia sehat*) has been implemented to provide socio-economic protection to people who are part of the responsibilities and obligations of the state. JKN-KIS one of the most single payer social health insurance programs in the world, provided coverage to around 186 million people in Indonesia by the middle of 2018 (Pinto et al. 2016; BPJS Kesehatan 2017).

This study examined how the JKN program affected people's ability to receive healthcare as indicated by how often they used it. Several previous studies reveal that the JKN program has raised the likelihood that people may seek both inpatient and outpatient care. The contributing group is more affected, and this is probably because they are a wealthier and better educated population (Erlangga, et al 2019). However, the effect on visit frequency is more susceptible to time-varying variables that are not observed, suggesting that estimated treatment effects may be overestimated in relation to the actual treatment effect on visit frequency. however, the impact of this increase is more susceptible to unobserved time-varying factors. In summary, this findings

provided scant evidence in favor of the JKN program's advantages for the subsidized group.

Abstract Submission No. 101811

P-0996

Burden of cirrhosis and other chronic liver diseases due to hepatitis B in children and adolescents

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Background: The global burden of cirrhosis and other chronic liver diseases due to hepatitis B (collectively referred to as hepatitis B-associated cirrhosis in this paper) in children and adolescents must be understood and investigated.

Methods: Data were extracted from the GBD database, and calculations were performed at global, regional, and national level. We calculate the incidence, prevalence, and disability-adjusted life years (DALYs) and annual average percentage changes (AAPCs).

Results: Globally, the prevalence of children and adolescents with hepatitis B-associated cirrhosis decreased from $125,053.98 \times 10^3$ in 1990 to $46,400.33 \times 10^3$ in 2019 (Table 1, Figure 1). Compared with 1990, the incidence of cirrhosis increased in low (95.51%) and low-middle SDI areas (26.47%), whereas it decreased in other SDI areas. The AAPC of incidence has increased in low-middle SDI areas (AAPC 0.12 [95% CI: 0.04–0.20]) (Table 2, Figure 2). Individuals over 10 years old accounted for 70.6% of the incidence and 65.2% of the prevalence of cirrhosis cases in 2019 (Figure 3). At the regional level, the East Asia region has experienced the largest reduction. Conversely, Western Sub-Saharan Africa was the most serious region. Notably, South Asia was the only region where the AAPC of cirrhosis incidence (AAPC 0.77 [95% CI: 0.68–0.86]) increased.

Conclusions: Globally, the overall burden of hepatitis B-associated cirrhosis has declined significantly, but the number of cirrhosis incidence cases in low-middle and low-SDI areas has increased. The incidence in South Asia is rising, and the burden on Africa remains serious.

Abstract Submission No. 101819

P-0997

Dynamics of Liver Cancer Incidence and Mortality in Hong Kong: A Join Point Regression Analysis

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Background: Liver cancer is the fifth leading cancer in Hong Kong. We aimed to identify the temporal trends in liver cancer incidence and mortality in HK from 2001 to 2020.

Methods: Data grouped by sex and age were obtained from Surveillance of Viral Hepatitis in Hong Kong (2021 report). Joinpoint regression program (version 5.0), with annual percentage change (APC) and average annual percentage change (AAPC), was used to assess trends.

Results: Liver cancer incidence and mortality declined overall, with slower declines in older age groups. Mortality had no join points for men, but women aged 65+ experienced a faster post-2012 decline in mortality ($APC = -4.3\%$ [-8.1 to -2.6]). In terms of incidence, women aged 65+ showed four periods (jointed in 2003, 2014, 2018), with a notable increase (9.7%, 2.9 to 16.6) in 2001/2003 and a significant decrease (-7.9%, -12.3 to -5.2) in 2014/2018; men aged 20-44 and 45-64 had significant decrease in post-join points in 2018 and 2016 (-24.8% and -5.0% respectively). TDF introduction in 2008-9 and TAF in 2015-16 significantly impacted mortality in women aged 65+ but not in men, with a greater decrease post-2015/16 (-4.3%, vs. 0.8% in 2001-2008). Similar impact was observed on incidence in men of younger age groups.

Conclusion: Decrease in liver cancer incidence and mortality in HK was driven mainly by younger age groups. HBV treatment changes significantly accelerated this decline, particularly in women. Universal screening and timely HBV treatment are crucial for achieving HBV elimination in Hong Kong.

Abstract Submission No. 101859
P-0998

Assessing Pricing and Affordability of HBV Treatment in Asia-Pacific Region: Barrier to Elimination

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Background: The Asia-Pacific (AP) region carries a substantial burden of HBV. Affordable HBV treatment is crucial to attain the WHO's elimination goal. This study assesses the pricing and affordability of HBV treatment in AP.

Methods: A survey conducted among APASL members from Aug 2nd to Oct 30th, 2023, gathered data on antiviral HBV treatment costs, covering CHB, DC, CC, HCC, liver transplant, and monitoring expenses. Drug costs for TDF and ETV were compared to their production minimums (TDF: \$23, ETV: \$36), generating a minimum price ratio (MPR) where $MPR < 1$ indicated an acceptable local price. Affordability was evaluated by comparing yearly CHB treatment cost to the yearly minimum wage in each country/region, all converted to 2023 US\$.

Results: TDF costs ranged from \$42 in Pakistan to \$2,640 in Malaysia, while ETV costs varied from \$12.9 in mainland China to \$2,446 in Hong Kong. All MPR exceeded 1, except for ETV in mainland China. Affordability of HBV treatment varied, with CHB patients in Australia paying 1.4% of the minimum yearly wage to get one-year CHB treatment, in contrast to Myanmar's 118%. Affordability disparities were also evident for patients with CC, DC, HCC, and liver transplant needs, though monitoring costs were generally affordable.

Conclusions: Despite patent expiration and the availability of low-cost generics for TDF and ETV, HBV medication costs in the Asia-Pacific region remain high compared to production minimums. CHB treatment is generally unaffordable for patients, potentially posing a significant barrier to HBV elimination in this endemic region.

Abstract Submission No. 101965
P-0999

Rapid decline of acute and chronic HBV and HCV prevalence in Mongolia over the last decade

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Introduction: We aimed to assess the prevalence of HBV and HCV among apparently healthy population of Mongolia over the last 10-15 years

Method: The research was carried out by combining the statistics and health indicators of the Center for Health Development of Mongolia, articles and WHO reports.

Results: According to our research, chronic C virus infection decreased from prevalence of 15.6% in 2008, to 11.1% in 2013, 9.4% in 2017, and 0.39% in 2022-2023. Acute HCV incidence was 167 cases in 2012, 117 in 2013, 126 in 2014, 131 in 2015, 103 in 2016, 91 in 2017, 93 in 2018, 71 in 2019, 75 in 2020, and 39 in 2021 respectively, decreasing by 4.2 times from 2012.

HBsAg positivity was 8.2% in 2005, 10.6% in 2013, 4.3% in 2017-2018, and 0.23% in 2022-2023 decreasing by 35.6 times. While acute HBV incidence was 748 in 2009, 747 in 2010, 749 in 2011, 632 in 2012, 615 in 2013, 574 in 2014, 483 in 2015, 367 in 2016, 304 in 2017, 269 in 2018, 219 in 2019, 2020 143 and 60 cases in 2021 was recorded and it was 12.4 times lower than in 2009.

Conclusion:

Prevalence and incidence B and C virus infections has decreased dramatically over the years 2009-2023, which may be due to the following factors: Vaccination against the B virus. Hospital disinfection has improved and more disposable equipment is used. C virus DAA treatment was introduced in 2016. Improved public health education. This trend might be global.

Abstract Submission No. 101982
P-1000

Empowering People Who Inject Drugs for Hepatitis C Screening through Peer-Led Education

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Background/Aim: In response to the heightened risk of hepatitis C (HCV) transmission among people who inject drugs (PWID), this cluster randomized controlled trial aimed to evaluate the impact of peer-led educational workshops on HCV screening uptake. The study, conducted in communities with prevalent injection drug use, sought to assess whether a peer-led approach could effectively increase awareness, diminish stigma, and improve engagement with HCV screening services.

Methods: Clusters within high-risk communities were randomized to either receive peer-led educational workshops or standard care. Peers, individuals with lived experience in drug use, facilitated workshops covering HCV transmission, prevention, and the significance of screening. Screening uptake was monitored through healthcare records and self-reporting. Participant feedback on the peer-led approach was collected through surveys and qualitative interviews.

Results: The peer-led educational workshops yielded a remarkable 40% (95% CI: 35-45) increase in HCV screening uptake compared to the control group. Participants reported diminished stigma and heightened comfort in accessing screening services. Qualitative data underscored the unique value of peer-led education in fostering trust and understanding within the PWID community.

Conclusions: This research provides compelling evidence for the effectiveness of peer-led educational workshops in significantly enhancing HCV screening uptake among PWID. The findings emphasize the potential of community-driven interventions to address health disparities, reduce stigma, and promote active participation in essential healthcare services among high-risk populations.

Abstract Submission No. 102025
P-1001

Importance of implementation of reliable tests for HDV and HEV-infections diagnosis in Armenia

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Background: Of the five main forms of viral hepatitis, the most neglected are hepatitis caused by delta virus (HDV) and hepatitis E virus (HEV). It was estimated that globally approximately 5% of patients with chronic hepatitis B virus (HBV) infection co-infected with HDV leads to the most serious form of chronic viral hepatitis; on average, progression to cirrhosis occurs within 5 years and to hepatocellular carcinoma within 10 years. Autochthonous zoonotic HEV-infection caused by genotypes 3 and 4, is diagnosed in developed countries during last decades. HEV-infection can occur via transfusion of blood products and poorly cooked contaminated food, predominantly pork. The improvement of diagnostic techniques and increased awareness have influenced on increase EU cases since 2010.

Methods: All HBV-positive patients should be screening on HDV to improving diagnostic rates, subsequently outcomes disease and reduce the transmission of HDV. The screening of HEV RNA in blood products for transfusion and diagnosing high risk populations including pregnant women, patients with liver disease and immunocompromised patients especially in low income areas remains challenging.

Results: The prevalence of HDV-HBV-co-infection, especially in high-risk sexual behavior and intravenous drug users and HEV-infection, include HEV-associated extrahepatic manifestations remains unclear in Armenia. The problems with availability and accuracy of HDV and HEV testing contribute to underdiagnosis. The lack of international standards for serological and molecular detection result to misdiagnosing of two serious viral hepatitis.

Conclusion: It is necessary to introduce high accuracy and standardized serological and molecular assay to estimate the real burden of HDV and HEV-infections in Armenia.

Abstract Submission No. 102072
P-1002

The legal basis of treatment for Hepatitis C patients caused by stimulant use

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Background: In Japan, Hepatitis C was mostly infected through blood transfusions and the use of blood products. However, there are currently no cases of Hepatitis C virus infection associated with blood transfusions, and most cases are due to stimulant drug use.

Methods: We analyzed the reasons for infection in 51 Hepatitis C patients who received interferon-free therapy at our clinic from May 2018 to November 2023.

Results: The mean age was 60 years (± 17 years), there were 49 men and 12 women. 34 (66.7%) were stimulant users. Among those born after 1960, 21 out of 25 (84%) were stimulant users.

Discussion: Since 1989, the Japanese Red Cross Society has been conducting HCV antibody testing. The number of people infected with Hepatitis C related to medical procedures is decreasing, and the proportion of stimulant users is expected to continue rising. In Japan, most of the medical costs for antiviral therapy are covered by public insurance and welfare. For this reason, some are skeptical that large amounts of medical costs will be spent on Hepatitis C patients infected through criminal activity. However, in Japan, Article 11 of the Constitution, which came into effect in 1947, enshrines "respect for fundamental human rights," and Public Assistance Act (effect in 1950) also abolishes disqualification items (provisions that prohibit those with poor behavior from receiving protection). We should provide treatment based on political stances based on scientific insight and fairer social policies.

Abstract Submission No. 200173
P-1003

Analysis of Influencing Factors of anxiety and fatigue in patients with abnormal liver function

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Abstract】 Objective: To explore the related influencing factors of anxiety and fatigue in patients with abnormal liver function.

Methods: GAD-7 and FS-14 were used to investigate 175 patients and 40 healthy adults in the Department of Infectious Diseases of the First Affiliated Hospital of Soochow University. Two-sample rank sum test and Kruskal-Wallis test were used to explore the influencing factors of anxiety and fatigue.

Results: The score of GAD-7 in female patients was higher than that in male patients, and the difference was statistically significant ($P < 0.05$), but there was no significant difference in FS-14 score between them ($P > 0.05$). There was no significant difference in GAD-7 and FS-14 scores among all age groups ($P > 0.05$). There were statistically significant differences in the scores of GAD-7 among all etiological groups ($P < 0.05$), the scores of GAD-7 in cirrhosis group and other groups were significantly higher than those in healthy group. There were prominent differences in the scores of FS-14 among all etiological groups ($P < 0.05$), and the score of FS-14 in cirrhosis group was significantly higher than that in healthy group.

Conclusions: Female patients with abnormal liver function need psychological counseling more than male patients. Fatigue and anxiety are common symptoms in patients with abnormal liver function.

Abstract Submission No. 200211
P-1004

Gardeniae Fructus Attenuates Thioacetamide-Induced Liver Fibrosis via NF- κ B and Nrf2 Signaling

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Liver fibrosis, which means a sort of the excessive accumulation of extracellular matrices (ECMs) components through the liver tissue, is considered as tissue repair or wound-healing status¹. This pathological stage potentially leads to cirrhosis, if not controlled, it progressively results in hepatocellular carcinoma. Gardeniae Fructus (GF, the dried ripe fruits of *Gardenia jasminoides* Ellis) not only has been popularly applied to traditional medicine to treat hepatic disorders or to decrease various inflammation but also epidemically used as an excellent natural colorant. In the current study, as purposed to investigate the pharmacological properties of GF against TAA (i.p.) to induce liver fibrosis of mice model, and our data elucidated new knowledge about anti-hepatofibrotic effects of GF. GF attenuated liver fibrosis through both of AMPK/SIRT1 pathway and the Nrf2 signaling cascades. Therefore, GF could be considered a potential drug candidate for the treatment of liver fibrosis. However, further studies are needed to demonstrate its safety and toxicity for future clinical applications.

Abstract Submission No. 101198
P-1005

Enhancing Abdominal Ultrasound Training Through an Integrated Video and Testing Instruction System

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Background: Abdominal ultrasound (US) is noninvasive and highly versatile test, but it depends on the skill of the examiner and it is difficult to learn the technique. Normally, one-on-one instruction is provided, but there are problems such as it is time-consuming, puts a heavy burden on the instructor, and the instruction methods vary depending on the instructor. We have constructed a US instruction system using videos and tests with basic observation points.

Methods: In this system, one training session lasted for one hour, and one instructor taught five trainees. We conducted a trainee satisfaction survey and test to evaluate the learning effect. 1) We compared the learning effects before (n=119) and after (n=107) the introduction of the system. 2) We compared the differences in effectiveness due to differences in instructors.

Results: 1) The trainee satisfaction level (out of 10) at the end of the training was 7.1 before and 7.5 after the introduction of the system, with no significant difference (p=0.14). The test scores (out of 26) before and after the training using this system were 14 and 23 points, respectively, and the scores were significantly higher after the training

(p<0.001). 2) The test scores of instructors A and B were 20 and 18 points, respectively, with no significant difference (p=0.05).

Conclusions: This system, which uses videos and test tools, allows one instructor to instruct multiple trainees at the same time in a short period of time, and even if the instructor changes, the same content and level can be maintained.

Abstract Submission No. 200085
P-1006

Use of Gel Immersion Technique in Colonic Diverticular Bleeding

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OBJECTIVES:

1. To demonstrate the consistency of the gel
2. To compare the visibility of water from the gel once mixed with fresh blood
3. Demonstrate the effectiveness of gel immersion technique in active colonic diverticular bleeding

MATERIALS AND METHODS:

Materials:

Viscoclear gel #1, 50cc Syringe filled with fresh blood #1, Liter Glass bottles #2, Water

Methods:

Two different 1.0 Liter glass bottles were filled with same amount of water in one bottle and viscoclear in another bottle. Fresh blood in a 50cc syringe was poured on both bottles consecutively. The mixtures were observed up to 1 hour.

Clinical:

An 87 year old male with a Lower Gastrointestinal bleeding from an ascending colon diverticulosis underwent colonoscopy. Gel was flushed to the bleeding site.

RESULTS:

Water immediately mixed with blood upon contact. Gel appeared to hold and prevent blood from scattering throughout the gel medium. After 1 hour, water appeared to mix thoroughly with blood while the blood in the gel did not scatter.

Clinical:

The bleeding lesion was easily identified because the bleeding was slowly oozing from the site and did not scatter. A hemoclip was deployed on the bleeding site. Hemostasis was achieved afterwards.

CONCLUSION:

1. The gel immersion technique is an effective method of improving endoscopic visualization during active colonic diverticular bleeding

Abstract Submission No. 100353
P-1007

Efficacy and Safety of Terlipressin in the Treatment of ESLD Complicated with Intestinal Obstruction

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Background: Dynamic intestinal obstruction(DIO) is a common complication of end-stage liver disease(ESLD). Traditional treatments typically offer limited relief, which affect a patient's quality of life and overall prognosis.

Objective: To evaluate the efficacy and safety of low-dose terlipressin in treating ESLD complicated with DIO.

Method: The research was divided into the exploratory phase (January 2018 to December 2020) and the clinical study phase (January 2021 to September 2022). The DIO patients were randomly assigned to receive terlipressin or placebo. The placebo group received treatments including fasting, glycerin enema, gastrointestinal decompression, and the terlipressin group was administered terlipressin (1 mg mixed with 48 ml of 0.9% sodium chloride solution, adjusted based on patient tolerance, every 8-12 hours) in addition to the standard treatments. The differences in alleviation of DIO, time to symptom relief, and adverse reactions between the two groups were compared.

Results: From the exploratory study, 26 DIO patients treated with terlipressin, 46.2% (12/26) achieved complete relief, 42.3% (11/26) experienced partial relief. The median time for abdominal distension relief was 2.0 (1.0, 3.0) days, and the median time to anal defecation and bowel movement was 1.0 (1.0, 1.8) days. The results of the clinical study phase demonstrated that out of the total 1,120 patients admitted for ESLD, 131 (11.7%) cases were complicated with DIO. 33 were assigned to the terlipressin group and 98 to the placebo group. In the terlipressin group, the time to relief of abdominal pain and bloating, anal defecation and bowel movement was significantly shorter compared to the placebo group (2.0d vs 4.0d, 1.0d vs 3.0d, $P < 0.001$), and the rate of relief of DIO was higher than the placebo group (93.9% vs 78.6%, $P < 0.05$). Multivariate logistic regression analysis showed that enema, gastrointestinal decompression, and terlipressin use were the independent factors influencing the resolution of DIO. The incidence of adverse events was similar in both groups.

Conclusion: Terlipressin use combined with the conventional treatment notably accelerates symptomatic relief in those ESLD patients with concurrent DIO, improves both the relief rate and overall clinical prognosis, and no additional side effect.

Abstract Submission No. 101166
P-1008

Minimal Hepatic Encephalopathy in patients with Budd Chiari syndrome (BCS)

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Introduction: Prevalence of minimal hepatic encephalopathy (mHE) covert is largely unknown in BCS.

Aims and Methods: To study prevalence of mHE in BCS and its outcome following endovascular intervention. 127 newly diagnosed patients with BCS (18-65y) between July 2017 to January 2020 were included and subjected to a pencil-paper based Psychometric Hepatic Encephalopathy Test (PHET). At baseline and post intervention days 1, 7, 30, 90 and 12mo PHET scores was expressed as z scores (-3 to +1) and then analyzed as per baseline liver disease severity.

Results: Total 30 patients [27.5 (22, 32)y, 17 (56.7%) males] were included in the study. 15 (50%) had mHE at baseline. Age ($p=0.93$), MELD score ($p=0.30$), CTP ($p=0.27$), MELD Na ($p=0.25$) and total bilirubin ($p=0.44$) were similar among those with (bmHE+) or without baseline mHE (bmHE-). In bmHE- group (n=15), new onset mHE was more common at 3 months ($p=0.039$) and 12 months ($p=0.039$) but not at 7 day ($p=0.53$) and 30 day ($p=0.22$, among those with MELD ≥ 15 as compare to MELD < 15 . In bmHE+ group, baseline scores was not associated with a new onset mHE. In bmHE- group, those with

improvement/normalization of total serum bilirubin at 30 days show a significantly lower 30-day mHE ($p=0.039$) with significant correlation between the two parameters ($p=0.04$, $r=0.53$). Age at > 27.5 years was associated with higher 30 days mHE.

Conclusion: mHE is common before and after intervention in BCS. Baseline disease severity, baseline mHE, age of intervention and trend of liver functions at 30 days influence presence of mHE in BCS after therapy.

Abstract Submission No. 102026
P-1009

Very low detection limit for a novel POC test of HCV viremia using smart polymer technology

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Background and aim: We previously developed a novel technology for extraction and enrichment of HCV antigen using a thermo-sensitive smart polymer (NIPAAm-co-HIPAAm-co-SAKIPAAm) as a point of care testing which has the same diagnostic accuracy as the gold standard PCR (1). The laboratory-based Roche COBAS®TaqMan® HCV test is able to detect and measure HCV RNA down to 15 international units per milliliter (IU/ml) with $>99\%$ sensitivity. Our aim is to determine the target limit of detection (LOD) of this technology.

Method: The limit of detection or the minimal amount of the viral antigen that can be detected using the developed LFI-HCV antigen test was determined as follows: a serial dilutions of HCV recombinant core protein/1 mg/ml were tested with our novel POC test compared to HCV core protein ELISA kit results. We determined our POC limit of detection as 50 Pg/mL.

Results: The novel thermo-sensitive smart polymer technology can extract and enrich HCV antigens with Lower limit of detection of < 10 IU/ml.

Conclusion: The novel thermosensitive smart polymer technology with an LOD of < 10 IU/ml could facilitate development of an affordable POC test.

Abstract Submission No. 100232
P-1010

Influence of Stereotactic Body Radiotherapy on Hepatic Reserve Capacity in HCC patients.

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Aim: Stereotactic body radiotherapy is effective in the treatment of hepatocellular carcinoma (HCC) for intrahepatic lesions. It is especially indicated when the lesion is untreatable or unsuitable for percutaneous ablation (radiofrequency/microwave). In this study, we

investigated the effect of stereotactic radiotherapy on hepatic reserve capacity for intrahepatic lesions.

Methods: Patients underwent stereotactic radiotherapy (Cyber-Knife®) for intrahepatic lesions of HCC between April 2014 and December 2022 at our institution. Background data, tumor status, and treatment status of the treated cases were examined. The trend of hepatic reserve capacity was examined before, one month, three months, and one year after treatment.

Results: Ninety-four cases were treated during the above period. Child classification was A 82, B 9, and C 3. BCLC stage was early 3, intermediate 13, advanced 75, and terminal 3. Tumor diameter was median 28mm (range 11-56mm). The number of stereotactic radiotherapy sessions was 3-10 (5 median), and the radiation dose was 40 Gy median (range 25-75 Gy). The liver reserve markers before, 1 month, 3 months, and 6 months after treatment were 3.6 ± 0.6 , 3.6 ± 0.5 , 3.7 ± 0.6 , and 3.7 ± 0.5 for albumin, 1.0 ± 0.7 , 1.0 ± 0.4 , 1.0 ± 0.5 , and 1.0 ± 0.6 for total bilirubin, and 91 ± 18 , 92 ± 20 , 89 ± 17 , and 92 ± 13 for PT% respectively. There were no characteristics in tumor diameter, irradiation dose, or tumor localization among the patients with decreased reserve. There were no cases of post-irradiation hepatitis exacerbation.

Conclusion: Stereotactic radiotherapy for intrahepatic lesions of HCC can be performed without reducing hepatic reserve.

Abstract Submission No. 100757

P-1011

Role of palliative radiotherapy in patients with chemo unfit gallbladder cancer - Time to rethink.

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Background: Gallbladder carcinoma (GBC) usually carries a poor prognosis. Pain and jaundice (either alone or in combination) are the presenting complaints for these patients. Although palliative chemotherapy (CT) is the treatment of choice for patients who are fit to receive CT, the rest all the cases are generally kept on best supportive care only. We hypothesized that palliative radiotherapy (RT) might be a useful methodology for GBC patients who otherwise are unfit for CT. Moreover, the role of RT has scarcely been documented for this entity. The present prospective pilot clinical study thus aimed to evaluate the role of palliative RT in unresectable/chemo-unfit GBC patients.

Patients and Method: Patients presenting with jaundice and/or pain were taken up for three-dimensional conformal radiation therapy (3DCRT) to a dose of 30 Gy/10 #. The response was assessed after 6 weeks of RT using RECIST criteria version 1.1. Acute toxicities, if any were assessed on weekly check-ups. A visual analog scale (VAS) was used for the assessment of pain. Also, EORTC QLQ C30 was used for assessing the quality of life (QOL). Results were analysed statistically.

Results: N=15 patients (6 males and 9 females) with a median age of 49 years (range 42-63 years) were evaluated. 8/15 (53.33%) patients showed partial response (PR) and 5/15 (33.33%) showed stable disease (SD) after RT while 2/15 (13.33%) patients defaulted treatment in between and were lost to follow-up. Grade II skin and gastrointestinal acute toxicities were observed in 3/15 (20%) patients. A statistically significant ($p<0.05$) reduction in VAS scores and GBC mass was observed. QOL at 6 weeks also shows better scores post-RT.

Conclusion: Palliative RT seems a feasible option in GBC patients who are otherwise not fit for definitive management. We propose its routine use in such patients who otherwise are deemed unfit for definitive therapy. Studies with larger sample sizes are warranted.

Abstract Submission No. 101731

P-1012

Patients with PBC-specific antibodies and cholestasis may not be primary biliary cholangitis

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Background & Aims: Patients with positive primary biliary cholangitis (PBC)-specific antibodies and evidence of cholestasis fulfill the diagnostic criteria of PBC. However, PBC-specific antibodies can appear in various diseases, and abnormal liver biochemistry might have non-PBC origins. Do these patients have PBC? Our study focused on patients with PBC-specific antibodies and cholestatic index elevation attributable to non-PBC etiologies.

Methods: We enrolled patients with positive PBC-specific antibodies at Beijing Friendship Hospital, Capital Medical University, between February 2017 and May 2023. Changes in liver biochemistry after non-ursodeoxycholic acid (UDCA) etiological treatments were monitored via electronic medical records and/or telephone interviews.

Results: One hundred and fifty-five patients with positive PBC-specific antibodies and elevated ALP and/or GGT levels due to non-PBC diseases were enrolled. One hundred patients had non-PBC liver diseases including non-alcoholic fatty liver diseases (n=36), drug-induced liver injury (n=35), autoimmune hepatitis (n=9), and others (n=20). Fifty-five patients had non-liver diseases, predominately consisting of connective tissue diseases (CTDs) (n=28). The median follow-up was 15.9 (4.7-25.6) months, and patients taking UDCA were excluded. After treatment targeting primary diseases, 73 patients exhibited decreases in both ALP and GGT levels, eventually normalizing within normal ranges. Among patients with persistently elevated liver enzymes, 12 patients underwent liver biopsy, and no specific manifestations of PBC were observed. Additionally, 55 patients had elevated GGT levels but normal ALP levels.

Conclusion: Patients with PBC-specific antibodies and cholestasis may not be PBC. For patients with non-PBC liver diseases and CTDs, treatments of primary diseases can normalize cholestatic index instead of UDCA.

Abstract Submission No. 101739

P-1013

Shared genetic architecture between Primary sclerosing cholangitis and inflammatory bowel diseases

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Background: Several studies have found that primary sclerosing cholangitis (PSC) and inflammatory bowel disease (IBD) are closely associated. However, the direction and causality of their interactions remain unclear. Thus, this study employs Mendelian Randomization to explore whether there are causal associations of genetically predicted PSC with IBD.

Methods: Genetic variants associated with the genome-wide association study (GWAS) of PSC were used as instrumental variables. The statistics for IBD, including ulcerative colitis (UC), and Crohn's disease (CD) were derived from GWAS. Then, five methods were used to estimate the effects of genetically predicted PSC on IBD, including MR Egger, Weighted median (WM), Inverse variance weighted (IVW), Simple mode, and Weighted mode. Last, we also evaluated the pleiotropic effects, heterogeneity, and a leave-one-out sensitivity analysis that drives causal associations to confirm the validity of the analysis.

Results: Genetically predicted PSC was significantly associated with an increased risk of UC, according to the study (odds ratio [OR] IVW = 1.0014, $P < 0.05$). However, none of the MR methods found significant causal evidence of genetically predicted PSC in CD (All $P > 0.05$). The sensitivity analysis results showed that the causal effect estimations of genetically predicted PSC on IBD were robust, and there was no horizontal pleiotropy or statistical heterogeneity.

Conclusions: Our study corroborated a causal association between genetically predicted PSC and UC but did not between genetically predicted PSC and CD. Then, we identification of shared SNPs for PSC and UC, including rs3184504, rs9858213, rs725613, rs10909839, and rs4147359. More animal experiments and clinical observational studies are required to further clarify the underlying mechanisms of PSC and IBD.

Abstract Submission No. 101717

P-1014

Clinical features of immune-related liver injury caused by immune checkpoint inhibitors

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Background: Immune checkpoint inhibitors (ICIs) have been developed as promising treatments for many advanced malignancies. Despite their efficacy, ICIs occasionally induce liver injury. We revealed the clinical features of immune-related liver injury caused by ICIs (ILICI).

Methods: We evaluated the complication rates and the risk factor of ILICI in 1023 cases treated with ICIs between July 2014 and May 2022. Among those who developed ILICI, we revealed the clinical features of 40 patients whose follow-up could be observed.

Results: ILICI ($\geq$ Grade 2) occurred in 45 (4.4%) patients during the follow-up period (median 11.6 months). Factor that was significantly associated with the incidence of ILICI was use of ipilimumab [hazard ratio 11.49, $P < 0.001$]. The liver-injuries patterns of 40 patients (Grade 2, $n = 13$; Grade 3, $n = 23$; Grade 4, $n = 4$) were hepatocellular ($n = 23$), mixed ($n = 10$), or cholestatic ($n = 7$). The median period between the initial administration of ICIs and the incidence of ILICI was 62 days. Corticosteroids were administered to 29 (72.5%) patients and three with Grade 3 and one with Grade 4 needed secondary immunosuppression with mycophenolate mofetil (MMF). Furthermore, in one patient who did not improve with MMF, azathioprine was administered. Of the 39 patients in which liver injury improved, ICI was readministered in 23 patients, and ILICI relapsed in 2 (8.7%).

Conclusions: ILICI ($\geq$ Grade 2) was observed in 4.4%. In particular, attention must be paid to the incidence of ILICI in cases of ipilimumab administration.

Abstract Submission No. 100484

P-1015

Overexpressed CYP7A1 inhibits HBV replication via activating NF-kappa B pathway

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Background: Cholesterol 7 α -hydroxylase (CYP7A1) is a rate-limiting enzyme catalyzing cholesterol to synthesize bile acids, which can activate nuclear receptors to regulate hepatitis B virus (HBV) replication. However, due to the complexity of bile acid feedback regulation, the integral effects of CYP7A1 on HBV life cycle have not been fully revealed.

Methods: Different doses (0.5 μ g, 1.5 μ g, 2.5 μ g) of plasmid expressing CYP7A1 (pCYP7A1) were co-transfected with 1.3 $\times$ HBV (pHBV1.3) into Huh7 cells. Cell viability, transcription and gene expression of HBV, intracellular cholesterol levels were quantified. Total and phosphorylated protein levels of P65 were detected. After ammonium pyrrolidine dithiocarbamate (PDTC, an inhibitor of NF- κ B) treated, the indicators of HBV were reassessed.

Results: First of all, CYP7A1 overexpression at the experimental dosages didn't significantly inhibit cell viability. Compared with controls, the intracellular cholesterol level gradually decreased and was significantly lower at 2.5 μ g of pCYP7A1. Meanwhile, the levels of HBeAg and HBV DNA were reduced in the supernatant of Huh7 cells transfected with high dose of pCYP7A1. The HBsAg level decreased at 2.5 μ g of pCYP7A1, while increased at 0.5 μ g. In addition, CYP7A1 overexpression decreased the levels of intracellular HBV 3.5kb mRNA and precore mRNA. Western blot analysis showed the phosphorylated P65 protein level was downregulated at low dose of pCYP7A1 and upregulated at 1.5 μ g and 2.5 μ g dosages. And the inhibitory effect of CYP7A1 overexpression on HBV replication was partially reversed by the administration of PDTC.

Conclusions: High level of ectopic CYP7A1 expression can inhibit HBV replication by activating the NF-kappa B pathway.

Abstract Submission No. 100507

P-1016

Effects and mechanism of KDM1B on transcriptional activity of HBV covalently closed circular DNA

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Background: Lysine demethylase 1B (KDM1B) is a member of KDM family. KDM1A has been reported to cooperate with the HBx and

promote hepatitis B virus (HBV) replication. However, the effects of KDM1B on HBV have not been reported.

Methods: Plasmids pcccDNA/pCMV-Cre and pKDM1B/siKDM1B were co-transfected into Huh7 or HepG2 cells. Supernatant HBsAg/HBeAg or HBV DNA were quantified by chemiluminescence immunoassay or qPCR, respectively. Intracellular HBV RNAs and virus proteins were detected by qRT-PCR or Western Blot. Then KDM1B was knocked down in HepG2-NTCP cells, subsequently infected with HBV viral particles. Viral parameters were detected 4 days post infection. pKDM1B and pGL3-Enhancer I/BCP/Enhancer II+BCP-Luci were co-transfected into HepG2 cells. Luciferase assay was performed to determine the transcriptional activity of HBV promoter and enhancers.

Results: In human hepatoma cells, KDM1B overexpression significantly increased the levels of HBsAg, HBeAg, HBV RNAs and HBV DNA. Western blot analysis showed that KDM1B overexpression increased HBcAg/HBsAg but decreased p53 level. The results were converse after knocking down KDM1B. Consistently, knockdown of the endogenous KDM1B also significantly decreased the levels of the supernatant HBsAg/HBeAg and intracellular HBV RNAs in HepG2-NTCP cells. Luciferase assay showed that KDM1B could significantly enhance the transcriptional activity of BCP, Enhancer I, Enhancer II+BCP. Mechanistically, Western Blot analysis suggested that KDM1B overexpression could significantly reduce the protein level of HBV transcriptional suppressor p53.

Conclusions: KDM1B can promote HBV replication by mitigating inhibitory effect of p53 on the transcriptional activity of promoter and enhancers on covalently closed circular DNA.

Abstract Submission No. 100508

P-1017

Regulation and mechanism of AZI2 on HBV replication

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Background: The understanding of the interactions between hepatitis B virus (HBV) and host is still limited. It has been reported that 5-azacytidine induced 2 (AZI2) can induce the production of type I interferon. However, the role of AZI2 in HBV is elusive. In this study, we aim to clarify the effects and related mechanisms of AZI2 on HBV replication.

Methods: Plasmids pcccDNA/pCMV-Cre and pAZI2/siAZI2 were co-transfected into HepG2 cells. AZI2 was knocked down in HepAD38 cells using siRNA. The levels of supernatant HBsAg/HBeAg or HBV DNA were determined by chemiluminescence immunoassay or qPCR. Intracellular HBV RNAs and a serial of interferon stimulating genes were detected by qRT-PCR. Besides, levels of intracellular HBcAg were detected by Western Blot.

Results: In HepG2 cells, AZI2 overexpression significantly increased the level of HBsAg, HBeAg, HBV RNAs and HBV DNA. Western blot analysis showed that AZI2 overexpression could increase intracellular HBcAg. Agreed with results of AZI2 overexpression, knockdown of AZI2 decreased the levels of viral parameters in both supernatant and cell lysates. Furthermore, when AZI2 was knocked down, the mRNA level of IRF3 which can suppress HBV replication was decreased, while no significant change was observed in MX1, ISG20 and OAS2. In addition, knockdown of AZI2 also significantly decreased the levels of supernatant HBeAg/HBV DNA and intracellular HBV

RNAs in HepAD38 cells, and no significant change in mRNA levels of MX1, ISG20 and OAS2 was observed.

Conclusions: AZI2 is likely to promote HBV replication by elevating HBV RNA levels without increasing type I interferon levels.

Abstract Submission No. 101337

P-1018

Relationship between immune cells and chronic hepatitis B: A Mendelian randomization study

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Background: Chronic hepatitis B (CHB) is an immune related disease. Growing evidence has suggested that there is a close association between immune cells and the progression of CHB. However, establishing a causal relationship between immune cells and CHB remains a subject of investigation.

Methods: Based on publicly available genetic data, we conducted a two-sample, Mendelian randomization (MR) analysis to explore causal associations between 731 immune cells and CHB.

Results: We used the inverse variance weighted method as the primary analysis, and genetically predicted Sw mem %B cell (odds ratio [OR]=1.27, 95% confidence interval [CI]=1.04-1.56, $P=0.022$), IgD-CD38- %B cell (OR=1.34, 95% CI=1.09-1.65, $P=0.006$), CD39+ secreting Treg %secreting Treg (OR=1.18, 95% CI=1.05-1.32, $P=0.007$), EM DN (CD4-CD8-) %DN (OR=1.13, 95% CI=1.01-1.26, $P=0.038$), CD25 on CD24+ CD27+ (OR=1.10, 95% CI=1.02-1.18, $P=0.016$) and CD40 on CD14+ CD16- monocyte (OR=1.09, 95% CI=1.00-1.18, $P=0.041$) were associated with an increased risk of CHB. On the other hand, Plasmacytoid DC AC (OR=0.90, 95% CI=0.83-0.97, $P=0.007$), CD14+ CD16- monocyte AC (OR=0.84, 95% CI=0.73-0.97, $P=0.015$), CD14+ CD16+ monocyte %monocyte (OR=0.86, 95% CI=0.76-0.97, $P=0.012$), CD4 on EM CD4+ (OR=0.84, 95% CI=0.71-0.99, $P=0.037$) and HLA DR on CD33br HLA DR+ CD14dim (OR=0.85, 95% CI=0.73-0.98, $P=0.029$) exhibited a protective effect against CHB. The results of sensitivity analyses for these immune cells were consistent. The reverse MR analysis did not support the causal relationship between CHB and these 11 immune cells.

Conclusions: Our study has demonstrated the potential causal relationship between immune cells and CHB by genetic means, thus providing guidance for future clinical research.

Abstract Submission No. 101606

P-1019

E-CFCP exerts potent antiviral activity against drug-resistant HBV with a high genetic barrier

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Background: Nucleos(t)ide analogues (NAs) are efficacious in treating hepatitis B virus (HBV) infections; however, the multi-drug resistant HBV has been reported in chronic patients receiving long-term therapy. Here, we attempted to select *E*-CFCP-induced HBV variants and determined their susceptibility to NAs.

Methods: 1) Groups of PXB mice were inoculated with a mixture in sera obtained from 9 NAs-refractory patients and monitored the emergence of NAs resistance during *E*-CFCP treatment (5-6 passage/day504-525). 2) 1.24-fold replication-competent genotype Ce clones containing rtI91F and I91F/S223A, together with ETV resistance-associated rtS202G/L180M/M204V mutations were analyzed susceptibility to NAs *in vitro*.

Results: 1) *E*-CFCP effectively reduced the HBV viremia compared to LAM, TAF, and ETV. LAM and ETV accompanied the emergence of HBV mutations including LAM resistance-associated A181S mutation and TAF resistance-associated D134E mutation, and ETV resistance-associated V173L/L180M/M204V/M250V mutations, respectively. Particularly, two specific variants, I91F and S223A, were selected in the presence of *E*-CFCP. 2) I91F was sensitive to NAs (*E*-CFCP/EC₅₀: WT 1.4 nM, I91F 56.7 nM; ETV/EC₅₀: WT 12.1 nM, I91F 29.6 nM; TAF/EC₅₀: WT 32.8 nM, I91F 56.5 nM), in addition of the S223A mutation without altering sensitivity. ETV virtually failed to block ETVr replication, but the activity of *E*-CFCP against ETVr was comparable to that of TAF (*E*-CFCP/EC₅₀ ETVr 97.3 nM; TAF/EC₅₀: ETVr 52.5 nM; ETV/EC₅₀: ETVr 19,455.6 nM). The activity of NAs against ETVr/91 and ETVr/91/223 was also comparable to that against ETVr. *E*-CFCP and ETV showed less toxicity than TAF.

Conclusions: *E*-CFCP has a high genetic barrier to HBV development of resistance to *E*-CFCP.

Abstract Submission No. 100060

P-1020

Effectiveness and safety of TAF in chronic hepatitis B patients with decompensated cirrhosis.

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Background: TAF is a novel tenofovir prodrug which has a great amount of evidence of potent antiviral capability and good renal and bone safety. However, the administration of TAF in Chronic Hepatitis B (CHB) patients with decompensated cirrhosis (DCC) is being controversial. Meanwhile, real world studies regarding TAF in these special population are limited. Hence, our study is aimed to evaluate the effectiveness and safety of TAF in CHB patients with DCC.

Methods: This single center, retrospective study totally enrolled forty-one DCC CHB patients in the treatment of TAF 25mg daily from January, 2022 to June, 2023. The primary endpoint was the proportion of patients achieving virological response (HBV DNA < 20IU/mL) and safety of TAF at week 24. Other endpoints such as change of ALT, AST, creatinine, eGFR, Child-Pugh score (CTP), MELD score from baseline to week 24 were also observed.

Results: Among these 41 participants, 73.2% were male (n=30), mean age was 53.49 years. After 24 weeks treatment of TAF, the HBV DNA undetectable rate was 90.2% (LLOQ: 20IU/mL). The median ALT, AST and total bilirubin (TBIL) reduced significantly from 50.70U/L, 48.70U/L and 26.40μmol/L to 31.50U/L, 37.8U/L and 23.8μmol/L (p < 0.05), the median serum creatinine and eGFR were stable during the treatment. 58.6% (n=24) and 63.4% (n=26) patients experienced CTP and MELD score improvement respectively. No drug-related adverse

events or severe adverse events were detected during the treatment period, neither do liver transplantation, HCC or death.

Conclusion: This analysis demonstrated the good effectiveness and safety of TAF for decompensated CHB patients in a real-world setting.

Abstract Submission No. 100344

P-1021

Study on the effectiveness and safety of TAF in the treatment of elderly CHB patients in China

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Objectives: To investigate the effectiveness and safety of tenofovir alafenamide fumarate (TAF) in elderly (60 years and older) CHB patients and to clarify the influence of TAF on bone and renal.

Methods: 173 CHB patients were included from 2021 to 2023. Relevant indicator data were collected and analyzed.

Results: A total of 51, 44, and 20 elderly CHB patients completed the 24, 48, and 96-week follow-ups, respectively. At any time, there were no significant changes in BUN, eGFR, urinary protein, α1-MG, β2-MG, or URBP, and the serum creatinine at 96 weeks was significantly reduced (73.87μmol/L vs. 69.3μmol/L, *t* = -2.50, *P* = 0.02). From baseline to weeks 48 and 96, the difference in BMD for the lumbar spine and femoral neck was statistically significant. At week 96, the BMD for the lumbar spine and femoral neck were -0.72 SD and -1.11 SD, respectively, compared with baseline values of -1.09 SD and -1.36 SD. The complete virologic response (CVR) rate increased with extended exposure to TAF to 80%, 95%, and 100% at weeks 24, 48, and 96, respectively. Compared with baseline, HBsAg levels significantly decreased at weeks 48 (*P* = 0.02) and 96 (*P* = 0.002). The HBsAg seroconversion rates increased during the treatment with no difference.

Conclusion: After 2 years of TAF treatment in CHB patients aged 60 years and older, the BMD of the lumbar spine and femoral neck significantly improved, and the serum creatinine significantly decreased. The CVR rate gradually increased, and the HBsAg levels significantly decreased.

Abstract Submission No. 100376

P-1022

Conversion Strategies in chronic hepatitis B patients with Low-level Viremia: A Multi-Center Study

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Background: Low-level viraemia (LLV) may contribute to drug resistance, exacerbate liver fibrosis, and increase hepatocellular carcinoma risk. However, there's limited data on interferon therapy combined with NAs in LLV patients.

Aim: Our study aims to assess the efficacy and influencing factors of different conversion strategies for treating LLV patients.

Methods: We retrospectively collected data from 97 LLV patients. Patients were divided into three groups according to their continued antiviral treatment: NAs (n=34), NAs+NAs (n=16), NAs+IFN (n=47). We compared complete virological response(CVR), HBV DNA and HBsAg decline, laboratory indicators, and liver stiffness after 96 weeks of treatment. Factors influencing CVR at 96 weeks in LLV patients were analyzed.

Results: At 48 weeks, there were no significant differences among the three groups ($P>0.05$). At

96 weeks, CVR rate was significantly higher in the NAs+NAs and NAs+IFN groups compared to the NAs group (87.5% vs. 55.88%, 89.36% vs. 55.88%, $\chi^2=13.742$, $P=0.001$). For liver cirrhosis, continuation of the original plan, 48-week HBV DNA, and HBsAg were independent risk factors for non-negative at 96 weeks ($P<0.05$). The AUC of HBV DNA combined with HBsAg was 0.825 (95% CI: 0.731-0.918) with a cutoff value of 0.10 log₁₀ IU/ml. the HBsAg decline in the NAs+IFN group was significantly higher than in the NAs group and NAs+NAs group ($P<0.05$). Three patients in the NAs+IFN group achieved HBsAg negative conversion.

Conclusion: Combining another NAs or IFN therapy effectively improves the 96-week CVR rate in LLV patients after NAs treatment. Furthermore, combined IFN therapy significantly enhances decline the HBsAg levels.

Abstract Submission No. 100505

P-1023

48 weeks of initial treatment with TMF versus TAF for patients with CHB: a retrospective study

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Background: Tenofovir amibufenamide (TMF) utilizes innovative ProTide technology and a methylation strategy to add a methyl group to the amide bond group compared to tenofovir alafenamide (TAF), which improves lipid solubility and maintains higher stability in plasma. The Phase III clinical registration trial of TMF has shown that it has good antiviral efficacy. However, there is still limited clinical data on TMF in the real world.

Objective: To compare the antiviral efficacy and safety of TMF and TAF in the initial treatment of patients with high viral load chronic hepatitis B (CHB).

Methods: Clinical data of high viral load CHB patients who received initial antiviral treatment with TMF (n=58) or TAF (n=32) monotherapy in the outpatient department of Beijing You'an Hospital from March 2022 to June 2022 was collected retrospectively and the efficacy and safety of antiviral therapy for 48 weeks between two groups were compared.

Results: The baseline HBV DNA levels in the TMF group and TAF group were 7.85 IgIU/ml and 7.44 IgIU/ml, respectively ($P=0.343$). Compared with the baseline, the decrease in HBV DNA levels between the two groups after 4 weeks, 12 weeks, 24 weeks, and 48 weeks of antiviral treatment was 3.65 IgIU/ml vs 3.70 IgIU/ml ($P=0.863$), 4.63 IgIU/ml vs 4.84 IgIU/ml ($P=0.329$), 5.82 IgIU/ml vs 5.77 IgIU/ml ($P=0.817$) and 6.85 IgIU/ml vs 6.38 IgIU/ml ($P=0.071$) with no significant statistical difference. The HBV DNA clearance rates (<10 IU/ml) of the TMF and TAF treatment for 48 week were 41.5% (22/53) and 40.0% (12/30) respectively. The baseline median ALT levels in the TMF and TAF treatment groups were 102.0 U/L (56.0 U/L, 210 U/L) and 195.0 U/L (73.5 U/L, 371.0 U/L), respectively ($P=0.071$). The normalization rates of ALT at 12 weeks, 24weeks and 48 weeks

were 65.2%, 86.1%, 93.4%, vs 58.3%, 81.6%, and 92.7% respectively. Compared with baseline, there was no significant statistical difference in serum Cr, eGFR, and lipid levels between the two groups at 24 and 48 weeks ($P<0.05$).

Conclusion: Both TMF and TAF can achieve good antiviral efficacy and safety in newly treated CHB patients with high viral load.

Abstract Submission No. 100882

P-1024

The interim analysis of E-Cure study for inactive hepatitis B surface antigen carriers in China

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Objective: To investigate the efficacy of different Peg-IFN α based treatment strategies of inactive HBsAg carriers.

Methods: A multi-center real world study (E-Cure study) of 103 hospitals started in January 2022. The study enrolled inactive HBsAg carriers (IHCs) consistent with the definition of inactive CHB in the guideline of AASLD 2018. The patients received one of the following treatments: NAs monotherapy, Peg-IFN α monotherapy, Initial combination therapy (Peg-IFN α -2b with NAs for 12-24w followed by Peg-IFN α -2b monotherapy), Whole process combination therapy (combination of Peg-IFN α -2b and NAs for the entire period) and Sequential combination therapy (NAs for 12-24w followed by Peg-IFN α -2b add-on).

Results: By June 2023, 927 patients who completed 12 weeks of treatment and had completed clinical information were included in this analysis, of whom 671 completed 24 weeks of treatment. The HBsAg clearance rate at 12w and 24w were 11% and 22.1% ($P<0.001$), with no significant difference between five treatment groups (0%, 11.5%, 4.1%, 12.2%, 13% at 12w; 0%, 23.8%, 14.6%, 20.4%, 11.1% at 24w, respectively). Further stratified analysis was performed according to baseline HBsAg levels (<10 , 10-100, 100-1000, >1000 IU/mL). The HBsAg clearance rate were 35.9%, 10.5%, 1.9% and 0% at 12w ($P<0.001$) and 54.6%, 26.6%, 10.1% and 1.6% at 24w ($P<0.001$).

Conclusions: Peg-IFN α based treatments result in a high HBsAg clearance rate, especially in patients with low HBsAg level. The in-depth antiviral study of IHCs is valuable.

Abstract Submission No. 100956

P-1025

Hepatitis B serological screening: A single centre experience

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Background: Profiling of Hepatitis B virus infection (HBV) involves HBsAg, anti-HBc (total) and anti-HBs (titre) serological markers. Standard protocol involves routinely screening for HBsAg alone to identify HBV infection. This protocol can fail to provide information on occult Hepatitis B infection, past HBV infection and HBV vaccination status.

Aim: To determine the profile of chronic HBV infection using HBsAg, anti-HBs (titre) and anti-HBc (Total) serological markers.

Method: Patients registered in the Hepatology outpatient clinic between Jan 2018 and June 2022 were categorized as incidental HBV infection (HBsAg positive; anti-HBc (total) positive), past infection {anti-HBc (Total); anti-HBs positive}, occult HBV infection (HBsAg; anti-HBs negative, anti-HBc (total) positive), unprotected (all three markers negative), and those vaccinated (anti-HBs titre of ≥ 10 IU/L).

Results: Of the 931 patients registered, 637 were men (68.4%) and 294 were women (31.6%). 510 patients (54.9%) were incidental HBsAg positive, 55 (6%) had past infection, and 56 (6%) were anti-HBc (total) positivity (raised HBV DNA (100 IU/mL) in one). A significant number of patients between 41 to 59 years had present (p-value .00004) or an occult HBV infection (.0029). 37 had serological protective anti-HBs titre; 22 (59.5%) were < 40 years old (p-value .00015).

Conclusion: Approximately 12% of patients had either a past (5.9%) or an occult HBV infection (6%). Do these subsets of patients require a protocol surveillance for hepatocellular carcinoma? Is there a likelihood of reactivation in an immunocompromised state or under treatment with potent biologicals? These questions remain unanswered.

Abstract Submission No. 101135

P-1026

PegIFN alpha-2b in HBeAg negative CHB patients with normal ALT: A multicenter real-world study

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Background: The purpose of this study was to analyze the efficacy of pegylated interferon alpha-2b (PegIFN alpha-2b) in HBeAg negative CHB patients with normal ALT, and to explore the predictive factors of virological and serological responses.

Method: This is a multi-center, prospective, non-interventive, real-world clinical study conducted in China, involving 20 hospitals in 12 provinces or municipalities, which enrolled CHB patients with age of 18-60 years, HBsAg positive for more than 6 months, HBeAg negative, HBV DNA > 20 IU/mL and normal ALT, without antiviral treatment history. PegIFN alpha-2b 180 µg/week was applied.

Results: 53 patients with complete data collection have been summarized for 24 weeks of treatment. The median baseline HBV DNA was 1.01×10^3 IU/mL (Figure 1a), the median baseline HBsAg was 657.22 IU/mL (Figure 1b). After 24 weeks of PegIFN alpha-2b treatment, the median HBV DNA was 0 IU/mL, and the rate of HBV DNA negative was 62.3% (Figure 1c), the median HBsAg was decreased to 106.45

IU/mL, and the HBsAg loss rate was 11.3% (Figure 1d). The patients with HBV DNA undetectable at treatment week 24 had much lower baseline HBsAg level (p = 0.032). The rate of HBV DNA negative at 24 weeks was 71.1% in patients with baseline HBsAg ≤ 1500 IU/mL (p = 0.036).

Conclusion: For HBeAg negative CHB patients with normal ALT, PegIFN alpha-2b treatment for 24 weeks can achieve a high rate of HBV DNA negative and significant HBsAg decrease, even HBsAg loss.

Abstract Submission No. 101241

P-1027

Long-term outcomes of HBeAg-positive grey-zone patients

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Background and aims: HBeAg-positive patients consisted of immune tolerant (IT) and immune active (IA) groups. Recently, a more detailed classification beyond the original criteria of ALT levels or HBV DNA levels has placed these patients into a grey-zone (GZ). It remains unclear whether these patients will demonstrate different long-term outcomes from the conventional group.

Methods: Out of 256 HBeAg-positive IT and IA patients in a naive cohort from our hospital (published in year 2011) 201 without HCC were finally analyze. Currently, IT was strictly re-defined as HBV DNA >10⁷ IU/mL and ALT <40 U/L, while IT-GZ was defined by HBV DNA >10⁷ IU/mL and 40 ≤ ALT <80 U/L. IA was defined as ALT >80 U/L regardless of HBV DNA levels, IA-GZ defined by HBV DNA <10⁷ IU/mL and ALT <80 U/L. We evaluated the rate of de novo HCC development and cumulative rate of antiviral therapy (AVT) of IT versus IT-GZ, IA versus IA-GZ groups.

Results: Of the 59 original IT patients, 39 were in the strict IT group and 20 were in the IT-GZ group. Of the 142 original IA patients, 93 were in the IA group and 49 were in the IA-GZ group. Both GZ groups had significantly lower levels of HBsAg, HBeAg, HBV DNA levels and platelet levels than IT and IA patients (P<0.01). The IA-GZ group was older in the IA group.

During a long-term follow-up period (9.1 ± 4.4 year), 18 patients developed HCC (8 in IA, 10 in IA-GZ, and only 1 in IT-GZ). De novo HCC in IA-GZ group was slightly higher than in the IA group (P=0.040). At the baseline, starting rate of AVT in IA was higher in IA-GZ but de-novo AVT rate in IA-GZ was higher in IA. Finally, the cumulative rate of AVT was not significantly different between IT and IT-GZ, or IA and IA-GZ. In the IA group, de novo AVT or no AVT during follow-up compared to the starting AVT at baseline, was a significant risk factor (HR 4.747, P=0.035) for HCC development but not in the IA-GZ group (P=0.099). For the predicting the HCC in IA/IA-GZ group, male gender, HBeAg titer <200 IU/mL, HBV DNA <10⁷ IU/mL, and ALT <80 U/L were significant variables.

Conclusions: The present study showed the long-term outcomes of IT and IA phase of HBeAg-positive patients including those in the GZ. In the re-defined phases, there was only one case of HCC development in IT-GZ group. The IA-GZ group had slightly higher HCC development than the IA group.

Abstract Submission No. 101652

P-1028

Genomic landscape of non-Hodgkin lymphoma patients with current or past hepatitis B virus infections

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Background: As hepatitis B virus (HBV) infection is a risk factor for non-Hodgkin lymphoma (NHL), we aimed to assess the effect of current or past HBV infections on the development of NHL.

Methods: Patients who were diagnosed with NHL and underwent targeted next-generation sequencing (NGS) for NHL tissue at Seoul National University Hospital between 2019 and 2022 were consecutively enrolled. Targeted NGS was performed for 166 NHL-related genes to detect single nucleotide variant (SNV). Current and past HBV infections were defined by a positive HBV surface antigen (HBsAg) and a positive HBV core antibody (HBcAb) with a negative HBsAg, respectively. The incidence of SNV was compared among three groups.

Results: A total of 252 patients were included for analysis. The incidence of *MYD88* (control vs. current HBV infection vs. past HBV infection: 14.0% vs. 34.8% vs. 30.0%; $P=0.005$), *PIM1* (16.3% vs. 34.8% vs. 29.0%; $P=0.03$), and *MYC* (3.1% vs. 8.7% vs. 12.0%; $P=0.03$) gene mutation was significantly higher in the current or past HBV infection group compared to the control group. On the other hand, the current HBV infection group showed significantly higher incidence of *ATM* (4.7% vs. 13.0% vs. 0%; $P=0.004$), *BCL10* (3.9% vs. 17.4% vs. 6.0%; $P=0.046$), and *BIRC3* (0.8% vs. 13.0% vs. 0%; $P=0.003$) gene mutation than the other two groups.

Conclusion: Although current or past HBV infections share some of the gene mutations associated with the development of NHL, current HBV infection exhibited other distinct gene mutations.

Abstract Submission No. 100074

P-1029

HCV elimination: Relink of diagnosed but untreated patients in Yining City.

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Background: Identifying of HCV-infected patients but untreated (DBU) has been shown to be a rapid and effective strategy to improve the diagnosis and treatment rates, contributing to the WHO goal of HCV elimination by 2030.

Objective: To establish an optimal model for the management of DBU patients and linkage to treatment.

Methods: All HCV antibody positive patients were extracted from the local Center for Disease Control and Prevention (CDC) database and universal screening in Yining city, call-back approach (by telephone) were applied for all DBU patients, the designated hospital was responsible for HCV RNA testing and linkage to treatment and the patients who did not come to the hospital for further diagnosis or treatment would be reported back to the local CDC, then community health services workers will be triggered by the local CDC to provide on-site service to improve the lost patients linkage to care.

Results: A total number of 1197 HCV DBU patients were included. Of these, 431(36%) patients were successfully recalled and tested for HCV RNA, 766(64%) patients were unable to be connected, and 267(62%) patients were HCV RNA positive, 141(53%) active HCV patients were initiated DAAs treatment and 63(45%) have achieved

SVR12 until now, others were followed up, no patients experienced treatment failure.

Conclusions: This local CDC-initiated model involving designated hospital and community health services, using decentralization and task sharing, is highly effective in identifying more active HCV patients and relinking them to treatment.

Abstract Submission No. 100109

P-1030

Impact of antiviral therapy on HCV-infected patients with unresectable hepatocellular carcinoma

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Background: Direct-acting antiviral agents (DAAs) are the recommended treatment for HCV infection, with a benefit in reducing incident hepatocellular carcinoma (HCC) and patients' mortality. The aim of this study was to evaluate the affecting factors of survival outcomes in the patients with BCLC stage B/C HCC and HCV underwent DAA therapy.

Methods: Data for subjects with BCLC stage B/C HCC and HCV receiving DAA therapy at Taichung Veterans General Hospital and Taipei Veterans General Hospital from January 2017 to April 2022 was collected respectively.

Results: Among the 197 enrolled patients, the SVR rate was 93.9%. Logistic analysis found non-significant association between clinical variables and fail to achieve SVR. The clinical presentations of Child-Pugh B ($P=0.001$), viable ($p=0.003$) or progressive HCC ($P=0.009$) and non-SVR ($p=0.001$) had significant poor impacts to survival outcomes. The median OS of the patients with SVR and those with non-SVR to DAA therapy were 4.36 years and 1.71 years respectively. The stratified analysis showed that achieving SVR had a significantly impact to decrease risk of death in most patients, but not in the group of Child-Pugh B, ALBI grade 2/3, FIB4>3.25, BCLC stage C, progressive HCC and AFP>400.

Conclusion: The SVR rate of patients with BCLC stage B/C HCC receiving DAA therapy was high. Achieving SVR to DAA therapy was associated with better survival outcomes in these patients, but this benefit was lost in the subjects with severe cirrhosis stage or progressive HCC.

Abstract Submission No. 100129

P-1031

Retreatment of GT3b cirrhotic hepatitis C patients who failed a regimen with NS5A-containing DAAs

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Currently, patients with TN and TE genotype 3 have low SVR rates for DAA, especially cirrhotic chronic hepatitis C patients with genotype 3b. Its retreatment strategy for this special population is still

challenging. We report one case of failed treatment of DAAs containing NS5A inhibitors, who received SVR after 12 weeks of treatment with Sofosbuvir/Velpatasvir and ribavirin.

Case, a male, 50 years old, chronic hepatitis C cirrhotic patient, genotype 3b, took oral Sofosbuvir 400 mg/d, daclatasvir 60 mg, and ribavirin 1000mg/time, once a day for 24 weeks. The patients personally cut down the ribavirin dose after a few days to 400mg. RNA viral load less than 15 IU/ml at 4, 12, and 24 weeks of treatment. However, after 12 weeks of treatment, the viral load had increased to 6.76×10^2 IU/ml. Two mutations of L31M and A30K were found. 4 months later, initiation of salvage therapy with Sofosbuvir/Velpatasvir 1 tablet/d + ribavirin 1000 mg/d for 24 weeks. SVR12 was obtained.

The patient was infected with HCV genotype 3, which is currently one of the most difficult genotypes to treat in the field of DAA therapy and was co-infected with cirrhosis and drug-resistant variants. The patient self-reduced the dose of ribavirin during the treatment period, but the dose was insufficient, which caused the relapse. This suggests that in the treatment of hepatitis C, the dose and duration of ribavirin may be closely related to relapse and that an adequate dose and duration of ribavirin are essential.

Abstract Submission No. 100175

P-1032

HCV Reinfection in High-Risk Patients Following DAA Therapy – Real-World Data from a Medical Center

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Background: HCV reinfection in high-risk patient groups, such as people living with HIV (PLWH), individuals engaging in injection drug use (PWID), and those undergoing hemodialysis (HD), remains a significant concern even after achieving sustained virologic response (SVR). This study presents real-world data from a medical center regarding reinfection rates in these specific populations.

Methods: This retrospective study focused on three high-risk groups of HCV patients who achieved SVR12 after DAA therapy between January 2018 and June 2022. HCV RNA levels were rechecked at least once after SVR12, and reinfection was defined as the recurrence of detectable viremia post SVR12.

Results: A total of 140 HCV patients were recruited, including PLWH from sexual transmission (n=22), PLWH combined with PWID (n=51), PWID (n=36), and individuals undergoing HD (n=31). The number of patients experiencing reinfection was 3 in PLWH from sexual transmission, 6 in PLWH combined with PWID, 6 in PWID, and 0 in HD, respectively. The incidence of reinfection was 6.1 per 100 person-years of follow-up (PYFU), 5.3 per 100 PYFU, 6.7 per 100 PYFU, and 0 per 100 PYFU in each group. The median time to reinfection was shorter in PWID (1.79 years) and PLWH combined with PWID (2.55 years) compared to PLWH from sexual transmission (3.17 years).

Conclusions: The reinfection rate remains notably high in PLWH and PWID groups. Effective HIV prevention programs and syringe services programs are still crucial in addressing the needs of these high-risk populations.

Abstract Submission No. 100257

P-1033

Lysyl oxidase-like 2 as a predictor of hepatocellular carcinoma after HCV eradication.

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Background: The lysyl oxidase-like 2 (LOXL2) is an enzyme for crosslinking extracellular matrix, reflecting qualitative changes in liver fibrosis. The present study aims to verify the usefulness of LOXL2 as a predictive biomarker for hepatocellular carcinoma (HCC) development after achieving sustained virological response (SVR) in patients with chronic hepatitis C virus (HCV) infection.

Methods: This retrospective study included 137 patients with chronic HCV infection without a history of HCC development who achieved SVR with direct acting antivirals between 2014 and 2016. Post-SVR HCC development was investigated until December 2022. Serum LOXL2 levels at pre-treatment (pre-Tx) and 24 weeks after the end of treatment (post-Tx) were measured. The usefulness as a predictor of post-SVR HCC development was compared with previously reported markers.

Results: The median LOXL2 levels decreased significantly after SVR achievement (pre-Tx; 2.33, post-Tx; 1.31, $p < 0.001$). During the observation period, 20 patients developed post-SVR HCC; the cumulative incidence at 3 years was 11.0%. LOXL2 ≥ 2.08 ng/mL, FIB-4 index ≥ 2.9 , platelet counts $\leq 120 \times 10^9/L$, WFA⁺-M2BP ≥ 1.0 cut-off index, and AFP ≥ 5 ng/mL at post-Tx were identified as independent predictive factors for post-SVR HCC in the univariate analysis. Furthermore, patients with both LOXL2 ≥ 2.08 and AFP ≥ 5 had a significantly higher incidence of post-SVR HCC than patients with either LOXL2 ≥ 2.08 or AFP ≥ 5 and patients with both LOXL2 < 2.08 and AFP < 5 .

Conclusion: LOXL2 can serve as a predictive biomarker for post-SVR HCC development. The combination of LOXL2 and AFP levels enables risk stratification of post-SVR HCC, suggesting an enhanced surveillance strategy.

Abstract Submission No. 100271

P-1034

The epidemiological and clinical characteristics of hepatitis C virus infection in Dongguan City

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Background: Aims to provide evidence for the subsequent regional hepatitis C elimination and appropriate treatment for those affected.

Methods: We conducted a retrospective analysis of 617 HCV RNA positive patients in Dongguan from October 2020 to December 2022. Demographics, genotype and transmission route of hepatitis C were investigated.

Results: Of the 617 HCV RNA-positive patients, 69.2% were males, with a median age of 46 years. The proportion of 33-59 years old is the highest, accounting for 80.4%. Genotype 1,3 and 6 are the common genotypes, accounting for 37.4%, 18% and 28.2% receptively. The proportion of patients infected by unknown route was the highest (38.1%), while the proportion of patients infected by intravenous drug addiction, blood transfusion, sexual transmission and other invasive operations was 27.4%, 23.8%, 2.4% and 13.3%, respectively. Genotype 3 and 6 were more common among patients infected through

intravenous drug use (34.9% and 43.8%). Genotype 1 was more common in patients infected by blood transfusion (66.4%), while genotype 1, 3 and 6 were more common in patients infected by sexual transmission (35.7%; 17.9% and 32.1%), and the genotype 1 and 6 were more common in patients infected by other invasive procedure (43.4%, 25.3%), and the difference among the groups was statistically significant ($P < 0.05$).

Conclusion: Hepatitis C antibody screening in residents aged 33-59 years can significantly improve the screening efficiency of HCV. The proportion of HCV infection with unknown transmission route was gradually increasing, highlighting the needs for management and treatment of the population of high-risk of HCV population.

Abstract Submission No. 100362

P-1035

Treatment cascade of hepatitis C virus infection in patients undergoing surgery

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Background: A lack of awareness compromises appropriate consideration of hepatitis C virus (HCV) infections in patients undergoing surgery. We evaluated the status of HCV screening, confirmation, and treatment in patients undergoing surgery.

Method: Patients who underwent surgery in a tertiary academic center between 2019 and 2021 were eligible for this retrospective study. The testing and positivity rates for anti-HCV antibodies and HCV RNA were analyzed.

Results: Among 96,894 patients (40,121 males, 41.4%) who underwent surgery under general anaesthesia, 83,920 (86.6%) were tested for anti-HCV antibodies before surgery. Of these patients, 576 (0.7%) were positive for anti-HCV antibodies and had significantly higher rates of diabetes mellitus (32.6% vs. 18.5%), hypertension (50.5% vs. 28.6%), liver cirrhosis (13.2% vs. 1.7%), and unfavourable laboratory test results compared with those who were negative (all $P < 0.05$). The HCV RNA status was assessed in 215 (37.3%) of the anti-HCV antibody-positive patients, and the rate of HCV RNA positivity was 20.5% ($n = 44$ of 215). Of these 44 patients, 42 (95.5%) were referred for treatment, and all 29 treatable patients were successfully treated with direct-acting antiviral therapy. The HCV RNA positivity rate was significantly higher in the hepatobiliary and transplant surgery department (76.6%) than in other surgical departments (25.0–33.5%).

Conclusion: A significant number of preoperative anti-HCV antibody-positive patients did not receive appropriate HCV management. An automated alert system may be required.

Abstract Submission No. 100752

P-1036

HBV Reactivation Among Patients with HCV During Direct Acting Antiviral Therapy in Guizhou, China

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Background: This study aims to assess the risk of HBV reactivation and disease progression during direct-acting antiviral (DAA) therapy.

Methods: A retrospective analysis was conducted on the patients treated with DAA at the Guizhou Public Health Treatment Center between January 2018 and December 2022. HCV RNA, liver function, HBV markers, and HBV DNA, were assessed before and after DAA therapy.

Results: 1652 HCV patients were enrolled, 5.08% (84/1652) were HBsAg positive, and 44.79% (740/1652) had HBV exposure (HBsAg-negative/HBcAb-positive, HBV DNA < 20 IU/ml). Compared to mono-infection, HBsAg positive patients had a higher proportion of males, liver cirrhosis and HCC, and lower platelet counts ($\chi^2=15.482, 46.101, F=7.292$, all $P < 0.05$). The incidence of HBV reactivation was 16.67% (9/54) among HBsAg-positive patients and 0.1% (1/740) among those with a history of HBV infection. Baseline HBsAg levels were higher in patients who experienced HBV reactivation than in those who did not ($Z=-4.291, P < 0.05$). Moreover, patients with baseline HBsAg levels < 185 IU/ml have an extremely low risk of HBV reactivation. After HBV reactivation, there were no differences in liver function, platelet counts, or other parameters compared to baseline ($P > 0.05$), and no cases of liver failure were identified.

Conclusion: The prevalence of HBsAg positivity among HCV-infected individuals in Guizhou is higher than in other regions of China. There is a substantial proportion of individuals with a history of HBV infection. HCV/HBV coinfecting patients treated with DAA therapy may experience HBV reactivation, but the disease progression risk is relatively low.

Abstract Submission No. 100783

P-1037

Elimination of HCV in women of childbearing age at hospital in southern China

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Background: The disease burden of HCV infection in women of childbearing age is high in low - and middle-income countries. Data on HCV elimination in this population is lacking.

Methods: We initiated the "Program for the Elimination of Hepatitis C Virus in Women of Childbearing age". This program provided primary healthcare practitioners with education related to HCV disease and treatment and distributes corresponding promotional materials. Also, we cooperated with the IT department to build data collation platform for this program. Patients who are HCV-Ab (+) are called back by phone to complete the HCV RNA test. HCV RNA positive patients are reminded by phone to return to the hospital for antiviral treatment. Meanwhile, HCV RNA positive patients within the hospital are automatically referred to liver disease specialists, and subsequent treatment plans are developed for them.

Results: From January 2017 to January 2023, there are 458 women of childbearing age are enrolled in this project, 267 women with positive HCV antibodies, 191 women with HCV RNA positive. From February 2023 to August 2023, 152 of the 458 childbearing aged women were successfully contacted by phone, and 14.5% (22/152) patients were successfully call back to the hospital. Out of the 14.5% (22/152) HCV RNA positive patients, 5.3% (8/152) have initiated antiviral treatments, and a further 23.7% (36/152) patients have agreed to come to the hospital for antiviral treatments in the near future.

Conclusion: Many women of childbearing age with HCV infection have not received effective treatment. A clear callback plan can effectively clear Hepatitis C in this population.

Abstract Submission No. 101431
P-1038

Analysis of Hepatitis C Virus Infection in Women of Childbearing Age in Jilin Province, China

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Background: With the encouragement of China's birth policy, the second-child birth rate has gradually increased in recent years, which means more older women may choose to give birth again. Focusing on the prevalence of hepatitis C virus (HCV) infection in women of childbearing age can help further reduce the progression of liver disease in women of childbearing age and reduce the rate of mother-to-child transmission of HCV.

Method: In this study, women of childbearing age (defined as 20-49 years old) who underwent anti-HCV testing in our hospital from January to September 2023 were included. Patients with positive anti-HCV antibodies were tested for serum anti-HCV RNA using fluorescence quantitative PCR.

Results: A total of 14,279 women of childbearing age underwent anti-HCV testing, and 355 were positive for anti-HCV. Among them, 239 patients underwent further HCV RNA testing, and 70 cases were positive for HCV RNA, with a positive detection rate of 29.29%. In the 20-29 years old group, 30-39 years old group, and 40-49 years old group, the positive rates were 15.79%, 27.59%, and 32.33%, respectively.

Conclusion: With increasing age, the positive detection rate of HCV RNA in women of childbearing age significantly increased. Strengthening attention to the prevalence of hepatitis C in women of childbearing age can help further reduce the progression of liver disease in women of childbearing age and the mother-to-child transmission of HCV, which is of extremely important practical significance.

Abstract Submission No. 101445
P-1039

An Innovative Management Mode of Integrated Prevention and Treatment of HCV in Jilin Province

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Background: To further strengthen the prevention and treatment of hepatitis C, reduce the prevalence of hepatitis C and the incidence of liver cancer, we developed a research system for an innovative management mode of integrated prevention, detection, and treatment for hepatitis C public health hazards in the First Hospital of Jilin University. The aim of this study is to verify the effectiveness of this system.

Methods: The hospital has implemented various methods for integrated management, include improving relevant work systems for hepatitis C prevention and treatment, carrying out health education on hepatitis C testing, including hepatitis C screening rates in clinical departments into hospital performance assessment, and publicizing the results throughout the hospital. The detection rate of HCV RNA of inpatients with (data from January to September 2023) or without the new management model (data from January to September 2021) were compared.

Results: From January to September 2023 and January to September 2021, hepatitis C antibody testing was carried out in 114926 and 98259

inpatients, respectively, with 1920 (1.67%) and 1875 (1.82%) positive cases. Among them, HCV RNA testing was carried out in 1048 (54.58%) and 867 (48.57%) patients ($P < 0.05$), with 332 (31.68%) and 226 (26.07%) positive cases, respectively ($P < 0.05$).

Conclusion: Through the hospital's innovative management mode of integrated prevention, detection, and treatment for hepatitis C public health hazards, it can effectively improve the detection rate of HCV RNA in anti-HCV positive inpatients.

Abstract Submission No. 101697
P-1040

The Significance of DAA Therapies in Patients with Chronic HCV Infection Complicated by HCC

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Aim: Patients with previous HCC due to HCV infection remain at a high risk of HCC recurrence even after achieving SVR. Furthermore, there are no clear guidelines regarding antiviral therapy in patients with unresectable HCC. We evaluated the significance of DAA therapies in such patients.

Methods: A total of 1,196 patients that underwent DAA therapy after September 2014, with a follow-up observation of at least one year after SVR, were subjected. The subsequent clinical course was retrospectively analyzed.

Results: The cumulative rates of HCC development after SVR (1-, 3-, 5-year) were higher in patients with previous HCC ($n=82$) at 24%, 60%, 73%, compared to those without HCC ($n=1,116$) at 1%, 4%, 7% ($P < 0.0001$). Among patients with previous HCC, 56 patients experienced HCC recurrence over median interval of 33 months. Recurrence was associated with initial HCC treatment involving TACE (HR 3.93, $P=0.0019$) and RFA (HR 2.62, $P=0.0141$). At the time of HCC recurrence, the frequency of mALBI-2b or higher at HCC recurrence decreased from 52% at DAA therapy to 14% ($P < 0.0001$). With BCLC C (HR 53.70, $P < 0.0001$) and mALBI-2b or higher (HR 2.64, $P=0.0401$) were associated with outcome. Two patients with unresectable HCC and complications of esophageal varices and refractory ascites, making treatment impossible, later achieved SVR with SOF/VEL, and they became eligible for combination immunotherapy and radiation.

Conclusion: Achieving SVR improves liver function, enabling HCC treatment upon recurrence. Thus, in patients where the disease stabilizes after HCC treatment, prompt implementation of DAA therapy is advisable.

Abstract Submission No. 101415
P-1041

Non-Invasive Approaches to Liver Function Management Study

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Background: While effective strategies exist for managing hepatitis B and C viruses in our country, Delta hepatitis remains a severe and complex viral liver disease. Promisingly, non-invasive tests exhibit potential for early liver disease detection without requiring a biopsy. Currently, the only treatment for HDV is PEG-Interferon administered for 48-72 weeks, which has little therapeutic effect.

Material and method: This cross-sectional study involved 28 outpatients with liver fibrosis at the Mongolia-Japan Hospital of the Mongolian National University of Medical Sciences from July to August 2023. Serum levels of platelet count, prothrombin time, bilirubin, AST, ALT, albumin, and cholesterol were analyzed. Additionally, we calculated the AST-to-platelet ratio index (APRI) and FIB-4. Descriptive analysis characterized the data using SPSS version 19.0.

Result: Patients with viral hepatitis comprised 2.6% of the 1056 outpatients in our hospital. The majority of the patients (78.6%) had hepatitis B and Delta (HBV and HDV) co-infection, while patients with hepatitis B and hepatitis C accounted for 14.8% and 17.9%, respectively. The age range of the patients was 24 to 52 years, with no significant difference in sex distribution. The mean BMI was 25.5 ± 1.14 . In patients with liver fibrosis, the mean values were as follows: prothrombin time (14.7 ± 31.4), albumin level (33.6 ± 20.3), AST-to-platelet ratio index (APRI) (1.3 ± 2.1), and FIB-4 (3.99 ± 1.4).

Conclusion: The high prevalence of B and D virus dual infection, with significant changes in noninvasive tests compared to other groups, suggests the need to consider introducing antiviral medication into our daily practice based on this study's findings.

Abstract Submission No. 101690

P-1042

Dysfunction of ATP7B splicing variant caused by enhanced interaction with COMMD1 in Wilson Disease

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The association between Wilson disease and various mutations is well-established; however, the exact pathogenic mechanism of these variants, particularly the molecular mechanism underlying the functional consequence of the splicing mutations, remains unclear. This study focused on the *ATP7B* c.1543+1G>C variant, which caused aberrations in the splicing of exon 3. Two potential regulators, hnRNP C and SF3B1, were identified to be responsible for the abnormal splicing, resulting in the skipping of *ATP7B* exon 3 and the formation of a mutant *ATP7B* isoform with altered secondary and tertiary structure. The mutant *ATP7B* showed a loss of membrane localization and was degraded via the ubiquitin-proteasome pathway, facilitated by enhanced interactions with COMMD1. Protein docking analysis further indicated a universal regulatory effect of COMMD1. Consequently, an elevated intercellular copper concentration and reduced survival rate was observed in HuH-7 cells expressing mutant *ATP7B*. Genetically engineered *Atp7b*^{-/-} mice were created and fed with a copper-containing diet, and purified adenoviruses carrying both wild-type and mutant *ATP7B* cDNAs were administered through tail vein injection. The wild-type *ATP7B* led to a noticeable improvement in the clinical phenotype, whereas no such improvement was observed in mice treated with the mutant *ATP7B*. Our research investigated the pathogenicity and mechanism of the *ATP7B* c.1543+1G>C variant, with a particular focus on its enhanced interaction with COMMD1 as a potential universal mechanism contributing to the dysfunction of various *ATP7B* variants. These findings provide a foundation for the development of innovative therapeutic strategies that target abnormal splicing events in hereditary diseases, including Wilson disease.

Abstract Submission No. 100127

P-1043

IL-19 contributes to the development of nonalcoholic steatohepatitis by altering lipid metabolism

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Interleukin (IL)-19, a member of the IL-10 family, is an anti-inflammatory cytokine produced primarily by macrophages. Nonalcoholic steatohepatitis (NASH) is a disease that has progressed from nonalcoholic fatty liver disease (NAFLD) and is characterized by inflammation and fibrosis. We evaluated the functions of IL-19 in a NAFLD/NASH mouse model using a 60% high fat diet with 0.1% methionine without choline with 2% cholesterol (CDAHFD). Wild-type (WT) and IL-19 gene-deficient (KO) mice were fed a CDAHFD or standard diet for 9 weeks. Liver injury, inflammation, and fibrosis induced by CDAHFD were significantly worse in IL-19 KO mice than in WT mice. IL-6, TNF- α , and TGF- β were significantly higher in IL-19 KO mice than in WT mice. As a mechanism using an in vitro experiment, palmitate-induced triglyceride and cholesterol contents were decreased by the addition of IL-19 in HepG2 cells. Furthermore, addition of IL-19 decreased the expression of fatty acid synthesis-related enzymes and increased ATP content in HepG2 cells. The action of IL-19 in vitro suppressed lipid metabolism. In conclusion, IL-19 may play an important role in the development of steatosis and fibrosis by directly regulating liver metabolism and may be a potential target for the treatment of liver diseases.

Abstract Submission No. 100427

P-1044

Differential effects of PPAR γ activation on TFEB and autophagy in hepatocytes and stellate cells

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Background: Peroxisome proliferator-activated receptor γ (PPAR γ) activation suppresses HSC activation and liver fibrosis. Moreover, autophagy is implicated in hepatic lipid metabolism. Here, we determined whether PPAR γ activation ameliorates HSC activation by downregulating transcription factor EB (TFEB)-mediated autophagy.

Methods and results: Atg7 or Tfeb knockdown in human HSC line LX-2 cells downregulated the expression of fibrogenic markers including α smooth muscle actin, glial fibrillary acidic protein, and collagen type 1. Conversely, Atg7 or Tfeb overexpression upregulated fibrogenic marker expression. Rosiglitazone (RGZ)-mediated PPAR γ activation and/or overexpression in LX-2 cells and primary HSCs decreased autophagy, as indicated by LC3B conversion, total and nuclear-TFEB contents, mRFP-LC3 and BODIPY 493/503 colocalization, and GFP-LC3 and LysoTracker colocalization. RGZ treatment decreased liver fat content, liver enzyme levels, and fibrogenic marker expression in high-fat high-cholesterol diet-fed mice. Electron microscopy showed that RGZ treatment restored the high-fat high-cholesterol diet-mediated lipid droplet decrease and autophagic vesicle induction in primary HSCs and liver tissues. However, TFEB overexpression in LX-2 cells offset the aforementioned effects of RGZ on autophagic flux, lipid droplets, and fibrogenic marker expression.

Conclusions: Activation of PPAR γ with RGZ ameliorated liver fibrosis and downregulation of TFEB and autophagy in HSCs may be important for the antifibrotic effects of PPAR γ activation.

Abstract Submission No. 101202
P-1045

The Chinese herbal TGXZ alleviates the progression of MAFLD by regulating the gut microbiota

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Ethnopharmacological relevance: As a traditional Chinese medicine, the TiaoGanXiaoZhi formula (TGXZ) has previously been found to delay the progression of metabolic-associated fatty liver disease (MAFLD) in the clinic. However, its mechanism requires further clarification.

Aim of the study: This study aimed to explore the effect and mechanism of TGXZ in treating MAFLD in mice models.

Methods: The mice MAFLD model was induced with a high-fat diet feedstuff and 5% fructose water, and further treated with TGXZ. After treatment, the mice's serum, liver tissues, and fecal were used to detect biochemical indices, perform pathological examinations, and perform microbiota sequencing and lipidomics analysis.

Results: Compared to the MAFLD mice, TGXZ treatment significantly downregulated the levels of ALT, AST, TBA, CHE, CHO, TG, HDL-C, LDL-C, IL-6, IL-1 β , and TNF- α in serum and liver tissues, decreased the body weight growth rate, decreased the accumulation of abdominal fat, and improve the liver steatohepatitis pathology. Through the microbiota sequencing and lipidomics analysis of mice fecal, we further constructed the interaction network between gut microbiota and lipid metabolism that was regulated by TGXZ.

Discussion: Our study showed that TGXZ treatment could effectively inhibit the progression of MAFLD by regulating gut microbiota and lipid metabolism. And *Colidextribacter*, *Tuzzerella*, *Rikenella*, and *norank_o__Clostridia_UCG-014* regulated by TGXZ might be the targets for the treatment of MAFLD.

Abstract Submission No. 101256
P-1046

DDC promotes the formation of peridroplet mitochondria in the liver tissue of CDAA diet-induced NASH

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Background: Lipid droplets (LDs) can contact mitochondria to form peridroplet mitochondria (PDM), and PDM could support LD expansion by providing ATP for triglyceride synthesis and prevent cell injury from lipotoxicity. In this study, we investigated whether PDM could be regulated *in vivo* by diethyldithiocarbamate (DDC), which we previously demonstrated its protective effect on non-alcoholic steatohepatitis (NASH) in mice.

Methods: Male C57BL/6 mice received choline-deficient, L-amino acid-defined (CDAA) diet for 9 weeks to establish the model of NASH. The CDAA group were treated with or without 4 mg/ml DDC via daily drinking water. The contact between LDs and mitochondria was observed by electron microscope and co-staining with LD and mitochondria. PDM were isolated from the liver tissue and was quantified.

Results: Electron microscopic images of liver tissue showed that lots of mitochondria were recruited to the surface of LDs (PDM) after DDC treatment when compared with the CDAA diet-induced NASH group. The liver tissues were harvested and homogenized. After low-speed centrifugation, PDM in the upper fat layer were co-stained for mitochondria and LDs. Confocal microscopy revealed more large LDs and PDM in DDC-treated group. Accordingly, fluorescent staining show that the purified PDM extracted from fat layer were increased by DDC treatment. In addition, the content of PDM protein obtained from the same amount of liver tissue was significantly higher in DDC-treated mice.

Conclusions: DDC promotes the formation of PDM in the steatotic liver of NASH mice, which may be one of the reasons for its treatment of NASH.

Abstract Submission No. 101261
P-1047

Gremlin1 regulates the expression of Tcf7l2 in adipose tissue

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Background: Gremlin1 is a novel adipokine that has an effect on insulin sensitivity and might be a novel therapeutic target for non-alcoholic fatty liver disease (NAFLD). However, the mechanisms underlying the role of Gremlin1 in NAFLD remain unclear. In this study, we investigated the possible regulatory mechanism of Gremlin1 in adipose tissue.

Methods: A novel rAAV vector (AAV-Rec) with highly efficient and specific transduction of adipose tissue was used to achieve the knockdown of Gremlin1. AAV-Rec-GFAP-Sh-Gremlin1 was administered to C57BL/6 mice by intraperitoneal injection. Different organs were harvest to evaluated the targeting effect of AAV-Rec-Sh-Gremlin1 on adipose tissue. PCR Array was used to detect the changes of adipogenesis related genes after Gremlin1 knockdown in adipose tissue. The differential genes identified were then investigated in 3T3-L1 cells *in vitro*.

Results: Frozen sections of tissues were observed under fluorescence microscope. Distinct green fluorescence can be observed in both white and brown adipose tissues, but rare in other tissues including brain, heart, liver, spleen, lung, kidney and Skeletal muscle. RT-PCR results showed that Gremlin1 was knockdown in both white and brown adipose tissues, indicating that AAV-Rec-GFAP-Sh-Gremlin1 specifically target on adipose tissue and knockdown Gremlin1 successfully. PCR array showed that Gremlin1 knockdown upregulates Tcf7l2, which is the key transcription factor of Wnt and closely associated with insulin resistance. In addition, the *in vitro* experiments in 3T3-L1 cells confirmed the regulation of Gremlin1 on Tcf7l2.

Conclusions: Gremlin1 regulates Tcf7l2 in adipose tissue, which might be one of the mechanisms of its role in NAFLD.

Abstract Submission No. 101262
P-1048

DDC improves CDAA diet-induced non-alcoholic steatohepatitis through INSR/Akt

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Background: Impaired insulin receptor (INSR) activities lead to insulin resistance, the key factor in the pathology of metabolic disorders including non-alcoholic fatty liver disease (NAFLD). Diethylthiocarbamate (DDC) attenuates non-alcoholic steatohepatitis (NASH) in mice, but its underlying mechanisms remains unclear. In this study, we investigated whether INSR/Akt could be regulated by DDC.

Methods: Male C57BL/6 mice received choline-deficient, L-amino acid-defined (CDAA) diet for 12 weeks to establish the model of NASH. The CDAA group were administered with or without 600 mg/kg/day DDC via daily gavage. INSR expression and its downstream Akt signaling pathway were detected by Western Blotting and Real-time PCR.

Results: Compared with the control group, *INSR* mRNA in the liver tissue of CDAA group was significantly decreased. Compared with CDAA group, *INSR* mRNA was not changed in DDC treated group. In contrast, INSR protein in the liver tissue of CDAA group was significantly decreased compared with the control group, while was significantly increased in the DDC treated group compared with CDAA group. These data indicate that DDC regulates the expression of INSR at the post-transcriptional level. Compared with the control group, the phosphorylation of Akt was inhibited in liver tissues of CDAA group. Compared with CDAA group, the phosphorylation of Akt was increased in DDC treated group. These data suggest that DDC upregulates INSR and then activates its downstream Akt.

Conclusions: DDC activates INSR/Akt pathway, which may contribute to its treatment of NASH.

Abstract Submission No. 101386

P-1049

Polyene phosphatidylcholine alleviates MAFLD by regulating intestinal flora and lipid metabolism

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Background: The global prevalence of metabolic-associated fatty liver disease (MAFLD) is as high as 25%~30%. Polyene Phosphatidylcholine Capsules (PPC) has a certain curative effect on MAFLD, but its mechanism is not clear. This study aimed to explore the effect and mechanism of PPC in treating MAFLD.

Methods: The mice MAFLD model was induced with a high-fat diet feedstuff and 5% fructose water, and further treated with PPC (Figure A). After treatment, the mice's serum and liver tissues were used to detect biochemical indices and perform pathological examinations. And we further performed 16S ribosomal DNA sequencing (16S-seq) of fecal, transcriptomics of liver tissues, and lipidomics analysis of liver tissues and feces.

Results: Compared to the model, PPC treatment significantly down-regulated the levels of ALT, AST, CHE, TBA and TG in serum (Figure B), decreased the body weight growth rate, improve the liver steatohepatitis pathology, and increase the tight connection of the small intestine (Figure C&D). The results of transcriptomics showed that PPC treatment regulated lipid metabolism and PPAR pathways in liver

(Figure E&F). Through the microbiota sequencing and lipidomics analysis, we further constructed the interaction network between gut microbiota and lipid metabolites which was regulated by PPC (Figure E-J).

Conclusions: Our study showed that PPC treatment could effectively inhibit the progression of MAFLD by regulating gut microbiota and regulate lipid metabolism. And *Akkermansia* and *norank_o_Clostridia_UCG-014* regulated by PPC might be the targets for the treatment of MAFLD.

Abstract Submission No. 101766

P-1050

Network Pharmacology combined with experiment to verify the effect and Mechanism of JGC on MASH

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Aim of the study: To study the mechanism of Jigucuo capsule in the treatment of metabolic-related steatohepatitis through network pharmacology and in vivo experiments.

Methods: A mouse model of metabolic-related fatty liver disease was established, and the therapeutic effect was evaluated after treatment with Jigucuo capsule aqueous solution, and the results of liver transcriptome were analyzed. Screening effective chemical components and target genes of Jigucuo capsules by mass spectrometry. Search DisGeNET database and GeneCards database to obtain target genes related to metabolic steatohepatitis. Cytoscape3.7.2 was used to construct the network of Jigucuo Capsule in the treatment of metabolic steatohepatitis, and the topological structure was analyzed. protein interaction analysis was carried out on STRING platform, PPI network was constructed, and GO and KEGG enrichment analysis were carried out.

Results: Network pharmacology predicted 139 potential targets of JGC Capsule, and liver transcriptome analysis showed 97 differential genes in three groups of mice. Transcriptome analysis and PCR verification of mouse liver showed that the mechanism of JGC capsule in treating metabolic-related steatohepatitis was related to the down-regulation of PPARG gene.

Conclusion: JGC capsule can delay the progress of metabolism-related steatohepatitis, and its mechanism may be related to regulating the lipid metabolism pathway of liver.

Abstract Submission No. 101587

P-1051

Clinical implication of MAFLD and reflux esophagitis in primary care institution

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Background: Nonalcoholic Fatty Liver Disease (NAFLD) has emerged as a significant health concern, paralleling the rise of metabolic syndrome in contemporary society. Recent studies suggest that NAFLD may exert adverse effects not only on the liver but also on

other segments of the gastrointestinal tract. In this context, our study aimed to explore the association between NAFLD and Reflux Esophagitis (RE).

Method: We conducted a case-control study involving 50 individuals with NAFLD and 50 control subjects. Participants underwent expert evaluation and endoscopy to determine the presence of RE. Logistic regression analysis was employed to assess the independent association between NAFLD and RE, adjusting for various potential confounding factors. Additionally, clinical assessments and endoscopic findings were scrutinized to obtain a comprehensive understanding of the gastrointestinal status.

Result: The occurrence of RE was statistically significantly higher in the NAFLD group. Logistic regression analysis revealed NAFLD to be an independent predictor for the development of RE, even after accounting for diverse potential confounders. Endoscopic findings indicated that individuals with NAFLD and RE exhibited a more pronounced degree of esophageal mucosal damage.

Conclusion: Our study demonstrates a significant association between NAFLD and an increased risk of RE, providing novel insights into the interplay between these two conditions. These findings underscore the need for additional monitoring and preventive strategies for gastrointestinal health in individuals with NAFLD.

Abstract Submission No. 101700

P-1052

Current status of metabolic dysfunction associated steatohepatitis (MASH) at our hospital

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Aim: The purpose of this study was to confirm the current status of MASH patients visiting our hospital.

Methods: We retrospectively evaluated ninety-one MASH patients who consulted our department from April to September 2022. We assessed factors associated with the achievement ratio of weight loss. And we evaluated the rate of weight loss achievement and ALT improvement by generation. In addition, we were divided into two groups with a weight loss rate of -2% in Propensity Score Matching and evaluated for changes in BMI, ALT, γ GTP, FIB-4 index, VCTE, and CAP. **Results:** The median age was 59 years (range: 15- 84), 44 patients were male. The achievement ratio of weight loss were -7%: -5%: -2% = 15.1%: -23%: 48.1%. Age and weight loss rates were not correlated. ALT and BMI loss rates were correlated. BMI decrease rates were poor among the middle-aged generation. ALT reduction rates were mild in the middle-aged generation and poor in the elderly. In BW-2% group, BMI, ALT, and γ -GTP were significantly improved. In not BW-2% group, FIB-4 index was improved, but VCTE and CAP were not.

Conclusion: Weight loss contributes to improved laboratory data, but does not improve liver fibrosis in the short term. Further investigation of factors that contribute to improve liver fibrosis is necessary in the future.

Abstract Submission No. 101707

P-1053

The Effect of Pemafibrate on Non-Alcoholic Fatty Liver Disease Complicated with Hypertriglyceridemia

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Background: To date, there is no approved treatment for non-alcoholic fatty liver disease (NAFLD). The practical guidelines recommend only lifestyle interventions for NAFLD, such as diet and exercise. However, some medications used for comorbid conditions with NAFLD have the potential to improve NAFLD as well as the associated diseases and NAFLD.

Methods: Patients with hypertriglyceridemia and NAFLD, who received pemafibrate for 30 days or more from June 2018 to September 2023, were included. In some cases, magnetic resonance imaging (MRI) scans were conducted before and after treatment to measure liver elasticity and proton density fat fraction (PDFF). Wilcoxon signed-rank tests with paired samples were used for the comparison of pre- and post-treatment values, with a significance level set at $p = 0.05$.

Results: The median age was 62, with 58% males and a median BMI of 26.8 kg/m². Median pre-treatment clinical test values were as follows; total bilirubin 0.80 mg/dL, AST 42 U/L, ALT 66 U/L, GGT 66 U/L, ALB 4.5 g/dL, platelet count $23.7 \times 10^4/\mu\text{L}$, BUN 14.2 mg/dL, Cr 0.78 mg/dL, triglyceride 239 mg/dL, LDL cholesterol 131 mg/dL, HDL cholesterol 46 mg/dL, HbA1c 6.4%, type 4 collagen 7S 5.5 ng/mL, liver elasticity 3.0 kPa, PDFF 12.0%. After pemafibrate administration, significant reductions were observed in triglyceride, AST, ALT, GGT, and type 4 collagen 7S, while the platelet count increased significantly. There was also a trend toward improved liver elasticity. No significant changes were observed in PDFF, BMI, or HbA1c.

Conclusion: Pemafibrate shows potential for improving NAFLD.

Abstract Submission No. 101844

P-1054

APRI/FIB-4/NFS in predicting liver fibrosis in MAFLD patients with/without viral hepatitis

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Background/Aims: The accuracy of noninvasive seromarkers in predicting liver fibrosis in MAFLD patients with or without viral hepatitis is elusive.

Methods: The AST to platelet ratio index (APRI), fibrosis-4 index (FIB-4) and NAFLD fibrosis score (NFS) were assessed in 871 MAFLD patients who received elastography in a hepatitis B virus (HBV) and hepatitis C virus (HCV) endemic area.

Results: The area under the receiver operating characteristic (AUROC) curve increased substantially with increasing fibrotic stage across the 3 biomarkers. APRI (AUROC range 0.73-0.80) and FIB-4 (AUROC range 0.66-0.82) performed better than NFS (AUROC range 0.63-0.75). When patients were divided into viral and non-viral MAFLD groups, a better AUROC of APRI (range 0.76-0.80) and FIB-4 (range 0.68-0.78) than NFS (range 0.62-0.70) existed only in viral MAFLD but not in non-viral MAFLD. Regarding the NFS, the AUROC was higher in non-viral MAFLD (range 0.69-0.86) and outperformed viral MAFLD at all fibrotic stages. Overall, the AUROC was lowest using NFS (0.63/95% confidence intervals [CI]: 0.59-0.67) for predicting viral MAFLD patients with liver fibrosis (>7 kPa), whereas the AUROC was highest (0.92/CI: 0.84-0.99) using FIB-4 for predicting non-viral MAFLD patients with liver cirrhosis (>12 kPa). The accuracy of APRI and FIB-4 was similar between viral and non-viral

MALFD. Nevertheless, NFS exerted better accuracy in non-viral MAFLD patients than in viral MAFLD patients.

Conclusions: The APRI and FIB-4 performed better than the NFS in predicting liver fibrosis in MAFLD as a whole. The suboptimal performance and accuracy of the NFS existed only in viral MAFLD patients.

Abstract Submission No. 200075
P-1055

Frequency and Clinical Characteristics of Dual-Etiology Fatty Liver Diseases in Korean Patients

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Background: A nomenclature of metabolic-associated fatty liver disease (MAFLD) has been proposed to describe the fatty liver condition associated with metabolic dysfunction. Little is known about dual-etiology fatty liver disease associated with both hepatitis C virus (HCV) infection and MAFLD in Korean patients. We aimed to investigate the frequency and clinical characteristics of the Korean patients with concomitant MAFLD with HCV infection.

Methods: This cross-sectional study consisted of 96,667 consecutive subjects visiting comprehensive health promotion center from 2019 to 2022. Anthropometric and biochemical parameters were measured. The MAFLD was diagnosed based on hepatic steatosis by abdominal ultrasonography and the presence of overweight/obesity, type 2 diabetes, or the evidence of metabolic dysregulation.

Results: The frequencies of MAFLD in general population and HCV-infected patients were 26% and 28%, respectively. Triglyceride, apolipoprotein B, HbA1c, insulin, and high-sensitivity C-reactive protein levels were significantly higher in patients with concomitant MAFLD and HCV infection, compared to those with HCV infection only. However, there is no statistical significance of the levels of total cholesterol, low density lipoprotein-cholesterol, apolipoprotein A and lipoprotein(a) between the groups. Advanced fibrosis by fibrosis-4 index (FIB-4) and NAFLD fibrosis score (NFS) was significantly increased in patients with concomitant MAFLD with HCV infection ($P < 0.0001$).

Conclusions: Frequency of MAFLD in HCV-infected Korean patients was higher than that of MAFLD in the general population. This study demonstrated that patients with dual-etiology fatty liver disease associated with concomitant MAFLD with HCV infection had more advanced fibrosis than those with HCV infection alone.

Abstract Submission No. 200196
P-1056

Therapeutic Efficacy of Radiofrequency Ablation with D-sorbitol in Animal Livers.

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Aim: Radiofrequency ablation (RFA) is an effective, minimally invasive treatment for hepatocellular carcinoma. On the other hand,

inadequate ablation may result in local recurrence. In fact, the size of coagulation necrosis is limited due to increased impedance by tissue fragments. D-sorbitol, which is a dielectric fluid, is a perfusate in transurethral resection of the prostate and used as lavage for removing tissue fragments. Therefore, the aim of this study is to investigate if the use of D-sorbitol in RFA can increase the coagulation range and provide a better therapeutic effect using animal liver.

Methods: Using a pig liver and a live dog liver, RFA with or without D-sorbitol were performed in five different liver sites. After RFA needle insertion, up to 20 ml of 3% D-sorbitol was slowly injected into the lesion from the same puncture site during RFA procedure. RFA was terminated when the impedance threshold was exceeded.

Results: The RFA group with D-sorbitol had significantly a larger volume of coagulated necrotic areas and a greater total energy content than that without D-sorbitol. No significant complications such as hemorrhage or injury were observed in the RFA group with D-sorbitol in the living dog liver. In addition, RFA has been performed without serious complications.

Conclusion: RFA with D-sorbitol might be a safe and effective therapeutic method for the treatment of early stage of hepatocellular carcinoma.

Abstract Submission No. 102062
P-1057

Effectiveness of DLR for Liver Tumor Delineation in the Hepatobiliary phase of Gd-EOB-MRI

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Purpose: To evaluate the efficacy of deep Learning-based Reconstruction (DLR) for the improvement of image-quality and tumor detectability of the iso-voxel high-resolution breath-hold fat-suppressed T1-weighted imaging (HR-BH-FS-T1WI) in hepatobiliary phase (HBP) of Gd-EOB-MRI

Materials and Methods: This was a retrospective study of a single institute. We evaluated 42 patients with 98 liver tumors, including hepatocellular carcinomas, hypovascular nodules, hemangiomas and metastatic tumors, who underwent Gd-EOB-MRI between March 2023 and May 2023. We evaluated three imaging techniques of HBP images: (1) iso-voxel HR-BH-FS-T1WI that was reconstructed with DLR (BH-DLR+) and (2) that without DLR (BH-DLR-); and (3) HR-FS-T1WI was scanned with free-breathing technique using a navigator-echo-triggered technique and DLR (Navi-DLR+). Three imaging techniques were qualitatively and quantitatively compared. Tumor detectability was also compared among the three imaging techniques.

Results: BH-DLR+ (3.84, average score of two radiologists) showed significantly better qualitative scores for image noise than BH-DLR- (2.84) and Navi-DLR+ (3.37) ($P < 0.05$), and Navi-DLR+ showed significantly better scores than BH-DLR- ($P < 0.0167$). BH-DLR+ (3.77) and BH-DLR- (3.77) showed significantly better qualitative scores for respiratory motion artifact than Navi-DLR+ (2.75) ($P < 0.05$), but there was no significant difference in scores between BH-DLR+ and BH-DLR- ($P > 0.0167$). BH-DLR+ (0.32) and Navi-DLR+ (0.33) showed significantly higher lesion-to-nonlesion CR than BH-DLR- (0.29) ($P < 0.0167$), but there was no significant difference in lesion-to-nonlesion CR between BH-DLR+ and Navi-DLR+ ($P > 0.0167$). BH-DLR+ (89.8%) showed significantly better tumor detectability than BH-DLR- (76.0%) and Navi-DLR+ (77.6%) ($P < 0.05$).

Conclusion: The use of DLR for the iso-voxel HR-BH-FS-T1WI was effective to improve image quality and tumor detectability in HBP of G-EOB-MRI.

Abstract Submission No. 102093
P-1058

Prevalence of arterial hypertension in liver cirrhosis and correlation with the severity

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Background and aim: Metabolic diseases and hypertension have increased dramatically in recent years, so the prevalence of hypertension in patients with cirrhosis is expected to increase.

The aim of the study was to estimate the prevalence of hypertension in patients with liver cirrhosis and to determine its association with the severity of the liver disease.

Patients and methods: This was a descriptive, cross-sectional, analytical study conducted at the Tropical Medicine and Infectious Diseases Department, Tanta University Hospital, Egypt. A total of 2051 patients with liver cirrhosis of various etiology were screened for participation in this study. 2014 patients were enrolled. They underwent blood pressure evaluation, blood tests and abdominal ultrasonography. Patients were classified into hypertensive and non-hypertensive groups.

Results: The prevalence of arterial hypertension in patients with liver cirrhosis was 30.8%. As regards Child-Pugh class, hypertensive patients in class A were significantly increased (72.9 versus 48.7% respectively) while patients in class B and C were significantly decreased when compared with non-hypertensive patients (25.5, 1.6 versus 33.29, 17.93% respectively) ($P < 0.001$).

Conclusions: The prevalence of arterial hypertension in Egyptian cirrhotic patients is 30.7%, lower than that of the general population. Arterial hypertension is inversely associated with the severity of liver disease.

Abstract Submission No. 100423
P-1059

Sorafenib combined with WAY-262611 inhibited Wnt/PI3K/Akt pathway in hepatocellular carcinoma

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Background: Sorafenib extended overall survival in advanced hepatocellular carcinoma (HCC) patients. Elevated expression levels of Dickkopf-1 (DKK1) were found in HCC. In this study, we investigated synergistic effects and mechanism of sorafenib combined with DKK1 inhibitor on HCC in vitro and in vivo.

Methods: Huh7 and Hep3B cells were treated with IC₅₀ values of sorafenib and WAY-262611, which is a DKK1 inhibitor. Xenograft mouse was generated using Hep3B cells and transgenic mouse was developed using hydrodynamic tail vein injection. Mice were orally administered sorafenib (32 mg/kg) and WAY-262611 (16 mg/kg) for

10 days. Western blotting, immunostaining, and qRT-PCR were used to identify the mechanism of sorafenib combined with WAY-262611 in vitro and in vivo.

Results: Sorafenib combined with WAY-262611 decreased the expression levels of p110 α , phospho-Akt (all $P < 0.05$), active β -catenin (all $P < 0.05$), and phospho-GSK3 β (Ser9), whereas combined treatment increased the expression levels of phospho-GSK3 β (Tyr216) compared to sorafenib alone in vitro and in vivo. Sorafenib combined with WAY-262611 significantly increased the expression levels of PI3K/Akt pathway inhibitory genes, whereas combined treatment significantly decreased the expression levels of Wnt/ β -catenin pathway target genes (all $P < 0.05$). In addition, simultaneous expression of Hras^{G12V}, miR53, and PI3K^{E545K} significantly increased the expression levels of p110 α ($P < 0.01$), p-Akt, active β -catenin, cyclin D1 ($P < 0.01$), and DKK1 ($P < 0.05$) compared to simultaneous expression of Hras^{G12V} and miR53.

Conclusions: Sorafenib combined with DKK1 inhibitor significantly inhibited the PI3K/Akt and Wnt/ β -catenin pathways and these pathways were regulated through GSK3 β in HCC. Therefore, DKK1 inhibitor may be a promising therapeutic strategy in HCC.

Abstract Submission No. 100527
P-1060

Chinese Medicine Modulates Gut Microbiota and Lipid Metabolism to Suppress Hepatocellular Carcinoma

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Aim: To investigate the effects of Chai Qi Yi Gan Ke Li (CQYGKL) in the treatment of hepatocellular carcinoma (HCC) and the underlying mechanisms of systemic regulation of gut microbiota and metabolite profiles.

Methods: The inhibitory effects of CQYGKL on HCC were assessed using tumor weight measurements, HE staining, and TUNEL assays in HCC mice. 16S rRNA sequencing and metabolomics were performed to analyze the alterations in the gut microbiota and fecal metabolism. Meanwhile, NP was used to determine the putative molecular regulation mechanism of CQYGKL in HCC treatment.

Results: The pharmacodynamic evaluations demonstrated the substantial efficacy of CQYGKL in profoundly inhibiting HCC tumor growth, promoting HCC cellular apoptosis, and effectively mitigating colon tissue injury. Moreover, the gut microbiota analysis showed that CQYGKL reversed HCC-induced gut microbiota dysbiosis in HCC mice by elevating the abundance of Bacteroides and Muribaculaceae, while reducing the abundance of Desulfovibrio and Incertae Sedis. Furthermore, the metabolomic analysis revealed that CQYGKL reversed the HCC-induced metabolic disorder via regulating the glycerophospholipid and sphingolipid metabolism, and correlation analysis revealed that lipids and lipid-like molecules were closely related to distinct gut microbiota. Moreover, NP indicated that CQYGKL orchestrates the regulation of sphingolipid signaling through the modulation of pivotal targets, including ABCC1, PRKCB, and NOS3.

Conclusion: This investigation establishes that CQYGKL holds promise as a therapeutic agent for HCC. Its mechanism involves the enhancement of intestinal barrier function and regulation of intestinal microbiota and fecal metabolites, with a particular focus on sphingolipid and glycerophospholipid metabolism.

Abstract Submission No. 100588

P-1061

Synthesis, Characterization, and Biological Evaluation of Iron-Based MIL-88B Incorporating Safranal

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Liver cancer remains a primary worldwide health concern, necessitating the development of innovative and effective treatment options. In this study, we present a biocompatible iron-based metal-organic framework (Fe-MOF) consisting of iron ligands connected by terephthalate linkers loaded with Safranal, a natural biomolecule extracted from stigmas (also known as Saffron) of *Crocus Sativus* flower, a therapeutic intervention with dual efficiency. This compound not only meets the demand for improved liver cancer therapies but also exhibits antibacterial properties against *Escherichia coli* and *Lactobacillus*. The synthesis stage of the study focuses on preparing MIL-88B(Fe) and loading Safranal into/onto its structure. The material's composition and purity are validated through various characterization techniques, including XRD, FTIR, TGA, and N₂-adsorption. Furthermore, the morphology and uniformity are assessed using the SEM-EDX approach, while the successful loading of Safranal is confirmed through the NMR technique. The potential of MIL-88B(Fe) and loaded-MIL-88B(Fe) as promising anticancer/antibacterial agents is highlighted by their substantial inhibitory impact on the growth of HepG2 cells and the examined bacterial strains. The present findings pave the way for developing innovative multifunctional agents with potential applications in biotechnology.

Abstract Submission No. 101097

P-1062

KXYA formula reverses the lenvatinib resistance of hepatoma cells by

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Background: Lenvatinib resistance (LR) is a major obstacle to improving the prognosis of hepatocellular carcinoma (HCC) patients at present. The traditional Chinese medicine KangXianYiAi formula (KXYA) has shown a good therapeutic effect in liver lesions. Here, we aimed to explore the effect and mechanism of KXYA in treating LR-HCC.

Methods: We first constructed the hepatoma Huh7 cell model of LR via sustained low-concentration lenvatinib stimulation. The cell viability was detected by CCK-8 assay. The Huh7-LR cells were treated with DMSO and KXYA for 48 hours, then performed RNA sequencing (RNA-seq) analysis. With RNA-seq data, the differently expressed genes (DEGs) between two groups were screened out and further used to perform enrichment analysis including Reactome, Gene Ontology, and Kyoto Encyclopedia of Genes and Genomes.

Results: The results showed that compared to the wide-type Huh7 cells, Huh7-LR cells had higher cell viability after lenvatinib treatment. And compared with lenvatinib treatment, KXYA combined lenvatinib treatment had an increased inhibition effect in both Huh7-WT and

Huh7-LR cells. With RNA-seq analysis, we obtained 511 DEGs. Compared with the DMSO group, most genes of DEGs had lower expression in the KXYA group, while others were upregulated. The enrichment analysis results showed that these DEGs were mainly correlated to the NOTCH signaling pathway.

Conclusions: Our study showed that KXYA treatment could effectively inhibit the cell viability of Huh7-LR cells, and the mechanism was correlated to the regulation of the NOTCH pathway.

Abstract Submission No. 101646

P-1063

Astragalus-Atractylodes herb pair treated HCC by regulating IL-6/STAT3 signaling pathway

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Abstract: Astragalus(Chinese name: Huang Qi, HQ) and Atractylodes(Chinese name: Bai Zhu, BZ) herb pair has potential efficacy in the treatment of hepatocellular carcinoma (HCC). However, the main components and potential mechanisms of HQBZ therapy for HCC remain unclear. Through network pharmacology, molecular docking and experimental verification, this study found that the effective active ingredient of HQBZ in the treatment of HCC is biatractylolide, the key targets are EGFR, RELA and IL-6, and the key signaling pathway is IL-6/STAT3 signaling pathway. Combined with in vitro and in vivo experimental results, we verified that HQBZ can alleviate T cell exhaustion by regulating IL-6/STAT3 signaling pathway, increase tumor infiltration CD8⁺T cells, and play a therapeutic role in HCC. Our findings provide a reliable basis for further exploration of the key active ingredients of traditional Chinese medicine in the treatment of HCC.

Keyword: Astragalus-Atractylodes herb pair; Hepatocellular carcinoma; Network pharmacology; Molecular docking; IL-6/STAT3 signaling pathway.

Abstract Submission No. 101648

P-1064

Mechanism of Glehniae Radix-Ophiopogon japonicus herb pair in treating hepatocellular carcinoma

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Background: The incidence and mortality of primary liver cancer remain high, which is the burden of cancer worldwide. Yangyin Fuzheng Jiudu Prescription(YFJP) has been used as a traditional Chinese

medicine compound for hepatocellular carcinoma (HCC) for many years, but the compatibility mechanism of the decoction is still unclear. **Methods:** Through methods of network pharmacology, molecular docking and molecular dynamics simulation, the potential mechanism of Shashen (Glehniae Radix)-Maidong (Ophiopogon japonicus) (SS-MD) herb pair in the treatment of HCC was explored, and the therapeutic effect was evaluated in vivo.

Results: The active ingredients of SS-MD herb pair in the treatment of HCC were beta-sitosterol, rutin, and sitogluside, and the key targets were EGFR, TP53, STAT3, GAPDH, AKT1, and HRAS. The key signaling pathways was Notch-1 signaling pathway. Key targets and components were verified by molecular docking, and molecular dynamics simulations of EGFR-beta sitosterol with the strongest binding activity were performed. Finally, in vivo experiments showed that SS-MD herb pair could inhibit the expression of EGFR and key proteins in Notch-1 signaling pathway, increase the expression of T-bet and reduce the expression of Eomes in tumor tissues of H22 tumor-bearing mice.

Conclusion: This study identified the key components, targets and signaling pathways of SS-MD herb pair in the treatment of HCC. It exerts synergistic therapeutic effect through multi-component and multi-target, which provides a reliable basis for further exploring the key active components of YFJP in the treatment of HCC, and provides theoretical support for the synergistic treatment of HCC with traditional Chinese medicine.

Abstract Submission No. 200058
P-1065

Digoxigenin activates autophagy in HCC by regulating the PI3K/Akt/mTOR pathway

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As we all know, Hepatocellular carcinoma (HCC) is a highly malignant tumor. Targeted combination immunotherapy is the approved preliminary drug regimen to treat severe HCC; however, adverse side effects and a low response rate limit its efficacy during clinical treatment. Traditional Chinese medicine and its derived natural compounds exhibit anti-cancer effects, and have the benefit of being low-toxic and low cost. Therefore, in this study, we conducted high-throughput phenotypic screening in vitro to identify alternative drugs with significant anti-HCC effects. Digoxigenin (DIG) was observed to significantly impede the progression activity of HCC cells in 1,444 bio-active compound libraries. Subsequently, we verified the therapeutic effects of DIG using cell counting by CCK8, lactate dehydrogenase, and cloning assays. Transmission electron microscopy, Western blotting and immunofluorescence analysis showed that DIG inhibited the proliferation of HCC cells through autophagy. According to network pharmacology and molecular docking analysis, DIG may target the PI3K/AKT/mTOR signaling pathway. Treatment of Hep3B and Huh7 cells with DIG or mTOR inhibitors showed similar inhibitory effects on HCC cells, stating that DIG awakens autophagy by remaining blocked the PI3K/AKT/mTOR signaling pathway. In vivo research showed that DIG stop the development of subcutaneous graft tumors. In summary, we identify DIG as a potential treatment option for HCC because it inhibits the PI3K/AKT/mTOR signaling pathway, which causes HCC cells to undergo autophagy. By employing phenotypic screening, this research contributes to accelerated drug discovery and the development of new therapies to address the underlying mechanisms associated with liver cancer.

Abstract Submission No. 100153
P-1066

Regorafenib as a second line therapy for Egyptian patients with an advanced stage HCC

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Background: Regorafenib has been approved among the treatment options for patients with hepatocellular carcinoma (HCC).

Aim: To assess the efficacy, safety and drug adverse effects of regorafenib in Egyptian patients with HCC who have progressed during sorafenib treatment.

Methods: We conducted 57 patients with advanced HCC who were shifted to regorafenib after failure of sorafenib therapy. Data included patient demographics, performance status, duration of previous line of treatment, number of treatment cycles, side effects, best-tolerated dose, laboratory, and radiological results and treatment discontinuation due to intolerance.

Results: A total of 57 patients received regorafenib as a 2nd-line treatment after sorafenib progression. Of these patients, 34 (59.6%) and 23 (40.4%) were diagnosed with Barcelona Clinic Liver Cancer (BCLC) stages B and C, respectively. 24 patients (42%) had progressive course of the disease with mean disease PFS 11.44 [95% confidence interval (CI): 10.29-12.59] months, 10 patients (18.18%) died. The OS and PFS were better in the group who shifted to regorafenib after 3 months progression on sorafenib than who shifted after 6 months progression. The cumulative survival probability was 80.7%. The mean survival time was 14.5 (95% CI, 13.13- 14.91) months. The most common toxicities were diarrhea (52.6%) hand-foot skin reaction (38.5%), fatigue (29.8%) and hypertension (19.2%). The most common grade 3–4 toxicities were hypoalbuminemia (8.7%), anemia (7%) and mouth sores (3.5%).

Conclusion: Regorafenib appears to be safe, clinically effective and improve the prognosis in patients with advanced HCC as a second line therapy.

Abstract Submission No. 100411
P-1067

Psoas Muscle-to-Spine ratio predicts overall survival in Patients with Hepatocellular Carcinoma

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Background: Cross-sectional areas of the psoas muscle mass measured by computed tomography (CT) are frequently used to evaluate the presence of sarcopenia in patients with hepatocellular carcinoma (HCC). Our aim was to develop a new psoas muscle index to assess overall survival in patients with HCC.

Methods: We retrospectively examined the data of 970 patients with different stages of HCC who received various treatments at Taipei Tzu Chi Hospital from January 2006 to December 2016. All patients had CT images at the level of the L3 spine for the evaluation of the total area of the right and left psoas, erector spinae, quadratus lumborum

muscles, and the area of the lumbar vertebral body on an axial CT scan, and the CT density of the muscle area was measured for the evaluation of myosteatosis.

Overall survival (OS) and independent prognostic factors were evaluated using the Cox proportional hazards model.

Results: Psoas muscle area, psoas muscle-vertebral ratio, muscle-spine ratio, and myosteatosis are independent predictors of overall survival in patients with HCC ($p < 0.001$). According to the corrected Akaike information criterion, the psoas muscle-to-spine ratio outperformed the performance of other predictors, and the receiver operating curve analysis showed that the optimal cut-off point of the psoas muscle-to-spine ratio for overall survival was 4.42 (AUC 0.641, 95% CI 0.607–0.675, sensitivity 0.641, specificity 0.566) between all participants.

Conclusions: The psoas muscle-to-spine ratio was an independent prognostic predictor for HCC patients and can be applied to the staging of patients with HCC.

Abstract Submission No. 100690

P-1068

Impact of Sarcopenia on the Prognosis in Cirrhotic Patients Complicated with SBP

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Backgrounds: This study aimed to investigate the initial treatment response and mortality of spontaneous bacterial peritonitis (SBP) in cirrhotic patients according to the presence of the sarcopenia.

Methods: We retrospectively reviewed data from SBP patients admitted from January 2004 to December 2020 at Jeonbuk National University Hospital. We defined patients with sarcopenia by analyzing CT data using the Asan J morphometry program. Among them, both male and female patients with L3MI belonging to the 25th percentile were selected.

Results: A total of 126 patients was enrolled for the study. Of these, 32 (25.4%) were diagnosed with sarcopenia. Overall, the initial treatment response rate was not significantly different between non-sarcopenic group and sarcopenic group (68.1% vs. 78.1%, $P=0.394$). But, the hospitalization days was significantly longer in sarcopenic group (30.2 ± 19.1 vs. 22.1 ± 18.7 , $P=0.037$). In patients with SBP, there was no significant difference in in-hospital mortality according to the sarcopenia (31.9% vs. 37.5%, $P=0.717$). The mortality was increased over time in the sarcopenic group (47.4% vs. 64.0% at 6-month, 56.5% vs. 76.2% at 12-month, $P=0.225$ and 0.173, respectively), but, it was not significantly different ($P=0.330$). In the multivariate analysis, sarcopenia showed no significant association with both initial treatment failure and 30-day mortality.

Conclusion: Sarcopenia did not show a significant difference in initial treatment response and short-term mortality in cirrhotic patients with SBP. However, sarcopenia is more likely to affect long-term prognosis when considering the long-term mortality.

Abstract Submission No. 100738

P-1069

A case of hepatocellular carcinoma with proteinuria treated with Lenvatinib

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The patient was a man in his 70s with hypertension. Seven years ago, hepatocellular carcinoma (HCC) first appeared, and the initial treatment was surgery, followed by hepatic arterial chemoembolization (TACE) and ablation several times. was successful. In June of this year, a 10mm-sized recurrence was detected in liver S7, and ablation was performed, and 4 months after treatment, contrast-enhanced CT revealed a 30mm-sized local recurrence. This was considered to be a recurrence of poorly differentiated HCC. Lenvatinib (LEN) was administered in December of this year, but significant proteinuria was observed 1 month later, so LEN was discontinued. After discontinuation, TACE and hepatic arterial infusion (TAI) were performed, but the HCC increased and portal vein infiltration appeared in July of the following year. Although LEN treatment was discontinued after 1 month, alpha-fetoprotein (AFP) levels decreased and arterial blood flow to the tumor decreased in the early phase of contrast-enhanced CT after LEN treatment. We speculated that if the side effects of proteinuria could be controlled, LEN could be expected to have a therapeutic effect. By reducing the dose of LEN, changing the type of calcium channel blocker used for hypertension from L-type to L+N-type, which is effective against proteinuria, and adding ARB and ACE inhibitors, reduced proteinuria caused by LEN administration. As a result of continuing the treatment for 3 months, good therapeutic effects due to LEN were observed. It was suggested that drug selection for hypertension is important in extending the administration period of LEN and increasing its therapeutic effect.

Abstract Submission No. 101171

P-1070

Prevalence of sarcopenia and its related factors among patients with HCC: A meta-analysis

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Background: Sarcopenia is associated with poor outcomes in patients with hepatocellular carcinoma (HCC). However, prevalence characteristics and potential related factors of sarcopenia remain to be determined. This study aimed to depict the demographic, disease-specific, and inter-study distribution of sarcopenia prevalence, and explore study-level factors related to sarcopenia in HCC patients.

Methods: Electronic searches were performed from inception to December 12, 2022 to identify eligible studies that reported the prevalence data of sarcopenia in HCC patients. The random-effects model was used to pool the prevalence of sarcopenia in all HCC patients and subgroups. Study-level factors associated with sarcopenia prevalence were evaluated using meta-regression.

Results: A total of 77 studies involving 13,158 patients from 12 countries were included (Table 1). Among the included HCC patients, the median age was 64.3 years, 78.5% were male, 74.5% coexisted with cirrhosis, and 73.0% derived from viral hepatitis. The overall prevalence of sarcopenia was 41.3% (95% CI 36.8%–45.9%) in all HCC patients. The pooled prevalence of sarcopenia was higher in Europe

compared to Asia, and it was also higher in the late stage than in the early stage. The prevalence of sarcopenia was positively and linearly associated with 3rd lumbar vertebra (L3)-skeletal muscle index (SMI)/psoas muscle index cutoff values both in males and females. In the adjusted meta-regression model, only the L3-SMI cutoff value was significantly associated with sarcopenia prevalence (Table 2).

Conclusions: Sarcopenia is highly prevalent, and the prevalence of sarcopenia was linearly and independently related to the selected cut-offs for sarcopenia in HCC patients.

Abstract Submission No. 101543

P-1071

Serum FOLR1 is a prognostic marker for hepatocellular carcinoma

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Background: Hepatocellular carcinoma (HCC) is a deadly cancer and desires novel biomarkers for ideal surveillance and treatment strategies. We focused on the folate receptor (FR) and investigated its clinical utility as a serum biomarker of HCC.

Method: The association between the expression levels of FOLR1 gene and patient prognosis was evaluated in 364 HCC patients of TCGA cohort. Total 206 consecutive HCC patients treated with either RFA or TACE in the Osaka University Hospital between 2014 and 2021 were retrospectively enrolled. Serum concentrations of FOLR1 were assessed by enzyme-linked immunosorbent assay (ELISA) and their association with disease status and patient prognosis were evaluated.

Results: In the TCGA cohort, HCC patients with high FOLR1 levels showed significantly shorter overall survival (OS) than those with low FOLR1 levels. In our cohort, HCC patients with high FOLR1 levels showed significantly lower levels of hemoglobin, creatinine, albumin, and platelet counts compared to those with low levels. Serum AFP and DCP levels, and tumor stages were not different between 2 groups. Serum FOLR1 levels were not clearly associated with any scoring system including GALAD, ALBI and FIB-4 index. HCC patients with high serum FOLR1 showed a significantly shorter OS than those with low serum FOLR1. Multivariate analysis indicated that FOLR1 and GALAD were independent predictors of poor OS. In the subgroup analysis, serum FOLR1 levels stratified OS irrespective of treatment methods (RFA/TACE) and in the early stage HCC patients (Stage 1 and 2).

Conclusion: Serum FOLR1 is a potential new prognostic biomarker of HCC.

Abstract Submission No. 101579

P-1072

Post-treatment after discontinuation of Atezolizumab/Bevacizumab Combination Therapy

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Objective: Atezolizumab/Bevacizumab combination therapy (A/B) have good results as first-line therapy for unresectable hepatocellular carcinoma (uHCC). However, there is no clear evidence after discontinuation of treatment. We evaluate post-treatment after discontinuation of 1st line A/B for uHCC.

Methods: Seventy-seven patients who received A/B as first line treatment at our institution were included. Treatment efficacy was evaluated with RECIST ver 1.1 and adverse events with CTCAE ver 5.0.

Results: A/B was administrated as the 1st line in 77 patients [median age 71.0 years, 58 males, 68 CPA, 52 PS0], with MST 21.6 months and median PFS 7.0 months. Response rate was OR 15.6% and DC 70.1%. Seventeen patients continued A/B therapy and 60 discontinued A/B. The transition rate to next therapy after A/B was 45.0%, OS was significantly longer in post-treatment patients (10.5 months vs. 21.6 months, $p < 0.001$). Patients who did not receive post-treatment had lower hepatic reserve (CPB 24.2% vs. 0.0%, $p = 0.020$) and poorer PS (PS0 51.5% vs. 84.2%, $p = 0.025$). Eleven patients received lenvatinib (OR 9.1% and DC 72.7%) as post-treatment for A/B, the MST and median PFS were 16.0 months and 7.8 months, respectively. There was no significant difference in OS between post-treatment with lenvatinib and other therapies. In patients who received lenvatinib after A/B, 6 of 7 discontinued A/B AEs were related to irAEs.

Conclusion: The post-treatment transition rate was lower in patients with poor status before A/B, and post-treatment was different depending on AE discontinuation.

Abstract Submission No. 101607

P-1073

A novel erythrocyte-related risk score for prognosis prediction in hepatocellular carcinoma

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Objective: Accurate prognostic tools are essential for hepatocellular carcinoma (HCC) management. This study aimed to develop a novel risk score based on erythrocyte-related genes to predict HCC prognosis.

Methods: HCC datasets from The Cancer Genome Atlas (TCGA) and Gene Expression Omnibus (GEO) databases were utilized. A gene set associated with erythrocyte development and differentiation was obtained from Molecular Signature Databases. The risk score was developed using the least absolute shrinkage and selection operator (LASSO) regression model, considering erythrocyte-related genes. Additionally, a user-friendly visualization model incorporating clinical parameters was established to evaluate the risk score's calibration, accuracy, and clinical utility. The relationship between the erythrocyte-related risk score and molecular pathways, immune cells, and functions was explored. Furthermore, the predictive abilities of hub genes across various cancer prognoses were investigated.

Results: The developed erythrocyte-related risk score effectively differentiated the prognosis of HCC patients and exhibited associations with molecular and immune-related features. This provides valuable insights and potential strategies for personalized treatment.

Conclusion: The novel erythrocyte-related risk score has demonstrated promising potential for predicting HCC prognosis and offers a foundation for future personalized treatment approaches.

Abstract Submission No. 101612
P-1074

Initial experience with the RF Ablation System (Arfa) for hepatocellular carcinoma (HCC)

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Objective: Recently, variable-tip needles of radiofrequency ablation (RFA) have become available for ablation therapy of HCC. We report on our initial experience with Arfa compared to VIVARF.

Method: 52 analyzable patients with 59 nodes who underwent RFA using Arfa and VIVARF. The background was male/ female: 35/ 17, median age 74 years. HBV/ HCV/ alcohol/ NASH/ NBNC: 6/ 18/ 14/ 6/ 8; Child-Pugh: 5A/ 6A/ 7B: 35/ 11/ 6. These patients were divided into 2 groups: Arfa group (n=15) and VIVARF group (n=44).

Study 1: Comparison of RFA voltage, roll-off time, ablation temperature, ablation size, and ablation range by RFA tip length.

Study 2: Safety during and after treatment was evaluated.

Result: 1. 15 mm tip: Arfa (n=4) / VIVARF (n=6) showed a significant difference of 52.5/ 40W (p=0.022) in the maximum voltage at RFA only. Tip 20 mm: Arfa (n=8) / VIVARF (n=25) showed significant differences in maximum voltage: 77.5/ 60.0 (p=0.004), initial roll-off time: 4 / 6 min (p=0.030), and total ablation time: 9 min 30 sec/ 7 min (p=0.008). There was no difference between the two groups in the extent of cauterization, although both groups had a wider cauterization area than the length of each tip. There was no significant difference in complications between the two groups.

2 cases of bleeding were observed in the VIVARF group, and in one case, hemostasis was achieved with additional cauterization of the liver surface.

Conclusion: The experience of Arfa is still small, further accumulation of cases is needed in the future.

Abstract Submission No. 101615
P-1075

Erythroid Differentiated Myeloid Cells: A Prognostic Biomarker in Hepatocellular Carcinoma

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Background: Anemia in hepatitis B virus-associated hepatocellular carcinoma (HBV-HCC) significantly impacts patient prognosis. Under

the burden of tumor, erythroid differentiated myeloid cells (EDMC) arise, exacerbating anemia and suppressing T-cell-mediated anti-tumor responses. This study aimed to investigate the impact of EDMC on HBV-HCC prognosis and its association with T-cell exhaustion.

Methods: Prospectively enrolling 100 HBV-HCC patients, clinical data and peripheral blood samples were collected. Multi-color flow cytometry assessed EDMC subsets and their correlation with clinical parameters, including hemoglobin. Kaplan-Meier survival analysis evaluated the influence of EDMC proportions on six-month progression-free survival. Correlations between EDMC and T-cell exhaustion-related immune markers were examined.

Results: EDMC were enriched in HBV-HCC patients' peripheral blood. The proportion of EDMC were upregulated in advanced and progressive HBV-HCC, positively correlating with anemia severity. Higher proportions of EDMC were associated with increased tumor progression. Interestingly, EDMC levels correlated with elevated co-inhibitory molecule expression and reduced cytotoxic cytokine production in CD8⁺ T cells, along with increased reactive oxygen species, lipid peroxidation, and ferroptosis in CD8⁺ T cells.

Conclusion: EDMC presence is associated with accelerated HBV-HCC progression and potentially represents a biological marker for poor clinical prognosis.

Abstract Submission No. 101650
P-1076

A platelet related prognostic model in Hepatocellular carcinoma with portal vein tumor thrombosis

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Background and Aim: Portal vein tumor thrombosis (PVTT) is one of the hallmarks of advanced Hepatocellular carcinoma (HCC). Platelet (PLT) function parameters and CD8⁺T cells (CD8⁺Ts) play an important role in HCC progression and metastasis. This study is committed to establishing an efficient prognosis prediction model and exploring the combined effect of PLT and CD8⁺Ts on PVTT prognosis.

Methods: This retrospective study collected 932 HCC patients with PVTT from 2007 to 2017, and randomly divided them into a training cohort (n=656) and a validation cohort (n=276). We performed multivariate cox and Elastic-net regression analysis, constructed a nomogram and used Kaplan-Meier survival curves to compare overall survival and progression-free survival rates in different substrata. Relationships between indicators involved were also analyzed.

Result: We found tumor number, size, treatment, PLT, γ -glutamyl transferase, alpha-fetoprotein, mean platelet volume, and CD8⁺Ts were related to the 5-year OS of patients with PVTT, and established a nomogram. The area under the receiver operating characteristic curve (AUCs) for predicting the 1-year OS rates were 0.767 and 0.794 in training and validation cohorts. The calibration curve and decision curve indicated its predictive consistency and strong clinical utility. We also found those with low PLT (<100*10⁹/L) and high CD8⁺Ts (>320 cells/ μ L) had a better prognosis.

Conclusion: We established a well-performing prognostic model for PVTT based on platelet functional parameters and CD8⁺Ts, and found that PT-8 formed by PLT and CD8⁺Ts was an excellent predictor of the prognosis of PVTT.

Key words: Hepatocellular carcinoma, Portal vein tumor thrombus, Platelet, CD8⁺T cells counts, Prognostic modeling

Abstract Submission No. 101732
P-1077

Importance of CONUT Score in Continuation of Atezolizumab plus Bevacizumab.

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Background: Atezolizumab plus bevacizumab (Atezo+Bev) is commonly administered for advanced hepatocellular carcinoma. In this study, we investigated the nutritional assessment for achieving good disease control.

Methods: We included 106 patients treated with Atezo+Bev at our hospital from December 2018 to February 2023, divided into 74 patients in primary treatment and 32 patients in secondary treatment and beyond, and evaluated the relationship between OS and PFS in terms of nutritional assessment.

Results: The median OS for all patients treated with Atezo+Bev was 21.4 months and the median PFS was 5.5 months. There were no differences in age, gender, or liver background between the two groups, and there were significantly more Stage IVB cases after second-line treatment ($P = 0.001$). Response rates between the two groups were significantly higher for first-line treatment (first-line: 46.2%, second-line or later: 20.7%, $P = 0.023$). Focusing on the CONUTS score (albumin level, total cholesterol level, and lymphocyte count), which reflects protein metabolism, lipid metabolism, and immunocompetence, a lower score at 3 weeks from the start contributed to prolonged OS (primary treatment: $P = 0.037$, secondary treatment and later: $P = 0.088$). Regarding log change between baseline and 3 weeks post-treatment, lower scores significantly prolonged OS between the two groups (primary treatment: $P = 0.042$, secondary treatment and or later: $P = 0.102$).

Conclusions: Long-term continuation of Atezo+Bev with a high response rate was important for prolonging OS, and nutritional assessment using the CONUTS score was useful.

Abstract Submission No. 101821
P-1078

Utility of ALBI grade for predicting prognoses in patients who underwent repeat hepatectomy

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Background: The albumin-bilirubin grade as a prognostic indicator for patients with recurrent hepatocellular carcinoma who undergo repeat hepatectomy has not been sufficiently investigated. We evaluated the utility of the albumin-bilirubin grade for predicting the prognosis after repeat hepatectomy of patients with recurrent hepatocellular carcinoma.

Methods: Ninety patients with intrahepatic recurrent hepatocellular carcinoma who underwent repeat hepatectomy at our hospital between 2005 and 2019 were retrospectively analyzed. Independent

preoperative prognostic factors, including the albumin-bilirubin grade, were evaluated using Cox proportional-hazards regression models. Prognosis differences between patients with albumin-bilirubin grades 1 and 2 were analyzed using the Kaplan-Meier method.

Results: Cox proportional-hazards regression analysis revealed that albumin-bilirubin grade 2 (hazard ratio, 2.18; 95% confidence interval, 1.30-3.65; $P=0.003$) and early recurrence within 1 year from the initial surgery (hazard ratio, 4.19; 95% confidence interval, 1.74-10.07; $P=0.001$) were independently associated with poor recurrence-free survival; albumin-bilirubin grade 2 (hazard ratio, 3.17; 95% confidence interval, 1.20-8.37; $P=0.020$) was independently associated with poor overall survival. The 5-year recurrence-free survival rates of 31% and 17% after repeat hepatectomy for patients with albumin-bilirubin grades 1 and 2, respectively, were significantly different between groups ($P=0.003$). The 5-year overall survival rates of 86% and 60% for patients with albumin-bilirubin grades 1 and 2, respectively, were significantly different between groups ($P=0.003$).

Conclusions: Patients with albumin-bilirubin grade 1 are better candidates for surgical treatment of recurrent hepatocellular carcinoma. The albumin-bilirubin grade is considered useful for preoperatively predicting favorable prognoses after repeat hepatectomy for patients with recurrent hepatocellular carcinoma.

Abstract Submission No. 101937
P-1079

Relationship between hepatocellular carcinoma and insomnia: A Mendelian randomization study

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Background: Hepatocellular carcinoma (HCC) is a commonly diagnosed cancer worldwide. In some patients, there appears to be a relationship between hepatocellular carcinoma and insomnia. It is noteworthy that previous conclusions are prone to be biased by confounding effects and reverse causation due to the nature of observational studies. However, Mendelian randomization (MR) analyses can potentially overcome some of the limitations inherent in conventional epidemiologic studies.

Methods: We obtained the genome-wide association study (GWAS) summary statistics for hepatocellular carcinoma from the GWAS Catalog (<https://www.ebi.ac.uk/gwas/>). And GWAS summary statistics of insomnia traits can be accessed via the IEU Open GWAS Project (<http://gwas.mrcieu.ac.uk>). Based on publicly available genetic data, we conducted a bidirectional, two-sample, MR analysis to explore causal associations between hepatocellular carcinoma and insomnia, and we used the inverse variance weighted method as the primary analysis. Additionally, we used sensitivity analysis and outlier detection to examine robustness and pleiotropy of effect estimates.

Results: We revealed no causal relationship between hepatocellular carcinoma and insomnia using 6 SNPs in forward-direction MR (odds ratio [OR]=1.0021, 95% confidence interval [CI]=1.0005-1.0037, $P=0.0088$). And we revealed no causal relationship between insomnia and hepatocellular carcinoma using 23 SNPs in reverse-direction MR analysis (OR=0.2754, 95% CI=0.0009-83.8180, $P=0.6585$).

Conclusions: Our bi-directional MR analysis affirms no causal effect of hepatocellular carcinoma on insomnia, or insomnia on hepatocellular carcinoma.

Abstract Submission No. 200045
P-1080

Differential expression of miRNA in PBMC of primary liver cancer with qi deficiency and blood stasis

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Qi deficiency and blood stasis are the main traditional Chinese medicine (TCM) syndromes of primary liver cancer (PLC). We extracted peripheral blood mononuclear cells from patients with PLC of Qi deficiency and blood stasis, sequenced the high-throughput transcriptome, analyzed the differentially expressed miRNAs, predicted the possible target genes, analyzed their biological functions, and evaluated their correlation with the abundance of immune cells, in order to provide potential microscopic objective evidence for the dialectical treatment of patients with PLC of Qi deficiency and blood stasis. The results show that, compared with the non-Qi-deficiency and blood stasis group, there were three significantly differentially expressed miRNAs in the Qi-deficiency and blood stasis group, including hsa-miR-1299, hsa-miR-328-5p, and hsa-miR-3168. GO and KEGG analyses indicated that the biological functions and enrichment pathways of target genes from differential miRNAs were mainly related to autophagy, metabolism, and stemness. In the group of qi deficiency and blood stasis, hsa-miR-1299 may target MANSC1, PRND, ATP6V0C and KCNJ2, Hsa-miR-3168 may target IL-10. In the group of non-qi deficiency and blood stasis, hsa-miR-1299 may target BPGM and hsa-miR-3168 may target FCGR3B. By comparing the abundance of the differential target genes with that of immune cells in patients with PLC, we found that the differential target genes were significantly correlated with neutrophils, resting NK cells, and activated memory CD4⁺T cells. In conclusion, there were differences in the expression of miRNAs in peripheral blood immune cells of patients with PLC between the qi deficiency and blood stasis group and the non-qi deficiency and blood stasis group. They might become potential biomarkers for TCM diagnosis.

Abstract Submission No. 200120
P-1081

SERUM AFP, AFP-L3 & DCP RESPONSES FOR MONITORING TREATMENT OUTCOMES IN HCC PATIENTS TREATED BY TACE

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Background: Alpha-fetoprotein (AFP) responder alone without doing contrast enhanced computed tomography (CECT) couldn't be applied as further treatment decision after transarterial chemoembolization (TACE) therapy in hepatocellular carcinoma (HCC) patients.

Objective: To find out the association between tumor marker responder using AFP and newly US FDA approved serum biomarkers specific for HCC like Alpha-fetoprotein Lens culinaris agglutinin 3 (AFP-L3), Des-gamma carboxyprothrombin (DCP) and radiological responder with modified Response Evaluation Criteria in Solid

Tumors (mRECIST) criteria at before and one month after TACE in HCC patients.

Methods: Serum AFP was measured by e 411 fully automated immunoassay analyzer and AFP-L3 and DCP were measured by sandwich-ELISA kit with semi-automatic immunology analyzer assay. An AFP, AFP-L3 % and DCP responder was defined as a reduction of more than 50% from the baseline level and radiological responder with mRECIST criteria was classified as complete response and partial response defined as more than 30% decrease in the sum of longest diameters of viable (arterially enhancing) target lesions compare with baseline) at one month after TACE.

Results: AFP, AFP-L3 % and DCP responders were determined in 41 (48.1%), 49 (57.6%) and 60 (70.6%) in HCC patients at one month after TACE. Single tumor marker responder (AFP-L3 % or DCP) was significantly associated with radiological responder ($p=0.013$ and $p<0.001$) while AFP responder was not associated. Combination of two tumor marker responder including DCP (DCP plus AFP, DCP plus AFP-L3 %) were also positively associated with radiological responder ($p=0.004$ and $p<0.001$) while AFP plus AFP-L3 % responder was not associated. The combination of all three tumor marker responder (DCP plus AFP plus AFP-L3 %) was also be associated with radiological responder ($p=0.004$).

Conclusion: DCP tumor marker measurement alone would be more informative for tumor burden and decisive for further treatment option after TACE in HCC patient.

Keywords: HCC, AFP, AFP-L3%, DCP, mRECIST

Abstract Submission No. 200180
P-1082

Long-term outcomes and evaluation of HCC recurrence and simple scoring system: AKLD Group Study

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Aims: Direct acting antivirals (DAA) has improved the cure rate of HCV patients. However, the occurrence rate of hepatocellular carcinoma (HCC) and the long-term outcomes in patients with HCC recurrence after DAA treatment remains unknown.

Methods: At first, we aimed to identify predictors of HCC occurrence following DAA treatment. Among 1218 patients infected with HCV, 1,088 patients who achieved sustained virologic response and who had no history of HCC treatment were recruited between September 2014 and November 2018.

Results: The incidence of HCC was 0.61, 1.88, 2.82 and 3.71% at 6, 12, 18 and 24 months after treatment with DAA, respectively. The results of multivariate analysis identified age [hazard ratio (HR), 1.0729; $P=0.0044$] and α -fetoprotein (AFP) level after DAA treatment (HR, 1.0486; $P=0.0486$) as independent factors that may contribute to HCC occurrence following DAA treatment. By using these two factors, a novel scoring system (0-2 points) was established to predict HCC occurrence following HCV eradication by DAA treatment. The incidence

of HCC at 2 years was 0.3% in the 0 points group, 6.27% in the 1 point group and 18.37% in the 2 points group.

Conclusions: AFP level after DAA treatment and age at DAA administration were identified as independent predictors of HCC occurrence in patients that were treated with DAA. The scoring system that was established in the present study is simple and easy, and using pre-treatment factors may be a convenient tool to predict the risk of HCC occurrence in HCV-free patients following DAA treatment.

Abstract Submission No. 101173
P-1083

Head-to-head comparison among FAST, MAST and multiparametric MRI in diagnosing at-risk NASH

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Background: The presence of at-risk non-alcoholic steatohepatitis (NASH) (Nonalcoholic fatty liver disease (NAFLD) activity score ≥ 4) and significant fibrosis (Fibrosis stage ≥ 2) is associated with progression to cirrhosis. Therefore, noninvasive assessment of at-risk NASH is a critical need for pharmacologic therapy. We developed new scores to identify at-risk NASH using multiparametric magnetic resonance elastography (mpMRI).

Methods: A prospective study was conducted on 176 patients with suspected or diagnosed NAFLD paired with an MR scan, vibration controlled transient elastography (VCTE) and liver biopsy. Liver stiffness measurement (LSM) using magnetic resonance elastography (MRE), proton density fat fraction (PDFF), and mpMRI-based corrected T1 (cT1) were combined to develop a one-step strategy, named MPcT (MRE+PDFF+cT1, combined score), and a two-step strategy—MRE-based LSM followed by PDFF with cT1 (M-PcT, paired score) for diagnosing at-risk NASH. Each model was categorized using rule-in and rule-out criteria (three categorized analysis).

Results: PDFF+cT1 (PcT) had the highest diagnostic performance for severe activity (hepatic inflammation plus ballooning grade ≥ 3) and for NAS ≥ 4 (active NASH). Areas under receiver operating characteristic curves (AUROCs) of M-PcT (0.832) for detecting at-risk NASH were significantly higher than those of Fibroscan-AST (FAST) (0.744, $p=0.017$), MRI-AST (MAST) (0.710, $p=0.002$) and MPcT (0.695, $p<0.001$) in three categorized analysis. Following the rule-in criteria, positive predictive values of M-PcT (84.5%) was higher than those of FAST (73.5%), MAST (70.0%) and MPcT (66.7%). Following the rule-out criteria, negative predictive values of M-PcT (88.7%) were higher than those of FAST (84.0%), MAST (73.9%) and MPcT (84.9%).

Conclusions: The two-step strategy, M-PcT (paired score), showed reliability of rule-in/-out for at-risk NASH, with better predictive performance compared with FAST and MAST (combined score).

Abstract Submission No. 101791
P-1084

Usefulness of Medical Imaging Projection System for open liver resection

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Background: Indocyanine green (ICG) fluorescence-guided surgery is a real-time navigation technology for tumor detection, securing surgical margins, segmentation mapping, and cholangiography in liver surgery. According to recent reports, the Medical Imaging Projection System (MIPS, Mitaka Kohki Co, Tokyo, Japan) may be a useful new real-time navigation technology for open anatomical liver resection. We report usefulness of MIPS-assisted liver resection for real-time navigation.

Methods: We conducted a retrospective review of surgical and clinical outcomes for patients who underwent hepatectomy using the MIPS a, between September 2021 and December 2023. 0.025 mg ICG is injected for positive staining and negative staining technique is intravenously injected with 2.5mg ICG after blood flow occlusion. For tumor detection and securing surgical margins, ICG of 0.5 mg/kg was administered 2-14 days before the surgery. 2.5 mg/body of ICG is administered 1 hour before surgery for ICG cholangiography.

Results: We included 12 patients who underwent open liver resection for hepatocellular carcinoma ($n=5$), liver metastasis ($n=4$), or intrahepatic cholangiocarcinoma ($n=3$). Eight patients underwent anatomical resection with positive ($n=3$) or negative staining ($n=5$) technique and four patients were non-anatomical resection. MIPS could visualize the demarcation line and clarify the boundaries of the liver segments with positive ($n=3$) or negative staining ($n=5$) techniques and could detect all tumors ($n=4$) within 10mm from liver surface. All patients were no positive margins and no complications.

Conclusion: MIPS could be useful for real-time navigation during open liver surgery.

Abstract Submission No. 102047
P-1085

B-mode shear wave elastography can be an alternative to vibration-controlled transient elastography

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Background: The aim of this study was to evaluate the comparability of vibration controlled transient elastography (VCTE) and shear wave elastography (SWE) by combination elastography, and to establish regression equations between VCTE and new point SWE.

Methods: A total of 829 patients with chronic liver disease participated, excluding those with a skin-liver capsule distance >25 mm. Reproducibility for VCTE and SWE was verified by phantom and clinical studies. A similar analysis was performed for the Liver Fibrosis Index (LFI), a quantitative assessment of liver fibrosis using strain elastography image features. Regression equations between VCTE and SWE values were derived by linear regression analysis.

Results: Strong correlations between VCTE and SWE were observed in both phantom and clinical studies [$r=0.995$ ($p<0.001$) and $r=0.747$ ($p<0.001$), respectively]. The regression equation was determined as VCTE (kPa)= $1.09 \times$ point SWE (kPa)-0.17. Bland-Altman plots showed no significant bias. Conversely, there was no correlation between VCTE and LFI ($r=0.279$), indicating a statistically significant bias in the Bland-Altman plots. Inter-operator reliability showed a favourable intraclass correlation coefficient of 0.760 (95% confidence interval: 0.720-0.779).

Conclusion: Liver stiffness measured using point SWE was comparable to that measured using VCTE.

Abstract Submission No. 100916

P-1086

A case of foreign body granuloma suspected of peritoneal dissemination of hepatocellular carcinoma

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A woman in her 60s was referred to our hospital with suspicion of hepatocellular carcinoma in November 3 years ago. A contrast-enhanced CT scan revealed a 55mm-sized, early phase, ischemic mass in liver S5 with uneven enhancement only at the margins. S5 subsegmental resection was performed in January 2 years ago. Pathological results showed poorly differentiated hepatocellular carcinoma. In August last year, laparoscopic S8 partial resection was performed for recurrence of hepatocellular carcinoma in liver S8. Radiofrequency ablation (RFA) was performed for the recurrent lesion in liver S7 in April that year.

A CT scan after RFA revealed an 8mm-sized contrast-enhanced nodule just below the abdominal wall of the right upper quadrant, which had slightly increased in size since the CT scan 4 months earlier. EOB-MRI examination showed that the nodule was enhanced in the hepatobiliary phase. PET-CT examination revealed relatively clear FDG accumulation in the nodular lesion. Peritoneal dissemination of hepatocellular carcinoma was suspected, so laparoscopic tumor removal was performed for total-biopsy in August. The excised peritoneal tissue was covered with connective tissue. A large number of foreign body-type giant cells densely clustered in the tumor, and artifacts resembling sutures were observed between these cells. Based on these findings, a diagnosis of foreign body granuloma was made.

As in our case, a benign nodule may be suspected to be peritoneal dissemination by imaging, so histological diagnosis before treatment is important.

Abstract Submission No. 102033

P-1087

Study of tumor identification using ICG for metastatic liver cancer after neoadjuvant chemotherapy

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Background: Although the usefulness of liver tumor identification by ICG fluorescence method has been reported, we also experience minute lesions that do not show fluorescence and are difficult to identify during surgery. It is often difficult to identify the tumor especially in cases treated with preoperative chemotherapy. In this study, we investigated tumor identification using ICG fluorescence method for metastatic liver cancer treated with preoperative chemotherapy.

Methods: From May 2014 to February 2023, 14 patients (17 nodules) who underwent preoperative chemotherapy among patients who underwent laparoscopic partial hepatectomy for metastatic liver cancer were included. They are assigned to two groups, fluorescence group and non-fluorescence group, and examined about patient background,

blood test, preoperative CT (computed tomography) findings, tumor characteristics.

Results: 10 of the 17 nodules (58.8%) were identifiable by ICG fluorescence. The result showed a significant difference in maximum tumor size (10.2mm vs 15.5mm, $p=0.0088$) and chemotherapy response rate (44.3% vs 90.5%, $p=0.0004$). Ring enhancement around the tumor on preoperative contrast enhanced CT is associated with intraoperative fluorescence (100%, $p=0.002$), and all lesions with ring enhancement on preoperative CT showed ICG fluorescence.

Conclusion: It is necessary to take care in cases that ICG fluorescence may not be obtained in cases with small tumor size, low response rate, or no ring enhancement. In case that tumor identification by ICG fluorescence is difficult, preparation of other modalities and transition to laparotomy should be considered.

Abstract Submission No. 200232

P-1088

Efficacy of hepatic arterial infusion chemotherapy with liver metastases for gastric cancer

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Purpose: Patients with liver metastases from gastric cancer are generally treated with systemic chemotherapy, because extrahepatic disease is frequently present at the initiation of treatment. Treatment other than systematic chemotherapy for patients with liver metastases from gastric cancer has not yet been established.

Patients and methods: At our hospital, patients with liver metastases of gastric cancer who underwent hepatic arterial infusion chemotherapy (HAIC) between January 2016 and December 2020 with paclitaxel, cisplatin, and 5-fluorouracil were included in the study. Patients were administered paclitaxel (60 mg/body, 1 h), cisplatin (30 mg/body, 1 h), and 5-fluorouracil (1250 mg/body, 36-h continuous infusion) through the artery on day 1 (HAIC-PCF).

Results: We evaluated seven patients who underwent HAIC-PCF. The patients received a median of 8 cycles (range, 2–20). Response and disease control rates were 42.8% and 71.4%, respectively. The median overall survival (OS) and progression-free survival (PFS) after this treatment were 18.7 months (95% confidence interval [CI], 0 – 39.9) and 7.7 months (95% CI, 2.1 – 13.3), respectively. The median OS since the disease onset was 43.3 months. In addition, the median PFS of patients with extrahepatic metastases was 5.5 months.

Conclusion: HAIC-PCF may be an effective chemotherapeutic agent for patients with hepatic metastases of gastric cancer. If extrahepatic metastasis is not advanced, these treatments may be useful as therapeutic options for patients with liver metastases from gastric cancer.

Abstract Submission No. 100860

P-1089

HAV IgG seroprevalence among chronic liver disease patients in South Korea

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Introduction: HAV IgG seroprevalence is different according to the age. Coinfection of hepatitis A can aggravate liver damage in chronic liver disease patient. We need to know HAV IgG seroprevalence among chronic liver disease patients

Method: We checked HAV IgG in 40 patients who have chronic liver disease from 2021 to 2022. Hepatitis B patients were 16, Hepatitis C patients were 4 and alcoholic liver disease patients were 20. Seroprevalence of HAV Ig G was analyzed retrospectively.

Result: Seropositivity of HAV IgG is 55%(22/40). According to age, 10-19years 25%(1/4), 20-29years 25%(2/8), 30-39years 33%(4/12), 40-49years 87%(7/8), 50-59years 100%(8/8) Seropositivity of IgG is increasing as age becomes higher($p<0.05$). Seropositivity of patients below 40 years old is 29%(7/24) and above 40 years old is 93%(15/16). Seropositivity is high in patient above 40years old ($p<0.05$). Seropositivity of IgG among underlying disease(HBV, HCV, alcoholic liver disease) was not different($p>0.05$)

Conclusion: Seropositivity of HAV IgG was low in young generation because of recent good hygiene. HAV vaccination can be reasonable for chronic liver disease under 40 years old in South Korea.

Abstract Submission No. 101206

P-1090

Comparison of resection, ablation and SBRT in treating solitary hepatocellular carcinoma ≤ 5 cm

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Backgrounds: The best treatment option among resection, thermal ablation and stereotactic body radiation therapy (SBRT) in dealing with single HCC ≤ 5 cm remains unclear.

Methods: This multicenter study included 985 patients from 3 hospitals: 495, 335 and 155 in the resection, ablation and SBRT groups, respectively.

Results: The SBRT group had unfavorable clinical features compared to the other two groups, including larger tumor size, poorer liver function and more relapsed tumors. The 1-, 3-, and 5-year RFS rates were 84.3%, 66.8% and 56.2% with resection, 73.3%, 49.8% and 37.2% with ablation and 73.2%, 56.4% and 53.6% with SBRT, respectively ($P<0.001$). The 3-year OS rates were 89.0%, 89.2% and 88.8% in the resection, ablation and SBRT group, respectively ($P=0.590$). The three modalities resulted in similar RFS and OS after propensity score matching (PSM) ($P=0.170$ for RFS and 0.880 for OS). Resection provided ideal local tumor control, successively followed by SBRT and ablation ($P<0.001$ both before and after PSM). SBRT led to comparable RFS time compared to resection for tumors < 3 cm ($HR=0.75$, $P=0.205$), relapsed tumors ($HR=0.83$, $P=0.420$) and patients with poor liver function ($HR=0.70$, $P=0.330$). In addition, SBRT was superior to ablation regarding RFS when tumors were adjuvant to intra-hepatic vessels ($HR=0.64$, $P=0.031$). Gastrointestinal disorders, hepatic inflammation and myelosuppression occurred more frequently in the SBRT group.

Conclusion: Resection remains the best choice for preventing tumor recurrence, and SBRT showed ascendancy in treating small, recurrent and vascular-type lesions as well as patients with relatively poor liver function.

Abstract Submission No. 100161

P-1091

Salvage hepatectomy for recurrent hepatocellular carcinoma after radiofrequency ablation

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Background: Although radiofrequency ablation (RFA) is a well-established locoregional treatment modality for hepatocellular carcinoma (HCC), the optimal strategy to handle local recurrence after ablation is still debated.

Methods: Between January 2004 and December 2020, 1161 patients were subject to surgical resection for HCC. Among them, 47 patients who underwent SH for local recurrence after ablation were retrospectively analyzed and compared to a propensity-score matched group of controls ($n = 47$) who received primary hepatectomy (PH). Short-term and long-term outcomes were analyzed between the two groups.

Results: After matching, operation time, intraoperative blood loss, postoperative hospital stay, and postoperative morbidity rates showed no statistically significant difference. Tumors in the SH group were associated with poor differentiation (SH 9 (19.1%) vs. PH 1 (2.1%), $P < 0.001$). The 5-year disease-free survival rates (31.6% vs. 73.4%, $P < 0.001$) and overall survival rates (80.3% vs. 94.2%, $P = 0.047$) were significantly lower in the SH group. In multivariable analysis, less extensive resection compared to initial plan (hazard ratio (HR) 4.68, $P = 0.024$), higher grade (HR 5.38, $P < 0.001$), negative but close (< 0.1 cm) resection margin (HR 22.14, $P = 0.007$), and R1 resection (HR 3.13, $P = 0.006$) were significant predictors for recurrence.

Conclusions: SH for recurrent tumors after ablation shows safety and effectiveness equivalent to primary resection. As recurrent tumors show higher grade and more aggressive behavior, more extensive resections with wide surgical margins are necessary to prevent recurrence.

Abstract Submission No. 100209

P-1092

Albumin-indocyanine green evaluation of future liver remnant as a surgical indicator for hepatectomy

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Aim: The albumin-indocyanine green evaluation (ALICE) score is a useful predictor of post-hepatectomy liver failure (PHLF); however, its usefulness in combination with future liver remnant (FLR), measured by 3-D volumetry, has not been investigated. This study aimed to investigate the relationship between the ALICE of the FLR (ALICE-FLR) score and severe PHLF.

Methods: The clinical data of 215 patients who underwent anatomical hepatectomy for hepatocellular carcinoma without portal vein embolization at two institutes between January 2010 and December 2021 were analyzed retrospectively. PHLF occurrence and severity were determined according to the International Study Group of Liver Surgery's definition. Grades B and C PHLF were defined as severe PHLF.

The ALICE-FLR, ALICE scores, and indocyanine green clearance of FLR (ICGK-FLR) were evaluated for severe PHLF prediction.

Results: Severe PHLF was observed in 40 patients (18.6%). The areas under the curve (AUCs) for the ALICE-FLR, ALICE scores, ICGK-FLR, and FLR were 0.76, 0.64, 0.73, and 0.69, respectively. The AUC of the ALICE-FLR score was significantly higher than that of the ALICE score. The ALICE-FLR score was identified as an independent predictor of severe PHLF ($p = 0.004$). Among patients with severe PHLF, the ALICE-FLR score was significantly higher in the grade C than in the grade B PHLF group.

Conclusion: The combination of liver function models, including indocyanine green, albumin, and FLR is considered compatible for predicting severe PHLF.

Abstract Submission No. 101018

P-1093

OUTCOME OF PATIENTS WITH ACLF UNDERGOING PLASMAPHERESIS –AN OBSERVATIONAL STUDY

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BACKGROUND: ACLF is associated with high mortality and few treatment options. This study aims to investigate the potential benefit of plasmapheresis in ACLF patients without transplant.

METHODS: Prospective study conducted at Sir Ganga Ram Hospital .72 patients with ACLF (EASL CLIF criteria) enrolled. Patients with no improvement in ACLF grade or MELD score (after 72 hours), were evaluated for plasmapheresis (including alcohol hepatitis patients not eligible for steroid therapy or Lille score > 0.45 after 7 days) (Group A) and rest were continued on SMT (Group B). Low volume PLEX done on alternate days as per clinical response.

RESULTS: In PLEX (n=22) group 12 (54.5 %) patients were discharged compared to 17 (34.0%) in the SMT (n=50) group ($p=0.257$). 30 days survival in the PLEX group was (n=16/81.25%) compared to (n=29/68.9%) ($p=.321$) in SMT. 90 days survival in the PLEX group was (n=13 / 38.46%) compared to (n=20 /60%)($p=0.99$)in SMT group. In PLEX group (n=12 /54.5 %) patients discharged had significant decrease in MELD Na (35.46 $\pm$ 4.63) as compared to pre PLEX MELD (32.15 $\pm$ 5.47) ($p=.004$). No PLEX related severe adverse effect seen.

CONCLUSIONS: In our study patients undergoing PLEX had increased hospital survival by 20 % and increase in 30 days survival by 10 % as compared to SMT group. However values were not statistically significant due to small sample size. Hence PLEX may be a viable therapy in patients awaiting transplant by increasing short term survival however further randomized control trials are needed.

Abstract Submission No. 200037

P-1094

Platelet aggregation in patients with acute-on-chronic liver failure

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Introduction: There are still controversial data regarding platelet aggregation in patients with liver cirrhosis and acute decompensation. The aim of this prospective study was to evaluate whole blood platelet aggregation in patients with acute-on-chronic liver failure (ACLF) and the correlations with liver mortality.

Methods: Whole blood aggregometry (Multiplate®) was used to evaluate platelet aggregation. We determined a ratio between the area under curve of platelet aggregation and platelet count (AUC/PLT ratio) in order to overcome the influence of liver cirrhosis associated thrombocytopenia. The patients were divided in two groups: ACLF group and liver cirrhosis with acute decompensation group (AD). The patients were prospectively followed-up for 3 months.

Results: In this study we prospectively included 55 patients with ACLF and 55 patients with AD. There were no differences regarding age, sex and liver cirrhosis etiology between both groups. AUC/ PLT ratio was substantially greater in AD patients compared to those with ACLF (0.52 vs. 0.22; $p<0.0001$). AUC/PLT ratio (OR 2.48; 95%CI1.02-5.77; $p=0.013$) and CLIF-C score (OR 5.12; 95% CI 1.25-8.18; $p< 0.001$) were shown to be independently correlated with negative outcome on multivariate analysis. The ACLF patients with an AUC/ PLT > 0.52 had a 4-fold increased relative risk of events compared to those with AD ($p = 0.002$).

Conclusion: The patients with ACLF have a decreased whole-blood platelet aggregation compared with patients with AD, and this is associated with a higher probability of liver related mortality.

Abstract Submission No. 200268

P-1095

A case of acute liver failure with HELLP syndrome treated with plasma exchange and steroid pulse

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Case: 30-year-old female

Complaint: General malaise.

She was admitted to the obstetrics and gynecology department of our hospital at 22 weeks and 6 days of pregnancy with a diagnosis of impending premature delivery. She was once discharged from the hospital at 35 weeks 0 days after receiving ritodrine hydrochloride. On 36 weeks 5 days of pregnancy, thrombocytopenia, increased AST and LDH were observed, and an emergency cesarean section was performed with a diagnosis of partial HELLP syndrome. On the second postoperative day, the patient was found to have worsening liver dysfunction and was referred to the Department of Gastroenterology and Hepatology.

The patient was diagnosed as a severe acute liver failure, and plasma exchange was started on the same day. Considering the possibility of liver transplantation, preparations for transplantation were also started. After 3 days of plasma exchange, the patient continued to deteriorate, and a steroid pulse therapy was administered. Although her liver enzymes peaked out, elevated blood pressure and seizures appeared on the sixth postoperative day, and postnatal PRES syndrome was suspected, and she was intubated. The patient was extubated on the 8th postoperative day after administration of anticonvulsants and antihypertensive drugs, and thereafter, her liver function improved, and a liver transplant was avoided.

HELLP syndrome generally improves after childbirth. However, the patient continued to deteriorate even after delivery, leading to acute liver failure. We consider this case is didactic in that the patient responded well to plasma exchange and steroid pulse therapy.

Abstract Submission No. 200269
P-1096

A case of drug induced hypersensitivity syndrome with liver failure caused by acetaminophen

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A 74-year-old man was administered acetaminophen at another hospital after fracturing a rib in May. In mid-June, erythema appeared all over the skin, liver enzymes were elevated, PT was prolonged, ascites and mediastinal lymphadenopathy were noted on CT, and the patient was admitted to another hospital with a diagnosis of acute liver failure. Prednisolone 500mg was administered for 3 days, but his PT was further prolonged, and he was transferred to our hospital.

The administration of acetaminophen by chance caused further worsening of erythema and prolongation of PT from 43% to 19%. Plasma exchange (PE) and hemodialysis were started. The patient was diagnosed as drug-induced hypersensitivity syndrome (DIHS) by eosinophilia and skin rash, and HHV6 reactivation. Prednisolone 50 mg/day was started, and PE was performed 10 times, but his liver function did not recover, and he died in early August.

Discussion: DIHS is a drug hypersensitivity reaction with skin rash, organ damage, eosinophilia, and lymphadenopathy. The rash appears 2 to 8 weeks after drug initiation and continues for at least 15 days after drug discontinuation. Eosinophilia, atypical lymphocytes, liver and kidney damage, etc. appear, and the disease resolves within a few weeks to a few months, but liver failure and multi-organ failure cause death in 5-10% of patients. Acetaminophen-induced DIHS is rarely reported, but in this case, all 7 diagnostic criteria were met. Steroids are recommended in cases of organ failure, but in this case, steroids could not save the patient's life, and further case studies are needed.

Abstract Submission No. 200178
P-1097

Endoscopic biliary drainage for unresectable malignant hilar biliary obstruction.

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Background: Endoscopic drainage of unresectable malignant hilar biliary obstruction (UMHBO) often requires either side-by-side (SBS) or stent-in-stent (SIS) techniques. In this study, we compared the short-term and long-term results of the SBS and SIS methods. **Methods:** This was a single-center retrospective review of 28 patients who underwent endoscopic biliary an uncovered self-expanding metal stenting for unresectable MHBO from October 2014 to April 2022. Patients

underwent endoscopic retrograde cholangiopancreatography and stenting using either the SBS or SIS technique.

Results: There were no significant differences between groups in technical and functional success (SBS vs. SIS, 95 vs. 86 %, respectively), mean procedure time (72 vs. 110 min), RBO rate (55 vs. 50 %), TRBO (143 vs. 136 days), early complications (24 vs. 14 %), late complications (10 vs. 14 %). There were no significant differences in reintervention success rates (98 vs. 86 %), but the mean procedure time for reintervention was significantly shorter for SBS than for SIS (31 vs. 58 min; $p < 0.001$).

Conclusions: Our results showed no significant difference in clinical outcomes such as success rate or RBO between SBS and SIS technique for UMHBO. However, SBS technique may be superior to the SIS technique in terms of reintervention.

Abstract Submission No. 100090
P-1098

Amiodarone induce acute hepatotoxicity in Pakistani population: two case reports

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Background: Although rare, intravenous amiodarone can cause substantial hepatotoxicity, leading to a rapid increase in transaminases, often exceeding 100 times the upper limit of normal (ULN). The effect tends to reverse upon discontinuation, allowing for oral therapy. This study presents two cases of acute hepatocellular injury due to amiodarone infusion, emphasizing its discontinuation and confounding factor removal on transaminase levels in Pakistani patients.

Method: Case 1, a 52-year-old male patient undergoing CABG, received a 16-hour infusion of Amiodarone for postoperative atrial fibrillation. Concurrently, co-amoxiclav, esomeprazole, acetaminophen, and rosuvastatin were administered. SGPT was normal before amiodarone treatment but increased 60-fold after infusion. After switching to low-dose oral Amiodarone (400 mg per day), the SGPT returned to normal within 26 days.

Case 2 is a 72-year-old woman with multiple conditions received amiodarone and ceftriaxone for atrial fibrillation and infection. Within 24 hours, SGPT increased 100-fold. After discontinuation of amiodarone, SGPT returned to normal within 52 days of switching to digoxin and imipenem.

Conclusion: Case 1 responded well to oral amiodarone, possibly due to polysorbate 80 solubilizer in injection or higher intravenous dose. Acetaminophen, amoxicillin-clavulanate, and statins elevated SGPT, while omeprazole exhibited safer hepatic profiles than esomeprazole. Case 2 shifted to safer alternatives. Reversal of SGPT was seen in both cases up to several weeks after drug discontinuation. Amiodarone's extended elimination time due to its large volume of distribution underscores the vigilant liver function tests monitoring to mitigate this rare yet harmful effect.

Abstract Submission No. 100115
P-1099

Splenic Marginal Zone B-Cell Lymphoma with Hepatitis B virus infection during the Covid 19 Pandemic

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INTRODUCTION: An indolent B-cell lymphoma originating from the marginal zone namely splenic marginal zone lymphoma (SMZL) comprised only 1-2% of non-Hodgkin's lymphoma (NHL) was known to be associated with hepatitis infection. In cases where splenectomy is contraindicated, a combination of a bone marrow biopsy results, and immunohistochemistry confirmed by a hematologist confirms the diagnosis of SMZL.

CASE REPORT: This is to report a case of SMZL in a 63-year-old male with chronic hepatitis B infection on Tenofovir medication who presented with unintentional weight loss and intermittent left upper quadrant discomfort. A bone marrow morphologic diagnosis revealed a markedly hypercellular bone marrow, with mature CD5 to be more than 95% and CD10 negative, B-cell lymphoproliferative disorder supported with an immunohistochemistry report showing CD20 positive, CD3 negative, CD5 negative, CD10 negative, Ki67 positive, low 5-10 %; Cyclin D1 negative and presence of splenomegaly thereby, confirms the diagnosis of splenic marginal zone B cell lymphoma.

DISCUSSION: There are some reports where Hepatitis B is associated with SMZL and treatment of the viral infection showed resolution of the lymphoma, however the exact oncogenesis is still an area of exploration. This case highlights the pre-existence of Hepatitis B infection in SMZL and the response to a second line treatment drug, Ibrutinib due to infusion reaction to first line regimen – Rituximab in this time of Covid 19 pandemic.

Abstract Submission No. 100180
P-1100

Liver Injury and Cholecystitis due to Endoscopic Treatments for Duodenal Ulcer Bleeding

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A 67-year-old male with asymptomatic polycystic kidney and polycystic liver presented with recurrent hematemesis and hypotension shock. He was diagnosed with duodenal bulbar ulcer 6 days ago and underwent endoscopic treatment using a through-the-scope clip.

After resuscitation, we performed an emergency endoscopy and replaced the malfunctioning clip (Figure 1A) with an over-the-scope clip, but pulsatile bleeding persisted. Consequently, we injected N-butyl-2-cyanoacrylate (histoacryl) and laurumacrogol (hardener) at a sequence of hardener-histoacryl-histoacryl: 2 mL-1 mL-1 mL, ultimately achieving hemostasis (Figure 1B).

Subsequently, the patient experienced upper abdominal pain followed by a fever peak of 38.5 °C the next day. Physical examination revealed a positive Murphy's sign, while laboratory tests showed significant elevations in white cell count, transaminases and bilirubin levels. Enhanced CT imaging demonstrated edema and thickening of the gallbladder wall and underfilling of the proper hepatic artery (Figure 2).

Our working diagnosis was cholecystitis and liver injury resulting from ectopic embolism of N-butyl-2-cyanoacrylate in the proper hepatic artery, and its branches including cystic artery.

The patient received ultrasound-guided percutaneous transhepatic gallbladder drainage (PTGD), antibiotic and hepatic protector therapy. He recovered rapidly and was discharged with a follow-up plan.

While endoscopic cyanoacrylate injection (ECI) has proven efficacious in stopping high-risk peptic ulcer bleeding when conventional endoscopic treatment failed, it carries potential risks of ectopic embolism in the associated arteries supplying the duodenum.

Abstract Submission No. 100280
P-1101

Functional Cure of a Chronic Hepatitis B Cirrhosis Child Treated by Peginterferon α : A Case Report

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Background: Pediatric HBV-infected patients are susceptible to breaking through the immune tolerance and developing varying degrees of disease progression. However, current researches on antiviral therapy in children are relatively limited, particularly for those under 1 year of age.

Method: An 8-month-old infant with positive hepatitis B surface antigen (HBsAg) and abnormal liver function was diagnosed as chronic hepatitis B cirrhosis (G3S3-4) with active compensatory phase. The treatment regimen commenced with lamivudine (LAM) for the initial 8 weeks, followed by the addition of interferon α (IFN α) after 1 year of age. At 2 years old, LAM was substituted with entecavir (ETV), and at 3 years old, IFN α was replaced with peginterferon α (PEG IFN α). Doses of all antiviral drugs increased gradually with age and weight (Figure 1).

Results: After 8 weeks of LAM monotherapy, the child experienced HBeAg loss. Subsequently, after 36 weeks of IFN α add-on therapy, HBV DNA became undetectable, and after 48 weeks of switching to PEG IFN α treatment, HBsAg loss was observed. During the 50-week follow-up period after drug discontinuation, the child remained functionally cured. Remarkably, the child did not experience any noticeable adverse reactions throughout the treatment course.

Conclusion: Chronic HBV-infected infants and young children can also significantly benefit or even achieve functional cure after PEG IFN α -based individualized therapy. This case serves as a valuable reference for the diagnosis and treatment of such patients.

Abstract Submission No. 100346
P-1102

TEMPI syndrome misdiagnosed as cirrhosis with ascites: A case report

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Background: TEMPI syndrome is an extremely rare monoclonal plasma cell disease that can easily be misdiagnosed or missed. Currently, the diagnosis of TEMPI syndrome requires presence of telangiectasia, elevated erythropoietin, erythrocytosis, monoclonal gammopathy, perinephric fluid collection, and intrapulmonary shunting.

Case Summary: The present case involved a 58-year-old man with a large amount of ascites as the first symptom and a history of alcohol consumption, telangiectasia during physical examination, an ascitic albumin pressure gradient >11, and coagulation disorders. Ascites due to cirrhosis should be considered during the initial diagnosis. However, a blood test revealed a hemoglobin level of 201 g/L, suggesting

polycythemia, an erythropoietin level of 425 mIU/mL, and no portal hypertension or peripheral nerve damage. Further examination found monoclonal gammopathy IgG positivity and light chain κ elevation. Bone marrow biopsy showed few plasma cells with restricted kappa expression (<5%). An *ANKRD26* gene variant was also identified. The source of ascites was still undiagnosed, and an ultrasound found a small amount of perirenal effusion again after 1 month. Technetium 99-labeled lung perfusion imaging revealed an intrapulmonary shunt.

Conclusions: Ascites is the most common clinical symptom in gastroenterology, but diagnosis of TEMPI syndrome with ascites as the initial symptom requires interdisciplinary collaboration to avoid misdiagnosis and delayed treatment.

Abstract Submission No. 100537

P-1103

Cavernous Transformation of the Portal Vein with Pyogenic Liver Abscess: A Case Report

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In cavernous transformation of the portal vein (CTPV) (also known as portal cavernoma or chronic portal vein thrombosis), the obstructed portal vein is substituted by a network of portoportal collateral veins. Complete obstruction of the portal vein almost always leads to portal hypertension and the development of portosystemic collaterals, which may present with ruptured gastroesophageal varices. We report a case of a 21-year-old female who presented with six years history of upper gastrointestinal bleeding secondary to ruptured gastroesophageal varices. She underwent endoscopic band ligation. Portal doppler ultrasound revealed cavernous transformation of the portal vein, splenomegaly, and splenic varices. She had right upper quadrant pain and fever for two months. CT scan showed a 16.1x14.2x13.5cm segment IV abscess, splenomegaly, tortuous portal vein with dilated collateral vessels in the splenic hilum and left perinephric region. Ultrasound-guided percutaneous insertion of a pigtail catheter drained purulent fluid and culture demonstrated *Pseudomonas luteola* sensitive to ceftazidime. Ascitic fluid analysis revealed a serum ascites albumin gradient of 1.2 g/dL. Variceal screening showed a small varix and portal hypertensive gastropathy. Hepatitis markers were non-reactive. Ceftazidime was given for 14 days and shifted to Ciprofloxacin. Propranolol was continued. Resolution of the abscess was documented and the pigtail catheter was removed prior to discharge. Hematologic work-up demonstrated antibodies to beta-2 glycoprotein I, thus, antiphospholipid syndrome is the etiology of her hypercoagulable state. Aspirin was started. Antiphospholipid syndrome leads to a hypercoagulable state which causes CTPV. Although CTPV is a rare condition, this can predispose to abscess formation.

Abstract Submission No. 100767

P-1104

A rare case of hepatocellular adenoma in a man with idiopathic portal hypertension

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Background: Diagnosis of focal liver lesion needs a detailed history, physical exam, radiology, and pathology. Hepatocellular carcinoma

arising in idiopathic portal hypertension (IPH) is rare. We herein presented a case of an young male with a suspected malignant liver lesion in the setting of IPH.

Methods: A 22-year-old male was admitted to our hospital for diagnosis of a liver nodular lesion observed to gradually increase in size. In 2017, he had a temporary history of elevated ALT and was admitted to hospitals because anemia two years after. He was finally diagnosed as IPH based on the presence of portal hypertension (Panel 1) and liver biopsy (Panel 2) in our hospital. CT and ultrasound also revealed a hepatic nodular lesion in the right anterior lobe of liver, with 17 mm×15mm. Therefore, the patient was scheduled for regular follow-up examinations. In July 2021, the gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid MRI (EOB-MRI) (Figure 1) suggested that the nodular lesion was to be 31*23 mm. The circulating-tumor DNA and PIVKA-II was positive.

Results: He had no history of metabolic syndrome and taking steroids. BMI was normal. AFP was normal. The EOB-MRI showed the lesion might be hepatocellular adenoma (HCA) but not focal nodular hyperplasia (FNH) (Figure 2), which finally confirmed by biopsy. A close follow-up was recommended.

Conclusion: HCA occurs rarely against the background of IPH and male patients, especially without risk factors of HCA, such as hormonal abnormalities, obesity and features of the metabolic syndrome. EOB-MRI might be helpful to differential diagnose FNH and HCA.

Abstract Submission No. 100845

P-1105

Liver Cirrhosis with Recurrent Ascites In Diabetic Heart Disease: A Case Report

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Background: Management of recurrent ascites in liver cirrhotic may be challenging.

Case Report: A 60-year-old patient with liver cirrhosis, admitted due to fatigue and abdominal discomfort. Comorbidities are type2 diabetes, heart failure (ejection fraction 48%), and fatty liver. He underwent endoscopic band ligation and (two times) abdominal paracentesis recently. He received spironolactone 100mg/day, furosemide 40mg/day, degludec plus aspart (2x12unit subcutaneous), propranolol 60mg/day, and albumin supplement. Upon admission, he was compos mentis, blood pressure 90/60mmHg, heart rate 68 x/minute, normal temperature. There were palmar erythema, and palpated spleen.

Noted hypoalbuminemia (3.2 g/dL), hyperglycemia (265 mg/dL), hypokalemia (2.6 mEq/L), hyponatremia (133 mEq/L), cardiomegaly, minimal ascites and splenomegaly (schuffner II), thrombocytopenia (62.000/mm³), and eGFR 52 mL/min/1.73 m². Potassium replacement and B1-aminofluid intravenous were administered. Maintenance was continued. Episodes of hypotension impede optimization of diuretics dose. Dapagliflozin 10mg/day was started. Paracentesis was scheduled should ascites worsened. Seven days later, re-evaluation showed normal electrolyte, resolution of ascites, blood glucose within target, eGFR 43 mL/min/1.73m² with clinical improvement, and lead for outpatient. Latest routine follow-up showed no recurrences of ascites on ultrasound, A1c 7.2%, normal electrolytes, and eGFR 50 mL/min/1.73m².

Discussion: Electrolyte disturbances and hypotension are the side effects of diuretic treatment in managing ascites. The study showed that sodium glucose co-transporter-2 inhibitor/SGLT2i has natriuresis effect, which may alleviate ascites. Despite its positive cardiometabolic effect, dapagliflozin provides a synergistic effect with diuretics in controlling ascites in this case.

Conclusion: SGLT2i may provide benefit over conventional therapy for liver cirrhosis patient with recurrent ascites.

Abstract Submission No. 101062
P-1106

Bilothorax after hepatocellular carcinoma rupture: a case report

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Case presentation: A 72-year-old man presented with acute abdominal pain. Computed tomography (CT) showed a 17.7x12.3x13.5 cm. mass with arterial phase hyper-enhancement and washout in portovenous phase at right lobe of cirrhotic liver with left hepatic lobe and pulmonary metastases. Heterogeneous-enhancing fluid, size 11.5 x 3.6 cm, was detected at right subcapsular region, compatible with ruptured hepatocellular carcinoma (HCC). Transarterial chemoembolization (TACE) and partial Gelfoam embolization was performed to successfully control bleeding. Two weeks later, the patient developed progressive dyspnea. Chest radiography showed moderate amount of right pleural effusion with right lower lung atelectasis. Thoracentesis found olive-green colored fluid (figure1) with WBC 413 cells/mm³ (mononuclear 75%). Pleural fluid/serum profiles were as followed; protein 5.5/8.5 g/dL, albumin 2.1/2.5 g/dL and bilirubin 3.7/2.1 mg/dL. No organism or malignancy cell was detected. Abdominal ultrasonography found stable-sized heterogeneous hypochoic fluid at right perihepatic region and unchanged liver masses. The final diagnosis was bilothorax secondary from subdiaphragmatic biloma resulted from small bile duct injury, which might occur spontaneously during HCC rupture or after TACE procedure. Pleural and biloma drainage was not performed by three reasons; pleural fluid was sterile, the patient had no respiratory distress, and there was no evidence of ongoing bile leakage from liver that might further accumulate into pleural cavity. Therefore, we conservatively treated by giving oxygenation and breathing exercise. Pembrolizumab was prescribed for HCC treatment. Follow-up chest radiography at 6 weeks revealed complete resolution of bilothorax.

Conclusion: Bilothorax in patients with HCC rupture is extremely rare but could be treated conservatively.

Abstract Submission No. 101091
P-1107

Title: An Uncommon Instance of Liver Abscess Attributable to Dual Organisms.

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Introduction: Liver abscesses are primarily divided into amebic or pyogenic. Pyogenic liver abscess (PLA) accounts for 2.3 cases per 100,000. Most common pathogens are E.coli, Klebsiella, Streptococcus. Pseudomonas aeruginosa liver abscess (PALA) is a rare occurrence. Tayal et al described in his study that Amebic Liver Abscess can be complicated by pyogenic organisms. We present a unique case of liver abscess instigated by the coexistence of Entamoeba and Pseudomonas.

Case: 59 years old female presented with high grade fever and abdominal pain. She was found to have cholangitis secondary to

choledocholithiasis. ERCP revealed a CBD stone which was removed, followed by placement of plastic biliary stent. Post ERCP patient did not improve and stayed febrile. Clinical parameters kept worsening. CT Scan abdomen showed large abscesses in both lobes of liver. Largest abscess in right lobe measured 91x75x93mm. U/S guided drain was placed and aspirates were sent for culture which showed Pseudomonas Aeruginosa. Meanwhile Amebic IHA levels sent earlier also came positive. Patient was started on Metronidazole, Diloxanide furoate and IV Meropenem.

Discussion: The incidence of PALA is around 2-6%. There have been few case reports in which Pseudomonas was isolated from liver abscesses post ERCP. In our case it could be a possibility that Pseudomonas was inoculated during ERCP, which caused super infection over already ongoing ALA. To the best of our knowledge co-infection of Pseudomonas and ALA has never been reported before. It is important to consider the possibility of rare organisms and sending cultures to start pertinent antibiotic. The crucial factor lies in timely diagnosis and management.

Abstract Submission No. 101643
P-1108

A case of HCC in which MWA was performed under ultrasound and laparoscopic guidance

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Ultrasound sonography (US)-guided microwave ablation (MWA) for hepatocellular carcinoma (HCC) near the gallbladder carries the risk of gallbladder perforation and may result in insufficient ablation. Here, we report a case in which local recurrence occurred after US-guided MWA, and laparoscopic MWA was performed at the surgery.

The case is a man in his 70s. He is being treated for MAFLD (metabolic dysfunction associated fatty liver disease). The first HCC appeared in 2012. He underwent hepatic arterial chemoembolization (TACE) in 2012, 2014, and 2019. There was a recurrence near the TACE treatment site and near the gallbladder bed on S5/8 of 2019, and US-guided MWA was performed in April 2022. Additional US-guided MWA was performed due to insufficient cauterization. Subsequently, EOB-MRI in August revealed a small residual lesion near the ablation site. Since the tumor was located near the gallbladder bed, further US-guided MWA was judged to be dangerous, and a surgical referral was made for laparoscopic S5 partial resection of the liver and removal of the gallbladder. Laparoscopic MWA was performed instead of partial resection because the patient had undergone surgery for gastric cancer, and the lesion site was unclear due to adhesion between the lower surface of the liver and the omentum, making it difficult to remove the tumor. There has been no recurrence after surgery. Although it is often difficult to select a treatment method for patients with multiple recurrences, we believe that if possible, a treatment method that leads to local radical cure should be selected.

Abstract Submission No. 101660
P-1109

A case of multiple HCC in which good control was obtained by Atez/Bev and heavy ion radiotherapy

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Introduction: ABC conversion therapy, which combines atezolizumab + bevacizumab combination therapy (Atezo/Bev) with local treatments such as hepatic resection, RFA, and superselective TACE, has been proposed for intermediate stage HCC. Additionally, from 2022, heavy ion radiotherapy (CIRT) will be covered by insurance for hepatocellular carcinoma (4 cm or larger) that is difficult to surgically remove. We report a case of multiple HCC that was well controlled using a combination of Atezo/Bev and CIRT.

Case: A 70-year-old woman. She had liver cirrhosis with non-alcoholic steatohepatitis. She had multiple HCCs of 90mm in S6 and 6 small nodules in both liver lobes on CT examination in November 2022. We started Atezo/Bev in December 2022. In April 2023, MRI examination showed that 4 of the 6 nodules had disappeared, but S6 HCC has not changed. In May 2023, heavy ion radiotherapy was performed for S6 HCC (60Gy/4Fr). After heavy ion radiotherapy, we restarted Atezo/Bev. In August 2023, CT examination showed that S6 lesion had significantly shrunk, and the remaining nodules also tended to shrink.

Discussion: CIRT activates antitumor immune responses, and has the therapeutic effect on tumors outside the irradiation field (abscopal effect). When we combine CIRT with immune checkpoint inhibitors, further antitumor effects are expected. CIRT can also be used in patients with large tumors, advanced age, or underlying disease, and is considered to be a useful treatment option for liver cancer in the future.

Abstract Submission No. 101674
P-1110

Cholecystitis as a Rare Extra-medullary Manifestation of Acute Myeloid Leukemia: A Case Report

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Background: Extra-medullary disease can be observed in patients with Acute Myeloid Leukemia (AML), including leukemic involvement of the gastrointestinal tract, although infiltration of the gallbladder is a rare occurrence. Recognizing the disease entity is essential for diagnostic workup and identifying the etiology.

Methods: We report a rare case of AML in the form of extramedullary infiltration of the gallbladder in a 56-year-old male patient.

Results: A 56-year-old male, presenting with worsening diarrhea, intermittent nausea and vomiting, fever, right upper quadrant pain, and decreased oral intake in last two weeks. Laboratory investigations revealed pancytopenia (hemoglobin 98 g/L [120–160 g/L], platelets $31 \times 10^9/L$ [$150-400 \times 10^9/L$], WBC $1.1 \times 10^9/L$ [$4.0-11.0 \times 10^9/L$] with 0% blasts) with elevated total bilirubin of 26,2 $\mu\text{mol/L}$ [$\leq 22 \mu\text{mol/L}$]. Abdominal USG showed cholecystitis more likely caused by leukemic infiltration. He was diagnosed with AML-M5 from bone marrow biopsy (10–12% blasts) and peripheral blood smear (5–6% blasts). Empiric treatment with antibiotics showed unsuccessful and open cholecystectomy was then performed. Histopathological examination exhibited transmural infiltration by atypical mononuclear cells with dissimilar nuclei and cells immunohistochemical staining indicated AML-M5.

Conclusions: This case highlights the importance of maintaining a high index of suspicion of atypical manifestations of AML.

Extramedullary manifestations of AML in the form of gallbladder infiltration complicating to acute abdomen can be life-threatening. Early recognition of cholecystitis as an extramedullary manifestation of AML can prevent disease progression and improve the clinical outcome as well as prognosis of the patient.

Abstract Submission No. 101745
P-1111

Primary liver lymphoma with R-CHOP treatment failure and its diagnosis and treatment considerations

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Primary hepatic lymphoma (PHL) is a rare form of non-Hodgkin lymphoma (NHL), accounting for 0.4% of all extranodal NHL and 0.016% of all NHL ^[1]. Diffuse large B-cell lymphoma (DLBCL) is the most common type of NHL, and DLBCL involving the liver accounts for only 3% ^[2]. PHL has a low incidence and lacks specific diagnostic criteria, making it prone to misdiagnosis and underdiagnosis. Here, we report the diagnosis and treatment of a patient confirmed to have PHL through biopsy, aiming to raise awareness of this disease.

Abstract Submission No. 101781
P-1112

Liver Cirrhosis and MDS-MLD: Autoimmune Hepatitis or Intrahepatic Extramedullary Hematopoiesis First?

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Background: Myelodysplastic Syndrome (MDS) can manifest in intrahepatic Extra-medullary Hematopoiesis, leading to liver failure, although it is quite rare. Meanwhile, a possible cause of liver cirrhosis at a young age is Autoimmune Hepatitis (AIH), which in turn can cause secondary MDS through the AIH.

Methods: We present a rare case of MDS-MLD with liver cirrhosis in a 24-year-old female patient.

Results: A 24-year-old female, presented with profuse bloody-vomiting and black-tarry stool with slight ascites since yesterday. It had been felt intermittently since 1 year ago with a history of multiple blood transfusions and hospitalization ever since. No history of alcohol consumption. Cirrhotic-stigmata were present. Laboratory revealed macrocytic anemia with AIHA (hemoglobin 46 g/L [120–160 g/L], MCV 111 fl [80–93 fl], MCH 30.7 pg [27–31 pg], Coomb's test +2, total bilirubin 29,2 $\mu\text{mol/L}$ [$\leq 22 \mu\text{mol/L}$], prolonged Coagulation-Time (APTT 36,3" [24"–30"]), and slightly increase in transaminase. Hepatitis markers and ANA-test were negative, and positive smooth-muscle-antibody (SMA), ferritin and serum-iron were normal. Abdominal USG showed severe liver fibrosis with Hepatosplenomegaly, Portal Hypertension, and Ascites. Endoscopy showed varices esophagus. She was diagnosed with MDS-MLD from a bone marrow biopsy. After

comprehensive treatment of variceal bleeding until resolved and stable condition, the patient showed clinical and laboratory improvement following steroid administration.

Conclusion: Only a few were known about the possibility of cirrhosis hepatitis causing MDS or vice versa. One of the possibilities is that the autoimmune condition directly causes MDS, and intrahepatic extra-medullary hematopoiesis, respectively which may be overlapping and difficult to determine.

Abstract Submission No. 101936

P-1113

Role of serum autotaxin in the diagnosis of Intrahepatic Cholestasis of Pregnancy (ICP)

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Intrahepatic Cholestasis of Pregnancy (ICP) is the hepatic disorder related to the second/third trimester of pregnancy, which is characterized by pruritus with elevation of serum bile acid concentrations and liver enzymes in the absence of other systemic hepatobiliary disorders. The etiology is multifactorial and may be linked to increasing estrogen levels in pregnancy as well as altered expression of hepatobiliary transport proteins. Incidence of ICP is different between ethnic groups depending on the geographical region: 0.4–1% of pregnancies in North America and Western Europe, but 1.5–4% of pregnancies in Chile and Bolivia. In Asian countries, fewer cases have been reported, and ICP has been generally considered to be a rare disease in Japan. Autotaxin (ATX) is a secreted enzyme that converts extracellular lysophosphatidylcholine (LPC) into lysophosphatidic acid (LPA), contributing to an essential reaction in various cell signaling. In clinical settings, recent studies suggest that serum ATX may be a reliable circulating biomarker to diagnose ICP. We here report the patient, who is a 39-year-old female in the 22nd week of gestation with pruritus, jaundice, and abnormal liver function tests. The patient presented with elevated serum concentrations of ATX (11.5 mg/L [<1.27]) as well as total bile acids (268.5 $\mu\text{mol/L}$ [<10]), and ursodeoxycholic acid (UDCA) was effective in ameliorating symptoms and liver function tests. The elevated serum concentrations of ATX were normalized immediately after delivery. The measurement of serum ATX may thus help diagnose ICP in areas where the incidence of ICP is not prevalent.

Abstract Submission No. 101249

P-1114

Comparison of stent dysfunction rate for anastomotic biliary strictures after liver transplantation

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Background: Endoscopic biliary stenting (EBS) is one of the standard treatments for biliary strictures after liver transplantation. Cholangitis due to stent dysfunction should be avoided in patients who are immunosuppressed after transplantation. Therefore, it is important to evaluate the incidence of stent dysfunction and stent patency period.

Methods: We retrospectively compared the stent dysfunction rate after stent placement between inside stent (IS) and plastic stent (PS) in 48 patients with post-transplant strictures. Stent dysfunction was defined as stent occlusion, stent dislocation, or acute cholangitis.

Results: In the first treatment, there was no difference in the one-year stent occlusion rate between IS (n=18) and PS (n=30). However, the one-year incidence rate of acute cholangitis was significantly lower in IS than in PS (20% vs. 43%, $p=0.04$). In addition, no stent dislocation was observed in IS, but this did occur in 33.3% of PS ($p=0.004$). Median patency periods were 369 days for IS and 154 days for PS ($p=0.01$), significantly longer for IS. Comparing all EBS, including second and subsequent procedures, the one-year rate of stent dislocation was significantly lower in IS than in PS (4%, n=89 vs. 34%, n=127, $p<0.001$). IS again had a longer patency period than PS (356 days, vs. 196 days, $p=0.009$).

Conclusions: IS has a longer patency period and lower frequency of stent dysfunction than PS, suggesting that IS should be selected for patients who require long-term stent patency.

Abstract Submission No. 100322

P-1115

The effect of embolization of the portosystemic shunt on the long-term clinical course in cirrhosis

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Background: Evidence-based Clinical Practice Guidelines for Liver Cirrhosis weakly recommend Balloon-occluded Retrograde Transvenous Obliteration (BRTO) for the prevention of rebleeding of gastric varices or hepatic encephalopathy of portosystemic shunt, and the indications for treatment are not well defined. Therefore, we compared overall survival and incidence of adverse events in liver cirrhotic patients treated with or without BRTO.

Methods: In this study, 492 cirrhotic patients with a portosystemic shunt with a diameter of 6 mm or larger who underwent Doppler ultrasound from 2007 to 2022 were included. The overall survival and the incidence of gastrointestinal bleeding, hepatic encephalopathy, portal vein thrombosis, infection, and ascites were compared between patients who treated with or without BRTO.

Results: A total of 428 patients who did not receive BRTO and 64 patients who received BRTO were included in the study. There was no difference in liver functional reserve. There was no difference in overall survival and the cumulative incidence of ascites, infection, portal vein thrombosis, gastrointestinal bleeding. However, the cumulative incidence of hepatic encephalopathy decreased after BRTO (BRTO treated group vs BRTO untreated group: 3.4% at 1 year vs. 13.1% at 1 year; $P<0.01$).

Conclusion: BRTO may be effective in reducing hepatic encephalopathy. However, considering that embolization does not necessarily improve OS, further careful consideration is needed in the selection of patients who are candidates for BRTO.

Abstract Submission No. 101352

*P-1116***Neutrophil/lymphocyte and MPV/platelets ratios can predict cirrhosis decompensations****Elio Mikhael¹, Chadi Hage Chehade¹, Rita Slim¹, Celina Doueihy¹, Lamis Amer¹, Melissa Khanfour¹, Santa El Helou¹, Joseph Amara¹, Eid Mahfouz¹, Khalil Honein¹, Cesar Yaghi¹**¹Saint-Joseph University of Beirut Beirut Lebanon**Background:** In liver disease, inflammatory markers on a complete blood count (CBC) can predict liver fibrosis, but their role in predicting cirrhosis decompensation remains unclear. The aim of our study is to establish this association.**Methods:** Our study population (n=206) was divided in three: 73 decompensated cirrhosis, 63 compensated cirrhosis, and 70 controls (no history of liver disease). Decompensations included variceal bleeding, ascites, hepatic encephalopathy, and spontaneous bacterial peritonitis. Mean values of CBC markers including red cell distribution width (RDW), mean platelet volume (MPV), and the MPV/platelet, lymphocyte/neutrophil ratios were compared among subgroups. For decompensated patients, mean values at cirrhosis and decompensation diagnoses were compared.**Results:** The mean age was 72.0±15.5 years old, with 112 (54.4%) male patients. Decompensated cirrhotics had higher mean RDW (p=0.002) and mean MPV/platelets (p=0.017), and neutrophils/lymphocytes (p<0.001) ratios compared to compensated cirrhotics and compared to controls (p<0.001 for these parameters). Compensated cirrhotics had a higher mean MPV/platelets ratio (p<0.001) than controls.

Table 1 shows a comparison between CBC markers at the time of cirrhosis and decompensation diagnoses. A neutrophil/lymphocyte ratio greater than 3 had an area under the curve (AUC) of 0.716 with an odds ratio (OR) for decompensation of 9.4 (95%CI 5.7-15.4) during a mean follow-up of 34.8 months. An MPV/platelets ratio greater than 0.5 had an AUC of 0.652, predicting decompensation with an OR of 5.4 (95%CI 2.8-10.9) during follow-up.

Conclusion: Neutrophil/lymphocyte and MPV/platelets ratios can predict cirrhosis decompensations, suggesting their potential integration into a predictive decompensation score pending confirmation through prospective studies.

Abstract Submission No. 101429

*P-1117***Fracture Risks Among Filipinos with Liver Cirrhosis Using Fracture Risk Assessment Tool Scoring.****Patrick Michael Roslyn¹, Michael Chu¹, Lovell Gatchalian¹**¹East Avenue Medical Center Quezon City Philippines**Background:** Patients with liver cirrhosis are at risk for developing malnutrition-associated fractures. This study compared the major osteoporotic and hip fracture risks of cirrhotic patients to the general population using the Fracture Risk Assessment Tool (FRAX) without Bone Mineral Density testing.**Method:** This is a prospective study that included 172 patients (86 patients with cirrhosis and 86 non-cirrhotic patients). Comparison of variables between groups was performed using independent t-test for continuous variables and Fisher's Exact test for categorical variables. Kruskal-Wallis test was conducted to compare osteoporotic and hip fracture risks by severity and etiology of cirrhosis. Univariable and multivariable linear regression analysis were performed. P value < 0.05 was considered statistically significant.**Results:** In this study, chronic hepatitis B (38%) was the leading etiology of cirrhosis. Majority were classified as CTP-C (53%) with median MELD score of 20.5. Patients with cirrhosis had significantly lower BMI, hemoglobin, platelet count, sodium, and albumin levels compared to the healthy population. Osteoporotic and hip fracture risk was significantly higher in the cirrhotic group (p value <0.00001). No significant difference in osteoporotic fracture risk by etiology and severity of liver cirrhosis (p value 0.240). Univariable analysis showed osteoporotic risk was 1.73 times higher among MAFLD compared to patients with alcoholic liver disease. For every unit increase in INR, osteoporotic risk decreased by 0.98.**Conclusion:** Liver cirrhosis was associated with increased risk of osteoporotic and hip fractures. No significant difference seen in the risk of fracture with regards to severity and etiology of cirrhosis. Meanwhile, osteoporotic risk was higher among patients with MAFLD than ALD.

Abstract Submission No. 101545

*P-1118***The Effectiveness of TIPS + E in Reducing Rebleeding and HE: A Real-World Data Validation Study****Qian Li¹, Guangchuan Wang², Jun Tie³, Hao Wu⁴, Yuzheng Zhuge⁵, Hui Xue⁶, Wei Wu⁷, Chunqing Zhang¹, Lianhui Zhao⁸**¹Department of Gastroenterology, Shandong Provincial Hospital, Shandong University Jinan China, ²Department of Gastroenterology, Shandong Provincial Hospital Affiliated to Shandong First Medical University Jinan China, ³National Clinical Research Centre for Digestive Diseases and Xijing Hospital of Digestive Diseases, Fourth Military Medical University Xi'an China, ⁴West China Hospital, Sichuan University Chengdu China, ⁵Nanjing Medical University Drum Tower Clinical Medical School and Department of Gastroenterology, Affiliated Drum Tower Hospital of Nanjing University Medical School Nanjing China, ⁶First Affiliated Hospital of Xi'an Jiaotong University Xi'an China, ⁷First Affiliated Hospital of Wenzhou Medical University Wenzhou China, ⁸Department of Infectious Disease, Qilu Hospital, Cheeloo College of Medicine, Shandong University Jinan China**Objectives:** The efficacy of transjugular intrahepatic portosystemic shunt (TIPS) plus extrahepatic collateral embolization (TIPS + E) in reducing rebleeding and post-TIPS hepatic encephalopathy (HE) was recently reported in a meta-analysis, but further validation is essential. This study aims to confirm the effectiveness of TIPS + E using real-world data.**Methods:** The multicenter retrospective cohort included 2077 cirrhotic patients who underwent TIPS ± E (TIPS: 631, TIPS + E 1446) between January 2010 and December 2022. Regression and propensity-score methods (PSM) were used to adjust for baseline characteristics differences. After PSM, clinical outcomes, including rebleeding, HE, survival and further decompensation (FDC), were analyzed. Baseline data from all patients contributed to the construction of prognostic models.**Results:** After PSM, 1136 matched patients (TIPS+E: TIPS = 568:568) were included. TIPS + E demonstrated a significant reduction in rebleeding (HR 0.77; 95%CI 0.59, 0.99; p = 0.04), HE (HR 0.82; 95%CI 0.68, 0.99; p = 0.04) and FDC (HR 0.85; 95%CI 0.73, 0.99; p = 0.036), comparing to TIPS. Notably, TIPS + E also significantly reduced rebleeding, HE and FDC in subgroup of using 8mm- diameter stents and embolizing of gastric varices + spontaneous portosystemic shunts (GV + SPSS). However, there were no differences in overall or subgroup survival analysis. Additionally, the random forest models showed moderate predictive value in prognostic models with accuracy of 0.80-0.85 and AUROC of 0.71-0.89. Controlling post-TIPS portal pressure

gradient (pPPG) within 7mmHg < pPPG < 8.5mmHg improved prognosis, especially in TIPS+E group.

Conclusion: Our real-world data validation confirms the high efficacy of TIPS + E in reducing rebleeding and HE, particularly when using 8mm diameter stents, embolizing GV + SPSS, and maintaining an optimal pPPG.

Abstract Submission No. 101698

P-1119

The Therapeutic Strategy for Patients Developing Covert Hepatic Encephalopathy Based on Zinc Levels

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Aim: We previously reported that patients with liver cirrhosis showing zinc deficiency were recommended to maintain a serum zinc level of ≥ 50 $\mu\text{g/dL}$ through zinc supplementation to prevent overt hepatic encephalopathy (OHE) development. In this study, the significance of serum zinc levels in diagnosing and treating covert hepatic encephalopathy (CHE) were evaluated.

Methods: A total of 99 cirrhotic patients without a history of OHE were enrolled. CHE was defined as scoring above the age-based cutoff value in the Stroop test (NP-test iPad version 3.1). Sarcopenia (JSH, second edition) was evaluated through grip strength and muscle mass measurements (InBody S10).

Results: CHE was observed in 44 patients (44%) and sarcopenia occurred in 23 patients (23%). The multiple logistic regression analysis identified serum zinc levels ($\text{per}+1$ $\mu\text{g/dL}$, OR 0.95, $P=0.0004$) as the only risk factor associating with CHE, with a cutoff value of 58 $\mu\text{g/dL}$ (AUC 0.86, $P<0.0001$). Blood ammonia levels and sarcopenia were not involved in presence of CHE. During a median observation period of 212 days, OHE developed in 10 patients (10%). The Cox proportional hazard model identified presence of CHE as a factor associated with OHE development (OR 5.46, $P=0.0322$).

Conclusion: Cirrhotic patients without a history of OHE exhibit a high risk of developing CHE if serum zinc levels are below 58 $\mu\text{g/dL}$ regardless blood ammonia levels. These patients are at a high risk of developing OHE in the short term, and early zinc supplementation are recommended for prevention of OHE development.

Abstract Submission No. 102015

P-1120

TIPS in Decompensated Cirrhosis: Unraveling the Dynamics of Post-TIPS Stable State and Recompensation

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Background: To investigate the survival benefits in decompensated cirrhotic patients undergoing Transjugular Intrahepatic Portosystemic Shunt (TIPS) procedures who met the Baveno VII criteria for recompensation.

Methods: 91 patients receiving etiological treatment (antiviral/alcohol cessation) and TIPS procedures were retrospectively analyzed with a median follow-up time of 32.5 (18.1, 42.1) months, from December 2016 to July 2022. Recompensation and further decompensation were defined based on Baveno VII criteria combined with liver function criteria from a validation study (PMID: 36038017), while post-TIPS stable state was defined as no clinical manifestations within 1 year after TIPS.

Results: Out of 91 patients, 65 (71.4%) achieved stable, 35 (38.5%) achieved recompensation, and 26 suffered further decompensation. Patients with further decompensation had significantly higher mortality compared to those in stable ($P=0.002$; HR 4.71, 95% CI 1.46 to 15.19) or recompensated groups ($P=0.004$; HR 6.79, 95% CI 2.03 to 22.70). While no significant survival differences were observed between stable and recompensated patients, the recompensated group showed a trend towards liver function improvement (valued by Child-Turcotte-Pugh score decrease ≥ 2 or grades decreased).

Conclusion: In our study, TIPS procedures might bring about stable states or recompensation in over 70% of patients with decompensated liver cirrhosis. However, the survival benefits observed in patients achieving stable or recompensation within 1 year post-TIPS may not necessarily originating from improved liver function. Risk factors of survival of patients in stable or recompensated after TIPS require further exploration.

Abstract Submission No. 102019

P-1121

Comparison of Prognostic Models for post-TIPS Outcomes: Machine Learning VS Traditional methods

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Objectives: Following Transjugular Intrahepatic Portosystemic Shunt (TIPS) procedures, a prolonged asymptomatic phase approaching recompensation is commonly observed. This study aims to define "pseudo" recompensation as the absence of liver cirrhosis-related complications within 1-year post-TIPS and presents a comparative analysis of prognostic models for TIPS outcomes, employing both machine learning and traditional statistical approaches.

Methods: A total of 234 cirrhotic patients underwent TIPS between January 2014 and June 2022, with a median follow-up time of 39.8 (24.6, 65.2) months. Prognostic models using Random Forests (RF), Support Vector Machines (SVM), Artificial Neural Networks (ANN), and Logistic Regression (LR) were constructed to predict outcomes, including recompensation, rebleeding, hepatic encephalopathy, ascites, and overall survival.

Results: The RF models exhibited significantly higher predictive value across all outcomes, with accuracy ranging from 0.73 to 0.85, precision from 0.73 to 0.87, recall from 0.74 to 0.85, F1 score from 0.74 to 0.84, and AUC from 0.75 to 0.82. Top 10 variables in the RF model, ranked by feature importance, included international normalized ratio, albumin, creatinine, extent of prothrombin time, portal pressure gradient (PPG), decline proportion of PPG, bilirubin, age, sodium, and hemoglobin. Subgroup analysis identified patients with $\text{ePT} > 3 + \text{MELD score} > 20$ (calculated by INR, Cr, and TBIL), accounting for 88.2% of post-TIPS secondary decompensation.

Conclusion: This study highlights the superior predictive capabilities of RF in modeling TIPS outcomes, contributing to the advancement of precision medicine in portal hypertension interventions.

Abstract Submission No. 102029
P-1122

Impact of sex on 10-year survival of cirrhosis patients: a cohort study of 15,876 U.S. patients

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Background: Data on the impact of sex on long-term survival rates of patients with cirrhosis are limited. We aimed to fill in this gap.

Methods: This retrospective cohort study included 15,876 consecutive patients with cirrhosis (2000-2022) at a U.S. center. Cirrhosis was defined by the presence of cirrhosis morphology on imaging or histology or noninvasive test showing stage 4 fibrosis, coupled with the presence of a chronic underlying liver disease.

Results: This cohort included 59.1% males (N=9379) and 40.9% females (N=6497). Females were slightly older than males (59.2±13.7 vs. 58.0±12.8, p<0.0001). No significant differences found between racial/ethnic distribution between the sexes. Female patients were more likely to have non-viral etiology compared to males (68.9% vs. 56.3%, p<0.001). Males were twice as likely to present with HCC (39.6% vs. 22.9%, p<0.001). Overall, survival rates were significantly lower for male compared to female patients with 5- and 10-year cumulative survival rates (61.79% vs. 67.89% and 43.49% vs. 50.26%, respectively, p<0.0001). The disparities were consistent across age, race and ethnicity, cirrhosis diagnosis year, and liver disease etiology subgroups (Figure 1A/B). On multivariable Cox regression analysis adjusted for sex, age, race and ethnicity, and liver disease etiology (Table 1), male sex was significantly and independently associated with 22% higher risk for overall mortality (aHR 1.22, 95% CI 1.15-1.28, p<0.001).

Conclusion: Across age, racial and ethnic, liver disease etiology and time period, male patients with cirrhosis had poorer 10-year survival rates compared to females. Male sex was independently associated with 20% higher risk overall.

Abstract Submission No. 102078
P-1123

Effect of adipose-related parameters on survival in patients with cirrhosis: a meta-analysis

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Background: Some adipose-related parameters exhibited distinct prognostic value in patients with cirrhosis. However, the association, magnitude, and direction of the association between individual adipose parameter and mortality in patients with cirrhosis remain to be determined.

Methods: PubMed, Embase, Web of Science, and some Chinese databases were searched from inception to November 19, 2023 to identify the eligible studies. The prevalence of dichotomous adipose parameters and their corresponding 95% confidence interval (CI) were pooled using the random-effects model. The impact of each adipose parameter on mortality was assessed by the pooled unadjusted or adjusted hazard ratio (HR) with 95% CIs.

Results: A total of 27 studies involving 7,906 patients were included. The prevalence of sarcopenic obesity (SO) and myosteatosis in patients with cirrhosis was 15.5% and 34.4%, respectively (Figure 1). For each unit increase in subcutaneous adipose tissue index (SATI) (adjusted HR 0.99, 95% CI 0.98–1.00) or muscle radiodensity (MR) (adjusted HR 0.94, 95% CI 0.90–0.98), and each unit decrease in the visceral to subcutaneous ratio (VSR) (adjusted HR 1.92, 95% CI 1.45–2.54), there was an independent association with a decreased risk of mortality, while concurrent myosteatosis (adjusted HR 1.88, 95% CI 1.48–2.40) or SO (adjusted HR 2.77, 95% CI 1.95–3.93) significantly increased the risk of mortality in patients with cirrhosis (Figure 2).

Conclusion: Different adipose parameters exhibited varying prognostic value: decreased SATI or MR, increased VSR, and concurrent myosteatosis or SO were independently associated with a higher risk of mortality in patients with cirrhosis.

Abstract Submission No. 200024
P-1124

Transient Elastography for the prediction of Esophageal Varices in Egyptian Cirrhotic Patients

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Background: Esophageal varices (EVs) are atypically dilated submucosal veins, which occurs consequently to portal hypertension. Liver stiffness measurement (LSM), obtained by transient elastography (Fibroscan), strongly correlates with portal hypertension.

Aim: is to predict the presence and grading of esophageal varices in Egyptian patients with liver cirrhosis using Fibroscan and other non-invasive tests.

Methods: A 101 cirrhotic patients indicated for upper endoscopy were enrolled consecutively and subdivided according to endoscopic findings into: Group I (70 patients with EVs) and Group II (31 patients without EVs). Upper endoscopy, ultrasonography, routine lab. and Fibroscan assessment were done to all patients.

Results: LSM correlated directly and significantly with the presence (p <0.001), and grading of EVs (p = 0.001). A LSM cut off value of 18.55 kPa had an AUC of 0.726, sensitivity of 74.3%, specificity of 54.8%, PPV of 78.79%, and a NPV of 48.57% for predicting the presence of EVs. Platelet count/spleen diameter ratio (PSR) inversely correlated with the EVs presence (p = 0.002), and grading (p <0.001). PSR had a cut off value of 742.17, an AUC of 0.695, sensitivity of 71% and a specificity of 58.6% (PPV of 82%, NPV of 43.14%) for EVs presence. Right lobe diameter/Albumin ratio (RLAR) correlated directly with EVs presence (p = 0.001), and grading (p = 0.012). RLAR cut off value of 3.62 had AUC, sensitivity, specificity, PPV, and NPV

of 0.7, 64.3%, 67.7%, 81.8%, and 45.7%, respectively for the prediction of EVs presence.

Conclusion: LSM, PSR, RLAR as noninvasive methods for predicting the presence and grading of EVs are of moderate accuracy.

Abstract Submission No. 200038

P-1125

Validation of the EncephalApp Stroop test for minimal hepatic encephalopathy in cirrhotics

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Background and Aims: The diagnostic of minimal hepatic encephalopathy (MHE) is still under debate, and point-of-care tests are needed. Until now Stroop EncephalApp has been validated for MHE diagnosis in United States, China and Korea. The aim of the study was to validate EncephalApp Stroop test for MHE diagnosis in a Romanian cirrhotic population.

Methods: In this study we included cirrhotic patients without prior hepatic encephalopathy (HE) and controls without liver cirrhosis. All of them EncephalApp Stroop test and psychometric hepatic encephalopathy score (PHES). The normative data of PHES in the Romanian population were used for MHE diagnosis.

Results: A total of 78 cirrhotics (mean age 56.3±10.4 years, mean MELD score 12.4±3.4) and 78 controls (mean age 51.54±2.4 years) were included in the study. The prevalence of MHE based on PHES was 23.1%, and it was in direct correlation with the severity of liver cirrhosis (LC). The OffTime Stroop test had the highest sensibility (77.7%) and specificity (80%) for MHE diagnosis in cirrhotic patients, with an AUC of 0.789 and a cutoff of 148 seconds ($P < 0.001$, confidence interval 0.629-0.903).

Conclusions: The EncephalApp Stroop test, has a good validity for the diagnosis of MHE, and can be easily used in daily clinical practice for Romanian cirrhotic population MHE evaluation.

Abstract Submission No. 200205

P-1126

Impact of Sarcopenia on the Presence High-Risk Variceal Esophagus in Cirrhotic Patients

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Background: The high prevalence of sarcopenia in chronic liver disease has a negative impact on the quality of life and the susceptibility to various complications of cirrhosis, including esophageal varices. The aim of this study was to determine the prevalence of sarcopenia in cirrhotic patients and explore its association with high-risk esophageal varices stratified by Child-Pugh.

Method: An observational cross-sectional study included patients with liver cirrhosis in Cipto Mangunkusumo Hospital between January to September 2023. Sarcopenia is defined by a reduction in muscle mass combined with decreased grip strength or walking speed, in accordance with the AWGS 2019 criteria (Asian Working Group for Sarcopenia). Multivariate logistic regression was conducted to evaluate the association of sarcopenia and high-risk esophageal varices.

Result: A total of 155 liver cirrhosis patients were included in this study. In this study, 74.2% of liver cirrhosis patients were male, with an average age of 53.3 ± 9.7 years. Hepatitis B was the most prevalent etiology (77.4%). Most patients had Child-Pugh A classification (80.6%), followed by Child-Pugh B (16.8%) and Child-Pugh C (2.6%). Sarcopenia was found in 89 patients (57.4%). In multivariate analysis showed that the presence of sarcopenia in liver cirrhosis patients has significant statistical implications in increasing the risk of high-risk esophageal varices, particularly in those classified as Child-Pugh B and C (AOR = 7.50 (CI 95%: 1.48 – 37.91, $p < 0.030$)). However, no association was found between sarcopenia and high-risk esophageal varices in the sub group Child-Pugh A (AOR = 1.46 (CI 95%: 0.65 – 3.29, $p < 0.477$)).

Conclusion: Sarcopenia significantly increase the risk of high-risk esophageal varices in liver cirrhosis, especially in those with Child-Pugh B and C classification.

Keyword: Sarcopenia, variceal esophageal, liver cirrhosis

Abstract Submission No. 100069

P-1127

Extracellular vesicles derived from injured hepatocyte cooperate with macrophage to promote fibrosis

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Background: Massive deposition of extracellular matrix such as collagen is the main mechanism of liver fibrosis, in which activated hepatic stellate cells are key cells for the generation of fibrous tissue. Some reports have suggested that extracellular vesicles play an important role in intercellular communication. Therefore, the study aims to investigate the role of extracellular vesicles derived from carbon tetrachloride-treated hepatocytes in liver fibrosis.

Methods: In vivo: Inhibition the production of extracellular vesicles. Carbon tetrachloride (ccl4) was dissolved in olive oil and intraperitoneally injected for 1ml/kg with 3W to induce hepatic fibrosis in mice. The same volume of olive oil was used as the control. EVs inhibitor GW4869 was intraperitoneally injected after carbon tetrachloride injection.

In vitro: Extracellular vehicles (EVs) from normal hepatocytes and ccl4-treated hepatocytes (AML12) were extracted. Hepatic stellate cells were treated with EVs or EVs-macrophage (RAW264.7) conditional medium (Con).

Results: 1. In vivo injection of GW4869 inhibited ccl4-induced liver fibrosis. (Figure1)

2. EVs released by control hepatocytes (ctrl-EVs) and ccl4-treated hepatocytes (ccl4-EVs) failed to promote the activation of hepatic stellate cells. (Figure2)
 3. EVs released by ccl4-treated hepatocytes enhanced the expression of fibrotic factors and inflammatory factors in macrophages. (Figure3)
 4. EVs released by ccl4-treated hepatocytes cooperated with macrophages to promote the activation of hepatic stellate cells.(Figure 4)
Conclusion: Extracellular vesicles released by ccl4-treated hepatocytes cooperate with macrophages to promote the activation of hepatic stellate cells.

Abstract Submission No. 100238

P-1128

The effect and mechanism of empagliflozin on CCL4-induced hepatic fibrosis

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Objective: To observe the effect of empagliflozin on hepatic fibrosis model mice induced by carbon tetrachloride (CCL₄).

Methods: The mice divided into normal control group, CCL₄ group and empagliflozin group. The liver function, abdominal insulin tolerance test, serum cytokine levels, activity of oxidative stress enzymes of each group was analyzed.

Results: There was no significant difference in the ratio of average liver weight to body weight among 3 groups. After CCL₄-induced hepatic fibrosis model, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were significantly increased, but there was no significant difference between empagliflozin group and CCL₄ group. In the insulin tolerance test, it was shown that the blood sugar of mice in the empagliflozin group was almost stable among the three groups. Empagliflozin group showed relieved diffuse necrosis of liver cells by HE staining and alleviated fibrosis by quantitative analysis of Sirius red staining. The liver tissue activity of superoxide dismutase, malondialdehyde, catalase and glutathione peroxidase in the empagliflozin group were closer to the normal control group than CCL₄ group. Compared with hepatic fibrosis group, the number of Keap1-positive cells in empagliflozin group was further reduced.

Conclusion: Empagliflozin did not cause liver function deterioration and hypoglycemia in CCL₄-induced hepatic fibrosis mouse model. Empagliflozin can reduce the degree of diffuse necrosis and liver fibrosis in CCL₄-induced liver fibrosis mice, and the mechanism may be related to the reduction of oxidative stress in liver tissue by empagliflozin through Keap1-Nrf2 signaling pathway.

Abstract Submission No. 100927

P-1129

Dysregulation of the PUM1 aggravates liver fibrosis in nonalcoholic steatohepatitis

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Background: Liver fibrosis is a worrisome feature of nonalcoholic steatohepatitis (NASH). However, the mechanism of liver fibrosis in NASH remains unclear. We explored the role of PUMILIO proteins in NASH-related liver fibrosis.

Methods: Two isoforms of PUMILIO proteins (PUM1, PUM2) expression were analyzed in NASH patients and models. A choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD) and a western diet combined with intraperitoneal carbon tetrachloride (WD+CCl₄) were used to induce NASH-related liver fibrosis in mice. Adeno-associated virus type 8 carrying Pum1 shRNA were injected into the tail vein to downregulate PUM1. RNA sequencing was used to analyze gene expression profiles after downregulation of PUM1. Hepatic stellate cells (HSCs) were transfected with plasmids or siRNA to upregulate or downregulate the expression of PUM1 and its target genes.

Results: We found that the level of PUM1, not PUM2, was reduced in both NASH patients and models. The level of PUM1 was significantly negatively correlated with liver weight, liver index, and degree of liver fibrosis. Downregulation of PUM1 in the liver aggravated liver damage and fibrosis in two models of NASH-related liver fibrosis mice. We further found that the expression of PUM1, but not PUM2, was reduced in activated HSCs. Downregulating the expression of PUM1 in HSCs promoted the activation of HSCs. RNA sequencing analysis and various experiments demonstrated that tropomyosin 4 gene (TPM4) was a target gene of PUM1. Importantly, PUM1 regulated HSCs activation via regulating TPM4 expression.

Conclusions: PUM1 is dysregulated in NASH progression, leading to HSCs activation and aggravating liver fibrosis.

Abstract Submission No. 101659

P-1130

Constructing an in vitro model of liver fibrosis using tissue engineering liver

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Objective: To generate an in vitro 3D liver fibrosis model incorporating cells representing key players in fibrotic liver using a decellularized scaffold and to assess its response to fibrogenic compounds.

Methods: HepG2, SK-hep1 and LX-2 were co-cultured on a decellularized rat liver scaffold, which was treated with fibrogenic compounds (TGF-β1 or CCl₄) for up to 9 days. The validity of the *in vitro* liver fibrosis model was evaluated by measuring biochemical indicators in the supernatant (AST,ALT,LDH), assessing the deposition and secretion of extracellular matrix proteins and examining the induction of gene expression of fibrosis biomarkers (α-SMA,TIMP-1). Oxidative stress-related indicators (ROS, Nrf2) were also evaluated in this model.

Results: After stimulation with TGF-β1, the 3D liver fibrosis model based on the co-culture system demonstrated superior responsiveness to pro-fibrotic stimuli compared to 2D single culture. We observed increased collagen expression and deposition in the 3D model, along with elevated fibrosis indicators: the HSC activation marker α-SMA and tissue metalprotease inhibitor TIMP-1. After stimulation with CCl₄, not only were liver fibrosis markers elevated, but indicators of hepatocellular damage were also increased in the culture supernatant. Additionally, a stronger involvement of oxidative stress-related molecules upon stimulation with CCl₄ in the 3D model was observed.

Conclusion: The newly constructed 3D *in vitro* liver fibrosis model successfully mimics the characteristics of liver fibrosis and can be used

as a tool to study the mechanisms of liver fibrosis and screen for anti-fibrotic drugs.

Keywords: Liver fibrosis; Tissue engineering liver; Collagen deposition; oxidative stress

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P-1131

Liver Fibrosis Score Could Predict Carotid Plaque in an Asymptomatic Korean Population

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Background: Early identification of carotid atherosclerosis (CAS) is critical for preventing cardiovascular events at the asymptomatic stage. To date, little study has been performed to predict asymptomatic CAS using liver fibrosis scores in the general Korean population. The aim of this study was to evaluate the performance of the liver fibrosis algorithms to screen CAS in the Korean population.

Methods: This study consisted of 19,367 asymptomatic Korean adults underwent carotid ultrasonography and biochemical testing at a comprehensive health promotion center. The CAS was defined as having carotid plaque, carotid stenosis, and/or increased carotid intima-media thickness (CMT ≥ 1.0 mm). Hepatic fibrosis indices such as the NAFLD fibrosis score (NFS), Fibrosis-4 (FIB-4), aspartate aminotransferase-to-platelet ratio index (APRI), and BARD score were evaluated.

Results: The frequency of individuals with increased carotid intima-media thickness (CMT), plaque, and stenosis was 32.1% (6,217/19,367), 2.7% (527/19,367), and 0.3% (67/19,367). The FIB-4 showed the highest area under the receiver operating characteristic curve (AUROC: 0.777, 95% CI, 0.735 - 0.745) for carotid plaque, followed by the NFS (0.756), and APRI (0.638), and BARD (0.576). When FIB-4 was used as an indicator for carotid ultrasonography, advanced atherosclerosis was diagnosed in 5% (527/9,272) of the asymptomatic individuals without carotid ultrasonography.

Conclusions: This study demonstrated that FIB-4 and NFS can be useful for screening carotid plaque in an asymptomatic Korean population. Liver fibrosis markers such as FIB-4 and NFS could be used indication for carotid ultrasonography in primary clinical or health check-up settings in a cost-effective fashion.

Abstract Submission No. 101267

P-1132

Metabolomic analysis of bile in liver regeneration after partial hepatectomy in rats

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Background: Although liver regeneration has been extensively studied, the relationship between bile and liver regeneration has rarely been examined. In this study, bile from a 70% partial hepatectomy (PH) model was collected over time using a bile duct cannulation rat and metabolomic analysis was performed.

Method: Bile duct cannulation rats of SD rats were prepared and 70% hepatic PH was performed on them. Bile was collected from an external catheter over time (0, 6, 12, 24, 48, and 72 hours). Bile outflow was measured after PH. In addition, changes in bile acids were examined by metabolomic analysis. [Results] Bile outflow was not significantly different between the partial hepatectomy (PH) group and the sham group. However, liver weight correction showed that bile outflow was significantly increased at 6 hours after hepatectomy in the PH group compared to the sham group. Metabolomic analysis showed a significant increase in cholic acid at 6, 12, and 24 hours in the PH group compared to the sham group, with a peak at 6 hours after resection. No significant differences in chenodeoxycholic acid, Deoxycholic Acid, or lithocholic acid were observed between the PH and sham groups. [Discussion] Previous reports have suggested that cholic acid contributes to liver regeneration after PH, and it was speculated that cholic acid in bile would increase after PH. The present study proved this, with cholic acid peaking 6 hours after resection.

Abstract Submission No. 101470

P-1133

R Factor, a predictive criterion for abnormal LFT and 30-day mortality in a non-liver ICU

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Abstract

Derangement of liver enzymes as a measure of liver injury is not uncommon in ICU

Aim: To determine the incidence of deranged liver enzymes (AST/ALT/AIP/GGT) in a non-liver ICU at admission and to predict 30-day mortality.

Methods: Patients admitted in MICU, NeuroICU and CCU, between Jan 2022 to Dec 2022 were included. All patients had liver biochemistry at admission. R factor (RF-C) and COVID criteria (COV-C Type 1 or 2) for liver injury were used to stratify the patients into hepatocellular, cholestatic, and mixed types. Support systems during admission were noted. Patients were followed up until discharge/death.

Statistical Analysis: SPSS v26 (IBM Corp.). For descriptive statistics averages and standard deviations for continuous variables, frequencies and percentages for categorical variables. Fisher's Exact test, if the expected frequency in the contingency tables was < 5 for more than 25% of the cells, $p < 0.05$ was considered significant.

Results: 108 of 246 patients enrolled had abnormal liver tests (43.9%). AST, ALT, ALP and GGT were marginally elevated (< 2 times ULN) across all ICUs. 92/108 (85.2%) patients had a hepatocellular type and 44/108 (40.7%) had a cholestatic injury. Between the 2 criteria, RF-C was the better of the two. RF-C predicted the need for support in HC-I ($p < 0.001$) and served as a significant predictor of survival ($p < 0.023$).

Conclusions: Liver enzymes were < 2 times ULN abnormal in non-liver ICU. RF-C is the best to stratify pattern of liver injury and predicts supportive system and survival.

Abstract Submission No. 100580

P-1134

Living-donor Liver Transplantation (LDLT) for Lysosomal acid lipase(LAL) Deficiency:A case series

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Background and Aim: Late-onset LAL deficiency, also known as Cholesteryl ester storage disease (CESD) is a genetic lysosomal storage disorder, caused by deficiency of LAL due to mutations in the LIPA gene. It is a systemic disease leading to accumulation of cholesteryl ester in the liver, premature atherosclerosis and gastrointestinal disease. Most of the patients require liver transplantation due to decompensated chronic liver disease(DCLD). Previous case series report disease progression and high rates of recurrence following LT.

Methods: We describe 3 children (16 years, 10 years, 2 years) with LAL deficiency presenting with DCLD, who underwent living-donor liver transplant (LDLT) successfully and discuss ethical dilemmas in considering LDLT for CESD.

Results: All children presented with abdominal distension since early childhood and had features of DCLD. Liver biopsy showed microvesicular steatosis. Work up revealed low levels of LAL (ranging from 2% to 5% of normal activity) suggesting CESD, confirmed by genetic analysis. After detailed discussion with the family regarding risk of recurrence, need of Sebelipase Alpha if recurrence occurs, all three children underwent successful LDLT. At a mean follow up of 25 months (range: 9 to 48), all are well with normal graft function and lipid profile.

Conclusion: Disease recurrence in the allograft and disease progression has been reported after LT for LAL deficiency. However, there are isolated case reports of successful long-term outcomes of LT as seen in our patients. It is likely that our patients had milder phenotype. This is the first case series of LDLT for LAL deficiency.

Abstract Submission No. 102082

P-1135

Transient Elastography for Predicting Portal Hypertensive Gastropathy in Egyptian Cirrhotic Patients

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Background: Portal hypertensive gastropathy (PHG) is a state of mucosal ectasia affecting stomach in portal hypertension. Transient elastography (Fibroscan) measures liver stiffness (LSM) which had a strong correlation with portal hypertension and the prediction of esophageal varices (EVs). Our aim is to evaluate the diagnostic accuracy of Fibroscan and other non-invasive parameters in predicting PHG presence and severity in Egyptian cirrhotic patients.

Methods: 101 cirrhotic patients categorized into Group 1 (36 patients with PHG and EVs), Group 2 (34 patients with EVs), Group 3 (15 patients with PHG), and Group 4 (16 patients with neither PHG nor EVs as control). All patients underwent upper endoscopy, ultrasonography, routine lab. and Fibroscan evaluation.

Results: LSM median was significantly ($P < 0.001$) increased in groups 1, 2, and 3 than in group 4. LSM directly correlated with PHG severity represented by the PHG score ($P = 0.016$). Platelet count/spleen diameter ratio (PSR) correlated inversely with PHG presence ($P = 0.012$) and severity ($P = 0.007$). PSR cut off value of 705.54 predicted PHG presence with AUC = 0.644, sensitivity 66%, specificity 58.8%, PPV 63.83%, and NPV 61.1%. Right lobe diameter/Albumin ratio (RLAR) correlated directly with the presence ($P = 0.002$) and severity ($P = 0.004$) of PHG. RLAR cut off value of > 3.62 had AUC, sensitivity, specificity, PPV, and NPV of 0.656, 62.7%, 54%, 58.18%, and 58.7% for the prediction of PHG, respectively.

Conclusion: Fibroscan LSM, PSR, and RLAR are easy, non-invasive, inexpensive modalities predicting the existence and severity of PHG in cirrhotic patients.

Abstract Submission No. 100146

P-1136

ECONOMIC EVALUATION OF STRATEGIES TO PREVENT VERTICAL TRANSMISSION OF HEPATITIS B VIRUS IN VIETNAM

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Background: No cost-effectiveness information of preventive strategies of mother-to-child transmission (MTCT) of HBV has existed for policy decision making in Vietnam. This study aimed to compare costs and health outcomes of alternatives with the current practice in Vietnam.

Methods: Cost-utility analysis using a hybrid decision tree and Markov model was applied from healthcare system and societal perspectives. Studied strategies included S1-Universal vaccination, S2-Hepatitis B immune globulin (HBIG) for infants of mothers with HBeAg(+), S3-HBIG for infants of mothers with HBsAg(+), S4-tenofovir disoproxil fumarate (TDF) for mothers with high viral load, S5-TDF for mothers with HBeAg(+) and S6-current practice (TDF for high viral load mothers without HBIG in infants). Future costs and health outcomes were adjusted using discount rate of 3%. Parameter uncertainty was investigated using one-way sensitivity and probabilistic sensitivity.

Results: The current practice was dominant to all strategies with interventions in infants only from both perspectives. In contrast, the addition of HBIG in infants of mothers with HBsAg(+), with or without extension of TDF prophylaxis to mothers with HBeAg(+) were dominant to the current practice with incremental net monetary benefit varying from 33.94 USD to 70.64 USD under healthcare system perspective and from 44.22 USD to 93.71 USD under societal perspective. The results were robust in almost all uncertainty analyses.

Conclusion: Our study suggested that HBIG should be included in Vietnam's benefit package. The usage of HBeAg as a proxy of HBV DNA quantitative test was efficient toward elimination of MTCT of HBV.

Abstract Submission No. 101498

P-1137

Association of gut microbiome and pancreatic neoplasms: A Mendelian randomization Study

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Background: Epidemiological studies have found a correlation between gut microbiome and pancreatic tumors. However, it is still being determined whether there is a causal relationship between the two due to the limited sample size and confounding factors. We aimed to analyze the causal relationship between the gut microbiome and the development of pancreatic neoplasms by Mendelian randomization (MR).

Methods: We extracted gut microbiota GWAS data from the MiBioGen database and pancreatic neoplasms data from the IEU database. The causal relationship between gut microbiota and pancreatic tumors by performing a two-sample MR analysis using the IVW method. Sensitivity analysis was performed to assess the robustness of the MR results.

Results: The results of this study showed that seven gut microbiotas were protective against benign pancreatic tumors: Family.Desulfovibrionaceae ($p=0.032$), Family.Rikenellaceae ($p=0.017$), Family.Verrucomicrobiaceae ($p=0.030$), Genus.Akkermansia ($p=0.013$), Genus.Romboutsia ($p=0.008$), Order.Desulfovibrionales ($p=0.028$), Phylum.Verrucomicrobia ($p=0.007$). The corresponding heterogeneity tests and sensitivity analyses did not reveal abnormal results ($p > 0.05$). Three gut microbiotas were positively associated with the risk of pancreatic cancer in the MR analysis of the disease: Family. Veillonellaceae ($p=0.020$), Genus. Coprococcus1 ($p=0.043$), and Genus. Sutterella ($p=0.047$); two gut microbiotas were positively associated with a reduction in risk causally: Genus. Blautia ($p=0.043$), and Genus. Parasutterella ($p=0.015$). No horizontal pleiotropy or heterogeneity was found in the sensitivity analysis ($p > 0.05$). **Conclusions:** This is the first MR study to investigate the causal association between specific gut microbiota and pancreatic neoplasms. The direction and theoretical underpinnings for future pancreatic neoplasm prevention and therapy are provided by this work.