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Abstracts

Acute Liver Failure

A01 - Acute liver failure

Abstract #91

Does sepsis-like performance in hepatitis B virus related acute-on-chronic liver failure accord with the existed definition of sepsis?

Ran Xue[1], Qinghua Meng[1]

[1]Beijing You-An Hospital, Capital Medical University

Aim: Early diagnosis of sepsis is the key to improving the survival rate of patients with hepatitis B virus related acute-on-chronic liver failure (HBV-ACLF). However, it is still unknown that whether sepsis with HBV-ACLF fit into the conventional diagnostic criteria of sepsis. Therefore, it is urgent to identify the clinical feature of sepsis with HBV-ACLF so as to performing the timely and effective prevention and treatment. Our aim was to investigate the potential clinical parameters for the diagnosis of HBV-ACLF with sepsis.
Methods: A retrospective study was conducted in 43 patients with HBV-ACLF and sepsis who underwent orthotopic liver transplantation. Immunohistochemistry (IHC) staining, routine hematoxylin-eosin (HE) staining and Gordon Sweet's reticulin staining were performed in this study. Alanine aminotransferase (ALT), aspartale aminotransferase (AST), total bilirubin (TBiL), cholinesterase (CHE), albumin (ALB), prothrombin activity (PTA), blood routine examination were detected. The results being chosen at admission and before transplantation were analyzed.
Results: TBiL had a significant increase (563.5 ± 191.8 μmol/L vs. 383.9 ± 157.6 μmol/L, 438.3 ± 154.7 μmol/L, P = 0.031) and ALT significantly decreased (81.6 ± 66.4 U/L, 754.5 ± 1084.7 U/L, 120.6 ± 102.5 U/L, P = 0.005) in sepsis group before liver transplantation. When sepsis appeared in patients with HBV-ACLF, the ratio of PLT to WBC count before liver transplantation was much lower than it at admission (4.6 ± 2.0 vs. 16.1 ± 7.2, P = 0.000).
Conclusions: The clinical parameters of sepsis in patients with HBV-ACLF should be reset. When sepsis appeared, TBiL and WBC count remarkably elevated, while PLT significantly decreased. The ratio of PLT/WBC and (WBCBLT/WBCAA)/(PLTBLT/PLTAA) could remind us the occurring of sepsis in patients with HBV-ACLF.

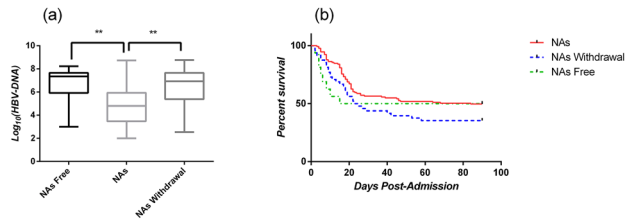
Abstract #160

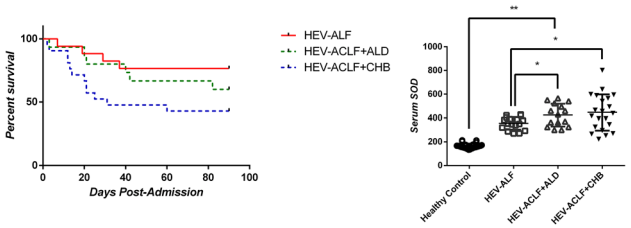
Withdrawal of Nucleoside Analogs Leads to Poor Prognosis in HBV-Related Acute-on-Chronic Liver Failure

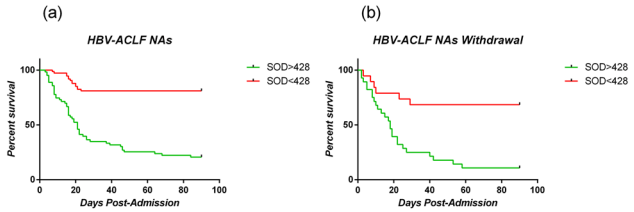
Zhen Tian[1], Jinfeng Liu[1], Tianyan Chen[1], Yingren Zhao[1]

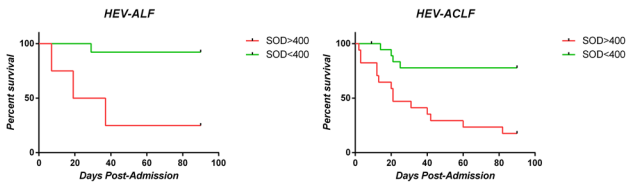
[1]Department of Infectious Diseases, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an City, Shaanxi Province, China

Objectives: HBV-related-acute on chronic liver failure (HBV-ACLF) accounts for 80% of all ACLF cases in China, and fewer than 50% of HBV-ACLF patients recover spontaneously. HBV reactivation due to withdrawal of Nucleoside Analogs (NAs) therapy is now the most important intrahepatic reasons leading to HBV-ACLF in China. Here, we focused on the prognosis of HBV-ACLF caused by NAs withdrawal and the relationship between plasm HBV-DNA level and oxidative stress, which has been shown mediate inflammation during liver failure.
Methodology: We analyzed plasma samples (collected at time of hospital admission) and clinical data from 200 patients included in the HBV-ACLF Group from January 2013 to November 2017. We compared data with those from all patients enrolled in the study, as well as from healthy individuals with no evidence of liver disease (healthy controls) of similar ages. Plasma levels of HBV-DNA were measured using Roche Cobas and SOD were measured using a polyclonal antibody and colorimetric assay.
Results: HBV-ACLF patients in NAs withdrawal group showed increased mortality rate compared to those in NAs treated group (69.95 vs 46.71). Elevated HBV-DNA and SOD levels were found in NAs withdrawal group (6.49 ± 0.24 vs 4.79 ± 0.14, $P < 0.01$) Log10 (HBV-DNA), (446.1 ± 30.69 vs 390.0 ± 12.47, $P < 0.05$). A level of SOD above 428 U/mL was associated with a statistically significant increase in risk for mortality in HBV-ACLF patients.
Conclusion: A one-time measurement of plasma SOD level can be used to assess prognosis of HBV-ACLF patients. Withdrawal of NAs leads to reactivation of HBV and then elevated oxidative stress in HBV-ACLF patients.









Abstract #161

Association Between Serum SOD Level and Survival of Patients with HEV-Induced Liver Failure

Zhen Tian[1], Yingli He[1], Tianyan Chen[1], Yingren Zhao[1]

[1]Department of Infectious Diseases, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi Province, China

Objectives: 2 billion people live in hepatitis E virus (HEV) endemic areas. The disease spans from acute viral hepatitis (AVH) to acute liver failure (ALF) and acute-on-chronic liver failure (ACLF) after HEV infection. ROS have been reported to mediate liver inflammation during liver failure, and SOD transforms toxic superoxide into hydrogen peroxide and diatomic oxygen and thereby limits the detrimental effects of ROS. Here, we investigated whether plasma levels of SOD are associated with outcomes of patients with HEV liver failure.

Methodology: We analyzed plasma samples (collected at time of hospital admission) and clinical data from 101 HEV liver failure patients from January 2013 to November 2017. We compared data with those from all patients enrolled in the study, as well as from healthy individuals (healthy controls) of similar ages. Plasma levels of SOD were measured using a polyclonal antibody and colorimetric assay.

Results: HEV-ACLF patients based on CHB or ALD showed increased mortality rate compared to HEV-ALF patients (57.14% vs 40% vs 23.52%). Patients with HEV-ACLF and HEV-ALF showed significantly higher plasm SOD level compare to HEV-AVH patients (446.7 ± 33.11 U/mL vs 150.3 ± 3.29 U/mL, $P < 0.01$) (355.6 ± 12.72 U/mL vs 150.3 ± 3.29 U/mL, $P < 0.01$). A level of SOD above 400 U/mL was associated with a statistically significant increase in risk for mortality or liver transplantation due to ACLF.

Conclusion: A one-time measurement of plasma SOD level can be used to assess prognosis of HEV liver failure patients. The elevated oxidative stress was induced by liver failure and enhanced by CHB or ALD.

Abstract #167

Association between Plasma Level of SOD and Survival of Patients with Acute-on-Chronic Liver Failure

Juan Li[1], Zhen Tian[1], Tianyan Chen[1], Yingren Zhao[1]

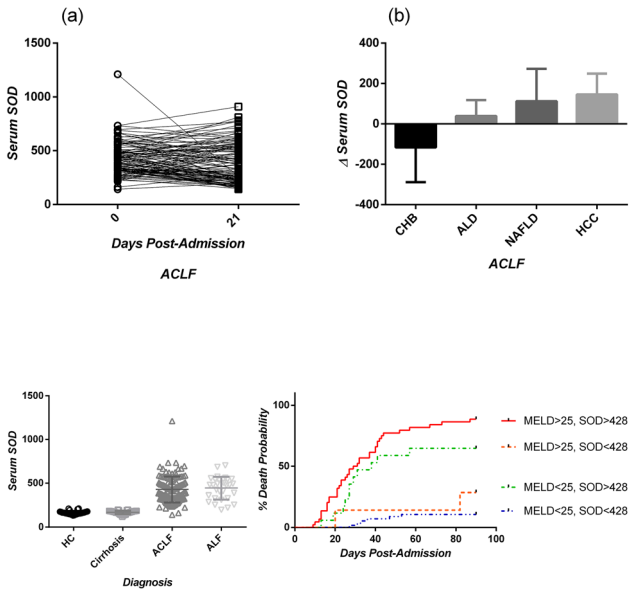
[1]Department of Infectious Diseases, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi Province, China

Objectives: Fewer than 50% of patients with acute-on-chronic liver failure (ACLF) recover spontaneously, and ACLF has high mortality without liver transplantation. ROS have been reported to mediate liver inflammation during the process of liver failure. SOD transforms toxic superoxide into hydrogen peroxide and diatomic oxygen and thereby limits the detrimental effects of ROS. We investigated whether plasma levels of SOD are associated with outcomes of ACLF patients.

Methodology: We analyzed plasma samples (collected at time of hospital admission) and clinical data from 150 patients from July 2013 through November 2017. We compared data with those from all patients enrolled in the study, as well as from healthy individuals with no evidence of liver disease (controls) and patient with liver cirrhosis (cirrhosis) of similar ages. Plasma levels of SOD were measured using a polyclonal antibody and colorimetric assay.

Results: Patients with ACLF had statistically higher plasma levels of SOD than controls (428.3 ± 13.04 U/mL vs 164.2 ± 3.82 U/mL, $P < 0.01$), and levels also differ significantly from patients with cirrhosis (428.3 ± 13.04 U/mL vs 169.3 ± 3.69 U/mL, $P < 0.01$). A level of SOD above 428 U/mL was associated with a statistically significant increase in risk for mortality or liver transplantation due to ACLF. Competing risk analyses associated level of SOD with transplant free survival, independently of model for end-stage liver disease (MELD) score.

Conclusion: The combination of SOD level and MELD score was more closely associated with patient outcome than either value alone. This system might be used to determine patient prognoses and prioritize patients for liver transplantation.



Abstract #217

Case report: Fulminant Hepatic Failure caused by Acute Hepatitis B virus infection

Peng Yuan He[1], Ruo Man Ke[1], Wen Tao Luo[2], Chong Jie Gan[2], Mign Xing Huang[2], Jin Yu Xia[2]

[1]The Fifth Affiliated Hospital, Sun Yat-Sen University, [2]Department of Infectious Diseases, The Fifth Affiliated Hospital, Sun Yat-Sen University

Background: Hepatitis B virus (HBV) infection leading to chronic hepatitis, liver cirrhosis and hepatocarcinoma is a global problem. Fulminant hepatic failure (FHF) is very rare by acute HBV infection in adult. Herein we present a case of FHF caused by acute HBV infection.
Methods: Case description
Result: A 51-year-old male presented with fever, chilly, headache and sore throat after catching a cold on March 15, 2018. He developed acute watery diarrhea, upper abdominal pain and vomiting 2 days later. His laboratory results were significant higher in alanine aminotransferase (ALT) of 6420 U/L, aspartate aminotransferase (AST) of 3513 U/L and creatinine (Cr) of 466 μmol/L and the significantly decrease in prothrombin activity (PTA) of 17.6% and the maximum of total bililubin (TB) of 318 μmol/L and serum ammonia of 106.5 μmol/L. Therefore, FHF was diagnosed. HBsAg was positive and HBV DNA levels was 4.09 log10 IU/ml (Table 1). Acute HBV infection was diagnosed according to the change of HBsAg and HBV DNA level within 1 week. The patient developed severe complications and died of multiple organ failure 5 days after admission.
Conclusion: Acute HBV infection in adults is usually self-limiting. However, this case indicates that FHF could be induced by acute HBV infection. We speculate specific host immunity and viral strains can cause FHF in the patients with HBV acute infection. More attention should be paid to the HBV acute infection in the future.

DATE	HBsAg (IU/ml)	HBsAb (s/co)	HBeAg (s/co)	HBeAb (s/co)	HBcAb (s/co)	HBV-DNA (log 10 IU/ml)
2018-3-20	0.05	197.83	6.858	2.04	2.98	4.093
2018-3-26	0.00	239.56	0.239	0.39	4.30	2.966

Table1. The changes in immunological markers of hepatitis B virus in the patients in one week.

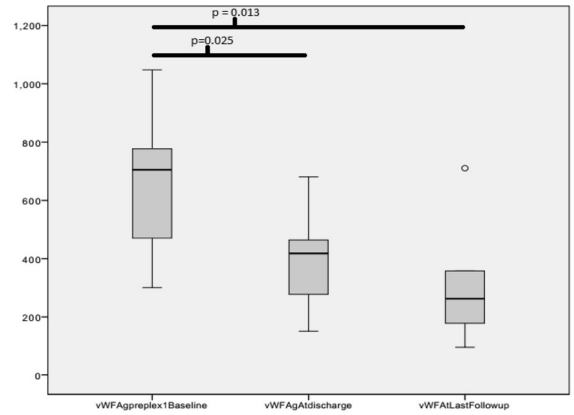
Abstract #272

von Willebrand factor (vWF)-pheresis : a possible explanation how plasma exchange is beneficial in liver failure.

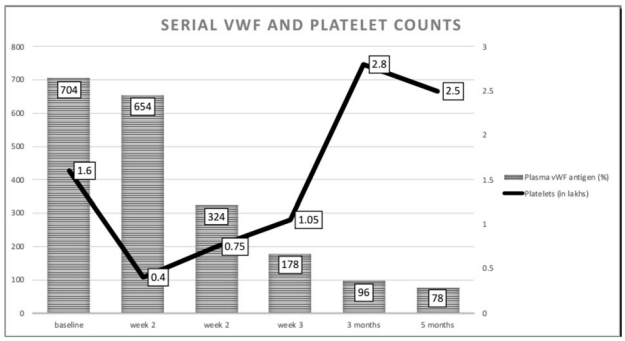
Prashanth B. Gandhi[1], Nitty Mathews[1], Joy Mammen[1], Sukesh Nair[1], Shibu Jacob[1], Vijayalekshmi B[1], Balasubramanian Ka[1], Subramani K[1], Binila Chacko[1], Shankar Zanwar[1], Ashish Goel[1], Uday Zachariah[1], Elwyn Elias[1], Eapen Ce[1]

[1]Department of Hepatology, Christian Medical College, Vellore

Introduction: Mechanism of Plasmapheresis (PLEX) improving survival in acute liver failure (ALF) and acute on chronic liver failure (ACLF) is unknown.
Objectives: To study whether vWF removal by PLEX could explain how it benefits liver failure patients.
Methodology: Prospectively collected database of ALF /ACLF patients who had PLEX (October 2017–June 2018) was retrospectively analysed. Serial plasma vWF antigen and MELD scores were analysed in patients with $\geq$ 1 month follow up after discharge from hospital. vWF levels in PLEX filtrate were analysed.
Results: Out of total of 45 post PLEX patients, 5 ALF and 4 ACLF patients, 32 (16–59) years, median (range) old, 7 males, had follow up $\geq$ 4 weeks after PLEX. MELD scores at admission, at discharge and at last follow up reduced (27 (21–40); 19 (17–30); 10 (6–21) respectively). Markedly raised plasma vWF levels reduced from 705 (300–1048) u/dl at admission to 418 (151–681) u/dl at discharge (after PLEX) and 262 (96–710) u/dl at last follow up. PLEX treatment reduced plasma vWF levels (median estimated daily decrease in plasma vWF level was 13% during PLEX treatment compared to 1% after discharge from hospital, no further PLEX given). In PLEX filtrate tested in 7 patients, vWF levels were 249.7 (24–496.5) u/dl.
Conclusion: Plasma vWF reduction was higher while patients were on PLEX compared to later follow up. vWF was demonstrated in PLEX filtrate. This data suggests vWFpheresis as a possible mechanism to explain why PLEX is beneficial in ALF and ACLF patients.



Graph1 : Serial vWF Levels in the 9 patients with liver failure treated with PLEX. Outlier shows the trend in the patient who eventually died.



Graph 2: Serial plasma vWF antigen levels (%) and platelet counts ($X10^5$/cmm) in a single ALF patient with good recovery over a long term follow up.

Abstract #298

Bench-to-clinic development of plasminogen as a novel prognostic biomarker for patients with HBV related acute-on-chronic liver failure

Da Xian Wu[1], Ze Yu Sun[2], Sai Nan Zhang[3], Qun Fang Rao[4], Zhou Hua Hou[5], Bing Jie Liu[6], Hai Nv Gao[7], Lan Juan Li[8]

[1]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases; Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases; The First Affiliated Hospital, College Of Medicine, Zhejiang University, 310003 Hangzhou, China, [2]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases; Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases; The First Affiliated Hospital, College of Medicine, Zhejiang University, 310003 Hangzhou, China, [3]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases; Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases; The First Affiliated Hospital, College of Medicine, Zhejiang University, 310003 Hangzhou, China, [4]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases; Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases; The First Affiliated Hospital, College of Medicine, Zhejiang University, 310003 Hangzhou, China, [5]Xiangya Hospital, Centralsouth University, [6]The First Affiliated Hospital, Nanhua University, [7]Shulan Hospital, Zhejaing University, [8]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases; Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases; The First Affiliated Hospital, College of Medicine, Zhejiang University, 310003 Hangzhou, China

Aims: HBV related acute-on-chronic liver failure (HBV-ACLF) deteriorates rapidly in short term, which necessitates accurate initial clinical decision-making. Present study aims to develop a novel prognostic biomarker for HBV-ACLF patients.
Methods: Three batches of Tandem Mass Tag (TMT) labeled quantitative proteomic were executed with 10 acute decompensation (AD) and 20 ACLF patients. The biomarker candidates were preliminarily verified by a cross-sectional cohort (n = 144) and further verified by two prospective cohorts (n = 207, and n = 121 respectively).
Results: Plasminogen, a novel prognostic biomarker for HBV-ACLF patients, was identified by TMT quantitative proteomic and preliminarily verified by the cross-sectional cohort. In the further verification with a prospective cohort (n = 207), plasminogen was significantly lower in ACLF non-survivors than survivors ($P < 0.001$). The cumulative survival time in patients with higher plasminogen was significantly longer than whom with lower plasminogen ($P < 0.001$). During the 14-day longitudinal observation, the plasminogen level significantly decreased in the deterioration groups ($P = 0.008$), but significantly increased in the improvement group ($P < 0.001$). Additionally, the plasminogen level gradually increased in survivors ($P < 0.001$) but gradually decreased in nonsurvivors ($P = 0.019$) during patients' hospitalization. PHAIT, a novel prognostic score based on plasminogen, hepatic encephalopathy, age, international normalized ratio, total bilirubin was significant better than Child-Pugh, MELD, CLIF-C ACLF, COSSH, and HINT (all $p < 0.05$). This score was validated by another multi-center prospective cohort (n = 121).
Conclusions: Plasminogen is a novel promising biomarker for HBV-ACLF, sequential plasminogen measurements may facilitate prediction of the clinical course of ACLF. PHAIT is a novel prognostic score and superior to Child-Pugh, MELD, CLIF-C ACLF, COSSH, and HINT.

Abstract #402

Bacillus cereus ameliorates D-galactosamine-induced liver injury in rats by modifing gut microbiota and enhancing intestinal barrier

Yating Li[1], Lanjuan Li[2]

[1]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China; & Collaborative Innovation Center For Diagnosis and Treatment of Infectious Diseases, Hangzhou, China, [2]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China & Collaborative Innovation Center For Diagnosis And Treatment Of Infectious Diseases, Hangzhou, China

Introduction: Acute liver failure is a drastic, unpredictable clinical syndrome with high mortality. Various preventative therapies for hepatic injury have been proposed by modulating the gut flora.
Objectives: To explore whether *Bacillus cereus* (*B. cereus*) could protect acute liver failure and its possible physiological and immunological mechanisms.

Methodology: The random components of 21 rats were divided into 3 groups, positive control group, negative control group and experimental group. *B. cereus* was administered 1 ml/d of solution (3×10^9 CFU/m). After 14 days, D-galactosamine (1 g/kg, Sigma, America) was intraperitoneally injected to induce acute liver failure. After 24 hours, liver pathology, bacterial translocation, 16S high-throughput sequencing, combined with serum liver function test, BioPlex multi-factor detection, immunohistochemistry was detected to analyze the correlation and explore possible mechanisms.
Result: The liver pathological score of B. cereus group was significantly lower than that of the control group. ALT level was lower than the untreated group ($P < 0.05$), and the globulin and albumin levels were significantly increased. Under the intervention of B. cereus, the level of anaerobic bacteria in liver, kidney and lymph node metastasis was reduced. The proportion of intestinal flora is also different from that of acute liver failure model disease group, which is characterized by lower abundance of Streptococcus and Escherichia coli. Correlation analysis suggests that TLRs play an important role in microbial changes and cytokine changes.
Conclusion: It was confirmed by experiments that Bacillus cereus could play an effective protective role in the model of acute liver failure in rats, and the inflammatory factors was reduced.

Abstract #606

High-volume plasma exchange in patients with acute liver failure: Initial experience in single liver-transplantation center

Jung Hee Kim[1], Byung Chul Yoo[2], Dong-Hyun Sinn[3], Wonseok Kang[3], Geum-Youn Gwak[3], Yong-Han Paik[3], Moon Seok Choi[3], Kwang Cheol Koh[3], Joon Hyeok Lee[3], Seung Woon Paik[3]

[1]Hallym University Hangang Sacred Heart Hospital, [2]Kon Kuk University Medical Center, [3]Samsung Medical Center

Acute liver failure is a serious condition which results in multiple organ failure. Recent study suggested that high-volume plasma exchange (HVP) defined as exchange of 8–12 or 15% of ideal body weight with fresh frozen plasma, improves survival in acute liver failure (ALF) patients. Herein, we report initial experience using HVP as a bridge treatment in patients with ALF at our center.

We retrospectively reviewed consecutive 36 patients who were enlisted for a liver transplantation (LT) due to ALF between 2014 and 2017 at Samsung medical center in Korea. The primary endpoint was comparison of overall survival before and after the implementation of HVP with intention-to-treat analysis.

There were 18 cases of ALF before HVP was adopted and 18 cases of ALF afterwards. Mortality was observed in 12 patients (33.3%). Among 18 patients who presented with ALF after implementation of HVP program, 9 patients received HVP (50.0%). The 60-day mortality rate was 88.9% and 59.3% for patients who received HVP and for patients who did not ($p = 0.111$). In intention-to-treat analysis, overall outcome was improved after implementation of HVP (77.8% vs. 55.6% at 60-days), although the difference was statistically marginal ($p = 0.207$). When stratified according to HVP and LT, 60-day survival rate was 100%, 80.0%, 66.7% and 33.3% for those with LT +/HVP + (n = 6), LT +/HVP− (n = 15), LT-/HVP + (n = 3), and LT-/HVP-(n = 12), respectively ($p = 0.013$).

In this real-world, outcome was improved after HVP implementation for ALF patients. HVP can be a viable option to improve outcome for patients presenting with ALF.

Abstract #678

Acute-on-Chronic Liver Failure (ACLF) in Patients with Liver Cirrhosis

Iwanaga Terunao[1], Kamezaki Hidehiro[1], Senoo Junichi[1], Sakamoto Dai[1]

[1]Eastern Chiba Medical Center

Introduction: We analyzed patients with liver cirrhosis and investigated the state of ACLF.
Methodology: The study included 186 patients with a history of hospital admissions related to liver cirrhosis between April 2014 and June 2018. (1) The patients were classified into ACLF and non-ACLF groups to analyze possible variables leading to the development of ACLF. (2) Additionally, the clinical courses and outcomes in the ACLF group were discussed.
Results: (1) 16 patients (8.6%) were classified as having ACLF whereas 170 (91.4%) did not. The two groups showed no significant difference in age (66.3 ± 17.3 years vs. 68.7 ± 12.6 years [$p = 0.478$]) or sex (8 [50%] vs. 107 [62.9%] male patients in the ACLF and non-ACLF groups, respectively [$p = 0.308$]). Patients in whom liver cirrhosis was caused by hepatitis C virus displayed a significantly lower incidence of ACLF (2 [12.5%] vs. 68 [40.0%] patients, respectively [$p = 0.030$]). (2) Heavy alcohol consumption triggered ACLF in 6 patients (37.5%), gastrointestinal bleeding and infection in 3 (18.8%), exacerbation of underlying diseases in 2 (12.5%), and fracture and an unknown trigger in 1 (6.3%). Cumulative mortality at 1 month was 33.7%, 48.4% at 3 months, and 55.8% at both 6 and 12 months.
Conclusion: Examining retrospectively and individually, ACLF could have been avoided with thorough management in 10 patients (62.5%) out of 16. Only 2.9% of patients with hepatitis C experienced ACLF, possibly indicating these patients were relatively well-managed.

Abstract #695

The short-medium prognosis of different subtypes of HBV-related ACLF are homogeneous irrespective of whether preexisting with cirrhosis or decompensation or not

Guanya Guo[1], Yichen Han[2], Jianhe Gan[2], Xinmin Zhou[1]

[1]Department of Digestive Disease, Xijing Hospital, The Military Medical University of Air Force, [2]Department of Infectious Disease, First Affiliated Hospital of Soochow University

Objective: The definition of acute-on-chronic liver failure (ACLF) remains contested between the west and the east, mainly focused on what qualifies as chronic. A proposed classification divides ACLF into 3 subtypes according to the basic condition of cirrhosis, is promising to unify the different definitions. This study aimed to explore prognostic features of the 3 subtypes in patients with HBV-related ACLF.
Methods: 720 hospitalized patients with acute decompensation of cirrhosis or severe liver injury due to CHB in two Chinese centers were enrolled. ACLF was diagnosed according to EASL-CLIF criteria with the exception of cirrhosis, and categorized as noncirrhotic ACLF (type A), cirrhotic ACLF (type B) and cirrhotic ACLF with previous decompensation (type C).
Results: 275 patients met the ACLF criteria. The 28-day and 90-day mortality had no significant difference between the 3 types (both p values > 0.3). Patients with type A ACLF (49%) trended to a lower 1-year mortality than type B (59%, $p = 0.19$) and type C (64%,

p = 0.07), while patients with type B and type C were similar (p = 0.51). The prognosis scores including MELD, CLIF-C OF, CLIF-C ACLF and COSSH-ACLF were comparable between the 3 types. Both CLIF-C ACLF and COSSH-ACLF could accurately predict the 28/90 days mortality of all 3 types patients with auROCs more than 0.8.
Conclusion: HBV-related ACLF developed from CHB, compensated cirrhosis, and decompensation cirrhosis could be unified as a prognosis homogeneous group with high short-medium mortality, which could be early evaluated by CLIF-C ACLF and COSSH-ACLF in all subtypes with high accuracy.

Abstract #764

Role of trans-cranial Doppler in Children with Acute Liver Failure" – A Prospective Observational Pilot Study

Mridul Chandra Das[1], Anshu Srivastava[2], Rajanikant Yadav[3], Surender Kumar Yachha[4], Ujjal Poddar[5]

[1]Department of Pediatric Gastroenterology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [2]DM & MD & Professor, Department of Pediatric Gastroenterology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [3]MD & MBSS & Assistant Professor, Department of Radiology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [4]DM & MD & Professor and Head, Department of Pediatric Gastroenterology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [5]DM & MD & Professor, Department of Pediatric Gastroenterology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India.

Objective: Early detection of raised intracranial pressure improves outcome in acute liver failure (ALF). We evaluated role of bedside transcranial dopler (TCD) in ALF children for feasibility, correlation with severity of hepatic encephalopathy (HE) and predicting outcome.
Methods: 28 ALF children with HE and 47 healthy controls were prospectively enrolled. Demographic, clinical and laboratory parameters were recorded. TCD of middle cerebral artery (MCA) were performed. Peak systolic velocity (Vs), end diastolic velocity (Vd), mean flow velocity (mFV), pulsatility (PI) and resistive index (RI) were calculated by electronic calipers. PI $\geq$ 1.2 was suggestive of raised ICP
Results: TCD could be performed in all children except one with poor window. TCD parameters are shown in table 1. The Vs, PI and RI showed an increasing trend from controls to HE grade I–II to grade III–IV. ALF children with HE grade III–IV had significantly higher Vs, PI and RI as compared to controls. However, the difference in Vs, PI and RI in ALF with HE grade I–II versus controls and ALF with HE I-II versus III–IV was not statistically significant. ALF children with PI $\geq$ 1.2 (n = 7) more had severe grade (III–IV) of HE (7/7 vs. 12/21; p = 0.03) and poorer outcome (0/7 vs. 8/21 survival without transplantation; p = 0.05) than those with PI $<$ 1.2 (n = 21).
Conclusions: TCD is feasible in ALF children. The PI, RI and Vs of MCA are higher in ALF with grade III–IV HE than controls but they do not differentiate between grades of HE. PI $\geq$ 1.2 is a predictor of poor outcome.

Abstract #772

Natural History and Predictors of Poor Outcome Among Patients with Non-Acetaminophen Induced Acute Liver Injury

Ajeet Kumar Lohana[1], Shahab Abid[2], Farheen Lubna[2], Maira Mustafa[3]

[1]Department of Medicine, Section of Gastroenterology, Aga Khan University Hospital, [2]Department of Medicine, Section of Gastroenterology, Aga Khan University Hospital, [3]Department of Medicine, Dow University of Health and Sciences

Background: Acute Liver Injury (ALI) occurring secondary to Non-Acetaminophen (non-APAP) etiologies with INR $\geq$ 2, ALT $\geq$ 10 $\times$ ULN and bilirubin of $\geq$ 3 mg/dl in absence of encephalopathy is defined as Non-APAP ALI. Considering paucity of literature about Non-APAP ALI, in this prospective cohort study we have described the spectrum and predictors of poor outcome among non-APAP induced ALI
Method: Out of 367 screened patients over a period of 3 years (Jan 2014 to Dec 2017); 120 patients met criteria for ALI. These patients were followed until full recovery, or developed any of poor outcome i.e. acute liver failure (ALF), death or transplantation
Results: A total of 120 patients had met ALI criteria, with median age of 25 years, and predominantly of male gender 69 (58%). The commonest cause ALI was HEV 47 (39.1%). A total of 32/120 (26%) patients developed at least one of the primary outcome i.e. ALF, death or liver transplantation, while rest of patients recovered liver insult as shown in Table-1. The patients with primary outcomes (non survivors) having many differences in comparison to those without primary outcome (non-survivors), such as; raised Prothrombin Time (PT) (31.20 vs. 22.25 p = 0.003), and others as shown in table 2. On multivariate logistic analysis the lower SGPT (OR 1.000 (1.000–1.000) p = 0.040) and higher SGOT (OR 1.000 (1.000–1.000) p = 0.031) were found to be the predictors of poor outcome.
Conclusion: ALI secondary to non-acetaminophen etiologies is a serious disease culminating to poor outcome in almost one fourth of patients. Reversed ALT/AST ratio is a detrimental factor for predicting the poor outcome

Abstract #774

Therapeutic Capacity Of Menstrual Blood Stem Cells In Treating Pig Models Of Acute Liver Failure

Linxiao Fan[1], Jiajia Chen[2], Jiajia Chen[3], Panpan Cen[4], Jie Wang[5], Lanjuan Li[6]

[1]Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases; State Key Laboratory for Diagnosis and Treatment of Infectious Diseases; First Affiliated Hospital, Zhejiang University School of Medicine; Hangzhou 310003, China, [2]Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases; State Key Laboratory for Diagnosis and Treatment of Infectious Diseases; First Affiliated Hospital, Zhejiang University School Of Medicine; Hangzhou 310003, China, [3]Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases; State Key Laboratory for Diagnosis and Treatment of Infectious Diseases; First Affiliated Hospital, Zhejiang University School of Medicine; Hangzhou 310003, China, [4]Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases; State Key Laboratory for Diagnosis and Treatment of Infectious Diseases; First Affiliated Hospital, Zhejiang University School of Medicine; Hangzhou 310003, China, [5]Collaborative Innovation Center for Diagnosis And Treatment of

Infectious Diseases; State Key Laboratory for Diagnosis And Treatment of Infectious Diseases; First Affiliated Hospital, Zhejiang University School of Medicine; Hangzhou 310003, China, [6]Collaborative Innovation Center for Diagnosis And Treatment Of Infectious Diseases; State Key Laboratory for Diagnosis And Treatment of Infectious Diseases; First Affiliated Hospital, Zhejiang University School of Medicine; Hangzhou 310003, China

Introduction: Menstrual blood stem cells (MenSCs) have promising potential for stem cell-based therapy. However, the effectiveness of MenSCs in treating acute liver failure (ALF) has not been well studied.
Objectives: The aim of our study was to investigate the therapeutic potential of MenSCs for treating ALF in pigs.
Methodology: Subjects: 40 miniature pigs were used to establish ALF models by D-galactosamine. Intervention: ALF pig models were equally divided into 5 groups (n = 8): A and B: group for survival analysis (A) and liver function analysis (B), which received saline; C and D: 0 h and 12 h treatment group, which received an immediate (C) or 12 h after the model established (D) transplantation of MenSCs (2.5 × 106/kg); E (N = 8): Tracing observation group, which received an immediate transplantation of PKH-26 labeled MenSCs (2.5 × 106/kg). Outcome measure: The blood samples, whole livers and liver tissues of pigs were collected on 0 h, 12 h, 24 h, 36 h, 48 h, 60 h, 72 h after ALF model established. Besides survival analysis, we use the samples for liver function examination, HE staning and Dynamic Tracing of PKH26-MenSCs.
Results: MenSCs transplantation at 0 h and 12 h after model established improved liver function, alleviated the progression of liver injury, prolonged the survival time of ALF animals. In addition, the In vivo imaging system (IVIS) imaging demonstrated the ability of MenSCs homing to injured liver post-transplantation.
Conclusion: Our study demonstrated the therapeutic efficacy of intraportal transplanted MenSCs in a large animal model of ALF for the first time.

Abstract #853

MicroRNA-19 Over-expressing Exosomes Improve Survival Rate of Rats with Acute Liver Failure through Anti-inflamatory Effect

Yinpeng Jin[1], Xi Wang[1], Qingchun Fu[1]

[1]Shanghai Public Health Clinical Center, Fudan University

Introduction: Some microRNAs in exosomes derived from human adipose-derived stem cells (hASCs) could promote or inhibit cytokine-related pathways to participate in inflammatory response in rats with liver failure.
Methods: MicroRNA-19 mimic or inhibitor were transfected into rat macrophages stimulated by LPS/D-gal. The expression of P47phox, ROS and inflammatory factors (IL-1a, IL-6, IL-10 and TNF) were detected. Macrophages activated by LPS/D-gal were treated with exosomes or miR-19 over-expressing exosomes respectively. Liver failure rats were treated with exosomes, miR-19 over-expressing exosomes and miR-19 over-expressing lentivirus respectively.
Results: In vitro experiment, the expression of P47phox, ROS, IL-1a, IL-6 and TNF in the mimic group was lower than that in the inhibitor group or the positive control group, and IL-10 in the mimic group was higher than that in the inhibitor group. In addition, the expression of P47pbox, ROS, IL-1a, IL-6 and TNF in miR-19 over-expressing exosomes was lower than that in the exosomes group, and the expression of IL-10 was higher than that in the exosomes group. In vivo experiment, compared with the control group, miR-19 over-expressing exosomes and viral therapy improved the survival rate and liver function of rats. The expression of cytokines, ROS and P47phox in the miR-19 over-expressing exosomes group were the lowest. Pathological examination of liver tissues showed that inflammation in liver in miR-19 over-expressing exosomes group were lightest, followed by the viral treatment group.
Conclusion: MiR-19 in hASCs derived exosomes could improve the inflammatory environment in vitro or in vivo by inhibiting P47phox-ROS pathway.

Abstract #880

Dysfunctional Circulating Monocytes With Altered Non Classical and Intermediate Subsets In Non-Acetaminophen Acute Liver Failure

Tanvi Agrawal[1], Rakhi Maiwall[2], Meenu Bajpai[3], Shiv Kumar Sarin[2], Nirupma Trehanpati[1]

[1]Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, [2]Department of Hepatology, Institute of Liver and Biliary Sciences, [3]Department of Transfusion Medicine, Institute of Liver and Biliary Sciences

Introduction: Non-acetaminophen etiologies are most common causes of acute liver failure (ALF) in Asia-Pacific region, however, frequency of circulating monocyte subsets and their functional status in these patients is not well studied.
Objectives: To study frequency and functional status of circulating monocytes in ALF.
Methodology: Monocyte subsets in ALF patients (n = 20) and age matched healthy controls (HC, n = 15) were analysed by flow-cytometry. Monocytes were isolated from PBMCs by adherence method and stimulated with LPS. Brefeldin A was added after 2 hours of LPS stimulation and after 16 hrs cells were harvested to analyse intracellular pro-inflammatory cytokine secretion (IL-1β, IL-6 and TNF-α) by flow cytometry.
Results: ALF patients (age 28 + 9 yrs, 48% males, 85% viral etiology), Jaundice to HE duration 4.4 + 3.5 days, HE grade III-IV, 82% with cerebral edema, 50% meeting KCH criteria, 40% with suspected sepsis were enrolled. Compared to HC, non-classical (CD14-CD16 +) monocytes were significantly reduced ($p < 0.05$) while intermediate monocyte (IM) (CD14 + CD16 +) significantly increased in ALF ($p < 0.05$). Compared to HC, all monocyte subsets in ALF had significantly lower expression of HLADR ($p < 0.05$). Monocytes from ALF patients showed significantly higher levels of IL-6 and TNF-α before stimulation as compared to HC, however upon stimulation with LPS, levels of IL-1β, IL-6 and TNF-α only marginally increased in ALF. In comparison monocytes from HC showed significant increase in cytokine production.
Conclusion: Circulating monocytes in ALF have lower HLADR expression and in response to LPS secrete reduced amounts of pro-inflammatory cytokines. These dysfunctional monocytes in ALF may enhance susceptibility to further infections.

Abstract #948

Hepatogenic differentiation of mesenchymal stem cell can be reverted by sequential and distinct external microenvironments when stimuli are removed

Chen Xia Hu[1], Lan Juan Li[1]

[1]Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases; State Key Laboratory for Diagnosis and Treatment of Infectious Diseases; School of Medicine; First Affiliated Hospital; Zhejiang University; Hangzhou, Zhejiang, Pr China

Introduction: Mesenchymal stem cells (MSCs) possess the ability to regenerate damaged tissue and rescue organ dysfunction due to their intrinsic plastic properties, while differentiated MSCs are progressively restricted from further differentiation. MSCs that are transplanted in vivo differentiate into functional cells at different stages according to their own specialty, but how MSCs respond to changing microenvironments and the detailed mechanisms underlying these responses are not well understood.
Objectives: We aim to explore the mechanisms of hepatogenic differentiation, transdifferentiation into adipocytes and dedifferentiation of MSCs.
Methodology: In the present study, placenta-derived MSCs (PDMSCs) were incubated in adipogenic medium to mimic an in vivo hepatogenic microenvironment and then were incubated in adipogenic medium to mimic a sudden and distinct change in microenvironment, hepatogenesis and subsequent adipogenesis were termed as a whole differentiation process.
Results: MSCs underwent hepatogenic and adipogenic differentiation cultured in general medium reverted to a primitive state. The adipocytokine signaling pathway and the PPAR signaling pathway are closely correlated with adipogenic and hepatogenic differentiation, pathways related to the cell cycle and DNA synthesis were initiated after stimuli were removed from the mixed cell lineages. Mixed lineages retained embryonic markers, metabolism homeostasis and differentiation ability.
Conclusions: These observations indicate that both MSCs and differentiated MSCs immediately respond to external stimulation and conserve their pluripotency after removal of the stimulation.

Abstract #978

Lifetimes, mortality and predictive factors of survival in patients with acute-on-chronic liver failure

Sayfullo Avezov[1], Manujehr Abdulloev[1], Rohatillo Odinaev[1], Behruz Ganiev[1], Mehroj Khuzhamurotov[1], Dilorom Ishankulova[1]

[1]Institute of Gastroenterology, Tajikistan

Background and Aims: There so little is known about diagnostic criteria, prevalence, survival rates and lifetimes of patients with acute-on-chronic liver failure (ACLF). We comparative investigated the lifetimes, mortality and predictive factors of survival in patients with liver cirrhosis (LC) and ACLF.
Methodology: We collected data from 310 hospitalized patients with LC. Diagnostic criteria for ACLF based on consensus recommendations of APASL. Survival was assessed according to the Kaplan-Meier method.
Results: 48 patients with LC reported clinical signs of ACLF. Patients with ACLF were younger than patients without OF. Prior decompensation of LC was in 34.9% of patients without ACLF and in 37.5% with ACLF. 28-day mortality was in 4.8% of patients without ACLF and in 18.9% of patients with ACLF. 90-day mortality of patients with ACLF was 50% versus 11.6% in patients without ACLF. 6-month survival rate of patients with the development of acute decompensation with organ failure was only 33.3%. The lifetimes of patients with ACLF was only 136.65 ± 18.96 days. The predictive factors of survival of patients with LC and ACLF are: the number of organ failure, indicators of CLIF-SOFA and MELD, Child-Pugh score, degree of hepatic encephalopathy, leukocytosis, hyperbilirubinemia, hypercreatininemia and increased INR.
Conclusion: The prevalence of ACLF in patients with LC is 15% and it is associated with a short-term mortality rate than that in patients without OF. The main predictive factors of survival of patients with LC and ACLF are: the number of organ failure, indicators of CLIF-SOFA and MELD.

Abstract #1015

Efficacy and Safety of N-Acetylcysteine in Patients with Non-Acetaminophen-Induced Acute Liver Failure: A Meta-Analysis

Enrik John Torres Aguila[1], Sherida Naing Edding[1], Ian Homer Yee Cua[1]

[1]St. Luke's Medical Center Global City

Introduction: Acute liver failure (ALF) is a rare but life-threatening medical emergency. While the role of N-acetylcysteine (NAC) in the treatment of acetaminophen-induced ALF has been well established, studies of its use on non-acetaminophen-induced ALF (NAI ALF) have shown inconclusive evidences.
Methodology: A comprehensive literature search from the PubMed, Embase, Cochrane Library, and Ovid was performed with the following search terms: N-acetylcysteine, non-acetaminophen, and liver failure. Four prospective clinical trials were selected and results were combined under a fixed-effects model. The Cochrane Review Manager Software version 5.0 was used for all analyses. The primary outcome of study was overall survival.
Results: Four trials comprising 499 patients were selected. 253 patients treated with NAC and 246 patients in the control group were included. In the fixed-effect model, it showed a statistically significant increase in over-all survival ($p < 0.00001$) among patients given NAC compared to control (75.09% vs. 44.31%; OR 3.65, 95% CI: 2.51–5.30). The four trials showed high heterogeneity ($I^2 = 92\%$) likely due to the study of Darweesh, et al having a population of lesser encephalopathy grades compared to the rest. A subgroup analysis removing the study of Darweesh still showed statistical significance ($p < 0.01$) in favor of NAC, with a lesser degree of heterogeneity ($I^2 = 30\%$). In terms of safety, only 78 out of 288 patients analyzed experienced side effects which include arrhythmia, vomiting, and allergic reactions.
Conclusion: NAC is an effective and safe treatment option for patients with NAI ALF. It significantly improves the over-all survival of these patients.

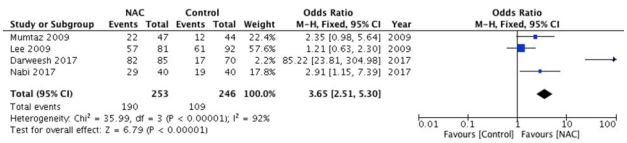


Figure 1. Forest plot of pooled incidence for over-all survival in NAI ALF patients given NAC vs. control, using Fixed Effects with 95% CI

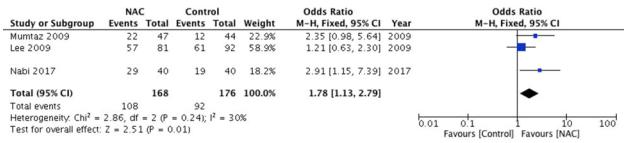


Figure 2. Subgroup Analysis on the over-all survival in NAI ALF patients given NAC vs. control *(without the study of Darweesh, et al)*

Abstract #1050

Low volume plasma exchange (LVPE) in the management of acute liver failure (ALF): A case series

Charles Panackel[1], Bipi Prasannan[2], Mathew Jacob[1], Rommel Sandhyav[1], Noushif Medappil[1]

[1]Aster Integrated Liver Care, [2]Aster Nephrology

Introduction: Larsen et al showed high volume plasma exchange (HVPE) to be effective in the management of ALF. We hypothesized that low volume plasma exchange (30–50 ml/kg/section) may be equally efficacious in ALF with less cost and less complications.
Methods: Retrospective analysis of prospective data base of patients undergoing LVPE. Patients with acute liver failure as per AASLD definition were included in the analysis. Patients with ALF and met King's college criteria were evaluated for liver transplantation. Patients on deceased donor waiting list or who were too sick for transplant underwent low volume plasma exchange (LVPE) along with standard medical therapy (SMT).
Results: Between August 2017 and September 2018, we had 42 cases of ALF meeting AASLD definition. Of these 29 met King's college criteria for liver transplantation. [Age 9 months to 58 years, M:F 14:15, Etiology-Zinc Phosphide-10, AIH-7, HAV-4, Drug-3, HBV-2, Wilson-1, Ischemic-1, Indeterminate-1]. Of these 10/29 underwent LVPE + SMT. 5/10 patients made a complete recovery and was taken off the waiting list and 1 patient was bridged to liver transplant. 2 patients died in hospital and 2 were discharged at request and lost follow up. Age 15–58, M:F 3:7, Etiology Zinc phosphide-4, Drug induced-3, HAV-1, HBV-1, Wilson-1.
Conclusion: In hospital mortality was 20% in patients with acute liver failure meeting Kings college Criteria and received LVPE + SMT. LVPE + SMT may improve transplant free survival in patients with ALF. Further large randomized control trials are needed to evaluate the efficacy of LVPE in ALF management.

Abstract #1082

Quality of life of elderly with chronic liver diseases

Raefa Refaat Alam[1], Abd-Elhady El-Gilany[1]

[1]Mansoura University

Abstract: Chronic liver disease (CLD) is a health and social problem in Egypt and its burden is expected to increase among elderly as the cohort of hepatitis C entering the geriatric age. We assessed the quality of life of 179 elderly with CLD using chronic liver disease questionnaire (CLDQ). The mean score of CLDQ was 3.55 and mean scores of the six domains were 3.6, 3.6, 3.4, 3.5, 3.6, and 3.4; respectively. The mean scores of the total CLDQ and its domains were statistically significantly lower in patients of 70 year; in males; in divorced and widowed elderly; in illiterate; in those living alone; in patients of non-alcoholic fatty liver than those with hepatitis B and C and in Child's B and C cirrhosis. It is the role of gerontological nurses and physicians to assess the effects of CLD on quality of life of elderly and council them. Key Words: Chronic liver disease questionnaire—Health related quality of life—Elderly—Hepatitis C

HEPATITIS B

B01 - Epidemiology and Natural history

Abstract #137

Enhanced liver fibrosis (ELF) score improves the accuracy of LSM-HCC score for predicting hepatocellular carcinoma (HCC) in patients with chronic hepatitis B received antiviral treatment

Lilian Yan Liang[1], Vincent Wai-Sun Wong[2], Kit Yee Tse[2], Henry Lik-Yuen Chan[2], Grace Lai-Hung Wong[2]

[1]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, [2]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong & Institute of Digestive Disease, The Chinese University of Hong Kong, Hong Kong

Background: Liver stiffness measurement (LSM)-based LSM-HCC score is accurate to predict hepatocellular carcinoma (HCC) in patients with chronic hepatitis B (CHB). Enhanced liver fibrosis (ELF) is a well-established serum biomarker for liver fibrosis. We aimed to evaluate a 2-step algorithm of using LSM-HCC and ELF scores sequentially to predict HCC in CHB patients received antiviral treatment.
Method: CHB patients who previously underwent transient elastography examination in 2006–2008 and 2009–2013 were defined; those at intermediate or high risk of HCC by LSM-HCC score (i.e. 11–20 or 21–30 respectively) were selected for an additional ELF score in order to improve the positive predictive value. ELF score was assessed by retrieved the stored serum samples 4 weeks within transient elastography examination. The primary endpoint is the cumulative incidence of HCC according to different strata of LSM-HCC/ELF scores.
Results: 453 CHB patients (mean age 51.7 ± 10.3 years; male 74.4%) were recruited. During a mean follow-up of 56 months, 45 patients (9.9%) developed HCC. Areas under receiver operating characteristic curves of LSM-HCC and ELF scores were 0.613 (95% CI 0.520–0.705, P = 0.014) and 0.644 (0.561–0.727, P = 0.002) respectively. An ELF score > 9.8 had a sensitivity of 75.6% to exclude HCC. In the combined algorithm, ELF score would be helpful to further stratify HCC risk in patients of LSM-HCC of intermediate risk (P = 0.039); but not in those of LSM-HCC of high risk (P = 0.823) (Figure).
Conclusion: A 2-step algorithm of LSM-HCC and ELF scores improve the accuracy of LSM-HCC intermediate risk in CHB patients received antiviral treatment.

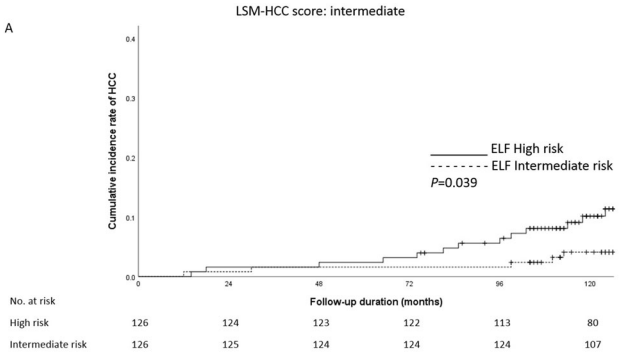
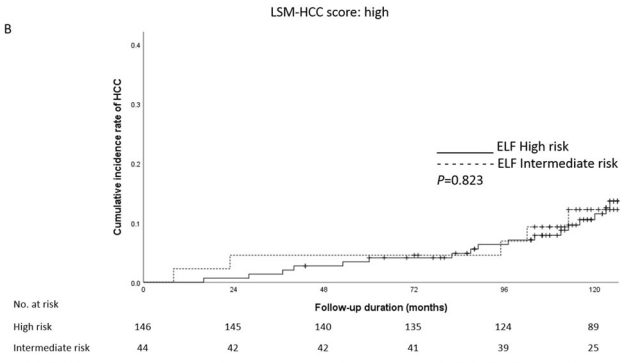


Figure. Kaplan-Meier analysis of the cumulative incidence of hepatocellular carcinoma in patients with A. LSM-HCC score of intermediate risk and B. LSM-HCC score of high risk at baseline, stratified by ELF score.



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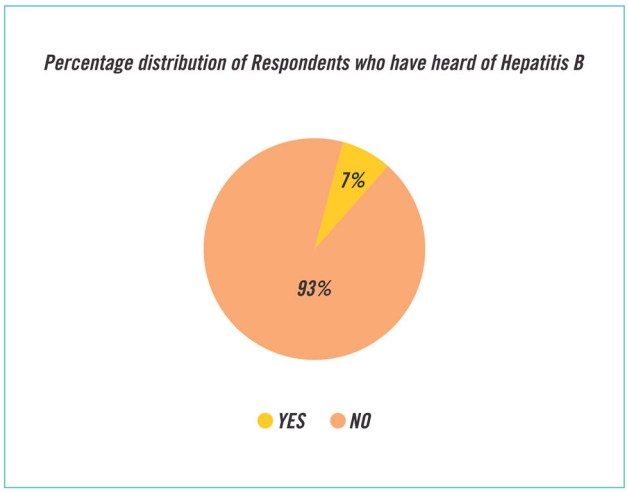


Abstract #180

Hepatitis B Knowledge, Attitude and Practices among Female Sex Workers in City of Mumbai, India

Anil Parmar[1], Jayanti Shukla[2]

[1]Director, Community Investment, United Way Mumbai & Visiting Faculty Member, Narsee Monjee Institute of Management Studies, [2]Chief Executive Officer, United Way Mumbai

Every year, over 100000 Indians die of Hepatitis B (HBV) related complications while 40 million are HBV carriers. (WHO, 2015) From the epidemiological point of view, female sex workers (FSWs) present risk of HBV infection with history of multiple sex partners, irregular condom use by partners and co-infection with sexually transmitted infection.

The objective of study was to assess the knowledge, attitude and practices with regards to (HBV) infection among brothel based FSWs in Mumbai.

Study was cross-sectional descriptive study with a two stage sample size of 400 FSW respondents who provided informed written consent. Data was collected using the screening and interview schedule covering five sections; demographic profile of the respondents, knowledge, attitude, practices towards HBV, health seeking behaviour for general health, and exposure to information-education-communication (IEC) campaigns on HBV. Descriptive statistical analysis was carried out of the collected data.

Findings indicate that there is lack of awareness about HBV infection among respondents. Risk behaviors such as early and unprotected sexual activity, limited or lack of condom use, illicit substance use by partners were highlighted. Almost all respondents had not been exposed to any print or electronic media messages on HBV on symptoms or prevention methods.

Research revealed gaps in knowledge, attitude and practices about Hepatitis B transmission among FSWs. This can lead to misinformation, missed opportunities for prevention and treatment, stigmatization of infected population. Need to design an effective behavior change communication program was established to advocate for public health IEC program on HBV in the communities.

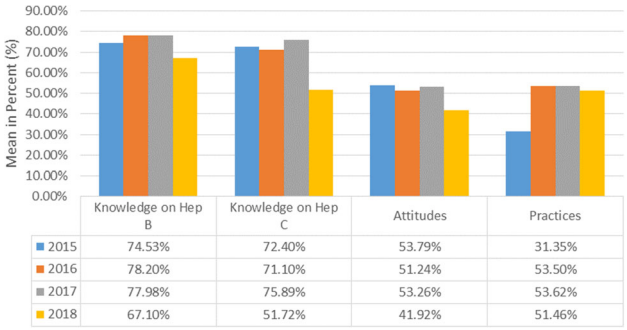
HEPATITIS B VIRUS TRANSMITTED THROUGH	YES (NUMBERS)
Unprotected Sexual contact with Hepatitis B infected person	24
Infected mother to new born during delivery	24
Sharing infected needle and Syringes	24
Infected Blood	24
Sharing personal hygiene products with Hepatitis B infected person	17

NOTE: Base-30 (Multiple responses

STATEMENTS	Strongly Disagree N (%)	Disagree N (%)	Neither Agree or Disagree N (%)	Agree N (%)	Strongly Agree N (%)
Condom use with paying clients (partners) in all types of sexual activities is one of the effective methods for Hepatitis B prevention	-	-	-	14	16
Condom use with non-paying clients (partners) in all types of sexual activities is not necessary to prevent from Hepatitis B	21	7	1	1	-
I am not at risk for getting Hepatitis B infection	2	8	11	3	6
Hepatitis B infection can occur to anyone	5	5	-	20	-
Person infected with Hepatitis B infection should not be isolated	11	4	10	5	-
It is okay to use personal hygiene products with anyone	16	2	7	3	2
Hepatitis B is not dangerous	26	1	1	1	1
It is important that every person is vaccinated for Hepatitis B prevention	-	-	4	11	15
Although I have been explained about preventive measures for Hepatitis B, I will hesitate to follow	18	5	6	-	1

SHARING OF PERSONAL PRODUCTS	YES (NUMBER)	PERCENTAGE
Comb	113	24
Nail Cutter	49	12
Razors	2	1
Towels	21	5

NOTE: Base-400



Abstract #191

A 4-year Comparison of the Knowledge, Attitudes and Practices on Hepatitis B and C among patients in the Out-Patient Department in Philippine Tertiary Hospital Setting

Marco Angelo Dominguez Tongo[1], Abigail L Valenzuela[2], Jennielyn C Agcaoili[3], Diana A Payawal[1]

[1]Cardinal Santos Medical Center, San Juan City, [2]De La Salle University Medical Center, Cavite, [3]De La Salle University Medical Center, Cavite & San Juan De Dios Hospital, Pasay City

Introduction: Approximately 400 million persons have chronic hepatitis B and 200 million have been infected by hepatitis C worldwide. The Philippines is hyperendemic for hepatitis B, with a prevalence rate of 6 to 12%. Determination of the current level of knowledge, attitudes and practices (KAP) regarding hepatitis B and C among the Filipino community will facilitate strategies for better health promotion planning.
Objectives: 1. To compare the level of KAP towards hepatitis B and C of Filipino patients in the past 4 years among those in the outpatient department in a tertiary hospital setting. 2. To describe the current status of KAP among those in the outpatient department.
Methods: This is a cross-sectional questionnaire-based study with 73 items. These were provided to participants during the celebration of the World Hepatitis Day in the past 4 years. .
Results: The comparison of KAP in the past 4 years yielded no statistical difference however, there has been a declining trend in all domains in the recent year. Those who were at least 60 years old, with a lower educational attainment and with lower monthly income demonstrated lower level of knowledge. Those who were at least 60 years old, and with lower educational attainment demonstrated more negative attitudes. Those who were females, at least 60 yrs old, and with lower educational attainment demonstrated poor practices.
Conclusion: KAP towards hepatitis B and C is influenced by different factors. The most consistently significant across all domains of evaluation is education.

Abstract #229

Need to test Anti-HBc-total for screening: An experience in Endoscopy unit of a tertiary level hospital of Bangladesh

Dr. A H M Rowshon[1], Dr. Mohammad Enamul Karim[2], Dr. Habib Ahmed[3], Dr. Dilip Kumar Ghosh[1], Dr. M A Muttalib[4]

[1]Shaheed Suhrawardy Medical College, Dhaka, Bangladesh, [2]Assistant Professor, Gastroenterology, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh, [3]Registrar, Gastroenterology Shaheed Suhrawardy Medical College, Dhaka, Bangladesh, [4]Consultant, Dentistry, Dhaka Dental College

Background: In practice, HBsAg is tested before invasive procedures like GI endoscopy to prevent transmission of Hepatitis-B (HBV). But HBsAg is surfaced in a few cases, while "AntiHBc total" remains for years after exposure to HBV and have potential to flare in immune-suppression by therapy or HIV infection. Universal antiseptic measures and immunization are expected to reduce HBV infection. But data are scarce.
Objectives: To see the status of 'AntiHBc total' and HbsAg in a large group people of Bangladesh.
Methodology: This cross sectional study was done in Endoscopy Unit of Shaheed Suhrawardy Medical College Hospital, Dhaka Bangladesh from January 2017 to December 2017. Demographic profile and medical history were taken, and then blood samples were collected. All were screened for HBsAg and Anti- HBc total. Data were recorded, processed and analyzed.
Results: A total of 2140 patients, HbsAg were found in 39 (1.8%) and Anti-HBc total were in 862 (40.3%) patients. Among anti-HBc total positive patients, 30 (3.48%) were HBsAg positive and 30 (76.92%) of 39 HBsAg positive were anti HBc-total positive. Among anti-HBc total positive patients, 452 (52.44%) were male, 282 (32.7%) had jaundice, 334 (38.7%) had dental procedures, 143 (16.6%) took blood, 2 (0.2%) were iv drug abuser and 104 (12.1%) had sexual exposure to unknown status.
Conclusion: AntiHBc total were found in two-fifth (40.3%) of patients while HBsAg were positive in 1.8% of patients attending GI procedures. So Anti-HBc total is to be tested in invasive procedures including endoscopy to prevent transmission of Hepatitis-B infection.

Abstract #250

Association of metformin use with risk of lactic acidosis in diabetic patients with chronic hepatitis B-related cirrhosis and different degrees of renal and liver impairment

Terry Cheuk-Fung Yip[1], Vincent Wai-Sun Wong[2], Yee-Kit Tse[3], Henry Lik-Yuen Chan[4], Grace Lai-Hung Wong[5]

[1]Institute of Digestive Disease and Department of Medicine and Therapeutics, The Chinese University of Hong Kong; Hong Kong Sar, China, [2]Institute of Digestive Disease, Department of Medicine and Therapeutics, and State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong; Hong Kong Sar, China, [3]Institute of Digestive Disease and Department of Medicine And Therapeutics, The Chinese University of Hong Kong; Hong Kong Sar, China, [4]Institute of Digestive Disease, Department of Medicine And Therapeutics, And State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong; Hong Kong Sar, China, [5]Institute Of Digestive Disease, Department of Medicine and Therapeutics, and State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong; Hong Kong Sar, China.

Introduction: The risk of lactic acidosis associated with metformin use in cirrhotic patients with diabetes mellitus (DM) has not been clearly documented.
Objectives: We evaluated the association of metformin use with risk of lactic acidosis in DM patients with different severity of chronic hepatitis B (CHB)-related cirrhosis.
Methodology: We identified a territory-wide cohort of DM patients with CHB-related cirrhosis from January 2000 to December 2017 in Hong Kong. Lactic acidosis was defined by diagnosis codes, and/or blood pH $\leq$ 7.35 with lactate $>$ 5 mmol/L or arterial bicarbonate $\leq$ 18 mmol/L or venous bicarbonate $\leq$ 21 mmol/L. Liver and renal function were modelled by time-dependent Child-Pugh class and estimated glomerular filtration rate (eGFR) category. Comorbidities and use of medications were adjusted as time-dependent covariates. Patients with eGFR $<$ 30 mL/min/1.73 m^2 or renal replacement therapy at baseline were excluded.
Results: 4,627 DM patients with CHB-related cirrhosis were identified; 2,762 (59.7%) had received metformin. At a median (interquartile range) follow-up of 5.3 (2.0–9.6) years, 1,119 (24.2%) patients developed lactic acidosis. The risk of lactic acidosis increased with degrees of liver and renal impairment (Figure). Use of metformin in Child-Pugh class A and eGFR $<$ 60 mL/min/1.73 m^2 during follow-up was associated with an increased risk of lactic acidosis; Child-Pugh classes B and C during follow-up were associated with a higher risk of lactic acidosis (Table).
Conclusion: Metformin therapy is safe in DM patients with Child-Pugh class A cirrhosis and eGFR $\geq$ 60 mL/min/1.73m^2. The use of metformin in Child-Pugh classes B and C should be cautious at any eGFR level.

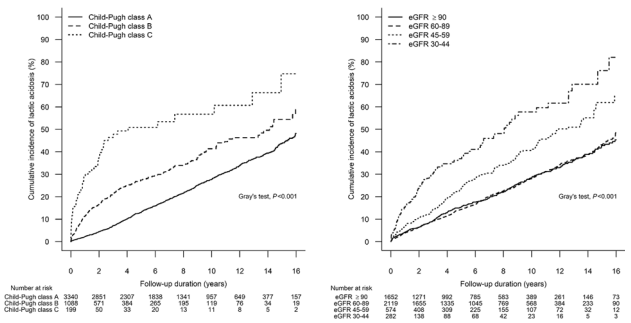


Table. Association of time-dependent metformin use with risk of lactic acidosis by time-dependent Child-Pugh class and estimated glomerular filtration rate (eGFR) category.

Time-dependent eGFR category*	Child-Pugh class A^ N=9,484		Child-Pugh class B^ N=11,269		Child-Pugh class C^ N=3,662	
	aHR (95% CI)$	*P* value	aHR (95% CI)$	*P* value	aHR (95% CI)$	*P* value
eGFR ≥90 N=10,468	0.96 (0.67–1.39)	0.842	3.91 (2.16–7.09)	<0.001	24.11 (12.58–46.20)	<0.001
eGFR 60-89 N=18,864	1.07 (0.70–1.62)	0.756	4.01 (2.42–6.64)	<0.001	16.40 (9.11–29.55)	<0.001
eGFR 45-59 N=13,107	2.26 (1.36–3.73)	0.002	15.59 (9.58–25.38)	<0.001	27.44 (14.20–53.02)	<0.001
eGFR 30-44 N=8,194	5.28 (3.17–8.80)	<0.001	24.45 (14.27–41.92)	<0.001	60.47 (32.21–113.51)	<0.001
eGFR <30 N=3,381	49.09 (30.05–80.21)	<0.001	148.33 (90.59–242.87)	<0.001	231.33 (139.60–383.32)	<0.001

* The eGFR category of patients changed during follow-up. Including records at baseline, 54,014 records of change in eGFR category were collected during follow-up of the 4,627 patients.
^ The Child-Pugh class of patients changed during follow-up. Including records at baseline, 24,415 records of change in Child-Pugh class were collected during follow-up of the 4,627 patients.
$ Reference group was patients with no metformin use, Child-Pugh class A, and eGFR ≥90 mL/min/1.73 m^2.
aHR = adjusted hazard ratio, CI = confidence interval, eGFR = estimated glomerular filtration rate.

Abstract #290

Aging population with increasing co-morbidities in patients with chronic hepatitis B – a territory-wide study of 135,414 patients from year 2000 to 2017

Grace Lai-Hung Wong[1], Becky Wing-Yan Yuen[1], Yee-Kit-Tse[1], Hester Wing-Sum Luk[1], Terry Cheuk-Fung Yip[1], Henry Lik-Yuen Chan[1], Vincent Wai-Sun Wong[1]

[1]The Chinese University of Hong Kong, Hong Kong

Introduction: Patients with chronic hepatitis B (CHB) are aging with improved survival under better healthcare. This has an important implication on choosing antiviral treatment, as long-term safety would be a concern in the presence of multiple co-morbidities.
Objectives: To determine the prevalence of co-morbidities in the territory-wide CHB cohort in Hong Kong over 18 years in 2000–2017.
Methodology: CHB patients who have been under the care at primary, secondary and tertiary medical centers in the public sector in Hong Kong were identified through the Clinical Data Analysis and Reporting System of the Hospital Authority. The demographics and prevalence of key co-morbidities, namely diabetes mellitus, hypertension, chronic kidney disease, osteopenia/osteoporosis based on diagnosis codes and relevant medications were determined according to patients' first appearance in four time periods: 2000–2004, 2005–2009, 2010–2013 and 2014–2017.
Results: 136,414 CHB patients were included; the mean age at presentation increased with time: 41 $\pm$ 15 years in 2000–2004; 46 $\pm$ 17 years in 2005–2009; 51 $\pm$ 16 years in 2010–2013; and 55 $\pm$ 15 years in 2014–2017. There was a trend of increasing prevalence of some common co-morbidities over the four periods: hypertension 25.5%, 23.8%, 27.2% and 28.6%; diabetes mellitus 10.6%, 12.5%, 16.1% and 20.1% respectively; cardiovascular disease 12.5%, 16.9%, 20.9% and 22.2% respectively, and malignancy 7.0%, 13.2%, 17.3% and 23.6% respectively (all P $<$ 0.001; Figure).
Conclusion: CHB patients are getting older with increasing prevalence of common co-morbidities. These co-morbidities should be taken into account when choosing antiviral treatment.
Funding: This work was supported by the Investigator Sponsored Research of Gilead Sciences (Reference: IN-US-988-5290).

Abstract #310

POLK, DNMT3B and EFTUD2 gene polymorphisms with the risk of HBV infection

Chuanlong Zhu[1], Anran Tian[2], Chen Dong[3], Jun Li[4], Ming Yue[5], Ming Yue[6]

[1]Department of Infectious Disease, The First Affiliated Hospital of Nanjing Medical University, [2]Department of Infectious Disease, The First Affiliated Hospital of Nanjing Medical University, [3]Department of Epidemiology and Statistics, Medical College of Soochow University, [4]Department of Infectious Disease, The First Affiliated Hospital of Nanjing Medical University, [5]Department of Infectious Disease, The First Affiliated Hospital of Nanjing Medical University, [6]Department of Infectious Disease, The First Affiliated Hospital of Nanjing Medical University

Background and Aims: Studies have shown that POLK, DNMT3B and EFTUD2 gene are connected with the pathophysiological processes of some diseases. Our study was to analyze the relationship between single nucleotide polymorphisms (SNP) of this genes and the risk of HBV infection.

Methods: A Chinese Han population, including 459 uninfected control cases and 437 cases with HBV infection, were genotyped for five SNPs (rs10077427, rs5744533, rs3809756, rs2424908 and rs73615605), using a TaqMan assay.

Results: There were significant differences in the distribution of cirrhosis, fatty liver, ALT and AST (all $P < 0.001$). The data confirmed that rs5744533 TT ($P = 0.035$), rs2424908 TC ($P = 0.033$) and rs3809756 AC ($P = 0.036$) genotype had higher risk of HBV infection; rs73615605 CT ($P < 0.001$) or rs10077427 AG ($P = 0.035$) genotype had lower risk of it. Stratified analysis showed rs10077427 G increased the risk of HBV infection in age < 47 and no cirrhosis subgroups; rs5744533 T increased it in age ≥ 47, no fatty liver, ALT and AST ≤ 40 U/L subgroups; rs3809756 C increased it in AST ≤ 40 U/L and no cirrhosis subgroups; rs73615605 T increased it in male, no cirrhosis, no fatty liver, age ≥ 47 and age < 47 subgroups; rs2424908 C increased it in ALT and AST ≤ 40 U/L subgroups.

Conclusion: Our data indicates that rs10077427 G and rs73615605 T significantly reduced the risk of HBV infection, while rs5744533 T, rs3809756 C, rs2424908 C increased it. We demonstrated that new locis associated with HBV susceptibility, may providing a novel insights into the prevention of HBV infection.

Table1: Demographic and clinical characteristics

Variables	Total (N=896)	Control (N=459)	Case (N=437)	*P*-value
Median age, year (IQR)	47.0 (40.0-55.0)	47.0 (41.0-55.0)	46.0 (38.0-56.0)	0.073[a]
Gender, n (%)				0.139[b]
Male	552 (61.6)	272 (59.3)	280 (64.1)	
Female	344 (38.4)	187 (40.7)	157 (35.9)	
Cirrhosis, n (%)				
No	558 (90.1)	383 (100.0)	175 (64.5)	<0.001[b]
Yes	61 (9.9)	0 (0)	61 (25.8)	
Fatty liver, n (%)				<0.001[b]
No	447 (74.9)	243 (63.4)	204 (95.3)	
Light	87 (14.6)	77 (20.1)	10 (4.7)	
Moderate or heavy	63 (10.5)	63 (16.5)	0 (0)	
ALT (U/L)				
≤40	636 (95.1)	407 (89.1)	228 (77.4)	<0.001[b]
>40	117 (4.9)	50 (10.9)	67 (22.6)	
AST (U/L)				
≤40	667 (88.5)	436 (95.4)	231 (77.8)	<0.001[b]
>40	87 (11.5)	21 (4.6)	66 (22.2)	

Abbreviations: IQR, interquartile range; ALT, alanine transaminase; AST, aspartate transaminase.

[a]*P* value of Mann-Whitney U test among two group.

[b]*P* value of χ^2-test among two groups.

Table 2:Association analysis between selected SNPs and the risk of HBV infection

SNPs (genotype)	Control, n (%) (N=460)	Case, n(%) (N=437)	OR(95%CI)[a]	*P*[a]
rs10077427				
AA	191 (52.9)	247 (60.5)	1.00	--
AG	152 (42.1)	144 (35.3)	**0.725 (0.538-0.978)**	**0.035**
GG	18 (5.0)	17 (4.2)	0.709 (0.354-1.419)	0.331
Dominant model			**0.724 (0.542-0.966)**	**0.028**
Additive model			**0.771 (0.603-0.985)**	**0.038**
Recessive model			0.807 (0.407-1.598)	0.538
rs5744533				
CC	234 (52.0)	202 (46.4)	1.00	--
CT	189 (42.0)	192 (44.1)	1.186 (0.899-1.565)	0.226
TT	27 (6.0)	41 (9.5)	**1.754 (1.041-2.958)**	**0.035**
Dominant model			1.258 (0.965-1.641)	0.090
Additive model			**1.259 (1.020-1.556)**	**0.032**
Recessive model			1.620 (0.977-2.688)	0.062
rs3809756				
AA	170 (39.2)	134 (32.0)	1.00	--
AC	188 (43.3)	205 (48.9)	**1.380 (1.021-1.866)**	**0.036**
CC	76 (17.5)	80 (19.1)	1.344 (0.912-1.982)	0.135
Dominant model			**1.370 (1.033-1.817)**	**0.029**
Additive model			1.191 (0.986-1.440)	0.070
Recessive model			1.121 (0.791-1.588)	0.522
rs2424908				
TT	116 (37.4)	103 (29.3)	1.00	--
TC	145 (46.8)	183 (52.1)	1.411 (1.000-1.992)	0.050
CC	49 (15.8)	65 (18.6)	1.467 (0.929-2.318)	0.100
Dominant model			**1.426 (1.029-1.975)**	**0.033**
Additive model			1.244 (0.995-1.554)	0.056
Recessive model			1.195 (0.794-1.798)	0.393
rs73615605				
CC	375 (86.6)	428 (99.3)	1.00	--
CT	68 (13.4)	3 (0.7)	**0.042 (0.013-0.136)**	**1.191×10^{-7}**
TT	0 (0)	0 (0)	--	--
Dominant model			**0.042 (0.013-0.136)**	**1.191×10^{-7}**
Additive model			**0.042 (0.013-0.136)**	**1.191×10^{-7}**
Recessive model			--	--

Abbreviations: SNP, single nucleotide polymorphism; HBV, hepatitis B virus; OR, odds ratio;CI, confidence interval.

[a]The *P* value, OR and 95% CIs of case versus control were calculated on the basis of the logistic regression model, adjusted by gender and age.

Bold type indicates statistically significant results.

Abstract #370

Prevalence of Hepatitis B and Hepatitis C in Non-professional Blood Donor in Tertiary Care Hospital in Bangladesh

Md Akmat Ali[1], Ahm Khairul Imam[2], Dr Khadija Begum[3]

[1]Ad-Din Women's Medical College And Hospital, Dhaka, Bangladesh, [2]Associate Professor of Medicine, Ad-Din Women's Medical College and Hospital, Dhaka, Bangladesh, [3]Associate Professor of Medicine, Ad-Din Women's Medical College and Hospital, Dhaka, Bangladesh

Introduction: Hepatitis B virus (HBV) and Hepatitis C virus (HCV) are the most common viruses causing liver cirrhosis and hepatocellular carcinoma globally. Blood transfusion related transmission of HBV and HCV also create serious health hazards in previously healthy persons.

Objectives: To determine the prevalence of seropositivity of Hepatitis B virus and Hepatitis C virus at the first screening in non-professional blood donor.

Methodology: This prospective observational study carried out in Transfusion medicine department of Ad-din Women's Medical College Hospital Dhaka, Bangladesh. Blood samples were collected from non-professional donors during the period of September 2017 to August 2018. Total 18908 persons were screened for HBV and HCV before blood transfusion. All data were analyzed by SPSS 20.
Result: Among 18,908 persons 94.2% (17,805) were male and 5.8% (1103) were female. Age ranges of voluntary blood donors were 18–55 years. Among 18,908 blood donors 0.6% (112) blood samples showed Hepatitis B surface antigen positive. Among them HBV seropositivity found 0.58% (103) in male and 0.82% (9) in female. There was no significant difference of Hepatitis B seropositivity between male and female (P = 0.99). HCV seropositivity detected in 0.02% (3) persons, all of them were male.
Conclusion: From this single center study, we have found the current status of seroprevalence of Hepatitis B and Hepatitis C among non-professional blood donors. Proper screening before transfusion and personal awareness may play role in the reduction of the prevalence of Hepatitis B and Hepatitis C in Bangladesh. However, multi-center large scale study is needed for further evaluation.

Abstract #449

Associated Factors of Early Stage Liver Fibrosis among Individuals with Hepatitis B Virus Infection, A Large-Scale Cross-Sectional Study

Claire Huang[1], Yu-Ju Lin[2], Yu-Han Huang[3], Chi Chan[4], Rebecca Hsieh[5], Mei-Hsuan Lee[6]

[1]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan & Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan, [2]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [3]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [4]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [5]Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan, [6]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan

Introduction and Objectives: This study aimed to examine risk factors associated with early stage liver fibrosis among individuals with hepatitis B virus (HBV) infection.
Methodology: This large-scale cross-sectional study included 16,500 adults 30 years or older. They were seropositive for hepatitis B surface antigen and participated in health examinations during 2008–2013. Demographic information, medical history, and life-style habits were collected via structured questionnaires. All subjects were examined for serological and biochemical tests. FIB-4 was used as a surrogate for liver fibrosis and was calculated by age, platelet counts, alanine aminotransferase and aspartate aminotransferase. Early stage liver fibrosis was defined by FIB-4 $\geqq$1.45. Logistic regressions were utilized to estimate odds ratios (ORs) and 95% confidence intervals (95% CIs) for associated factors.
Results: There were 14,478 (87.8%), 1,852 (11.2%), and 170 (1.0%) subjects with FIB-4 $<$ 1.45, 1.45–3.25, and $>$ 3.25, correspondingly. Age, sex, cigarette smoking, alcohol consumption, glucose and cholesterol levels, direct bilirubin, and γ-GT were significantly associated with early fibrosis ($p < 0.01$). The multiple adjusted OR and 95% CI was 1.24 (1.08–1.42) for males versus females and 1.19 (1.18–1.20) for 1-year incremental age. Elevated direct bilirubin ($\geqq$ 0.4 vs. $<$ 0.4 mg/dL) was positively associated with early fibrosis with adjusted OR of 2.21 (1.83–2.66). Individuals with abnormal γ-GT ($\geqq$ 50 IU/L for males and $\geqq$ 40 IU/L for females) had 4.36 (3.68–5.16) likelihood to have early fibrosis compared to those with normal γ-GT.
Conclusion: HBV infected subjects with factors positively associated with fibrosis need to be further monitored.

Abstract #450

Opportunistic Hepatitis B Vaccination Model for Hepatitis C Positive Patients

Zaw Zaw Aung[1]

[1]Myanmar Liver Foundation, Mandalay, Myanmar

Introduction: Both hepatitis B and C are endemic in Myanmar. This model is the integration of hepatitis B vaccination into hepatitis C treatment care.
Objective: To assess the effectiveness of opportunistic hepatitis B vaccination model in the study population.
Methodology: In hepatitis C treatment care center, consented hepatitis C positive participants with 18 years or older (n = 168) were tested with hepatitis B profile. Vaccine non-responders and unvaccinated participants were offered 3 doses of hepatitis B during the treatment course of hepatitis C infection.
Results: 168 hepatitis C positive participants tested with hepatitis B profile were categorized into three groups—HBsAg positive participants (2%, n = 3), HBsAg negative but anti-HBs Ab positive (27%, n = 46) and both HBs Ag and anti-HBs Ab negative participants (71%, n = 119). The first two groups were excluded from the study. The remaining 119 non-immune participants were further divided into four groups—ongoing primary 1st dose of hepatitis B (n = 11), ongoing primary 2nd doses (n = 13), non-responders after primary 3rd dose (n = 33) and unvaccinated participants (n = 62). The non-responders and unvaccinated participants were offered opportunistic hepatitis B vaccination. Uptake of non-responder was 26 and that of unvaccinated participants was 49. Therefore, utilization of opportunistic hepatitis B vaccination model was 79% (n = 75).
Conclusion: Targeting high risk population using opportunistic hepatitis B vaccination model in hepatitis C treatment care setting is found to be a very attractive model.

Abstract #499

Prevalence of HBV, HCV and their risk factors in an urban orphanage of Bangladesh

Abdullah Al Mahmood[1], Mohammad Asif Khan [2], Pritam Dasgupta. [3], Sytuha Binta Ali[4], Aloke Kumar Raha[5], Mamun Al Mahtab[6]

[1]Department of Hepatology, Chittagong Medical College, Chittagong, Bangladesh, [2]Department of Community Medicine, Chittagong Medical College, Chittagong, Bangladesh, [3]Mahidol-Oxford Tropical Medicine Research Unit, Department of Medicine, Chittagong Medical College Hospital, Chittagong, Bangladesh, [4]Mahidol-Oxford Tropical Medicine Research Unit, Department of Medicine, Chittagong Medical College Hospital, Chittagong, Bangladesh, [5]Department of Hepatology, Chittagong Medical College Hospital, Chittagong, Bangladesh, [6]Department of Hepatology, Bangabandhu Sheikh Mujib Medical University (Bsmmu), Dhaka, Bangladesh.

Introduction: Viral hepatitis is a major public health concern around the globe. Prevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) is markedly diverse in different parts and communities of

Bangladesh. Due to lower hygiene and health awareness among the residents of the orphanages, they are highly vulnerable to suffer from infectious diseases, particularly HBV and HCV. The prevalence of HBV and HCV is often under-reported and less studied in this population.
Objective: This study was conducted to evaluate the prevalence of HBV and HCV along with the distribution of their risk factors among orphans.
Materials and Methods: This descriptive, cross sectional study was conducted in August, 2018 in an urban orphanage of Chittagong, Bangladesh. A total of 202 subjects were tested for seropositivity by rapid test device and immunochromatographic test (ICT) positive samples were further tested by enzyme-linked immunosorbent assay (ELISA).
Results: 13 students (06.44%) were found to be ICT positive for HBV and among them 11 (05.45%) were found as ELISA positive. There was no case of HCV. The history of circumcision (63.86%) by traditional healers or unqualified medical practitioners was the highest reported risk factor in all the respondents and 08 (61.54%) out of 13 HBV positive cases had a history of circumcision by unqualified medical practitioners.
Conclusion: Immunization against hepatitis B and health awareness programs on HBV and HCV need to be initiated in the orphanages to prevent the spread of hepatitis in this underprivileged group of young members of the community.

Abstract #532

The Incidence of Chronic Viral Hepatitis B and C in the Kyrgyz Republic for the Period 2000–2017

Kalys Asanbekovna Nogoibaeva[1], Svetlana Ibragimovna Umarova[2]

[1]Kyrgyz State Medical Institute for Advanced Training And Retraining, [2]Kyrgyz Russian Slavic University

Introduction: The Kyrgyz Republic (KR) is a Central Asia country with 6 million people, borders China in the south-east.
In the KR, surveillance of Carriage of the B, C virus has begun since 2000, chronic viral hepatitis B, D, C—since 2010.
Goal: Morbidity study of chronic viral hepatitis B (CHBV) and C (CHCV) in last 17 years
Methodology: The data of the routine surveillance for chronic viral hepatitis have studied from 2000 to 2017.
Results: Rate "Carriers of the hepatitis C virus" 2000–2009 varied between 29.8–34.1 0/0000. In the period of 2010–2017—varied between 52.2–57.8 0/0000, with maximum in 2012—63.2 0/0000.
The incidence CHCV in 2010–2017 varied between 3.6–4.6 0/0000, with the increase in 2012 to 7.4 0/0000.

Hepatitis B virus carrier rates varied between 35.7–53.2 0/0000 in 2000–2010. In the period of 2011–2017, varied between 69.1–78.3 0/0000, with maximum in 2012—85.2 0/0000.

The incidence CHBV in 2010–2017 varied between 2.6–3.3 0/0000 with the increase in 2012 and 2014 to 6.6 and 6.3 0/0000, respectively.

Indicators of CHBV with a delta agent (CHDV) varied between 2.1–44 0/0000, with maximum in 2011 to 7.5 0/0000.
Conclusions: In the KR, chronic viral hepatitis is serious problem as well acute viral hepatitis. Present surveillance could not show the true picture of the incidence. The new system of surveillance for CHBV, CHBV and CHDV, liver cirrhosis and hepatocellular carcinoma in the outcome they, as recommended by WHO (2016), has been implemented since 2018.

Abstract #631

Increasing age and non-liver comorbidities in patients with chronic hepatitis B in Taiwan: a nationwide population-based analysis

Yao-Chun Hsu[1], Hsiu J Ho[2], Mindie H Nguyen[3], Chun-Ying Wu[4]

[1]Fu-Jen Catholic University Hospital, [2]Taipei Veterans General Hospital, [3]Stanford University Medical Center, [4]Taipei Veterans General Hospital

Background/Aim: Taiwan is endemic for chronic hepatitis B (CHB) with prevalence of 13% in the adult population. The study aims to characterize the temporal changes in age and non-liver comorbidities between 2001 and 2011 among CHB patients in Taiwan.
Methods: This study analyzed Taiwan National Health Insurance Research Database (NHIRD) to identify adult ($\geq$ 18 years) patients with CHB (at least one inpatient or two outpatient claims for a known diagnosis of CHB, using ICD-9-CM codes and disease-specific medications). Cross-sectional analyses in 2001, 2006, and 2011 were performed to compare the changes in demographics and non-liver comorbidities over the decade.
Results: A total of 102,158, 252,809, and 338,200 eligible patients were identified in 2001, 2006, and 2011, respectively. The proportions of male CHB patients decreased from 69.9% in 2001 to 67.0% in 2011 ($p < 0.001$). The median age significantly advanced from 44.5 in 2001, 47.8 in 2006, to 51.9 years in 2011 ($p < 0.001$). In 2011, the prevalence of diabetes mellitus (24.3%), hypertension (35.2%), dyslipidemia (11.2%), stroke (9.8%), heart failure (4.2%), malignancy (7.6%); all increased significantly from 2001 (Table 1). Furthermore, the prevalence of chronic kidney disease (4.2%) and bone fracture (13.3%) in 2011 also increased significantly from 2001. Moreover, the proportion with exposure to aspirin, non-steroidal anti-inflammatory drug, proton pump inhibitor, and steroid also increased over time (Table 1).
Conclusions: Between 2001 and 2011, the Taiwanese CHB population have aged and presented with a higher non-liver comorbidity burden. These findings may inform the management of CHB in treatment selection and safety monitoring.

Abstract #640

Increasing age and comorbidities in Chinese urban patients with chronic hepatitis B from 2013 to 2016: a retrospective claims data analysis

Yida Yang [1], Wendong Chen [2], Ying Han[3], Lei Wang [4], Ling-I Hsu [5], Rentao Gao[6], Dongying Xie [7], Xueru Yin[8], Fengqin Hou[9], Jinlin Hou[10]

[1]The 1st Affiliated Hospital of Zhejiang University, [2]Toronto Health Economics and Technology Assessment Collaborative, University of Toronto, Canada, [3]Xijing Hospital of the 4th Military Medical University, [4]The 2nd Hospital of Shandong University, [5]Gilead Sciences Inc, Foster City, CA, USA, [6]Anhui Provincial Hospital, [7]The 3rd Affiliated Hospital of Sun Yat-Sen University, [8]Nanfang Hospital, Southern Medical University, China, [9]The 1st Hospital of Peking University, [10]Nanfang Hospital, Southern Medical University, China

Introduction/Objectives: To characterize demographics and comorbidity burden in Chinese urban patients with chronic hepatitis B (CHB) from 2013 to 2016.
Methods: We used the China Health Insurance Research Association (CHIRA) annual claims database to identify patients $\geq$ 18 years of

age with at least one ICD-10 code for CHB (B18.1). CHIRA conducted independent national sampling annually among covered urban employees and residents to create the claims database. Each annual claims database was used to create the study cohort by calendar year. Descriptive analyses were performed to compare the distributions of age and comorbidities in the identified CHB patients between 2013 and 2016.

Results: The proportion of the population over 45 years of age increased significantly from 40.3% in 2013 to 49% in 2016 ($p < 0.01$). The median age of CHB patients increased from 40 in the 2013 study cohort ($N = 14,545$) to 44 in the 2016 cohort ($N = 11,648$) ($p < 0.001$). In 2016, 14.5% of CHB patients had hypertension, 7% with hyperlipidemia, 10% with cardiovascular disease; all of which have increased significantly from 2013 ($p < 0.001$) [Figure 1]. Furthermore, from 2013 to 2016, the proportion of patients with renal impairment increased significantly from 8.8% to 10.0% ($p < 0.001$) and osteoporosis and/or osteoporosis-related bone fracture (pathological/non-traumatic) significantly increased from 2.1% to 4.1% ($p < 0.001$).

Conclusions: Between 2013 and 2016, Chinese patients with CHB have aged and presented with more comorbidities including hypertension, hyperlipidemia, renal impairment, and osteoporosis and/or osteoporosis-related bone fracture. Careful selection of treatment options and monitoring should be considered in managing Chinese patients with CHB.

Abstract #641

Prevention of HIV transmission and optimization of HIV therapy among HCV-infected people who inject drugs (PWID) by engagement in long-term medical care

Julie Holeksa[1], Tianna Magel[1], David Truong[1], Rossitta Yung[1], Astou Thiam[1], Letitia Chu[1], Brian Conway[1]

[1]Vancouver Infectious Diseases Centre

Background: Among HCV-infected PWID, 10–20% are co-infected with HIV. Identification of HCV mono-infected PWID may provide us with an opportunity to prevent HIV acquisition as blood-to-blood transmission of HCV generally occurs more rapidly than for HIV.

Objective: We assessed the impact of long-term engagement in multidisciplinary care of HCV-infected active PWID on the rate of subsequent HIV seroconversion or response rates to antiretroviral therapy among HCV/HIV co-infected individuals.

Methodology: We conducted a retrospective review of HCV-positive patients who initiated HCV treatment. All patients are enrolled in care addressing medical, social, psychological, and addictions-related needs. Outcomes of interest: rate of HIV seroconversion (HCV mono-infected) or response to antiretroviral therapy (HIV/HCV coinfected).

Results: 486 individuals were considered, of whom 93 were co-infected with HIV, 77 (83%) were active PWID. Demographics of HIV co-infection: mean age 54, 6% female, 11% homeless, 38% on opioid substitution therapy (OST). The majority (88/93, 95%) were on antiretroviral therapy, with 76/88 (86%) having full virologic suppression. The only correlate of absent/ineffective antiretroviral therapy was male sex (18/18). Among 393 mono-infected patients, 189 (65%) were active PWID. Demographics: mean age 52, 43% female, 14% homeless, 55% on OST. In 617 person-years of follow-up, there were no cases of HIV seroconversion.

Conclusion: Within HCV-infected PWID, long-term engagement in care (continuing after HCV treatment) is associated with excellent HIV treatment responses (exceeding WHO 90-90-90) in co-infected individuals and reduction in HIV acquisition despite ongoing high-risk behaviors in mono-infected individuals, confirming an additional benefit of providing HCV care to PWID.

Abstract #648

The high incidence of infections complication lead to high mortality in patients with HBV related acute on chronic liver failure

Chen Wang[1], Deqiang Ma[1], Chuanmin Wang[1], Deping Ding[1], Youyou Tian[1], Yue Chen[1], Zhongji Meng[2]

[1]Department of Infectious Diseases, Taihe Hospital, Hubei University of Medicine, Shiyan, China, [2]Institute Of Biomedical Research, Taihe Hospital, Hubei University of Medicine, Shiyan, China

Introduction: Bacterial or fungal infection plays an important role in the development and prognosis of liver failure, acting as either the precipitating event or a common complication. Early diagnosis and control of the infections will improve the outcomes of patients with liver failure.

Objective: To investigate the frequency and the role of bacterial and fungal infection in patients with Hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF).

Methodology: Patients with HBV-ACLF hospitalized in Taihe Hospital, Hubei University of Medicine from Jan. 2014 to Dec. 2017 were retrospectively enrolled. The sites, types, and incidences of infections and the influence of infection on the prognosis of HBV-ACLF were statistically analyzed.

Results: 114/174 (65.52%) patients with HBV-ACLF were diagnosed with infection complication, including abdominal cavity (87 cases), respiratory tract (51 cases), urinary tract (18 cases), and bile duct (10 cases). Patients with infection complication showed significantly higher mortality (70.18%) than those without infection complication (62.5%, 40/64), and patients with infection complication exhibited much higher incidence of non-infectious complications (54.39%, 62/114), which led to extremely high mortality of 88.71% (55/62). The grade of liver failure, days of hospitalization $\geq$ 30 days, age $\geq$ 45 years, and percentage of neutrophils $>$ 70% are risk factors for infection complication.

Conclusion: The high incidence of infections complication in patients with HBV-ACLF is associated with the severity and deterioration of the disease, contributing mostly to the extremely high mortality.

Abstract #761

HCC Diagnosis at a Young Age (< 40) in Patients with HBV: Clinical Features and Comparison to Older Patients

Joseph Hoang[1], Myron Schwartz[2], Mindie Nguyen[3], Jennifer Leong[4]

[1]Division of Gastroenterology and Hepatology, Stanford University Medical Center, [2]Recanati Miller Transplantation Institute, Icahn School of Medicine at Mount Sinai, [3]Division of Gastroenterology and Hepatology, Stanford University Medical Center, [4]Division of Liver Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai

Introduction: Current guidelines focus on hepatocellular carcinoma (HCC) surveillance for older patients with chronic hepatitis B (CHB).

Objectives: We aimed to characterize HCC patients by age of diagnosis.

Methods: We performed a retrospective cohort study of 961 (112 age $<$ 40 [young] and 855 age $\geq$ 40 [older]) consecutive adult

patients age ≥ 18 diagnosed with HBV-related HCC at two U.S. medical centers. Patients were identified by ICD-9/ICD-10 diagnosis codes and confirmed to have CHB-related HCC by chart review. Kaplan-Meier analysis and Cox proportional hazard models were used to study survival outcomes.

Results: Most patients were male (86.6% age < 40 and 78.3% age ≥ 40) and 11.6% (n = 112) were < 40. Of patients age < 40, the mean age at diagnosis was 33.1 years and were primarily Asians and Blacks (65.2% and 14.3%). Young males, compared to young females, older male and females, were less likely to have history of HCC screening (37.9% vs. 60.0% vs. 60.6% vs. 62.5%, p = 0.14). There was a trend towards improved survival in young females compared to young males, older males and females, but this was not statistically significant (p = 0.15). In a multivariate analysis inclusive for age groups, gender, AFP, ALT, and HBV DNA, there was a trend for higher mortality in older males (HR = 1.81, p = 0.071).

Conclusion: The vast majority of young HCC were Asian or African. Young males were less likely to undergo HCC screening and older males have higher mortality. Further research is needed to identify high risk patients for surveillance, especially young male patients and those of Asian and African ethnicity.

Abstract #787

The basal core promoter and pre-core mutations dynamics in the natural history of chronic hepatitis B patients in Indonesia

Turyadi[1], Nu'man A.S. Daud[2], Susan Irawati Ie[3], Luthfi Parewangi[4], Meta Dewi Thedja[5], M Nasrum Massi[6], David Handojo Muljono[7]

[1]Hepatitis Unit, Eijkman Institute for Molecular Biology, Jakarta, Indonesia & Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [2]Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [3]Hepatitis Unit, Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [4]Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [5]Hepatitis Unit, Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [6]Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [7]Hepatitis Unit, Eijkman Institute for Molecular Biology, Jakarta, Indonesia & Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia & Faculty of Medicine and Health, University of Sydney, NSW, Australia

Introduction: Hepatitis B has wide range of liver disease manifestations. Chronic hepatitis B (CHB) is classified into four phases: immune-tolerant (IT), immune-clearance (IC), low/non-replicative (LR), and e-negative hepatitis (ENH). Hepatitis B virus (HBV) mutations, especially basal core promoter (BCP) and pre-core (PC) mutations are known to have important roles in CHB progression.

Objective: To investigate the dynamics of BCP and PC mutants in the natural history of CHB patients in Indonesia.

Methodology: Two-hundred-fifty-seven patients were enrolled following written informed consent and classified into CHB phases based on viral load, ALT titer, and HBeAg status. BCP/PC mutants were assessed with PCR and direct sequencing. HBV genotype was determined phylogenetically using S-gene fragment.

Results: Patients were mostly male (70.8%), genotype C (56.8%), and ENH (43.2%) with median age of 48 (20–76), followed by IT (27.6%; median age 37 (16–85)), LR (17.1%; 46.5 (25–76)), and IC (12.1%; 40 (14–74)). BCP/PC mutations T1753V, A1762T/G1764A, A1846T, and G1899A were comparably high in all phases. T1753 V, A1846T, and G1896A were significantly higher in HBeAg-negatives. A1762T/G1764A was higher in genotype C. BCP/PC mutations tend to be more frequent in later phases, whereas T1753V, A1762T/G1764A, A1814C, A1837V, A1846T, G1896A, and G1899A mutations were significantly more prevalent in older patients.

Conclusions: HBeAg-defective mutations have existed since the CHB early phases, with higher prevalence in later phases and older age. BCPA1762T/G1764A mutants are possibly associated with disease manifestation in genotype C. Precaution should be exercised against the existence of BCP/PC mutations, as they could be the predictors of severe disease development in CHB patients.

Abstract #789

Seroepidemiology of triple HBV, HCV, and HIV infections in an indigenous region of Eastern part of Papua, Indonesia

Dhita Prabasari Wibowo[1], Turyadi[2], Susan Irawati Ie[3], äMaghfira[4], Meta Dewi Thedja[5], David Handojo Muljono[6]

[1]Hepatitis Unit, Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [2]Hepatitis Unit, Eijkman Institute for Molecular Biology, Jakarta, Indonesia & Faculty Of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [3]Hepatitis Unit, Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [4]Hepatitis Unit, Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [5]Hepatitis Unit, Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [6]Hepatitis Unit, Eijkman Institute for Molecular Biology, Jakarta, Indonesia & Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia & Faculty of Medicine And Health, University of Sydney, Nsw, Australia

Introduction: Hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) infections are global health problems. Coinfections with these viruses may increase morbidity and mortality. There is scanty data on epidemiology and impacts of these infections in indigenous populations, particularly those with limited access to health facilities.

Objective: To investigate HBV, HCV, and HIV prevalence in an indigenous population in Keerom, Papua, Indonesia.

Methodology: Three-hundred-and-twenty-two subjects from a native population in Keerom, Papua were serologically examined for viral infection status, following written informed consent, using HBsAg, anti-HBs, HCV-AgAb, and HIV-AgAb ELISA kits. Data was analyzed statistically.

Results: Among 322 subjects (mean age 34.6 ± 15.7; 64.3% females), the same prevalence rates of 21.7% (70/322) were found for HBsAg and anti-HBs positivity, but only 2.1% (7/322) samples had simultaneous HBsAg and anti-HBs positivity. The prevalence of HCV was 2.8% (9/322) and HIV was 4.3% (14/322). No significant gender difference was observed in the prevalence of the three infections. Viral coinfection rate was quite low, with only 0.6% (2/322) HBV/HCV and 0.9% (3/322) HBV/HIV coinfections, and no HCV/HIV and triple HBV/HCV/HIV coinfections.

Conclusion: HBV and HIV infections were highly endemic in Keerom. HCV prevalence may be increasing, considering the high endemicity of HIV and HBV that shares similar transmission routes with HCV, and vice versa. High prevalence of these viral infections should be a high concern for public health policy maker in developing required prevention, health-care delivery, and management strategies.

Abstract #904

Factors Influencing Screening Of Family Members Among Index Cases of Chronic Hepatitis B

Maria Aloiza Joven Hadloc[1], Stephen Ng Wong[1]

[1]Section of Gastroenterology Chinese General Hospital

Introduction: Recent survey of hepatitis B (HBV)-infected patients showed that 28%didn't know HBV status of their immediate family members. Factors influencing family member screening are unknown.
Objectives: We aimed to determine proportion of patients who follow doctor's advice to have family members screened and determine factors influencing this among index HBV cases.
Methodology: HBV-infected patients in single outpatient hepatology clinic from February2007-October 2017 with atleast 1follow-upvisit were included. Patients were advised to have family members screened for HBV.
Results: 406 patients (62.8% male) included, with 180 excluded because of no follow-up. Only 132 (32.5%) had their family members screened, of which 65 (49.2%) had at least 1 member with active/resolved HBV infection. Patients likely to have their family screened were those with family history of liver disease (40% vs. 27.2%; $p = 0.008$) or HBV (40.4% vs. 26.3%; $p = 0.004$), who had HBV checked because of family history of HBV (42.5%) or incidentally (36.8% vs. 16% because of jaundice/HCC; $p < 0.001$), and patients who already had cirrhosis on initial visit (41.5%) or no liver complications (36.4%) versus those with jaundice/ALT flares (18.8%) or HCC (17.5%) ($p = 0.005$). Patients with more visits were likely to have their family screened ($5.4 + 5.4$ vs. $4.3 + 4$; $p = 0.035$). In contrast, neither patient's age, gender, liver enzymes/function tests and HBV markers were factors. Independent predictors for family screening were family history of liver disease ($p = 0.026$), number of clinic visits ($p = 0.033$), and reasons for having themselves checked for HBV (family history of HBV or incidental finding) ($p = 0.014$).
Conclusion: Despite reminders to have their family screened, only minority will comply. The strongest influence is presence of other having liver disease. Patients with jaundice, ALT flares, or HCC may be pre-occupied with their condition to remind family members need for screening.

Abstract #908

Unchanging High Prevalence Of Late Hepatitis B Virus Discovery Among Patients With Chronic Hepatitis B: A Comparison Between Two Time Periods

Maria Aloiza Joven Hadloc[1], Stephen Ng Wong[2]

[1]Section of Gastroenterology Chinese General Hospital

Introduction: Late discovery of hepatitisB virus (HBV) infection leads to high rate of cirrhosis and hepatocellular carcinoma (HCC) at initial consult, and be decreased by better screening practices.
Objectives: We aimed to determine prevalence of late HBV discovery among chronic HBV (CHB) patients in 2 time periods, and compare clinical characteristics with and without late HBV discovery.
Methodology: CHB patients seen at single hepatology clinic from 2007–2017 were included. Late discovery was defined as HBV infected when cirrhosis orHCC were already present, prevalence of which was compared between 2time periods (2007–2012 and 2013–2017). Baseline clinical and laboratory characteristics were compared between patients with and without late HBV discovery.
Results: Total 50 (8.8%) and 127 (22.4%) CHB patients were diagnosed with cirrhosis and HCC, respectively, on initial clinic visit, while 390 (68.8%) didn't have complications. Late discovery was evident in 123 (21.7%). Among Cirrhotics, 64% had late HBV discovery, while 3.5% didn't have complications or jaundice (30%). Among HCC patients, 71.7% had late HBV discovery because of cirrhosis (11%) or HCC (60.6%), while minority discovered before liver complications (27.6%) or jaundice (0.8%). Patients with late HBV discovery were likely be male (79.7% vs. 58.6%; $p < 0.001$), older ($54.7 + 33.5$ vs. $39.2 + 25.3$; $p < 0.001$), hypertensive/diabetic (29.2% vs. 12%; $p < 0.001$), with significant alcohol intake (40.5% vs. 16.8%; $p < 0.001$), higher INR ($1.3 + 0.6$ vs. $1.0 + 0.3$; $p < 0.001$) and AST ($134.7 + 169.5$ vs. $49.3 + 84.3$; $p < 0.001$), lower albumin ($33.8 + 8.6$ vs. $43.2 + 5.6$; $p < 0.001$), and less likely with HBV family history (32.5% vs. 47.9%; $p = 0.003$). There was no difference in patient's proportion with late HBV discovery in 2007–2012 (20.3%) vs. 2013–2017 (24.6%) ($p = 0.276$).
Conclusions: About a fifth of patients with CHB discovered HBV infection when cirrhosis/HCC was present. The fact that late HBV discovery rate hasn't changed in > 10 years emphasizes need for amplified efforts to screen everyone, not just those with high risk, in endemic countries.

Abstract #930

Occult hepatitis B among health-care workers with anti-HBc positivity from two provinces of Indonesia

Teguh Wijayadi[1]

[1]Faculty of Medicine Universitas Hasanuddin Makasar, Indonesia & Eijkman Institute for Molecular Biology, Jakarta, Indonesia & [2]Faculty of Medicine, Universitas Tarumanagara, Jakarta, Indonesia

Introduction: Hepatitis B virus (HBV) infection, defined by the presence of hepatitis B surface antigen (HBsAg) in serum/plasma, is an occupational hazard among health-care workers (HCWs). HBV may prevail without detectable HBsAg, but with the presence of HBV DNA in the serum and/or in the liver, i.e. the occult HBV infection (OBI). Anti-HBV core antigen (anti-HBc) has been used to trace OBI.
Objectives: To assess HBV infection status and OBI among HCWs, and investigate the occult HBV isolates.
Methodology: A total of 644 HCWs (male/female 134/510; median age 28, range 16–71 years) were recruited from South Sulawesi and Jakarta. They were classified into administration (19.1%), non-intervention (63.6%), and intervention (17.3%) groups, and serologically screened for HBsAg, anti-HBc, and anti-HBs. HBV DNA was tested in anti-HBc-positive samples by nested PCR, then analyzed by sequencing of the surface gene.
Results: HBsAg, Anti-HBc, and Anti-HBs prevalence was 4.7% (30/644), 18.5% (119/644), and 36.7% (235/641), respectively. The remaining 57.3% (367/641) were negative for all seromarkers, indicating susceptibility to HBV. A rising trend of anti-HBc positivity was observed by work type ($Ptrend < 0.001$) and service period ($Ptrend = 0.010$), suggesting increasing risk to HBV infection. HBV DNA was detected in 44.1% (49/111) of anti-HBc-positive subjects, of whom 79.6% (39/49) were OBI cases. With this OBI, at least 10.7% (69/644) HCWs had existing HBV infection. Of 22 OBI sequences, 15 (68.2%) had mutations, some associated with detection and/or vaccination failure.
Conclusion: HCWs had risks associated with work type and service period. OBI with mutations was observed among anti-HBc-positive HCWs

Abstract #942

Molecular analysis of discrepant results between HBsAg and HBV NAT assays in Indonesian blood donors

Rebriarina Hapsari[1], Turyadi Turyadi[2], Susan Irawati Ie[3], Arfat Lusinanto[4], Pierlita Rini[5], Meta Dewi Thedja[6], Yuyun Soedarmono[7], Bart L Haagmans[8], David Handojo Muljono[9]

[1]Faculty Of Medicine, Diponegoro University, Semarang, Indonesia, [2]Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [3]Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [4]Central Blood Transfusion Service, Indonesian Red Cross, [5]DKI Jakarta Transfusion Service, Indonesian Red Cross, [6]Eijkman Institute for Molecular Biology, Jakarta, Indonesia, [7]Central Blood Transfusion Service, Indonesian Red Cross & Indonesian Ministry Of Health, [8]Department of Viroscience, Erasmus Mc, Rotterdam, The Netherlands, [9]Eijkman Institute For Molecular Biology, Jakarta, Indonesia & Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia & Faculty of Medicine and Health, University of Sydney, Sydney, Australia

Introduction: Nucleic acid testing (NAT) has recently been introduced into the Indonesian blood transfusion setting in attempt to increase sensitivity and window-period negativity. For hepatitis B virus (HBV) detection, however, there were discrepant results between HBV surface antigen (HBsAg) and NAT assays.
Objective: This study aimed to characterise HBV surface (S) gene among samples with discrepant results.
Methodology: A total of 30,067 blood donations were screened for HBV infection using NAT (Ultrio HBV NAT) in parallel with routine chemiluminescence HBsAg assay. Samples showing discrepant NAT and HBsAg results were further tested for other HBV serological parameters (anti-HBs and anti-HBc). HBV DNA was determined using nested PCR, sequenced for S gene characteristics and analysed for HBsAg antigenicity index.
Results: HBsAg and NAT discrepancies were found in twenty donors. Of seven HBsAg-positive/NAT-negative donors, two had detectable HBV DNA by nested PCR, with T123I and Y161F mutations were found in one donor. Among thirteen HBsAg-negative/NAT-positive donors, of whom nine were repeat donors, twelve had detectable HBV DNA; in these donors, M133L, T140I, G145A, G145R, N146S, I150T, and W156R mutations were detected, with W156R having greater antigenicity index changes of HBsAg.
Conclusion: This study highlighted the presence of HBV infection harbouring mutants known to be associated with detection failure and vaccine escape among donors with HBsAg-negative/NAT-positive, irrespective of the presence of either or both anti-HBs and anti-HBc. Repeat donors might had transmitted HBV to recipients in the past due to negative HBsAg as the sole screening method for HBV infection.

Abstract #1005

Impact of hepatic steatosis on patients with chronic hepatitis B

George Boon Bee Goh[1], Vincent Wai-Sun Wong[2], Wah Kheong Chan[3], Rajneesh Kumar[4], Jian Gao Fan[5], Wai-Kay Seto[6], Wan Cheng Chow[7]

[1]Singapore General Hospital, [2]The Chinese University of Hong Kong, [3]University of Malaya, [4]Singapore General Hospital, [5]Shanghai Jiaotong University School of Medicine, [6]The University of Hong Kong, [7]Singapore General Hospital

Introduction: The prevalence of Nonalcoholic Fatty Liver Disease (NAFLD) is increasing worldwide, and may frequently co-exist with chronic hepatitis B (CHB) in endemic regions. However, the interaction between hepatic steatosis (HS) and CHB remains to be clarified. We studied the clinical characteristics of patients with CHB-HS and explored the impact of HS.
Methods: CHB patients recruited from the CAP Asia consortium, a collaborative network of Asian centres, were included in this study. Presence of HS was defined by fibroscan evaluation of controlled attenuated parameter cutoff of 248 dB/m. Advanced fibrosis (AF) was stratified using liver stiffness measurement of 9.6 kPa.
Results: 195 patients were included in the study, with 56.4% of patients having concurrent HS. Relative to those without HS, patients with HS were older and associated with more metabolic risk factors of diabetes mellitus (22.7 vs 8.2%), hypertension (37.3 vs 14.1%), dyslipidaemia (47.3 vs 28.2%) and obesity (68.2 vs 24.7%). While patients with HS had lower HBV DNA level (1.84 log (IU/mL) vs 2.16 log (IU/mL)), ALT (37 vs 21 U/L) and AST (30 vs 23 U/L) were significantly higher. Patients with HS had higher frequency of AF (13.6 vs 1.2%). On regression analysis, diabetes mellitus (OR 4.54, $p = 0.000$), presence of HS (OR 5.16, $p = 0.027$) and obesity (OR 2.67, $p = 0.004$) were independent factors affecting AF.
Conclusion: CHB patients with HS were associated with more metabolic risk factors, and while they had lower HBV viremia, higher ALT, AST and frequency of AF were demonstrated, suggesting that HS may be responsible for driving liver injury. The presence of HS was associated with 5-fold increased odds of AF.

Abstract #1038

Risk of Clinical Events in Inactive Hepatitis B According to Different Upper Limits of Normal for Alanine Aminotransferase Level

Gwang Hyeon Choi[1], Ha Il Kim[1], Dan Bi Lee[1], Ju Hyun Shim[1], Kang Mo Kim[1], Young-Suk Lim[1], Han Chu Lee[1], Young-Hwa Chung[1], Yung Sang Lee[1]

[1]Asan Medical Center

Background: The upper limits of normal (ULN) for ALT of 35 U/L for males and 25 U/L for females is recommended according to recent American guideline whereas traditional cut-off values is approximately 40 U/L according to European guideline. The aim of this study is to evaluate the incidence of HCC and death/transplant in inactive hepatitis patients according to each ULN for ALT.
Methods: A total of 3,572 consecutive HBeAg-negative adult CHB patients with HBV DNA levels $< 2{,}000$ IU/mL, but without evidence of cirrhosis, were identified at Asan Medical Center between 2000 and 2013. 'Within AASLD group' was defined as persistently normal ALT levels according to American guidelines ($n = 3096$); and 'Beyond AASLD group' was defined high normal ALT levels (American ULN between Traditional ULN for ALT) for at least 1 year ($n = 476$).
Result: During median followed-up of 9.9 years, 111 (3.1%) developed HCC, 177 (5.0%) died or received transplantation. By univariate analyses, Beyond AASLD group had significantly higher risk of HCC (hazard ratio [HR], 1.56; 95% confidence interval [CI], 1.02–2.41; $p = 0.04$) and marginal risk of death/transplantation (HR, 1.44; 95% CI, 1.00–2.09; $p = 0.053$) than Within AASLD group. By multivariable analyses, Beyond AASLD group had significantly higher risk of HCC (HR, 1.85; 95% CI, 1.18–2.90; $p = 0.007$) and death/transplantation (HR, 1.66; 95% CI, 1.13–2.43; $p = 0.01$) than Within AASLD group.

Conclusions: Beyond AASLD group develop significantly more HCCs compared to Within AASLD group. Management of inactive CHB using strict ALT reference may reduce the unnecessary clinical events.

Abstract #1085

Cross-sectional Analysis of Chronic Hepatitis B Patients in East China: A Retrospective Data Analysis

Jueqing Gu[1], Yida Yang[1*], Guodong Yu[1], Dezhou Li[2], Zhaowei Tong[3], Huajiang Shen[4], Huazhong Chen[5], Xijie Lai[2], Meiling Xu[3], Feng Ding[4], Junyan Liu[5], Weiti Wu[5], Xiaoli Zhang[1], Huan Cai[1], Shanyan Zhang[1], Chanyuan Ye[1]

[1]Department of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University.Hangzhou, Zhejiang, China, [2]Department of Infectious Diseases, Ningbo No. 2 Hospital, Ningbo, Zhejiang, China, [3]Department of Infectious Diseases, Huzhou Central Hospital, Huzhou, Zhejiang, China, [4]Department of Liver Diseases, Shaoxing Municipal Hospital, Shaoxing, Zhejiang, Zhejiang, China, [5]Department of Infectious Diseases, Taizhou Hospital, Taizhou, Zhejiang, China.
*Corresponding Author, Email: Yangyida65@163.Com

Objective: To explore the impact of longtime antiviral therapy with entecavir on the peripheral Th17/Treg cytokines and specific transcription factor (RORγt, Foxp3) in patients with chronic hepatitis B (CHB).
Methods: One hundred and thirty-six patients with chronic hepatitis B, who received entecavir therapy for 48 weeks, were enrolled the study. 20 normal individuals were as control group. Serum HBVDNA load was measured by Real-Time-PCR, and the HBV markers were detected with ELISA during 48 weeks of the treatment. Serum levels of IL-17, TGF-β, IL-10 and IL-23 were measured using ELISA. RT-qPCR method was applied to determine the expressions of RORγt and Foxp3 mRNA of peripheral blood.
Results: CHB patients had significantly increased serum levels of IL-17, TGF-β, IL-10 and IL-23 and the expressions of RORγt and Foxp3 mRNA compared with normal individuals ($p < 0.001$). At baseline, 12 weeks, 24 weeks and 48 weeks after treatment were significantly different in the levels of ALT, AST, TBIL, HBVDNA (all p less than 0.05). HBV viral load dropped sharply during the first two weeks. Along with the extension of treatment time, the clinical indexes gradually reduced. The rates of HBVDNA undetectable and HBeAg seroconversion in 48 weeks after treatment were 78.7% (107/136) and 14.7%(20/136), respectively. Compared with pre-therapy level, a significant decrease in serum levels of IL-17, TGF-β, IL-10, IL-23 and RORγt and Foxp3 expression were found from week 48 ($p < 0.001$).
Conclusion: Antiviral therapy with entecavir can improve liver function, inhibit virus replication and lower the levels of the cytokines of Th17 and Treg, and control the progress of liver disease.

Abstract #1090

A real world, prospective cohort study on mother-to-child transmission of HBV in China (Shield Project 01)

Zhihua Liu[1], Xueru Yin[1], Guorong Han[2], Hua Zhang[3], Mei Wang[4], Wenjun Zhang[5], Yunfei Gao[1], Po-Lin Chan[6], Mei Zhong[1], Xiaolan Wang[7], Xiaozhu Zhong[8], Guojun Shen[9], Chuangguo Yang[10], Huiyuan Liu[11], Zhihong Liu[1], Jinlin Hou[1*]

*Corresponding author: Jinlin Hou, Nanfang Hospital, Southern Medical university, jlhousmu@163.com*Corresponding author: Jinlin Hou, Nanfang Hospital, Southern Medical university, jlhousmu@163.com

[1]Department of Infectious Diseases, Nanfang Hospital, Southern Medical university, [2]Department of Obstetrics and Gynecology, Nanjing 2nd Hospital, [3]Department of Obstetrics and Gynecology,You'an Hospital, Capital Medical University, [4]Department of Obstetrics and Gynecology, 302 Hospital of PLA, [5]Department of Obstetrics and Gynecology,The Fifth Affiliated Hospital, Southern Medical university, [6]World Health Organization/ West Pacific Region Office (WPRO), [7]Department of Obstetrics and Gynecology, Maternal and Child Care Service Center of Jiujiang, [8]Department of Infectious Diseases, Zhujiang Hospital, Southern Medical university, [9]Department of Infectious Diseases, Jiujiang 3rd People's Hospital, [10]Department of Infectious Diseases, The Third Affiliated Hospital, Southern Medical university, [11]Department of Severe Liver Diseases, Guangzhou 8th People's Hospital

Introduction: World Health Organization (WHO) has set the goal to eliminate hepatitis as a threat to public health by 2030. To achieve the goal, preventing mother-to-child transmission (MTCT) of HBV is the pivotal step.
Objective: This study was carried out to investigate the implementation of preventive measures and incidence of MTCT. (ClinicalTrials.gov ID: NCT03539016).
Methodology: One thousand and eight HBsAg+ pregnant women were enrolled the study in ten hospitals since July 2015. All the enrolled mother-infants pairs were prospectively followed up from establishment of perinatal medical records to 28-48 weeks postpartum.
Results: In total, 8 infants were tested positive for HBsAg and HBV DNA and all of them were born to HBeAg+ mothers with HBVDNA>2x106IU/mL. The incidence of MTCT was 0.88%, 1.43%, and 1.60% among mothers with HBsAg+ , HBsAg+ and HBeAg+, and HBV DNA>2x106IU/mL, respectively. Of the pregnant women with HBV DNA>2x106IU/mL, 72.34% of them received antiviral treatment, compared to 20.99% in those with HBV DNA2x106IU/mL. The coverage of birth dose hepatitis B vaccine and HBIG reached 99.78% and 99.89%, respectively. The delivery mode, newborn's weight, height, head circumference, Apgar score and incidence of congenital deformity or defect were similar among infants with nucleos(t)ide analogues exposure and those without exposure.
Conclusion: Through comprehensive management comprised of immunoprophylaxis for infants and antiviral therapy for mothers, the incidence of perinatal infection of HBV could be reduced further to reach the criterion of eliminating MTCT of HBV set by the WHO.

B02 - Virology, Pathogenesis and Immunology

Abstract #221

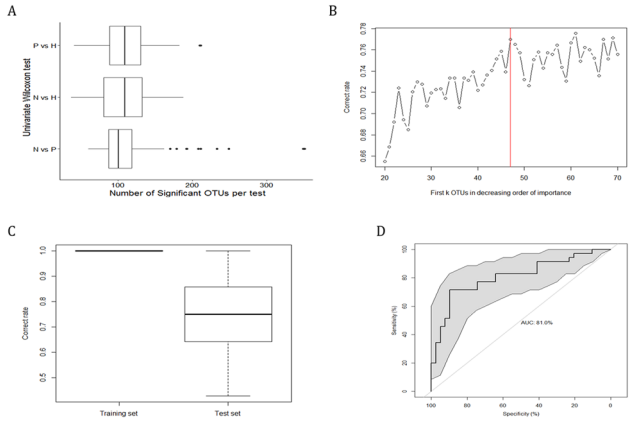
Intestinal Microbiota Signature Related to HBeAg Seroconversion after Oral Antiviral Therapy

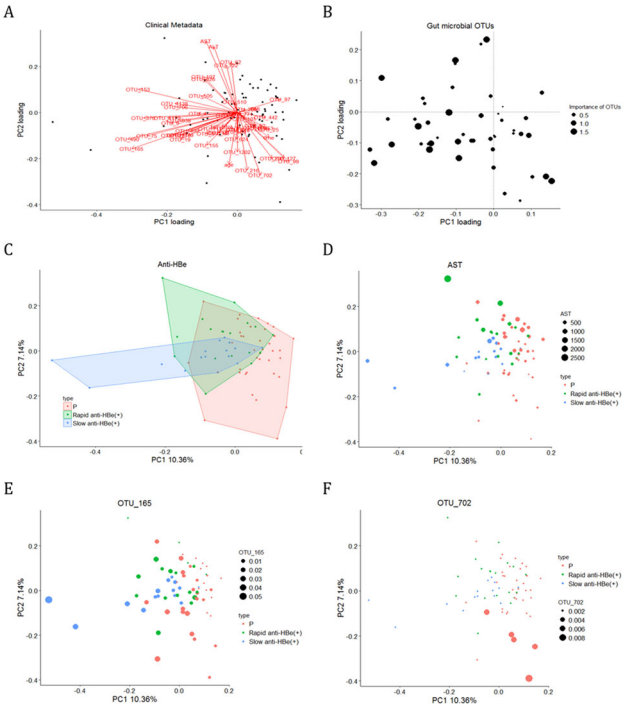
Jin-Shui Pan[1], Yu-Li Zeng[2], Lei Qin[3], Wen-Jun Wei[4], Hong Cai[5], Xiao-Fang Yu[6], Ben-Chang Shia[7], Mei-Zhu Hong[8]

[1]Department of Gastroenterology, Zhongshan Hospital Affiliated to Xiamen University, [2]Department of Gastroenterology, Zhongshan Hospital Affiliated to Xiamen University, [3]School of Statistics, University of International Business and Economics, [4]Department of Gastroenterology, Zhongshan Hospital Affiliated to Xiamen University, [5]Department of Hepatology, Xiamen Hospital of Traditional Chinese Medicine, [6]Department of Hepatology, Xiamen Hospital of Traditional Chinese Medicine, [7]School of Management & Big Data Research Center, Taipei Medical University, [8]Department of Traditional Chinese Medicine, Zhongshan Hospital Affiliated to Xiamen University

Currently, there is limited knowledge regarding the association between the composition of intestinal microbiota and HBeAg seroconversion after oral antiviral therapy. In this cross-sectional study, we collected information on fecal microbiota from the patients with CHB who have oral antiviral therapy and evaluated whether these were associated with HBeAg seroconversion. Thirty-five of these subjects displayed HBeAg seroconversion in the first 3 years after the initiation of oral antiviral therapy, while the remaining 39 subjects remained HBeAg positive even after over 3 years of therapy. Samples were analyzed using 16S ribosomal DNA sequencing. The HBeAg and anti-HBeAg levels were measured for each subject, and the HBV DNA was measured by quantitative PCR. Using classical approaches, no differences were found between the microbiota from patients with and without HBeAg seroconversion. However, a computational statistical and machine learning approach allowed us to identify a microbial signature for HBeAg seroconversion, consisting of 47 bacterial operational taxonomic units. The microbial signature was able to discriminate patients who achieved HBeAg seroconversion from those who remained HBeAg-positive. Using random forest method, we further constructed a prediction model based on the gut microbial signature, with the area under curve being 0.81 for the test set. Based on our results, HBeAg seroconversion was found to be associated positively with AST, and several genera belonging to TM7-3, and Actinomycetaceae families.

Conclusions: By analyzing the fecal microbiota from the patients with and without HBeAg seroconversion, we identified intestinal microbiota signatures that is associated with HBeAg seroconversion after oral antiviral therapy.





Abstract #251

Interferon alpha-induced IL6 triggers IL21 production by CXCR5 + CD4+T cells to facilitate effective B cell responses and HBeAg seroconversion in HBV infection

Yang Zhou[1], Shihong Zhong[2], Libo Tang[3], Ruihua Zhong[4], Chengcong Chen[5], Xuan Yi[6], Guofu Ye[7], Weibin Wang[8], Jian Sun[9], Jinlin Hou[10], Yongyin Li[11]

[1]State Key Laboratory of Organ Failure Research, Guangdong Provincial Key Laboratory of Viral Hepatitis Research, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, China, [2]State Key Laboratory of Organ Failure Research, Guangdong Provincial Key Laboratory of Viral Hepatitis Research, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, China, [3]State Key Laboratory of Organ Failure Research, Guangdong Provincial Key Laboratory of Viral Hepatitis Research, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, China, [4]Department of Infectious Diseases, The Fifth Affiliated Hospital of Sun Yat-Sen University, Zhuhai, China, [5]State Key Laboratory of Organ Failure Research, Guangdong Provincial Key Laboratory Of Viral Hepatitis Research, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, China, [6]State Key Laboratory Of Organ Failure Research, Guangdong Provincial Key Laboratory of Viral Hepatitis Research, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, China, [7]State Key Laboratory of Organ Failure Research, Guangdong Provincial Key Laboratory of Viral Hepatitis Research, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, China, [8]State Key Laboratory of Organ Failure Research, Guangdong Provincial Key Laboratory of Viral Hepatitis Research, Department of Infectious Diseases, Nanfang Hospital, Southern

Medical University, Guangzhou, China, [9]State Key Laboratory of Organ Failure Research, Guangdong Provincial Key Laboratory of Viral Hepatitis Research, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, China, [10]State Key Laboratory of Organ Failure Research, Guangdong Provincial Key Laboratory of Viral Hepatitis Research, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, China, [11]State Key Laboratory of Organ Failure Research, Guangdong Provincial Key Laboratory of Viral Hepatitis Research, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, China

Background: Interferon alpha (IFNα) is superior to nucleos(t)ides for the achievement of HBeAg seroconversion in CHB patients, but the mechanism is not well understood.
Methods: Twenty-four CHB patients with Peg-IFNα-2a treatment were longitudinally studied, 9 patients with HBeAg seroconversion were defined as complete response (CR) and 15 were noncomplete response (NCR). The profiles of CXCR5 + CD4+T cells, B cells, serum cytokines and the effects of Peg-IFNα-2a on immune cells were assessed. B cells from IL21R-KO or WT mice were transferred to μMT mice bearing pAAV-HBV1.2, serum HBsAg and HBeAg were detected.
Results: An elevated frequency of plasmablasts was observed only in CR patients after treatment (Fig.1). Although higher expression of IFNα-2a receptor was found in CD14 + monocytes and CD19 + B cells (Fig.2), the effects of Peg-IFNα-2a on the proliferation, STAT3 phosphorylation, and IgG production of B cells were inferior to IL21 (Fig.3). Notably, increased serum levels of IL6, not IL21, were observed only in CR patients after treatment. Correspondingly, Peg-IFNα-2a promoted marked production of IL6 from CD14 + monocytes, and this effect was also observed in HBV mice with the administration of murine IFNα (Fig.4). Importantly, IL6 promoted CXCR5 + CD4+T cells to produce IL21 (Fig.5), which facilitated HBeAb production from B cells. Strikingly, μMT mice receiving B cells from IL21R-KO mice showed higher serum levels of HBsAg and HBeAg than that receiving B cells from WT mice (Fig.6).
Conclusions: IFNα-induced IL6 from monocytes triggers the production of IL21 by CXCR5 + CD4+T cells, which may facilitate B cell responses and HBeAg seroconversion in HBV infection.

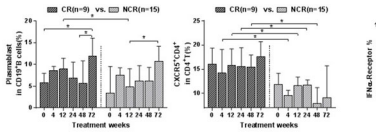


Fig. 1 Expanded plasmablasts in CR patients with Peg-IFNα-2a treatment.

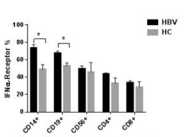


Fig. 2 The expression of IFN-α receptor on immune cells.

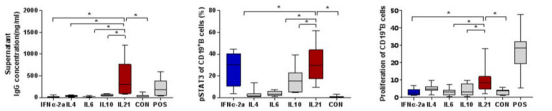


Fig. 3 The effects of IFNα-2a on B cells are weaker than that of IL21.

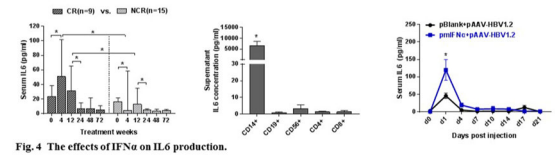


Fig. 4 The effects of IFNα on IL6 production.

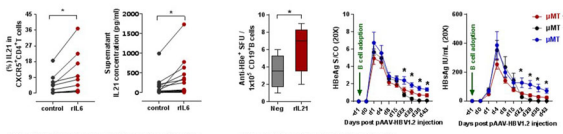


Fig. 5 IL6 enhances IL21producetion by CD4+CXCR5+T cells.

Fig.6 The role of IL21 on B cells.

Abstract #379

Hepatitis B virus Infection and its Genotypes in Sikkim Himalayas a Prospective Study

Mool Raj Kotwal[1]

[1]Sir Thutob Namgyal Memorial Hospital & Sikkim Manipal Institute of Medical Sciences & Govt of Sikkim

Objective: Hepatitis B virus infection causes substantial morbidity and mortality worldwide including India. To generate data on the Seropravelence of Hepatitis B infection and its genotypes total of 593 different types of liver disease cases were collected from 2012 to 2015.
Methods: Besides epidemiological data, Samples were collected in EDTA or clot activator vials. Hepatitis B surface Antigen, Anti Hepatitis B core Antigen, Hepatitis B core IgM, Anti HCV, Hepatitis A core IgM, Hepatitis E core IgM were done using specific kits. HBsAg positive cases were subjected to HBV DNA extraction and further polymerase chain Reaction with specific primers.
Results: A total of 182 (30.7%) acute viral hepatitis cases were collected. The prevalence of Hepatitis B surface antigen among acute viral hepatitis cases was 83.0% (151/182) with median age of 33 years (SD ± 14.9), from 12–86 years. Males accounted for 66.8% (101/151) of cases while females accounted for the rest 33.2% (50/151).
Among hepatitis B virus infection 47.0% (71/151) cases were DNA positive. Genotyping results were available for 71 cases. The most common genotype of hepatitis B virus infection detected in AVH cases was genotype D 83.0% (59/71) and genotype C 9.8% (7/71) followed by A 7.0% (5/71).
Conclusion: Prevalence of Hepatitis B among all the cases was found to be 27.2% (262/963). The most common genotype of Hepatitis B, genotype D 88.9%, genotype C 5.1% followed by genotype A 5.4%. Surveillance for chronic hepatitis will give valuable insights into long-term disease burden in Sikkim.

Abstract #437

Predictive Factors of Treatment in HBeAg Negative Chronic Hepatitis B Patients with Low HBV DNA Load and ALT less than 2-fold upper limit of normal

Jianchun-Xian[1]

[1]Li Xiao & Yang Li & Ai-Wen Geng

Objectives: The study was designed to determine the predictive factors for antiviral therapy in hepatitis B e antigen (HBeAg) negative chronic HBV infection [(HBeAg(-) CHBI)] patients with HBV DNA < 4.3 log10 IU/mL and ALT < 2-fold upper limit of normal (ULN).
Methods: A total of 179 patients were enrolled in this single-center and retrospective study from Jan. 2008 to Apr. 2017. Histology activity index (HAI) and fibrosis (S) were scored according to the Knodell HAI scoring system, and HAI > 3 and /or S ≥ 3 was adopted as indications for treatment.
Results: There were 81 cases with HAI > 3 (45.3%) and 72 with S ≥ 3 (40.22%), and the proportion of patients with indications of treatment was 54.7%. Univariate and multivariate analyses showed that age, γ-glutamyl transferase (GGT), platelet (PLT) and albumin (ALB) were the predictive factors for treatment needs ($p < 0.05$). The need for treatment increased significantly as age and GGT values increased and PLT and ALB values decreased.
Conclusion: Nearly 50% of HBeAg (-) CHBI with low viral load and ALT < 2ULN present abnormal hepatic histology and require

antiviral therapy, and older age, high GGT, and low PLT and ALB levels are the predictive factors for treatment.

Abstract #564

Hepatitis B virus mutation pattern rtL180M + A181C + M204V may contribute to entecavir resistance in clinical practice

Liu Yan[1], Zhou Yi[2], Li Xiaodong[3], Niu Ming[4], Chen Rongjuan[5], Shao Jinman[6], Si Lanlan[7], Luo Dan[8], Lin Yayun[9], Li Le[10], Zhang Kai[11], Xiao Xiaohe[12], Liu Min[13], Zoulim Fabien[14], Xu Dongping[15]

[1]Institute of Infectious Diseases, Beijing 302 Hospital (The 5th Medical Center Of General Hospital of Pla, [2]Department of Infectious Diseases, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China, [3]Institute of Infectious Diseases, Beijing 302 Hospital, [4]Institute of Infectious Diseases, Beijing 302 Hospital, [5]Institute of Infectious Diseases, Beijing 302 Hospital, [6]Institute of Infectious Diseases, Beijing 302 Hospital, [7]Institute of Infectious Diseases, Beijing 302 Hospital, [8]Department of Infectious Diseases, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China, [9]Department of Infectious Diseases, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China, [10]Institute Of Infectious Diseases, Beijing 302 Hospital, [11]Department of Infectious Diseases, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China, [12]Institute of Infectious Diseases, Beijing 302 Hospital, [13]Department of Infectious Diseases, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China, [14]Univ Lyon, Université Claude Bernard Lyon 1, Inserm 1052, Cnrs 5286, Centre Léon Bérard, Centre De Recherche En Cancérologie De Lyon, Lyon, France, [15]Institute of Infectious Diseases, Beijing 302 Hospital

Introduction: Entecavir (ETV) resistance of hepatitis B virus (HBV) conventionally requires rt184, 202, or 250 mutations concomitant with lamivudine-resistance mutation.
Objectives: This study aimed to clarify whether rtL180M + A181C + M204V mutations may contribute to HBV ETV resistance.
Methodology: Serum samples were collected from 22,009 patients who underwent resistance testing in Beijing 302 Hospital from 2007 to 2016. HBV reverse transcriptase (RT) gene was screened by direct sequencing and verified by clonal sequencing. Phenotypic analysis was performed for evaluating replication capacity and drug susceptibility.
Results: Classical ETV-resistance mutations of HBV were detected in 1,252 patients who were receiving ETV therapy. The rtA181C mutation was detected with rtL180M + M204V mutations in 18 lamivudine-experienced ETV-treating patients, and the emergence of the mutations was associated with virological breakthrough or inadequate virological response to ETV. Patient-derived representative rtA181C-containing mutants, rtL180M + A181C + M204V, rtL180M + A181C + M204V + M250V, and rtL180M + A181C + S202G + M204V, exhibited 45.7%, 25.9%, and 25.0% replication capacity and 85.6-, 356.1-, and 307.1-fold decreased susceptibility to ETV respectively compared to the wild-type strain, while the three mutants remained sensitive to tenofovir (TDF). Artificial elimination of rtA181C largely restored the rtL180M + A181C + M204V mutant's sensitivity to ETV. Molecular modeling of viral RT binding to ETV showed that the rtL180M + A181C + M204V mutant had a less stable conformation compared to rtL180M + M204V mutant. In clinical practice, undetectable serum HBV DNA was achieved in two of five longitudinally-followed rtA181C-positive patients who received switching-to TDF therapy, but not in the other three who received add-on adefovir therapy during observation.
Conclusions: Both clinical and experimental data support rtL180M + A181C + M204V as a novel non-classical ETV-resistance mutation pattern.

Abstract #570

Outcome of Different Precipitating Events in Patients with HBV-Related Acute-on-Chronic Liver Failure

Yinyun Lu[1], Lingling Yang[2], Jiang Li[3], Jiaojiao Xin[4], Dongyan Shi[5], Jing Jiang[6], Tan Li[7], Hozeifa Mohamed Hassan[8], Xin Chen[9], Jun Li[10]

[1]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [2]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [3]State Key Laboratory For Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [4]State Key Laboratory For Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [5]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [6]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [7]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [8]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [9]Institute of Pharmaceutical Biotechnology, Zhejiang University School of Medicine, [10]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine

Introduction and Objectives: Identification and management of precipitating events in patients with hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF) are essential for reducing unacceptable high mortality rate. This study aimed to clarify the precipitating events and outcome of patients with HBV-ACLF.
Methodology: A total of 479 hospitalized ACLF patients were enrolled according to the Chinese Group on the Study of Severe Hepatitis B-ACLF (COSSH-ACLF) criteria. Patients' laboratory data, precipitating events and short-term mortality were evaluated to identify their clinical characteristics and outcome.
Results: Among 479 HBV-ACLF patients assessed by COSSH-ACLF criteria, single HBV exacerbation accounts for 213 (44.5%) of all patients, followed by HBV exacerbation mixed with infection (49, 10.2%), other major precipitating events includes infection (31, 6.5%), HBV exacerbation with alcoholism (21, 4.4%), alcoholism (20, 4.2%) and more than two insults (10, 2.1%). However, no identifiable precipitating events was observed in 100 (20.9%) patients with HBV-ACLF at diagnosis. There were no significant differences in the precipitant distributions between cirrhotic or non-cirrhotic HBV-ACLF patients. The 28 day mortality rate was significant higher in patients with identified precipitating events compared to those without identified precipitating events (32.9% vs 20.0%, $p = 0.025$). ACLF patients precipitated with HBV exacerbation had the higher 28-day mortality rate compared to those without HBV exacerbation (34.4% vs 23.0%, $p = 0.015$).
Conclusions: HBV exacerbation has the high prevalence and prognostic significance in HBV-ACLF patients regardless of the presence of cirrhosis, the result might be useful to reduce the high ACLF mortality through preventing HBV exacerbation.

Abstract #574

The rtA186T mutation of hepatitis B virus contributes to entecavir resistance in multiple patients—analysis from a large cohort of Chinese patients

Liu Lujie[1], Liu Yan[2], Chen Rongjuan[3], Li Xiaodong[4], Luo Dan[5], Zhao Yangyang[6], Li Qi[7], Huang Bixia[8], Wang Fusheng[9], Liu Xinguang[10], Xu Dongping[11]

[1]Institute of Infectious Diseases, Beijing 302 Hospital (The 5th Medical Center of General Hospital Of Pla), [2] Institute of Infectious Diseases, Beijing 302 Hospital, [3]Institute of Infectious Diseases, Beijing 302 Hospital, [4]Institute of Infectious Diseases, Beijing 302 Hospital, [5]Institute of Infectious Diseases, Beijing 302 Hospital, [6]Institute of Infectious Diseases, Beijing 302 Hospital, [7]Institute of Infectious Diseases, Beijing 302 Hospital, [8]Institute of Biochemistry & Medical Molecular Biology, Guangdong Medical University, Guangdong Province, China, [9]Institute Of Infectious Diseases, Beijing 302 Hospital, [10]Institute Of Biochemistry & Medical Molecular Biology, Guangdong Medical University, Guangdong Province, China, [11]Institute Of Infectious Diseases, Beijing 302 Hospital

Introduction: Recently, rtA186T and rtI163 V mutations of hepatitis B virus (HBV) were detected in an entecavir (ETV)-refractory Japanese patient and shown to confer ETV resistance in concomitance with LAM-resistance mutation (Hayashi et al, J Hepatol 2015).
Objectives: This study aimed to clarify whether the rtA186T and rtI163 V contributed to ETV resistance in Chinese patients.
Methodology: A total of 22,009 patients with chronic HBV infection who received resistance testing at Beijing 302 Hospital from 2007 to 2016 were enrolled. Among them, 6,170 patients had been treated with ETV. HBV reverse transcriptase (RT) gene was screened by direct sequencing and verified by clonal sequencing. Phenotypic analysis was performed for evaluating replication capacity and drug susceptibility.
Results: Classical ETV-resistance mutations, rtA186T, and rtI163 V were detected in 1,252 (5.69%), 14 (0.06%), and 230 (1.06%) of the 22,009 patients, respectively. The rtA186T mutation coexisted with rtM204V/I ± L180M mutations (LAM-r), but not with rtI163 V. The 14 rtA186T-positive patients were all treated with LAM and ETV, and the emergence of the rtA186T + LAM-r was closely associated with poor response to ETV. In contrast, the emergence of rtI163 V was not related to ETV therapy. Compared to wild-type strain, two patient-derived mutant strains rtL180M + A186T + M204V and rtL180M + T184S + A186T + M204V had 86.7% and 89.2% decreased replication capacity, 210- and 555-fold increased ETV resistance, respectively; and artificial elimination of rtA186T largely restored their ETV sensitivity. The rtA186T mutants remained sensitive to tenofovir.
Conclusion: HBV rtA186T mutation plus LAM-r is proved to be a novel ETV-resistance mutation pattern which may confer ETV resistance in multiple Chinese patients.

Abstract #589

The rtS106C + H126Y + D134E triple variant of hepatitis B virus has no direct association with tenofovir resistance in Chinese patients

Liu Yan[1], Chen Rongjuan[2], Li Xiaodong[2], Niu Ming[2], Liu Lujie[2], Luo Dan[2], Lin Yayun[2], Lin Yayun[2], Lin Yayun[2], Xu Dongping[2]

[1]Institute of Infectious Diseases, Beijing 302 Hospital (The 5th Medical Center of General Hospital of Pla), [2]Institute of Infectious Diseases, Beijing 302 Hospital

Background: Whether hepatitis B virus (HBV) may develop tenofovir (TDF)-resistance mutation has been concerned. rtS106C + H126Y + D134E triple variant in the reverse-transcriptase (RT) region of hepatitis B virus (HBV) was recently reported to be a TDF-resistance-associated mutation pattern, and the triple variant plus rtL269I to be more resistant to TDF.
Objective: The study aimed to characterize the prevalent and phenotypic characteristics of above-mentioned mutants in a large cohort of Chinese patients with chronic HBV infection.
Methodology: Total of 22,009 nucleoside/nucleotide analogues treated patients who visited Beijing 302 Hospital from 2007 to 2016 was enrolled. HBV RT gene sequence and phenotypic analysis of drug resistance were performed.
Results: Direct sequencing showed that rtS106C, H126Y, D134E, and L269I were detected in 7.01%, 2.80%, 2.31% and 51.49% in 19,988 genotype C HBV-infected patients, and 0.60%, 1.23%, 0.09%, and 89.52% in 3,339 genotype B HBV-infected patients. Among these, rtS106C + H126Y + D134E triplet was only detected in 9 genotype C HBV-infected patients, and four of them harbored rtS106C + H126Y + D134E + L269I quadruplet. None of the 9 patients had TDF treatment history. Clonal sequencing verified the collocation of the triple/quadruple variations on the same viral genome. Compared to wild-type strain, 8 representative rtS106C + H126Y + D134E ± L269I variants had 30–60% decrease of replication capacity; and their TDF susceptibility decreased < 2-fold and < 10-fold with and without coexistence of adefovir-resistance mutation (rtA181 V/N236T), respectively. Molecular modelling showed that the rtS106C + H126Y + D134E variant had similar binding energy to TDF with that of wild-type strain.
Conclusion: rtS106C + H126Y + D134E exhibited the feature of HBV polymorphisms rather than a TDF-resistance-associated mutation pattern in Chinese patients.

Abstract #590

Analysis of intrahepatic HBV total DNA, covalently closed circular DNA and HBV RNA, and serum anti-HBc levels in HBsAg-negative/HBcAb-positive individuals

Li Zhiyan[1], Liu Yan[2], Liao Hao[3], Shi Xiaojuan[4], Wang Jie[5], Lu Fengmin[6], Zhao Jingmin[7], Xu Dongping[8]

[1]Institute of Infectious Diseases, Beijing 302 Hospital (The 5th Medical Center of General Hospital Of Pla), [2]Institute of Infectious Diseases, Beijing 302 Hospital, [3]Department of Microbiology & Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing, China, [4]Institute of Infectious Diseases, Beijing 302 Hospital, [5]Department of Microbiology & Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing, China, [6]Department of Microbiology & Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing, China, [7]Institute of Infectious Diseases, Beijing 302 Hospital, [8]Institute of Infectious Diseases, Beijing 302 Hospital

Introduction: Clinical implications of serum HBsAg-negative/HBcAb-positive have not been fully understood.
Objective: This study aimed to reveal characteristics of intrahepatic hepatitis B virus (HBV) total DNA (tDNA), covalently closed circular DNA (cccDNA) and RNA, and serum HBcAb levels in HBsAg-negative/HBcAb-positive people.

Methodology: A total of 130 adult people were enrolled in this study, including 100 HBsAg-negative/HBcAb-positive individuals without illness history of hepatitis B, twenty with chronic hepatitis B (CHB) as positive control, and ten without any HBV serum markers as negative control. All subjects received liver biopsy. Intrahepatic HBV tDNA, cccDNA and RNA and serum HBcAb levels were quantitated measured. Occult HBV infection (OBI)-related mutations in major hydrophilic region (MHR) of HBV S gene were sequenced
Results: The tDNA was detected in 22 HBsAg-negative/HBcAb-positive individuals [0.37 (0.26–1.63) copies/cell] and all 20 CHB patients [103.85 (35.75–231.56) copies/cell]. The cccDNA were detected in 9 of the 22 HBsAg-negative/HBcAb-positive individuals [0.04 (0.02–0.05) copies/cell] and all 20 CHB patients [1.98 (0.95–8.02) copies/cell]. A lower level of HBV RNA was detected from two cccDNA-positive HBsAg-negative/HBcAb-positive individuals. HBcAb was 300.0 (163.4, 442.5) IU/mL in the cccDNA-positive individuals, significantly higher than that in the cccDNA-negative individuals. No significant difference in OBI-related mutations in the MHR was observed between HBsAg-negative/HBcAb-positive individuals and CHB patients.
Conclusions: HBV tDNA and cccDNA were detectable in some HBsAg-negative/HBcAb-positive individuals and a relatively higher HBcAb level was closely related to cccDNA positivity. The study provides direct evidence for the risk of HBV reactivation in HBsAg-negative/HBcAb-positive people, in particular in those with relatively higher HBcAb level.

Abstract #609

Global Scientific Strategy for an HBV cure

Peter Revill[1], Capucine Penicaud[2], Fabien Zoulim[3]

[1]Melbourne Health, [2]Doherty Institute, [3]INSERM

Background and Aims: Over 257 million people worldwide are chronically infected with hepatitis B virus (HBV), resulting in over 880,000 deaths per year from cirrhosis and liver cancer. There is no known cure for chronic HBV, due in part to the continued presence of transcriptionally active DNA in the nucleus which is not directly targeted by current antiviral therapies. Our aim is to inspire and support the discovery of a safe, scalable and effective cure for the benefit of all people living with CHB.
Methods: The International Coalition to Eliminate Hepatitis B (ICE-HBV) is coordinating collaborative partnerships among researchers and stakeholders to accelerate the search for an HBV cure.
Results: ICE-HBV working groups have developed a joint global scientific strategy for HBV cure, with input from key stakeholders including the HBV affected community. ICE-HBV aims to drive changes in governmental policy to ensure more funds are channelled to HBV cure research and drug development. ICE-HBV fosters new collaborations among HBV researchers and industry worldwide and initiate new projects to fast-track the discovery of an HBV cure such as animal models for HBV, serum biomarkers, point-of-care assays, cost-effectiveness modelling, community engagement and scientific literacy, health policy.
Conclusion: The push for a cure for chronic HBV infection is particularly timely thanks to the recent development of cell culture infection models that, for the first time, empower truly curative research. Through its global network, ICE-HBV is striving to promote effective collaboration and facilitate opportunities that can produce a cure for chronic HBV infection.

Abstract #616

Determine™ HBsAg 2: A novel rapid test for the detection of hepatitis B virus infection

Robert Downing[1], Camilla Forssten[2], Patrick Kabbale[3], Robert Newton[4], Terry Robins[5], Yuko Tamanoue[6]

[1]Uganda Virus Research Institute, Entebbe, Uganda, [2]Alere International (Now Abbott), [3]Wagagai Health Centre, Wakiso District, Uganda, [4]MRC/UVRI & LSHTM Uganda Research Unit, Entebbe, Uganda, [5]Alere Scarborough Inc. (Now Abbott), [6]Alere Medical Co, Ltd. (Now Abbott)

Introduction: Determine™ HBsAg 2 is a novel CE-marked HBsAg (Hepatitis B Surface Antigen) rapid test. Circulating HBsAg is one of the earliest biomarkers present in patients infected with Hepatitis B virus.
Objectives: To characterise the analytical sensitivity and the clinical sensitivity and specificity of the test.
Methodology: The analytical sensitivity of Determine™ HBsAg 2 (Alere Medical Japan (now Abbott)) was determined using dilutions of the WHO International Standard for HBsAg (NIBSC code 12/226), and the detection of 14 mutations was investigated. A prospective, multi-centre study was conducted in Uganda.
Results: Analytical Sensitivity: Determine™ HBsAg 2 detects 0.1 IU/mL of the WHO International HBsAg Standard (NIBSC code 12/226). The test identified 11 mutations at 0.125 IU/mL and all 14 at 0.25 IU/mL.
Clinical Sensitivity and Specificity: 604 evaluable subjects were enrolled across 3 sites, including two cohorts with a total of 150 HBsAg-positive and 154 HBsAg-negative subjects, and an all-comers cohort of 300 subjects (29 HBsAg-positive). The test sensitivity and specificity using plasma was 98.9% (95% CI; 96.0, 99.9) and 100.0% (99.1, 100.0), respectively (n = 604) at 15 and 30 minutes. The test sensitivity using finger-stick whole blood was 98.0% (94.3, 99.6) at 15 and 30 minutes and the specificity was 98.1% (94.4, 99.6%) at 15 minutes and 96.8% (92.6, 98.9) at 30 minutes (n = 304). Following up a positive finger-stick test result with a Determine™ HBsAg 2 plasma test resulted in 100% specificity.
Conclusions: These analytical and clinical results demonstrate that Determine™ HBsAg 2 represents industry leading performance in HBsAg rapid testing.

Abstract #622

Serum HBV-RNA levels is a novel biomarker for liver fibrosis and cirrhosis in chronic HBV infection.

Liang Chen[1], Chenlu Huang[1], Xiaonan Zhang[2], Yuxian Huang[3], Qianqian Wang[1], Qiang Li[1], Wei Xu[1], Jie Cao[1]

[1]Department of Hepatology, Shanghai Public Health Clinical Center, Fudan University, Shanghai, China, Fudan University, Shanghai, China, [2]Shanghai Public Health Clinical Center, Fudan University, Shanghai, China, [3]Department of Infectious Disease, Huashan Hospital, Fudan University, Shanghai, China & Department of Hepatology, Shanghai Public Health Clinical Center, Fudan University, Shanghai, China

Introduction: It is urgent to develop tests that can been easily and conveniently used by all patients to detect liver fibrosis.
Objectives: This study aimed to determine whether serum hepatitis B virus (HBV)-RNA levels are correlated with the liver injury and histopathology and to develop a novel noninvasive assessment of liver

fibrosis and cirrhosis in patients with chronic hepatitis B(CHB) infection.
Methodology: A cross-sectional set of serum samples was obtained from untreated patients with CHB infection. The expression levels of serum HBV-RNA by quantitative Real-time (qRT)-PCR in 175 patients, were detected. We analyzed the correlations between serum HBV-RNA concentration and fibrosis stages and the independent predictor for advanced fibrosis. We also compared the diagnostic accuracy of the serum HBV-RNA, aspartate transaminase-to-platelet ratio index (APRI), and fibrosis index based on four factors (FIB-4).
Results: Serum HBV-RNA was associated with liver fibrosis progression, which was the best independent predictor for significant fibrosis (OR = 2.912; 95% CI 1.829–4.636, $p < 0.001$). It shows higher performance than APRI and FIB-4 (AUROC = 0.81, 0.75 and 0.69, respectively). Furthermore, the combination of the serum HBV-RNA and APRI indices showed better diagnostic performance for the evaluation of advanced liver fibrosis (AUROC = 0.83; 95%CI, 0.76–0.89; $p < 0.001$).
Conclusion: Serum HBV-RNA is a more accurate noninvasive test than APRI and FIB-4 to no or mild fibrosis and advanced liver fibrosis in Chinese CHB patients.

Abstract #655

Immune-metabolism disorder in progression of hepatitis B virus-related acute-on-chronic liver failure characterized by transcriptomics

Jiang Li[1], Liang Xi[2], Lingling Yang[3], Jiaojiao Xin[4], Jing Jiang[5], Jianing Zhang[6], Heng Yao[7], Dongyan Shi[8], Tianzhou Wu[9], Suwan Sun[10], Yinyun Lu[11], Beibei Guo[12], Xingping Zhou[13], Hozeifa Mohamed Hassan[14], Xin Chen[15], Jun Li[16]

[1]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [2]Institute of Pharmaceutical Biotechnology, Zhejiang University School of Medicine, [3]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [4]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [5]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School Of Medicine, [6]Institute of Pharmaceutical Biotechnology, Zhejiang University School of Medicine, [7]Institute of Pharmaceutical Biotechnology, Zhejiang University School of Medicine, [8]State Key Laboratory for Diagnosis And Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [9]The Infectious Disease Department, The First People's Hospital Of Wenling, [10]State Key Laboratory for Diagnosis And Treatment Of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [11]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [12]State Key Laboratory For Diagnosis And Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School Of Medicine, [13]State Key Laboratory For Diagnosis And Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [14]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [15]Institute of Pharmaceutical Biotechnology, Zhejiang University School of Medicine, [16]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine

Introduction: The pathophysiological etiology of hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF) remains unclear.
Objective: This study aims to characterize the molecular basis of HBV-ACLF using transcriptomics.
Methodology: Peripheral blood mononuclear cells of HBV-ACLF (n = 100), acute-on-chronic hepatic dysfunction (ACHD), liver cirrhosis, chronic hepatitis B and healthy controls (n = 50/group) from a prospective multi-center cohort were performed for sequencing and qPCR validation. Differential expression and network-driven functional synergy analysis was used to clarify the mechanism.
Results: Principal component analysis shows HBV-ACLF patients with or without cirrhosis were positioned together and separated from other groups, demonstrating the effectiveness of COSSH-ACLF criteria in diagnosing HBV-ACLF. Totally 2000 differentially expressed genes (DEGs) identified eight biological processes (immune, inflammation, metabolism, virus, etc.) that contribute to HBV-ACLF progression. Functional synergy analysis with 62 DEGs identified from CHB/LC patients progressing into ACHD/ACLF indicated that excessive immune response triggered by HBV reactivation drove ACHD to ACLF-1. Inflammation and metabolism disorder identified with 106 GO terms and subsequent multiple organ failures identified with 288 GO terms were respectively observed in ACLF-2/3 and deceased patients. The qPCR validation of 12 DEGs based on top significantly differential expression and functional synergy analysis confirmed the reliability of sequencing results, and demonstrated MERTK, PPARG, SEMA6B and THBS1 as potential HBV-ACLF biomarkers for diagnosis and prognosis.
Conclusions: This study highlights immune-metabolism disorder triggered by HBV reactivation as an important axis that aggravates HBV-ACLF, which brings new insights for the development of effective ACLF treatment.

Abstract #665

The Relation of serum Tenascin-C and Type IV Collagen with the severity of liver fibrosis in patients with chronic hepatitis B infection

Ahmet Sevki Kaya[1], Elif Yorulmaz[2], Ozcan Sonmez[3], Bilge Ozdemir[4], Fatma Eksi Polat[5], Umit Seza Tetikkurt[6], Can Davutoglu[7], Mikail Yetmis[8]

[1]Bagcilar Education and Research Hospital, Department Of Internal Medicine, [2]Bagcilar Education and Research Hospital, Department of Gastroenterology, [3]Bagcilar Education and Research Hospital, Department of Internal Medicine, [4]Bagcilar Education and Research Hospital, Department of Clinical Microbiology, [5]Bagcilar Education and Research Hospital, Department of Clinical Microbiology, [6]Bagcilar Education and Research Hospital, Department of Pathology, [7]Bagcilar Education and Research Hospital, Department of Gastroenterology, [8]Bagcilar Education and Research Hospital, Department of Internal Medicine

Introduction: Chronic hepatitis B (CHB) leads to the most common infectious disease worldwide and untreated CHB can cause liver cirrhosis and hepatocellular cancer. This study we aimed to newly diagnosed CHB patients liver fibrosis degree compare with the level of tenascin-C (TNC) and type IV collagen.
Methodology: Included this study liver biopsies were performed 35 CHB patients and healty control group. Serum type IV collagen and TNC levels and liver function tests, body mass index (BMI), waist circumference, alphafetoprotein and HBV DNA levels, liver biopsy is the degree of fibrosis and to investigate the relationship between hepatic activity index.

Results: Patient and control groups were not statistically significant differences between serum TNC and type IV collagen. TNC and type IV collagen levels between fibrosis levels were negative statistically significant correlatıon ($r = -0.405$, $p < 0.05$ ve $r = -0.340$, $p < 0.05$). TNC and type IV collagen levels between BMI found a statistically significant correlation ($r = 0.370$, $p < 0.05$ ve $r = 0.359$, $p < 0.05$). In the patient group women TNC and type IV collagen between BMI found a statistically significant correlation ($r = 0.423$, $p < 0.05$ ve $r = 0.438$, $p < 0.05$). TNC and type IV collagen levels between liver function tests, HBV DNA level, the degree of liver fibrosis, hepatic activity index not found a statistically significant correlation ($p > 0.05$).
Conclusion: Negative association between severity of liver fibrosis with serum TNC and type IV collagen in patients with mild fibrosis suggest the idea that these markers should be used in patients with severe liver fibrosis.

Abstract #677

Characterization of immunological features correlating with HBsAg loss and seroconversion in HBeAg-negative chronic hepatitis B patients

Shu E Xiong[1], Dan Zhu[2], Ming Yue Li[3], Bo Yun Liang[4], Hua Wang[5], Dong Liang Yang[6], Jia Liu[7], Xin Zheng[8]

[1]Department of Infectious Diseases, Institute of Infection And Immunology, Union Hospital, Tongji Medical College, Huazhong University of Science And Technology, [2]Department of Infectious Diseases, Institute of Infection and Immunology, Union Hospital, Tongji Medical College, Huazhong University Of Science And Technology, [3]Department of Infectious Diseases, Institute of Infection and Immunology, Union Hospital, Tongji Medical College, Huazhong University of Science And Technology, [4]Department of Infectious Diseases, Institute of Infection And Immunology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, [5]Department of Infectious Diseases, Institute of Infection and Immunology, Union Hospital, Tongji Medical College, Huazhong University of Science And Technology, [6]Department of Infectious Diseases, Institute of Infection And Immunology, Union Hospital, Tongji Medical College, Huazhong University of Science And Technology, [7]Department of Infectious Diseases, Institute of Infection and Immunology, Union Hospital, Tongji Medical College, Huazhong University of Science And Technology, [8]Department of Infectious Diseases, Institute Of Infection And Immunology, Union Hospital, Tongji Medical College, Huazhong University of Science And Technology

Background: Hepatitis B surface antigen (HBsAg) loss and seroconversion in chronic hepatitis B (CHB) is rare. So far, the immunological features of cellular immune responses during the course of HBsAg loss and seroconversion in CHB patients remain elusive.
Methods: In a single-center prospective trial, 15 HBsAg-negative CHB patients along with 30 HBsAg-positive and 20 healthy individuals were studied longitudinally. The PBMCs from these subjects were freshly analyzed for antigen presenting cell phenotypes, T cell activation and cytotoxicity phenotypes and HBV-specific T cell responses by flow cytometry.
Results: 7 out of 15 HBsAg-negative patients developed HBsAb during observation period. Compared to the healthy individuals and HBsAg-positive CHB patients, the patients with HBsAg loss and seroconversion showed significant increases of CD72 expression on B cells and dendritic cells (DCs), HLA-DR and CD25 expression on CD4+T cells and HLA-DR expression on CD8 + T cells compared to the healthy individuals and HBsAg-positive CHB patients. We could detect HBcAg-specific CD8 + T responses in 66.67% of patients with HBsAg loss and seroconversion versus in 30% of HBsAg-positive patients. And the intensities of HBcAg-specific CD8 + T cell responses were significantly higher in the patients with HBsAb than those without.
Conclusions: CD72 expressed by B cells and DCs, HLA-DR and CD25 expressed by T cells, as well as HBcAg-specific CD8 + T cell responses were identified as distinguish immune biomarkers for CHB patients with HBsAg loss and seroconversion. This adds to our knowledge of the immunological events taking place during the course of HBsAg seroconversion in CHB patients.

Abstract #681

The p.Ser267Phe in sodium taurocholate cotransporting polypeptide is associated with disease progression of chronic hepatitis B patients

Lina Wu[1], Fangji Yang[1], Limin Zhen[1], Gang Ning[1], Yongyuan Zheng[1], Liang Peng[1]

[1]The Third Affiliated Hospital of Sun Yat-Sen University

Introduction: The sodium taurocholate cotransporting polypeptide (NTCP) is universally accepted to be receptor binding hepatitis B virus to hepatocytes. Previous studies have proved that p.Ser267Phe variant (rs2296651 G>A) in NTCP may reduces risk of chronicity in hepatitis B virus infection through altering NTCP molecule structure. We aim to investigate whether the p.Ser267Phe variant is associated with chronic hepatitis B disease progression.
Cohort and Methods: We retrived five single nucleotide polymorphisms (rs201339654, rs202018997, rs2296651, rs61745930, and rs759531965) reported to be associated with bile acid metabolism and/or Chronic Hepatitis B (CHB) after carefully searching in mainstream databases. Then we performed SNaPshot multiplex assay for estimating these five SNPs among 574 DNA samples extracted from CHB patients' peripheral blood. However, no heterozygous or mutant homozygous individuals were found except for rs2296651 G > A. Therefore, only rs2296651 was genotyped in all the 3187 CHB patients, among which 1370 were genotyped using SNaPshot multiplex assay lately and 1817 had been genotyped using Sanger sequencing in previous studies. Apart from chi-square test, logistic modelling, corrected by gender, age, lg HBV DNA, AST, ALT and HBeAg status, were also applyed to estimate correlation between rs2296651 G > A and diagnoses (diagnoses of 1817 patients from our previous study were updated in April 2018) .
Results: The p.Ser267Phe variant in NTCP had the effect of protecting CHB patients from cirrhosis ($P = 1.408e{-}05$, $OR = 0.4963$), acute-on-chronic liver failure ($P = 0.00000006591$, $OR = 0.3098$), and hepatocellular carcinoma ($P = 0.003525$, $OR = 0.5838$), yet increased the risk of hepatic encephalopathy in foundation of acute-on-chronic liver failure ($P = 0.01282$, $OR = 2.905$).

Abstract #710

Detection of Hepatitis B Virus M204V/I Mutation qualitatively and quantitatively by Real-time PCR

Jingjing Liang[1], Cheng Zhang[1], Hong Ma[1], Leng Nie[2], Yu Wang[1]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [2]wuhan Wawasye Nanotech Company, Beijing, China

Introduction and Objectives: With the application of Nucleotide analogues (NAs), the problem of drug-resistance has been gradually prominent. It's essential to monitor the relative mutations of drug resistance. This study is aim to establish a sensitive, and convenient method to detect HBV mutation qualitatively and quantify mutations.
Methodology: Blood samples were collected from patients with viral breakthrough, primary nonresponse and poor response in NAs between 2015 and 2018. The serum of above samples were detected by sequencing. Primers and probes were designed based on the mutant gene of HBV polymerase, which were confirmed by the serum samples containing M204V/I mutation. The specificity of primers and probes were tested by a set of positive samples. The target genes (M204V/I) were extracted and amplified. We compared the results of real-time PCR assays with sequencing to evaluate the efficiency, which was defined as gold standard. To verify the accuracy and repeatability, a series of trials was conducted. To quantify mutations, specific plasmids relied on M204V/I mutations were established and then diluted to 10-fold in order to build standard curves.
Results: The primers and probes used are presented in Table 1. Its specificity and reproducibility were verified very well (Table2 and Figure 1). The amplification results of the new method were similar to sequencing and were repeatable. And the outcome of the plasmid containing M204V mutation showed a good linear relationship (Figure 2).
Conclusion: Real-time PCR could be used to detect HBV DNA gene variation, and is a quantitative system without complex and expensive instruments.

Abstract #733

The interaction of beta2-glycoprotein I and the large hepatitis B surface protein promotes endoplasmic reticulum stress in hepatitis B-related hepatocellular carcinoma

Yaming Liu[1], Jessica Maiers[2], Yajuan Rui[3], Pujun Gao[3], Jianlin Ren[1]

[1]Xiamen University Zhongshan Hospital, [2]Mayo Clinic, [3]First Hospital Of Jilin University

Introduction: Beta2-glycoprotein I (beta2-GPI) is an acute phase protein during HBV infection. It is upregulated by HBV and the large surface protein (LHBs). Intracellular retention of HBsAg induces endoplasmic reticulum (ER) stress in hepatocarcinogenesis.
Objectives: To explore the interaction of beta2-GPI and LHBs promotes ER stress in HBV-related hepatocellular carcinoma (HCC).
Methods: Beta2-GPI expression at protein and mRNA levels were assayed by Western Blot and RT-qPCR in different cells and liver tissues from patients with HBV-related HCC. Next, beta2-GPI and HBV expression vectors were co-transfected in 293T cells. Post-transfection 36hrs, beta2-GPI expression was detected by Western Blot, and intercellular HBsAg level and HBsAg titer in conditioned media were measured by ELISA. 293T cells were co-transfected with beta2-GPI and either HBV or LHBs for 36 hrs and examined for expression of ER stress markers Bip, XBP-1 and CHOP using Western Blot or RT-qPCR assay.
Results: Beta2-GPI is highly expressed in carcinoma liver tissues from patients with HBV infection compared to control or adjacent non-tumor tissues ($p < 0.05$). Beta2-GPI expression at protein and mRNA levels are much higher in HepG2.2.15, HepG2 and Huh7 cells compared to controls (L02, SMMC-7721, and BEL7402 cells). HBV upregulates beta2-GPI expression in 293T cells cotransfected with beta2-GPI and HBV expression vectors. Beta2-GPI overexpression inhibits HBsAg secretion, which upregulates the production of BiP, XBP1 and CHOP. This effect is mediated by the LHBs, as its retention in conjunction with beta2-GPI leads to ER stress.
Conclusion: The interaction of beta2-GPI and HBV promotes ER stress through the accumulation of HBsAg.

Abstract #744

FIB-04 score and APRI as non-invasive method for prediction of histopathological Activity score (HAS) and Fibrosis in patient with chronic hepatitis B

Most. Rokshana Begum[1], Professor Nooruddin Ahmad[2], Mamun Al Mahtab[2], Sheikh Mohammad Noor-E-Alam[2], Faiz Ahmed Khondaker[1], Jahangir Alam Sarker[1], Mohammad A Rahim[3], Kazi Zakir Hossain[1]

[1]Shaheed Suhrawardi Medical College Hospital, [2]BSMMU, [3]Abdul Malek Ukil Medical College, Noyakhali

Introduction: HBV (Hepatitis B virus) is a major global public health problem. About 686,000 people die every year due to its complications. Biopsy is sometimes prime determinant to start treatment. However, it is invasive, costly and complicated. So non-invasive methods like FIB-04 and APRI may validate alternative method predicting histological activity and fibrosis.
Objectives: To measure APRI & FIB-04, to determine HAS and fibrosis by Metavir scoring, to validate FIB-04 and APRI as non-invasive marker.
Methodology: This was an observational cross-sectional study, study population forty, per cutaneous liver biopsy was done at hepatology dept, BSMMU. Scorings were calculated and compared with histology. All data were analyzed by SPSS.
Results: Mean ALT 51.9 ± 29.4, AST 39.2 ± 16, platelet count 232.4 ± 67.4, HBV DNA 5.3 ± 1.7, significant fibrosis in 82.5% patient & significant HAS in 77.5%. The mean FIB-04 and APRI in F2-F4 group and A2-A3 group were higher but statistically significant for HAS. For measuring fibrosis, area under the receiver operator characteristic curve (AUROC) for FIB-04 was 0.519 with cut off value 1.11 and for APRI was 0.654, cut off value 0.33. AUROC for HAS of FIB-04 was 0.828 and of APRI, 0.829. Scatter diagram Showed significant positive correlation of FIB-04 and APRI for determining HAS.
Conclusion: FIB-04 and APRI can predict HAS but not fibrosis in patient with CHB.

Abstract #745

Association of Caspase-Cleaved Cytokeratin18 (CK18-Asp396) Fragment M30 with Hepatic Histological Severity in Patients with HBV Related Compensated Chronic Liver Disease

Dr Kazi Zakir Hossain[1], Prof Dr Mamun Al Mahtab[2], Dr Md Jahangir Alam Sarker[1]

[1]Shaheed Suhrawardy Medical College Hospital, [2]Bangabandhu Sheikh Mujib Medical University

Introduction: Chronic hepatitis B (CHB) remains a serious public health problem worldwide. Cytokeratin (CK) 18 is an intermediary filament protein, expressed in hepatocytes, which is proteolytically cleaved during liver damage. M30 epitope of cytokeratin18 (CK18-M30) is involved at different levels in apoptotic pathways. Objective: whether serum CK-18 fragment M30 level significantly correlate with the histological severity (activity and fibrosis) in patients with CHB.

Methodology: A total of 40 patients with CHB were enrolled in this study between January 2015 to August 2016. All CHB cases underwent liver biopsy for METAVIR score. Serum CK-18 M30 were measured by ELISA.
Results: Mean ALT and AST, HBV DNA levels were 66.4 ± 28.20 IU/L, 40.2 ± 20.2 IU/L and cx 5.3 ± 1.7 IU/ml. Serum M30 CK-18 levels significantly higher in both HBeAg positive and negative CHB in comparison to carrier groups. Serum CK18 were significantly increased in a stepwise fashion from F1 to F3 but not incase of necroinflammation. A significant correlation was found between ALT, AST level and the METAVIR histological activity scores (P = 0.036 and 0.016). We found highly significant positive correlation between the stages of fibrosis (F1 to F3) and Serum CK-18 M30 level (r = 0.839; p = 0.0157) but no correlation incase of necroinflammation (r = − 0.073; p = 0.357). Serum M30 CK-18 levels were able to discriminate patients with mild versus moderate-advanced fibrosis (AUC: 0.84)
Conclusion: This study indicates there is significant positive correlation between the stages of fibrosis (F1 to F3) and Serum CK-18 M30 level in patients with CHB. So CK-18 M30 can be used as a potential noninvasive biomarker of hepatic fibrosis.

Abstract #748

In vitro and in vivo models of HBV replication utilizing monomeric HBV genomes facilitate studies of the HBV cccDNA minichromosome

Thao Huynh[1], Michelle Clark[2], Liana Mackiewicz[3], Vitina Sozzi[4], Hugh Mason[5], Marc Pellegrini[6], Greg Ebert[7], Hans J Netter[8], Peter A Revill[9]

[1]Research and Molecular Development, Vidrl, Royal Melbourne Hospital at the Peter Doherty Institute for Infection and Immunity, [2]Infection and Immunity Division, the Walter and Eliza Hall Institute of Medical Research, [3]Infection and Immunity Division, the Walter and Eliza Hall Institute of Medical Research, [4]Research and Molecular Development, Vidrl, Royal Melbourne Hospital at the Peter Doherty Institute for Infection And Immunity, [5]Research and Molecular Development, Vidrl, Royal Melbourne Hospital at the Peter Doherty Institute for Infection and Immunity, [6]Infection and Immunity Division, The Walter and Eliza Hall Institute of Medical Research, [7]Infection and Immunity Division, The Walter and Eliza Hall Institute of Medical Research, [8]Research and Molecular Development, Vidrl, Royal Melbourne Hospital at the Peter Doherty Institute for Infection and Immunity, [9]Research and Molecular Development, Vidrl, Royal Melbourne Hospital at the Peter Doherty Institute for Infection and Immunity

The absence of appropriate in vitro and in vivo replication models enabling direct comparison of hepatitis B virus (HBV) replication across genotypes is hampering the progress of curative HBV research. HBV exists as nine distinct genotypes (A-I) which generally affect particular demographic groups in discrete geographic regions, with varying severity and treatment response. Differences in their replication efficiencies have also been identified and characterized, but molecular analyses have been hindered by the lack of a suitable model that enables thorough investigation of the complete HBV replication cycle, particularly the viral cccDNA reservoir which is a major source of viral persistence and barrier to HBV cure. Using complete genome PCR, we generated full-length HBV genomes ("1-mers", genotypes A, C and D), transfection of which induced the complete HBV replication cycle, including the generation of a cccDNA-like molecule, in vitro. We next introduced these plasmid-free monomeric HBV genomes into mice via hydrodynamic tail-vein injection, to investigate their utility as a novel in vivo replication model. Characterization of HBV replication from liver tissue demonstrated the production of cccDNA-like episomes via Southern blot, as well as the detection of major viral RNA transcripts by Northern blot. Taken together, these in vitro and in vivo models enable exploration of the interactions between cccDNA-like molecules and viral and host proteins, to further investigate their contributions to HBV replication across genotypes. This may unearth new insights into cccDNA transcriptional regulatory mechanisms and lead to discovery of novel pan-genotypic strategies for the control or inhibition of HBV replication.

Abstract #780

No Resistance to Tenofovir Alafenamide (TAF) Detected Through 96 Weeks of Treatment in Patients with Chronic Hepatitis B from China

Jinlin Hou[1], Yu Chen[2], Yang Liu[3], Bandita Parhy[3], Gregory Camus[3], Becket Feierbach[3], Hongmei Mo[3], John F Flaherty[3], Anuj Gaggar[3], Hong Tang[4], Qing Xie[5], Qin Ning[6]

[1]Nanfang Hospital, Southern Medical University, Guangzhou, China, [2]Chybeyond@163.Com, [3]Gilead Sciences, Foster City, CA, United States, [4]West China Hospital, Sichuan University, Chengdu, China, [5]Shanghai Ruijin Hospital, Shanghai Jiao Tong University, Shanghai, China, [6]Tongji Hospital, Tongji Medical University, Wuhan, China

Introduction: In the Phase 3 studies GS-US-320-0108 and GS-US-320-0110, TAF has shown efficacy non-inferior to that of TDF at Weeks 48 and 96.
Objectives: To conduct virology resistance surveillance in patients with chronic HBV participating in 2 Phase 3 studies in China through 96 weeks of TAF treatment.
Methodology: HBV polymerase (pol)/reverse transcriptase (RT) population sequencing was conducted for subjects with ≥ 24 weeks of treatment who experienced virologic breakthrough (VB) at Week 96, or at early discontinuation (ED) with HBV DNA ≥ 69 IU/mL. Sequence changes from Baseline at Week 96/ED are reported. Phenotypic analysis was performed for adherent subjects with VB, and those with emergent conserved site substitution(s), or polymorphic substitutions when detected in > 1 patient.
Results: At Week 96, only 16 of 223 subjects (7.2%) in the TAF group and 7 of 104 subjects (6.7%) in the TDF group qualified for HBV sequencing across the 2 studies. Of the 23 subjects who qualified for sequencing, 5 were unable to be sequenced, 8 had no change in pol/RT from baseline, 6 had unique polymorphic site substitutions, and 4 had conserved site substitutions in pol/RT. Overall, no site substitutions emerged in > 1 subject. Six subjects in the TAF group and 4 subjects in the TDF group met the criteria for phenotypic analysis; no reduction in susceptibility was shown in vitro.
Conclusion: Consistent with non-China results, no substitutions associated with resistance to TAF were detected through 96 weeks of treatment in CHB patients enrolled in China.

Abstract #793

Hyperactivation and proliferation of B cells in HBeAg positive Hepatitis

Yang Li[1], Yong Liu[2], Yuxin Chen[3], Shengxia Yin[4], Chao Wu[4]

[1]Nanjing University Medical School, [2]Scientific Research Office, Nanjing Drum Tower Hospital, [3]Laboratory Medicine, Nanjing Drum

Tower Hospital, [4]Infectious Diseases Department, Nanjing Drum Tower Hospital

To dissect expression profiling of circulating B cells from patients with HBeAg-positive chronic hepatitis B versus healthy volunteers with the history of HBV vaccine immunization. Peripheral blood CD19 + B cells isolated from 4 HBeAg-positive CHB patients and 4 HBV vaccinated healthy controls were analyzed by high-through RNA sequencing. GO analyses and signaling pathway enrichment analyses including KEGG and Reacome were used to identify differentially expressed genes (DEGs) among different groups. Our interested gene expressions were further validated by both of qPCR and flow cytometry. A total of 1401 DEGs were identified between B cells of HBsAg-positive chronic hepatitis B patients and vaccinated healthy controls. Interestingly, such DEGs were enriched in biological progress especially immune system process. The ribosome pathway was down regulated in HBsAg-positive CHB patients may result in p53 suppression leading to B cells activation and proliferation. Specifically, we identified that cell activation and proliferation related genes including BACH2, CTLA4, TLR4, NFAM1, ZAP70, NOD2, PELI1 and PRDM1 were remarkably upregulated, whereas negative regulators of B cell activation including ID3 and CTLA4 were significantly downregulated in patients. Of note, such B cell hyperactivation and proliferation in HBeAg-positive CHB patients were also confirmed in HBV mouse model was established by hydrodynamical injection of pAAV/HBV1.2 plasmid. For the first time, we identified a panel of potential genes and signaling pathways associated with the hyperactivation and proliferation of B cells in CHB patients and in a HBV mouse model which might serve promising targets for novel therapies to treat chronic hepatitis B infection.

Abstract #794

New Method of Next-generation Sequencing without Pre-amplification in Whole Genome Sequencing of Hepatitis B Virus

Hyun Woong Lee[1], Hye Young Chang[2], Jung Il Lee[2], Kwan Sik Lee[2]

[1]Department Of Internal Medicine, Yonsei University College Of Medicine & Gangnam Severance Hospital, [2]Department Of Internal Medicine, Yonsei University College Of Medicine

Background and Aims: In this study, we tried to overcome the limitations of previous amplification methods using non-amplification method directly using serum DNA for NGS test.
Methods: Eight newly diagnosed, untreated naïve HBV infected patients enrolled in this study. The DNA were fragmented into 300 to 1000-bp, and then analyzed on a MiSeqDx sequencer (Illumina) for paired-end sequencing (2 × 150 bp, 300 cycles). BWA-MEM (v0.7.17) was used to map the reads against the human reference sequence (GRCh38.p12). The reads unmapped or not well mapped (MAPQ < 60) were extracted and re-mapped to reference sequence of HBV of Korean (DQ683578.1). GATK Mutect2 (v4.0.3) was used to call SNPs and Indels in the result. We analyzed the whole genome of HBV including DNA polymerase, preS1/preS2/S, protein X, and precore/core region.
Results: Of the total data obtained from the NGS test, 97.3% (min–max; 90.1–99.7%) were human DNA and HBV DNA was 1.2% (min–max; 0.0–6.4%) on average. The average depth of coverage spanning 3215 nucleotides was 38.4 bp (min–max; 4.3–64.9). Total 181 variants (175 SNPs and 6 Indels) were detected. 57 variants in polymerase, 23 in preS1/preS2/S, 18 in X, 14 in precore/core region were non-synonymous variants or indels, which make changes in amino acid and protein.
Conclusions: We were able to detect the full-length genome of HBV without pre-amplification steps. Using this non-amplification direct NGS method, errors in the PCR process can be minimized and the whole genome of HBV could be more accurately examined.

Abstract #832

Serum hepatitis B core-related antigen is a valuable marker to predict regression of fibrosis in chronic hepatitis B patients after Entecavir 72-week treatment

Chang Xiu Juan[1], Yang Yong Ping[1], Sun Chao[1], Li Xiao Dong[1]

[1]Therathpeutic Research Center For Liver Cancer, The 5th Medical Center Of Chinese Pla General Hospital

The objective of study was to evaluate serum hepatitis B core-related antigen (HBcrAg) for predicting liver fibrosis stage and regression of fibrosis in chronic hepatitis B (CHB) after Entecavir 72 weeks treatment.
Methods: HBcrAg levels were measured by a chemiluminescence enzyme immunoassay in 320 patients with CHB, including 164 HBeAg-positive and 156 HBeAg-negative patients. All patients were treated with entecavir and were followed-up for 72 weeks. The CHB patients is divided into the high and low serum HBcrAg groups accroding to the median of baseline serum HBcrAg (6.33Log IU/ml).
Results: Baseline serum HBcrAg levels was correlated negatively with the liver fibrosis stage in HBeAg-positive patients and positively in HBeAg-negative patients. Ordered multi-class Logistic regression to fibrosis stage showed that baselise serum HBcrAg, platelet counts, chiolinesterase, quantitative of HBsAg and G1764A are independent factors of fibrosis stage. Baselise serum HBcrAg is correlated with fibrosis regression. The high serum HBcrAg group is more easily to reverse fibrosis than the low group in CHB patients. Multivariate logistic regression analysis showed that baseline serum HBcrAg, platelet counts and age are independent factors of regression of fibrosis in CHB (P = 0.004, 95%CI: 0.206–0.735, P = 0.033, 95%CI: 0.264–0.945, P = 0.040, 95%CI: 0.030–0.923). We further analyze HBV BCP/PC/C mutation is closely associated with the level of serum HBcrAg, particularly G1896A (P < 0.001), G1899A (P = 0.020), C1766T (P = 0.033), A1846T/C (P = 0.010) and T1753C/A/G (P = 0.038). Those variant sites is closely with progression of liver fibrosis.
In conclusion, baseline serum HBcrAg may be a valuable marker to predict liver fibrosis stage and regression of fibrosis, especially in CHB patients treated with nucleoside analogs.

Abstract #877

Early Antiviral Treatment (Tenofovir) Declines Hepatitis B Viral Load with Emergence of Functional T Cells with reduced PD1 expression in HBsAg Positive Pregnant Females

Pooja Negi[1], Ashish Kumar Vyas[1], Ritesh Khanna[1], Sharda Patra[2], Shiv Kumar Sarin[3], Nirupama Trehanpati[1]

[1]Department of Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, New Delhi, [2]Lady Harding Medical College, New Delhi, [3]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi

Background: HBV flares at delivery reconstitute immunity in HBsAg + ve pregnant females, however there is little data of immune reconstitution during kinetics of pregnancy in HBsAg + ve pregnant females with or without anti-viral therapy.

Methods: 12 HBsAg + pregnant-females treated with 300 mg/day tenofovir from first trimester (T, ~ 12 wks; Gr.I) and 12 HBsAg + non treated pregnant (NT, Gr.II) were analyzed for changes in HBV DNA, HBsAg, ALT/AST, HBeAg, HBV specific immune correlates in the 2nd, 3rd trimester, at delivery and 3 M post-partum. Healthy pregnant females (H, n = 10) were included as control.
Results: Continues decline in HBV DNA, HBsAg levels but significant reduction in HBsAg quant was observed at delivery in Gr.1. Manwitney and univariate analysis revealed decreased expression of exhaustion marker PD1 on CD4 + and CD8 + T cells in Gr.1 compared to Gr. II. Gr.I females also showed higher HBV specific IFN-γ, IL-17A and decreased IL-10 and TGF-β secreting CD4 and CD8 T cell compared to Gr.II. Along with increased HBV specific T cells, antibody secreting plasma B cells were also increased in Gr.I than Gr.II. In the subsequent 3rd trimester, at delivery and in post - partum, in addition to increased HBV specific effector Tcells, Tregs cells and inhibitory immune parameters largely declined with effectively increase in HBV specific pro-inflammatory cytokines in Gr.I compared to Gr.II. Spearman correlation showed significant negative correlation of ALT, CD4 +/CD8 + IFN-γ + T cells with HBV DNA levels and HBsAg quant.
Conclusion: Early start of anti-viral treatment in HBsAg positive pregnant females, reconstitute immunity better and could prevent viral flares postpartum

Abstract #883

GIV regulates HBV replication via enhancing cellular membrane trafficking machineries

Zhiqiang Wei[1], Yonghong Zhang[2], Yulin He[1], Bin Cheng[1], Jie Luo[5], Zhongji Meng[1]

[1]Institute of Biomedical Research, Taihe Hospital, Hubei University of Medicine, Shiyan 442000, Hubei Province, China, [2]Institute of Wudang Chinese Medicine, Taihe Hospital, Hubei University of Medicine, Shiyan 442000, Hubei Province, China, [3]Center for Evidence-Based Medicine and Clinical Research, Taihe Hospital, Hubei University of Medicine, Shiyan 442000, Hubei Province, China

Introduction and Objectives: The natural history of chronic Hepatitis B virus (HBV) infection can be classified into five phases. Patients in HBeAg-positive chronic infection and HBeAg-negative chronic infection phase had persistently normal ALT levels and low fibrosis but significant different viral loads. Through microarray analysis of liver biopsies, we found that Gα-interacting vesicle-associated protein (GIV) expression dynamic changed in different phases of chronic HBV infection. The aim of this study is to investigate the role of GIV in HBV replication and its mechanism.
Methodology: The effect of GIV on HBV replication and HBsAg production were evaluated in HepG2.2.15 and Huh7 cells lines. Cellular membrane trafficking system including autophagy and endocytosis was investigated to study the mechanism of GIV action on HBV replication.
Results: GIV overexpression significantly enhanced HBV replication and HBsAg production. However, GIV had no effect on HBV pgRNA transcription and promoter activity. Then, we found that GIV with its effector GTPase Gαi3 activation significantly decreased autophagy through enhancing insulin induced Akt/mTOR/ULK1 pathway. However contrary to GIV knockdown, HBV replication was increased by Gαi3 knockdown, which revealing GIV-regulated HBV replication is Gαi3 independent. Interestingly, GIV activation also enhances endocytosis. Furthermore, blocking the formation of early endosomes by silencing Rab5 significantly reduced HBV replication. These results indicated that GIV may enhance HBV replication through endocytosis.
Conclusion: Although GIV has the opposite effect on autophagy and endocytosis, both of which increase HBV replication, GIV enhances endocytosis more strongly than autophagy, ultimately enhancing HBV replication.
Keyword: GIV, Hepatitis B virus, endocytosis, autophagy

Abstract #888

The role of heat shock 70 kDa protein-9 (HSPA9) in Hepatitis C virus-related liver diseases

Korri Elvanita El Khobar[1], Enoch Tay[2], Eve Diefenbach[3], Jacob George[4], Mark W Douglas[5], David Handojo Muljono[6]

[1]Hepatitis Unit, Eijkman Institute for Molecular Biology, Jakarta, Indonesia & Storr Liver Centre, The Westmead Institute For Medical Research, The University of Sydney at Westmead Hospital, Westmead, Australia, [2]Storr Liver Centre, The Westmead Institute for Medical Research, The University of Sydney at Westmead Hospital, Westmead, Australia, [3]Protein Core Facility, The Westmead Institute for Medical Research, Westmead, Australia, [4]Storr Liver Centre, The Westmead Institute for Medical Research, The University of Sydney at Westmead Hospital, Westmead, Australia, [5]Storr Liver Centre, The Westmead Institute For Medical Research, The University of Sydney at Westmead Hospital, Westmead, Australia & Centre for Infectious Diseases and Microbiology, Marie Bashir Institute for Infectious Diseases and Biosecurity, The University of Sydney At Westmead Hospital, Westmead, Australia, [6]Hepatitis Unit, Eijkman Institute For Molecular Biology, Jakarta, Indonesia & Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia & Faculty of Medicine And Health, University of Sydney, Sydney, Australia

Introduction: Hepatitis C virus (HCV) infection is associated with oxidative stress and endoplasmic reticulum (ER) stress. This is typically marked by increased expression of ER chaperone proteins including the heat-shock protein (HSP) families. Thus, HSP expression may be used as marker to monitor oxidative and ER stress levels in HCV-related liver disease.
Objective: To determine the expression of various heat-shock proteins in HCV-related liver disease.
Methodology: 2-D electrophoresis (2DE) analysis was performed on isolated membrane proteins from HCV-Jc1-infected cells compared to HCV-replication-defective (GND) and uninfected cells. Differentially-expressed membrane proteins were identified using MALDI-TOF mass spectrometry and confirmed by quantitative-RT-PCR. Gene expression datasets from Gene Expression Omnibus and cBioPortal analysis of The Cancer Genome Atlas (TCGA) liver tumour samples (LIHC) were used to confirm changes in identified HSP expression in the setting of liver cancer, its effect on overall survival, and potential interacting proteins.
Results: Our 2DE results showed increased expressions of HSPA9, HSPA5, HSP90AA1, HSP90AB1, and HSP90B1 in membrane fraction of HCV-Jc1 cells. Two-fold increase of HSPA9 mRNAs in HCV-Jc1 cells was confirmed by qRT-PCR ($p < 0.05$). Increased HSPA9 mRNA was found in all tumour samples from the GSE14520 dataset ($n = 445$; $p < 0.001$) and in 17% (62/366) of the LIHC dataset, and was associated with reduced overall survival ($p = 0.157$). Changes in HSPA9 expression were associated with changes in expression of mitochondrial proteins TIMM17A and TOMM20.
Conclusion: HSPA9 mRNA was increased in HCV-related liver cancer. More functional studies are needed to confirm the exact role of HSPA9 in pathogenesis of chronic hepatitis C.

Abstract #925

Entecavir Reduced Serum Hepatitis B Core-related Antigen (HBcrAg) Level In Chronic Hepatitis B Patients With Hepatocellular Carcinoma

Lung-Yi Mak[1], Kwan-Lung Ko[1], Wai-Pan To[1], Danny Ka-Ho Wong[2], Justin Hei-Chun Ma[2], Teresa Lok-Yee Hui[2], Wai-Kay Seto[2], James Fung[3], Ching-Lung Lai[2], Man-Fung Yuen[2]

[1]Queen Mary Hospital, Hong Kong, [2]Department Of Medicine, The University Of Hong Kong, [3]Department Of Medicine, Queen Mary Hospital

Introduction: Hepatitis B core-related antigen (HBcrAg) was shown to predict risk of hepatocellular carcinoma (HCC) in chronic hepatitis B (CHB) patients on treatment.
Objectives: We investigated the longitudinal profile of serum HBcrAg in entecavir (ETV)-treated CHB patients with subsequent HCC development.
Methodology: We identified HCC cases diagnosed at $\geq$ 1 year after ETV initiation. CHB patients without HCC (matched for age, gender, cirrhosis, baseline DNA, ETV duration) were identified as controls in 1:2 ratio (HCC:non-HCC). Serum samples were retrieved at baseline (ETV initiation), 3-year and 5-year of ETV for serum HBcrAg measurement (log IU/mL).
Results: A total of 180 (60 HCC cases were matched with 120 CHB patients without HCC; median age 56.5 years, 80.6% male, baseline HBV DNA 5.9 log IU/mL, median follow-up 6.8 years) were recruited. Median time from ETV initiation to HCC was 3.2 years. Serum HBcrAg levels were higher in HCC cases compared to controls at all 3 time points: 5.69 vs. 5.02 log IU/mL ($p = 0.025$), 4.23 vs. 3.36 log IU/mL ($p = 0.007$), and 3.86 vs. 3.36 log IU/mL ($p = 0.009$), respectively. ETV treatment led to decline in serum HBcrAg from baseline to 3-year at similar rates in both groups (0.34 vs 0.39 log IU/mL/year, $p = 0.774$), although the decline from 3-year to 5-year slowed down more in the non-HCC group (0.05 log IU/mL/year) compared to the HCC group (0.09 log IU/mL/year; $p = 0.055$).
Conclusion: ETV reduced serum HBcrAg in HCC and non-HCC patients in a time-dependent manner. Interpretation of serum HBcrAg should take into account the duration of antiviral treatment.

Abstract #933

The specific transcription factors RORγt and Foxp3 take an important role in the imbalance of Th17/Treg in patients with chronic hepatitis B

Jing You[1], Ru Yi Zhang[1], Hon Ying Chen[1], Huai E Liu[1], Guan Hua Jia[1], Feng Xu[1], Jian Ming Chen[1]

[1]Department of Infectious Diseases, The First Affiliated Hospital of Kunming Medical University, Kunming, Yunnan, China

Objective: RORγt and Foxp3 are transcription factors for Th17 and Treg respectively. Th17 and Treg have antagonistic functions, pro-inflammatory and anti-inflammatory, respectively. The balance between Th17 and Treg is significant important for maintenance of immune homeostasis. The aim of the study is to exploring the causes of Th17/Treg imbalances and to revealing the immunology mechanism of HBV persistent infection and disease chronicity.
Methods: One hundred and eighteen CHB patients were involved in this study. Twenty were normal physical examination people as control group. The frequency of Th17cells and Tregcells in the peripheral blood of the patients group and control group were detected by flow cytometry. RT-PCR was used to measure levels of RORγtmRNA and Foxp3mRNA in the peripheral blood.
Results: The peripheral Th17/Treg ratio in CHB patients were higher than those of the control group ($P < 0.01$). Th17/Treg ratio in the moderate/severe group was higher than those of the mild group and the control group. The peripheral levels of RORγtmRNA and Fox-p3mRNA in all CHB patients were higher than those of the control group ($P < 0.01$). The levels of RORγtmRNA and Foxp3mRNA in the moderate/severe group patients were higher than those of the mild group and control group ($P < 0.01$). There were positive correlations between the peripheral levels of RORγtmRNA and Th17/CD4+T cells, and between the levels of Foxp3mRNA and Treg/CD4+T cells in CHB patients.
Conclusion: RORγtmRNA and Foxp3mRNA take an important role in the imbalance of Th17/Treg in CHB patients. It may be the important reason of chronicity and viral persistent infection in HBV infection.

Abstract #943

Early intrahepatic TLR4 activation facilitates HBV persistence through strengthening Kupffer cell mediated T cell suppression

Wenqing Zhou[1], Jinzhuo Luo[1], Qing Yu[1], Jia Liu[1], Dongliang Yang[1]

[1]Department of Infectious Disease, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology

HBV is considered as a "stealth" virus since it triggers no or only limited innate response during the acute phase of infection, yet most of the infected adult individuals resolved the infection. We investigated the impact of early activation of innate immune response on HBV clearance and the related immune mechanism by using the HBV hydrodynamic injection (HDI) mouse model. C57BL/6 mice were hydrodynamically injected with HBV replicating plasmid pAAV/HBV1.2 either in combine with TLR4 agonist LPS or not, and were monitored for HBV viremia, serum cytokine production and Kupffer cell (KC) function. We could show that HDI of pAAV/HBV1.2 in combine with LPS led to significant delay of HBV clearance in mice compared with pAAV/HBV1.2 HDI alone. HDI of LPS but not pAAV/HBV1.2 resulted in dramatic elevation of serum proinflammatory cytokine (IL-6, TNF-α and IL-10) levels within 3 hours. Compared to LPS HDI alone, HDI of LPS and pAAV/HBV1.2 significantly reduced serum IL-6, TNF-α and IL-10 concentrations, suggesting HBV inhibits TLR4 signaling in vivo. Besides, the KCs separated from HBV plus LPS HDI mice showed significantly increased IL-10 production as well as enhanced ability to suppress IFN-γ production of TCR-activated T cells than the KCs from HBV HDI alone mice. Taken together, our results suggest that early activation of intrahepatic innate immune responses by TLR4 agonist strengthens the suppressive properties of KCs and may facilitates the persistence of HBV infection. The role of HBV as a "stealth" virus in HBV clearance needs to be carefully and thoroughly reinterpreted.

Abstract #952

Histone deacetylases and acetylated histone H3 are involved in the process of hepatitis B virus DNA replication

Yao Wang[1], Zuojiong Gong[2]

[1]Department of Infectious Diseases, Renmin Hospital of Wuhan University, Wuhan, China

The aim of this study was to investigate the relationship between anti-HBV treatment and the regulation of HDACs in the process of HBV DNA replication. The HDAC activities and histone protein expression in the serum of CHB patients with different HBV DNA levels were measured and further validated the changes in HDAC2, HDAC6 and acetyl-histone H3 (AH3) levels in normal control and 4 CHB patient liver tissue samples before and after antiviral treatment. The HDAC inhibitor, TSA, and the anti-HBV agents, ETV and IFN-α, were used to stimulate HepG2.2.15 cells. The supernatant HBV DNA, pgRNA, and cccDNA levels in cells were determined. AH3 and H3 were tested at days 3, 6, and 9 after treatment. The levels of HDAC2, HDAC6 and AH3 were notably decreased in the liver tissue after 24 weeks of antiviral treatment. The HDAC activity and AH3 protein levels in the patients with higher HBV DNA levels were higher than those in the patients with lower HBV DNA levels. In an in vitro study, the level of HBV DNA, the HDAC activity, and the HDAC2, HDAC6 and AH3 protein levels decreased in the ETV, IFN-α and TSA groups compared with the control group. The supernatant pgRNA level declined in the IFN-α group and increased in the ETV and TSA groups. cccDNA expression was suppressed by IFN-α. Anti-HBV treatment inhibited HDACs, which promoted pgRNA expression and inhibited cccDNA, possibly due to changes in the acetylation sites of molecules in the viral mini-chromosomes mediated by AH3.

Abstract #957

MMP2/MMP9-mediated CD100 shedding is crucial for inducing intrahepatic anti-HBV CD8 T cell responses and HBV clearance

Shangqing Yang[1], Lu Wang[2], Wen Pan[3], Wibke Bayer[4], Christine Thoens[5], Ulf Dittmer[6], Joerg Timm[7], Dongliang Yang[8], Jia Liu[9]

[1]Department of Infectious Diseases, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, [2]Department of Infectious Diseases, Union Hospital, Tongji Medical College, Huazhong University Of Science And Technology, [3]Department of Infectious Diseases, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, [4]Institute for Virology, University Hospital of Essen, University of Duisburg-Essen, [5] Institute for Virology, Heinrich-Heine-University, University Hospital, [6]Institute for Virology, University Hospital of Essen, University of Duisburg-Essen, [7]Institute for Virology, Heinrich-Heine-University, University Hospital, [8]Department of Infectious Diseases, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, [9]Department of Infectious Diseases, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology

Background: CD100 is constitutively expressed on T cells and can be cleaved from the cell surface by matrix metalloproteases (MMPs) to become soluble CD100 (sCD100). Both membrane-bound CD100 (mCD100) and sCD100 play important immune regulatory functions that promote immune cell activation and responses. The aim of this study was to investigate the expression and role of mCD100 and sCD100 in regulating antiviral immune responses during HBV infection.
Methods: mCD100 expression on T cells, sCD100 levels in the serum and MMP expression in the liver and serum were analyzed in patients with chronic hepatitis B (CHB) and HBV replicating mice. The ability of sCD100 in mediating antigen-presenting cell maturation, HBV-specific T cell activation and HBV clearance were analyzed in HBV replicating mice and CHB patients.
Results: CHB patients had higher mCD100 expression on T cells and lower serum sCD100 levels than healthy controls. Therapeutic sCD100 treatment resulted in the activation of dendritic cells and liver sinusoidal endothelial cells, enhanced HBV-specific CD8 T cell response and accelerated HBV clearance, while blockade of its receptor CD72 attenuated the intrahepatic anti-HBV CD8 T cell response. Together with MMP9, MMP2 mediated mCD100 shedding from the T cell surface. CHB patients had significantly lower serum MMP2 levels, which positively correlated with serum sCD100 levels. Inhibition of MMP2/9 activity resulted in an attenuated anti-HBV T cell response and delayed HBV clearance in mice.
Conclusions: MMP2/9-mediated sCD100 release plays an important role in regulating intrahepatic anti-HBV CD8 T cell responses, thus mediating subsequent viral clearance during HBV infection.

Abstract #963

Distinct bile acid profiles in chronic viral hepatitis B patients

Zeyu Sun[1], Chenjie Huang[1], Yixian Shi[1], Miaomiao Zhao[1], Rusha Wang[1], Zhenggang Yang[1]

[1]Zhejiang University

Introduction: There are nearly 300 million HBV-infected population globally, and this incurable disease post great public health challenge particularly in developing countries. The recent identification of Na + taurocholate co-transporting polypeptide (NTCP) as the hepatocyte receptor for hepatitis B virus (HBV) entry has prompt interest to study relationship between HBV infection and host bile acid (BA) metabolism.
Objectives: This study aim to investigate the BA metabolism in chronic HBV infection (CHB) patients.
Methodology: Serum BA profiles including unconjugated, glycine or taurine conjugated primary and secondary BAs were compared among 92 CHB patients with normal ALT level (NALT), 34 CHB patients with abnormal ALT level (AALT) and 28 healthy controls (HCs) using UPLC-MS measurement. Multivariate modeling was used to illustrate the overall changes of BA profiles between groups.
Results: Total serum BAs were significantly higher in CHB-AALT patients, compared to CHB-NALT patients and HCs, suggesting the impact of liver injury on serum BA levels. Despite unchanged total level, the BA composition in CHB-NALT group did change as the unconjugated BAs decreased significantly in CHB-NALT patients while the ratio of conjugated/unconjugated BAs increased as compared to HCs. In addition, we found the ratio of primary to secondary BAs increased in CHB-NALT patients as compared to HCs and CHB-AALT patients.
Conclusions: Distinct changes of serum BA profiles were found in CHB patients. Changes of individual or combinatory BA profiles can be used to monitor CHB progression.

Abstract #997

The gamma-glutamyl transpeptidase to platelet ratio predicts liver inflammation in chronic hepatitis B patients with normal or mildly elevated alanine transaminase levels

Jian Wang[1], Rui Huang[2], Xiaomin Yan[3], Yong Liu[4], Yunxin Chen[5], Zhaoping Zhang[6], Weimao Ding[2], Chao Wu[1]

[1]Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, [7]Huai'an No. 4 People's Hospital

Background: The gamma-glutamyl transpeptidase (GGT) to platelet ratio (GPR) was proposed as an accurate index for predicting liver inflammation in patients with chronic hepatitis B (CHB) in our previous study. We aimed to validate the value of GPR for predicting significant inflammation in CHB patients with normal or mildly elevated alanine transaminase (ALT) levels.
Methods: Four hundred and thirty-one treatment-naïve CHB patients with normal ($\leq$ 40U/L) or mildly elevated ($\leq$ 80U/L) ALT who underwent liver biopsy were enrolled in this study. The predicting value of GPR for significant liver inflammation ($\geq$ G3) were compared with other conventional inflammation parameters by the areas under the receiver-operating characteristic curves (AUROCs).
Results: For patients with ALT $\leq$ 80U/L, the AUROCs of GPR in predicting significant liver inflammation were 0.837 (95%CI 0.796 to 0.878), 0.860 (95%CI 0.809 to 0.910) and 0.809 (95%CI 0.739 to 0.878) in entire patients, HBeAg positive and HBeAg negative CHB patients, respectively. Further comparisons showed the diagnostic performance of GPR for significant liver inflammation was significantly higher than that of ALT (0.673 and 0.666, $P < 0.001$, respectively), aspartate transaminase (AST) (AUC = 0.737, P = 0.001; AUC = 0.745, P = 0.003, respectively) and GGT (AUC = 0.796, P = 0.002; AUC = 0.802, P = 0.002, respectively) in entire patients and HBeAg positive CHB patients, but was comparable with AST (AUC = 0.720, P = 0.096) and GGT (AUC = 0.786, P = 0.273) in HBeAg negative CHB patients. Similar results were observed in patients with ALT $\leq$ 40U/L.
Conclusions: The GPR index has a better diagnostic value than conventionally predictive parameters to assess liver inflammation in CHB patients with normal or mildly elevated ALT levels, especially for HBeAg positive CHB.

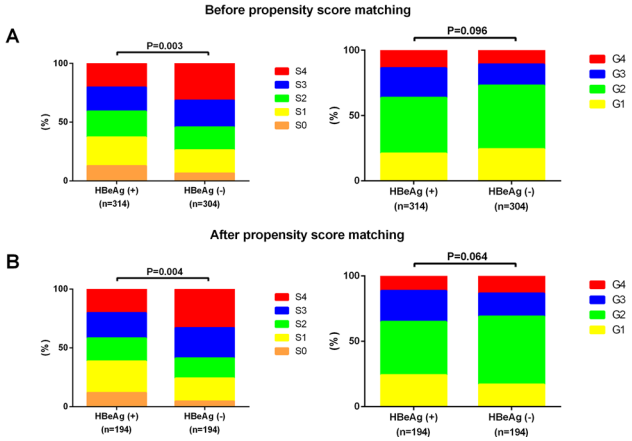
Abstract #1001

HBeAg negative CHB patients is associated with more severe liver fibrosis than HBeAg positive CHB patients: A propensity score matching analysis

Rui Huang[1], Jian Wang[1], Yong Liu[1], Yunxin Chen[1], Xiaomin Yan[1], Zhaoping Zhang[1], Weimao Ding[2], Chao Wu[1]

[1]Nanjing Drum Tower Hospital, The Affiliated Hospital Of Nanjing University Medical School, [2]huai'an No. 4 People's Hospital

Background: Serum hepatitis B e antigen (HBeAg) plays an important role in the progression and prognosis of hepatitis B virus (HBV) related liver diseases. However, few studies reported whether HBeAg status is related with the degree of liver injury in patients with chronic hepatitis B (CHB). We aimed to investigate the relationship between HBeAg status and liver pathological stages in CHB patients using propensity score matching (PSM).
Methods: A total of 618 treatment-naïve CHB patients who had undergone liver biopsy from two medical centers were enrolled in this study. PSM was performed to adjust the imbalance of baseline confounders between HBeAg-positive CHB patients and HBeAg-negative CHB patients.
Results: Of these 618 CHB patients, 194 patients were included in each group after PSM. HBeAg-negative CHB patients (n = 304) exhibited a significantly severity of liver fibrosis than HBeAg-positive CHB patients (n = 314) before PSM (P = 0.003). However, there were no significant differences of the distribution of inflammation grades between HBeAg-positive CHB patients and HBeAg-negative CHB patients (P = 0.096). After propensity matching, CHB patients with HBeAg-negative (n = 194) still showed a significantly severity of liver fibrosis as compared with HBeAg-positive CHB patients (n = 194) (P = 0.004). Furthermore, the distribution of liver inflammation grades was comparable between HBeAg-positive CHB patients and HBeAg-negative CHB patients (P = 0.064).
Conclusion: HBeAg negative CHB patients may have more serious degree of liver fibrosis than HBeAg positive CHB patients in the propensity score matching (PSM) analysis.



Abstract #1002

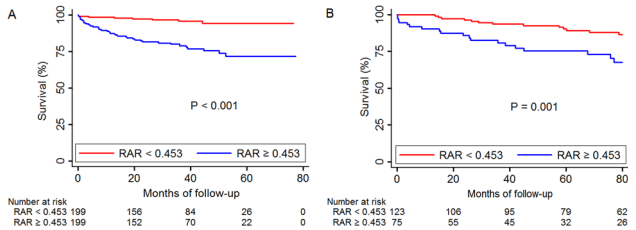
Red blood cell distribution width to albumin ratio as a novel prognostic indicator in patients with chronic hepatitis B-related liver cirrhosis

Rui Huang[1], Jian Wang[1], Juan Xia[1], Linda Henry[2], Yeehui Yeo[2], Zhaoping Zhang[1], Chuanwu Zhu[3], Mindie H Nguyen[2], Chao Wu[1]

[1]Nanjing Drum Tower Hospital, The Affiliated Hospital Of Nanjing University Medical School, [2]Stanford University Medical Center, [3]The Fifth People's Hospital Of Suzhou

Background: Simple, reliable non-invasive indexes to predict prognosis of chronic hepatitis B (CHB)-related liver cirrhosis (LC) are currently lacking. We aimed develop and test a novel index using routine laboratory results to predict the liver-related mortality of CHB-LC.
Method: The derivation cohort contained 398 CHB-LC patients from China. A validation cohort of 198 CHB-LC patients was independently enrolled from the United states. Multiple regression identified index predictors. The prognostic value was assessed using Kaplan–Meier analysis.
Results: Red cell distribution width (RDW) and albumin ($P < 0.001$) were independent predictors of CHB-related decompensated cirrhosis (CHB-DCC) in derivation cohort. The receiver operating characteristic curves (ROCs) analysis revealed that RDW to albumin ratio (RAR) (0.771, 0.737 and 0.727) was comparable with CTP score (0.800, 0.743 and 0.746, $P > 0.05$) for predicting 1-year, 3-year and 5-year liver-related mortality, and was superior to MELD score (0.624, P = 0.028) for predicting 3-year liver-related mortality, but was comparable with MELD score (0.694 and 0.639, $P > 0.05$) for predicting 1-year and 5-year liver-related mortality in the derivation cohort. Validation cohort had similar results. Over a median follow-up of 39.8 (IQR 22.8–62.1) months, CHB-LC patients with RAR $\geq$ 0.453 in both derivation cohort (22.1% vs. 4.0%, $P < 0.001$) and validation cohort (25.3% vs. 10.6%, P = 0.001) had significantly higher liver-related mortality.

Conclusion: The RAR, a novel easy-to-use index, accurately predicts CHB-LC related mortality in clinical practice.



Abstract #1010

The prognostic significance of HBeAg status on the long-term outcome for chronic hepatitis B-related liver cirrhosis: A propensity score matching analysis

Haiyan Chang[1], Rui Huang[1], Jian Wang[1], Xiaomin Yan[1], Juan Xia[1], Bei Jia[1], Chuanwu Zhu[2]

[1]Nanjing Drum Tower Hospital, The Affiliated Hospital Of Nanjing University Medical School, [2]The Fifth People's Hospital Of Suzhou

Background: Serum hepatitis B e antigen (HBeAg) status is a critical predictor of the progression in patients with chronic hepatitis B (CHB). We aimed to investigate the prognostic significance of HBeAg status on the long-term outcome for CHB related liver cirrhosis (CHB-LC) using propensity score matching.
Methods: 398 CHB-LC patients were enrolled from two medical centers (2011–2017). To adjust for the selection bias of patients between HBeAg positive and HBeAg negative, we performed 1:1 match using propensity score matching. The Kaplan-Meier curve and Cox regression analysis was performed for the risk of LC-related death.
Results: After propensity score matching, 77 patients were final included in each group. There were no significant differences of liver related mortality between HBeAg positive CHB-LC and HBeAg negative CHB-LC patients before propensity score matching (8.2% vs. 14.9%, P = 0.094). However, after propensity score matching, HBeAg negative CHB-LC patients (26.0%) exhibited a significantly higher mortality than HBeAg positive CHB-LC patients (9.1%, P = 0.019) over a median follow-up of 32.1 (IQR, 17.7–50.1) months. Furthermore, after propensity score matching, HBeAg negative status (HR, 2.859; 95% CI 1.207–6.770; P = 0.017) was significantly associated with increased risks of LC-related mortality in CHB-LC patients. After adjustment for other prognostic variables in the propensity score matched cohort, HBeAg negative status was still found to be associated with higher mortality (HR, 3.032; 95% CI 1.232–7.460; P = 0.016) in patients with CHB-LC.
Conclusion: HBeAg negative status appears to be an independently risk predictor of long-term mortality for patients with CHB-LC based on propensity score matching analysis.

Abstract #1030

Th17/Treg imbalance takes an important role in the progress of chronic liver disease and is closely related with the occurrence and development of hepatocellular carcinoma

Jing You[1], Ru Yi Zhang[2], Hon Ying Chen[1], Huai E. Liu[1], Guan Hua Jia[1], Feng Xu[1], Jian Ming Chen[1]

[1]Department of Infectious Diseases, The First Affiliated Hospital of Kunming Medical University, Kunming, Yunnan, China, [2]Department of Infectious Diseases, The First People's Hospital Of Yunnan Province, Kunming, Yunnan, China

Objective: To investigate the changes of peripheral Th17 cells and Treg cells and Th17/Treg balance in patients with chronic hepatitis B virus infection, and to exploring the possible role in development process of the disease of chronic HBV infection.
Methods: Two hundred and five patients with chronic hepatitis B virus infection were involved in this study. Including 35ASC patients, 102CHB patients, 37HBV-related liver cirrhosis (LC) and 31 HBV-related hepatocellular carcinoma (HCC). Twenty-six were normal physical examination people as control group (HC). The frequency of Th17cells and Treg cells in the peripheral blood of the patients group and control group were detected by flow cytometry.
Results: Th17 cells and Treg cells of the patients in CHB, LC and HCC-groups were significantly higher than those of HC-group ($p < 0.05$). Th17 cells in LC-group was significantly higher than the other four groups; CHB-group was significantly higher than the ASC, HCC and HC-groups ($P < 0.05$). Treg cells in HCC-group was significantly higher than the other four groups, CHB-group, LC-group and HC-group were higher than the ASC-group ($P < 0.05$). Th17/Treg ratio in LC-group was significantly greater than that of other four groups; HCC-group was significantly lower than that in the other four groups, ASC-group was significantly lower than that in CHB-group and HC-group ($P < 0.05$). Th17 cells, Treg cells and Th17/Treg in four groups, were positively correlated with severity of the liver diseases ($P < 0.05$).
Conclusion: Th17/Treg imbalance takes an important role in the progress of chronic liver disease and is closely related with the occurrence and development of hepatocellular carcinoma.

Abstract #1046

Down-regulation of Cell Membrane Localized NTCP Expression in Proliferating Hepatocytes Prevents Hepatitis B Virus Infection

Ying Yan[1], Danli Yang[1], Lena Allweiss[2], Maura Dandri[2], Jingmin Zhao[3], Fengmin Lu[1]

[1]State Key Laboratory of Natural and Biomimetic Drugs, Department of Microbiology and Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing 100191, P.R. China, [2]Department of Medicine, Center for Internal Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, [3]Department of Pathology and Hepatology, Beijing 302 Hospital, Beijing 100039, P.R. China

Background and Aims: Hepatocyte proliferation could result in the loss of covalently closed circular DNA (cccDNA) and the emergence of cccDNA-cleared nascent hepatocytes, which appear refractory to hepatitis B virus (HBV) reinfection with unknown mechanism(s). This study aims to uncover the underlying molecular mechanism(s) and its related clinical significance on HBV reinfection.
Methods: The transcriptional inhibition of NTCP and the impact of NTCP protein levels on HBV infection were assayed in vivo and

in vitro. The influence of NTCP level on the antiviral treatment efficacy were determined in a cohort of 68 HBeAg-positive chronic hepatitis B (CHB) patients.
Results: p53, cyclin D1, S-phase kinase associated protein 2 and interleukin-6 transcriptionally down-regulate NTCP expression. Arresting HepG2-NTCP-tet cells in G0/G1 phase greatly up-regulated cell membrane expression of NTCP and facilitated HBV infection. HBV infection happened only after most hepatocytes had stopped proliferating and cell membrane expression of NTCP returned to normal in HBV-infected liver humanized mice. Significantly lower NTCP protein expression was strongly correlated with higher levels of hepatocyte proliferation and less HBsAg expression in HBV-related focal nodular hyperplasia (FNH) tissues. More active hepatocyte proliferation was correlated with significantly lower NTCP protein expression in CHB patients with severe active necroinflammation and better antiviral treatment outcome.
Conclusions: Within the milieu of liver regeneration, cccDNA dilution and loss, together with lower NTCP expression level, render hepatocytes resistant to HBV reinfection. These processes may accelerate virus clearance during immune-mediated cell death and compensatory proliferation in CHB patients, thus raising the hope of finally curing CHB.

Abstract #1052

HBV virions produced under nucleos(t)ide analogues treatment are not infectious due to irreversible DNA chain termination

Yongzhen Liu[1], Hui Liu[2], Zhanying Hu[3], Jingyuan Xi[4], Ju-Tao Guo[5], Lai Wei[6], Fengmin Lu[7]

[1]State Key Laboratory of Natural and Biomimetic Drugs, Department of Microbiology & Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing 100191, P.R. China, [2]State Key Laboratory of Natural And Biomimetic Drugs, Department of Microbiology & Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing 100191, P.R. China, [3]Baruch S. Blumberg Institute, Doylestown, Pennsylvania 18902, USA, [4]State Key Laboratory Of Natural and Biomimetic Drugs, Department of Microbiology & Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing 100191, P.R. China, [5]Baruch S. Blumberg Institute, Doylestown, Pennsylvania 18902, USA, [6]Peking University People's Hospital, Peking University Hepatology Institute, Beijing Key Laboratory of Hepatitis C And Immunotherapy For Liver Diseases, Beijing 100044, P.R. China, [7]State Key Laboratory of Natural And Biomimetic Drugs, Department of Microbiology & Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing 100191, P.R. China

Background and Aims: Nucleos(t)ide analogue (NA) hepatitis B virus (HBV) DNA polymerase inhibitors have been used for treatment of patients with chronic hepatitis B (CHB) for nearly two decades. This study explored the nature of nascent HBV DNA and infectivity of progeny virions produced under NA treatment.
Methods: HBV infectivity was determined by infection of HepG2-NTCP cells. Real-time quantitative PCR (qPCR), Northern blot or Southern blot hybridization, sucrose gradient centrifugation and in vitro endogenous DNA polymerase assay were performed to investigate the biochemical properties of HBV DNA in the progeny virions.
Results: The progeny HBV virions produced under NA treatment are not infectious to HepG2-NTCP cells. Biochemical analysis revealed that HBV DNA in nucleaocapsids or virions under NA treatment were predominantly irreversibly terminated short minus strand DNA, which was supported by the observation of first disappearance of rcDNA and then the proportional decline of HBV DNA levels corresponding to the regions of PreC/C, S and X genes in serial sera of patients receiving NA treatment.
Conclusions: HBV virions produced under NA treatment are predominantly replication deficient because the viral genomes are truncated and elongation of DNA chains is irreversibly terminated. Clinically, our results suggest that the viral loads of CHB patients under NA therapy vary with the different regions of genome being detected by qPCR assays. Our findings also imply that NA prevention of perinatal and sexual HBV transmission as well as infection of transplanted livers works not only by reducing viral loads, but also by producing non-infectious virions.

Abstract #1055

A novel HBsAg assay based light initiated chemiluminesence technology: is it reliable for screening HBV infection and quantifying HBsAg?

Ruifeng Yang[1], Liyan Cui[2], Lai Wei[1]

[1]Peking University People's Hospital, Peking University Hepatology Institute, Beijing Key Laboratory of Hepatitis C and Immunotherapy for Liver Diseases, [2]Peking University Third Hospital

Introduction: HBsAg assay has been used to screen HBV infection for decades. The use of quantitative HBsAg assay is also clinically rejuvenated recently.
Objectives: We aimed to evaluate a new quantitative assay, the Chivd Lica HBsAg assay, which is based on a principle of light initiated chemiluminesence immunoassay (Lica).
Methodology: Consecutive routine clinical serum samples were tested in parallel using the Lica and Abbott Architect HBsAg assays. Samples with inconsistent qualitative results were subjected to the neutralization assay, or the Roche Taqman HBV DNA assay, or the Roche Elecsys HBsAg assay for further confirmation. Consistency was calculated, and performance characteristics including sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were compared. Correlation was also analyzed for the quantitative results.
Results: Totally, 5176 samples were tested. The Lica and Architect assays showed a consistency of 99.63% with a Kappa value of 0.99. Characteristics parameters were also satisfactory. The Lica assay showed a higher specificity (99.95% vs. 99.75%) and PPV (99.75% vs. 98.65%) than the Architect assay, while the latter showed better sensitivity (100.00% vs.99.25%) and NPV (100.00% vs.99.86%) than the former. Two assays displayed an excellent linear correlation for samples with HBsAg levels ranging from 0.05 to 150.00 IU/ml ($r^2 = 0.90$, $P < 0.001$).
Conclusion: The Chivd Lica HBsAg assay provides a reliable tool for screening HBV infection. It is also accurate to quantify the serum HBsAg, which makes it useful for monitoring the baseline and on-treatment HBsAg levels and benefiting the treatment option as well as the antiviral response prediction.

Abstract #1087

Correlation of liver fibrosis with HbsAg titer among chronic hepatitis B and HBV/HDV co-infected patients

Zolzaya Sumiyajav[1], Nasanbayar Tumurbaatar[1], Budmaa Dashlkhundev[1], Namuuntsetseg Gankhuyag[1], Ankhbayar Bat-Ochir[2], Enkhtuya Damba[2], Batbayar Purev [2], Badamgerel Chinzorigt [2], Erdenebayar Gonchig[3], Baatarkhuu Oidov[3], Bold Manaljav[1], Amarsanaa Jazag[3]

[1]Etugen University, [2]Happy Veritas Hospital, Mongolian Association for the Study of Liver (MASLD)

Background: Mongolia is a country with high prevalence HBV infection. Approximately 10% of apparently healthy population is infected with HBV. HBV is one of main causes of liver cirrhosis and HCC in our country. As a result Mongolia has the highest prevalence of HCC and HCC related mortality in the world. About 723 people die each year due to liver cirrhosis. Though quantitative HbsAg assays were introduced in Mongolia quite recently, this study focuses on HbsAg's contribution to develepment of liver cirrhosis.
Methods: Retrospective analysis 5672 patients who were assessed for liver stiffness by transient elastography at Happy Veritas Hospital was performed. Out of those patients 2,822 patients were positive for HBV or HBV and HDV. Only 231 patients had a full set of tests including both quantitative HbsAg assay and transient elastography. Transient elastography was performed using equipments Fibrotouch (HISKY) and Fibroscan (Echosens). There was no difference in results between the 2 equipment. Quantitative HbsAg assay was performed using Analyzer HISCL-800 by Sysmex Corporation. Because our objective was to assess HbsAg titer's contribution to development of liver cirrhosis and it is also well known that development of LC depends on time passed since infection we classified our patients into age groups 10–20, 20–30, 30–40, 40–50, 50–60, 60–70 and 70–80
Result: There was no significant difference in HbsAg amount in patients with absense of presense of liver fibrosis, except for age of 60–70. In this group of patients HbsAg amount was low in non-cirrhotic patients 421 IU vs. cirrhotic patients 7,549 IU. We observed differences in amount of HBsAg between HBV infected and HBV/HDV co-infected patients as fibrosis develops. In non-cirrhotic patients (fibrosis stage 0, F-0) mean HbsAg was 68.3% higher in HBV infected patients (10,343 IU) than HBV/HDV co-infected ones (3285 IU). In fibrosis stage 1 patients (F-1) mean HbsAg was 5.5% higher in HBV infected patients (4,818 IU) than HBV/HDV co-infected ones (4555 IU). In fibrosis stage 2 patients (F-2) mean HbsAg was 78% lower in HBV infected patients (1231 IU) than HBV/HDV co-infected ones (5,584 IU). In fibrosis stage 3 patients (F-3) mean HbsAg was 31.2% lower in HBV infected patients (4,686 IU) than HBV/HDV co-infected ones (6,810 IU).). In cirrhotic patients (F-4) the mean HbsAg was 25.9% lower in HBV infected patients (4,887 IU) than HBV/HDV co-infected ones (6,596 IU).
Conclusion: HbsAg titer is tend to increase as liver figrosis stage increases in HBV/HDV co-infected patients. But HBV mono-infected patients this trend is not that clear. We need to further study to explain molecular biologic causes of this result.

B03 - Treatment

Abstract #70

Improvement of hepatic fibrosis in naive chronic hepatitis B virus infected patientspost Entecavir antiviral therapy

Ali Abdelrahman Ghweil[1], Heba Osman [2], Ashraf Khodery[3]

[1]Qena Faculty of Medicine South Valley University, [2]Lecturer of Gastroentrology South Valley University, [3]Lecturer of Clinical Pathology Sohag University

Background and Aims: Chronic hepatitis B virus infection affects more than 3 million people worldwide. The present study aimed to evaluate the effect of entecavir on HBV related hepatic fibrosis and assess factors responsible for post treatment fibrosis regression.
Patients and Methods: This prospective cohort study has been conducted on 74 naieve patients with chronic HBV infection with variable degree of hepatic fibrosis (F2, F3, $\geq$ F4), viral load, and variable degree of abnormality in laboratory parameters of liver functions. All patients treated with Entecavir 0.5 mg/day or 1 mg/day according to severity of hepatic condition for 1 year. liver fibrosis assessed using fibroscan, factor IV collagen, (APRI) and (FIB-4) scores evaluation.
Results: All included patients in our study achieve post treatment Virological response with undetectable HBV DNA PCR (< 16 IU/ml). With significant post treatment reduction in mean fibroscan value 10.70 ± 5.80 ($p < 0.001$**). There were also significant end treatment improvements in mean FIB score and APRI score 1.56 ± 1.02 ($p < 0.0001$***) and 0.50 ± 0.28 ($p < 0.0001$***) respectively. There is significant end treatment improvement of mean factor IV collagen. In our study 49 (66.22%) of included patients showed post treatment reduction in their level of hepatic fibrosis (Responder) opposite to 25 (33.78%) had no post treatment improvement in Degree of hepatic fibrosis (Non- responder).
Conclusions: Entecavir therapy once daily for 12 months was associated with significant decrease in hepatic fibrosis with obvious improvement in liver function tests so its reasonable treatment option for HBV-associated hepatic fibrosis.
Keywords: Entecavir; hepatic fibrosis; HBV.

Abstract #118

Tenofovir treatment reduces hepatic decompensations, hepatocellular carcinoma and deaths in chronic hepatitis B patients with cirrhosis

Ken Liu[1], Jonggi Choi[2], An Le[3], Vincent Wai-Sun Wong[4], Stephen Lam Chan[5], Mindie H Nguyen[6], Young-Suk Lim[7], Grace Lai-Hung Wong[8]

[1]AW Morrow Gastroenterology And Liver Centre, Royal Prince Alfred Hospital, Sydney, Australia & Sydney Medical School, Sydney, Australia, [2]Department of Gastroenterology, Asan Medical Center, University of Ulsan, [3]Division of Gastroenterology and Hepatology, Stanford University School of Medicine, [4]Department of Medicine And Therapeutics, The Chinese University of Hong Kong, Hong Kong & State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong & Institute of Digestive Disease, The Chinese University of Hong Kong, Hong Kong, [5]Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong, [6]Division of Gastroenterology and Hepatology, Stanford University School of Medicine, [7]Department of Gastroenterology, Asan Medical Centre, University Of Ulsan,

[8]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong & State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong & Institute of Digestive Disease, The Chinese University of Hong Kong, Hong Kong

Introduction: Lamivudine and entecavir have been shown to reduce decompensation, hepatocellular carcinoma (HCC) and death in chronic hepatitis B (CHB) patients with cirrhosis. Tenofovir disoproxil fumarate (TDF) is a potent antiviral agent with no documented resistance to date, but its impact on cirrhotic patients is unclear. We aimed to investigate the effectiveness of TDF therapy in CHB patients with cirrhosis.
Methods: We studied 808 TDF-treated and 291 untreated CHB cirrhotic patients from 3 centres (Hong Kong, Korea, US). Cirrhosis was defined by liver histology, thrombocytopenia ($< 150 \times 10^9$/L) and/or features of portal hypertension on imaging. TDF cohort included consecutive patients from three tertiary centres who received TDF 300 mg/day for $\geq$ 12 months. Control cohort included historical untreated patients.
Results: TDF-treated patients were 69% men, mean age 54 $\pm$ 10 years, and 47% hepatitis B e antigen (HBeAg) positive. Untreated controls were 78% men, mean age 50 $\pm$ 9 years and 24% HBeAg positive. At 5-years follow-up, there were 72 decompensating events, 113 HCCs and 41 deaths from both groups combined. 5-year cumulative probabilities in TDF-treated vs. control cohorts were (Figure 1): 8% vs. 22% for decompensation (P = 0.002), 10% vs. 15% for HCC (P = 0.05) and 1% vs. 12% for death ($P < 0.001$). On multivariate Cox regression (Table 1), TDF treatment was independently associated with reduced risks of decompensation (hazard ratio [HR] 0.41, P = 0.046), HCC (HR 0.42, P = 0.001) and death (HR 0.05, $P < 0.001$).
Conclusions: Among patients with cirrhosis, TDF treatment reduces risks of hepatic decompensation and HCC by more than 2-fold and death by 95% at 5 years.

Figure 1. Kaplan-Meier analysis of cumulative probability of (A) Decompensation, (B) HCC, and (C) death in TDF-treated vs. untreated CHB patients with cirrhosis

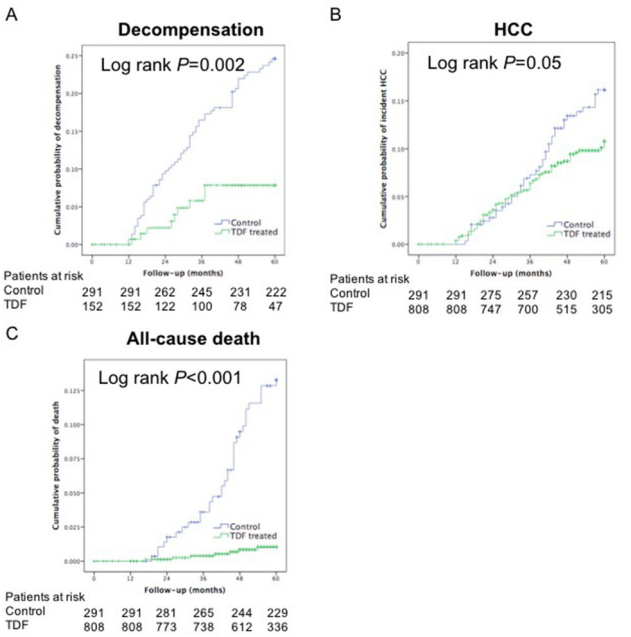


Table 1. Predictors of decompensation, hepatocellular carcinoma, and death at 5 years on multivariate Cox regression analysis

Decompensation predictors	**HR**	**95% CI**	***P***
TDF treatment (yes vs. no)	0.41	0.17-0.99	0.046
Platelet count (per 10^9/L increase)	0.99	0.98-0.99	0.017
Serum albumin (per g/L increase)	0.92	0.86-0.98	0.002
INR (per unit increase)	9.9	2.31-42.25	0.015
HCC predictors	**HR**	**95% CI**	***P***
TDF treatment (yes vs. no)	0.42	0.27-0.69	0.001
Serum albumin (per g/L increase)	0.94	0.90-0.97	<0.001
Death predictors	**HR**	**95% CI**	***P***
TDF treatment (yes vs. no)	0.05	0.02-0.12	<0.001
INR (per unit increase)	21.24	4.91-91.90	<0.001

HR = hazard ratio, INR = international normalised ratio, CI = confidence interval, HCC = hepatocellular carcinoma, TDF = tenofovir disoproxil fumarate

Abstract #184

Hepatitis B reactivation after stopping Nucleoside analogues in treatment naïve patients with low HBV DNA undergoing immunosuppression

Tan Yi Yuan[1], Rajneesh Kumar[2]

[1]Ministry of Health Holdings & Singapore General Hospital Department of Gastroenterology, [2]Singapore General Hospital & Singapore General Hospital Department of Gastroenterology

Introduction: In Singapore, 3.6% adults are chronic hepatitis B(CHB) carriers. Advances in medical therapy, especially in oncology and rheumatology, brings attention to increased risks in HBV reactivation from immunosuppression. Antiviral prophylaxis during and up until 6–12 months after discontinuation of immunosuppressive therapy has been recommended.
Aim: To observe the frequency of reactivation in treatment naïve patients with low HBV DNA who received antiviral prophylaxis during and up to 1 year after cessation of immunosuppression.
Methodology: A retrospective analysis of patients on follow-up for hepatitis B at Singapore General Hospital requiring immunosuppression was conducted. The studied population had low HBV DNA levels, defined as less than 1000 iu/ml prior to starting treatment and received nucleoside analogues (NA) for viral suppression. NAs were continued for 1 year after cessation of immunosuppression, during which monitoring of reactivation with HBV DNA loads and Alanine Transaminase (ALT) was carried out. Reactivation was defined as a rise in levels of HBV DNA of more than 1 log after stopping NA, from levels of < 20 iu/ml while on NA.
Results: 10 patients with low HBV DNA before starting immunosuppression were studied. The mean age was 64.6 years ($\pm$ 9.51), where 80% were Chinese. All patients received chemotherapy. Entecavir (80%) or lamivudine (20%) was used for prophylaxis. 20% had viral reactivation, none with elevation of ALT.
Conclusion: Even in patients with low HBV DNA, there was a risk of HBV reactivation. All patients even with low HBV DNA should be followed up closely for monitoring of HBV DNA to prevent a flare.

Abstract #188

A Single and Multiple Ascending Dose Study of Toll-Like Receptor 7 (TLR 7) Agonist (RO7020531) in Chinese Healthy Subjects

Andrea Luk[1], Joseph F. Grippo[2], Ilia Folitar[3], Miriam Triyatni[4], Katerina Glavini[5], Lynna Zhao[6], Ruchi Upmanyu[7], Tomas Racek[8], Steffen Hoppe[9], Benny Fok[10], Yonghong Zhu[11], Yuyan Jin[12], Qiudi Jiang[13]

[1]Prince Of Wales Hospital, Hong Kong, China, [2]Roche Innovation Center New York, Us, [3]Roche Innovation Center Basel, Switzerland, [4]Roche Innovation Center Basel, Switzerland, [5]Roche Innovation Center Basel, Switzerland, [6]roche Pharma Development Shanghai, China, [7]Roche Pharma Development Welwyn, Uk, [8]Roche Innovation Center Basel, Switzerland, [9]Roche Innovation Center Basel, Switzerland, [10]Prince Of Wales Hospital, Hong Kong, China, [11]Roche Innovation Center Shanghai, China, [12]Roche Innovation Center Shanghai, China, [13]Roche Innovation Center Shanghai, China

Introduction and Objectives: RO7020531, an oral double prodrug of the TLR7-specific agonist, RO7011785, is being developed for the treatment of chronic hepatitis B (CHB). Single and multiple doses up to 170 mg of RO7020531 were safe and well tolerated in healthy volunteers (HVs) and CHB patients in global first-in-human study. Here we present the data from the ongoing study in Chinese HVs.
Methodology: 4 single ascending dose (SAD) and 3 multiple ascending dose (MAD) cohorts were planned, with 10 subjects (8 RO7020531, 2 placebo) in each cohort. Safety and tolerability were monitored throughout the study. Blood samples for the assay of pharmacokinetics (PK) and pharmacodynamics (PD) markers were collected. The fourth SAD and MAD cohorts are ongoing.
Results: RO7020531 at single doses (40, 100 and 140 mg) was safe and well tolerated in Chinese HVs. No serious AEs and no clinically significant changes or patterns in ECG, vital signs, or laboratory safety test results were reported. Following single doses of RO7020531 from 40–140 mg, mean plasma Cmax and AUCinf of the active TLR7 agonist RO7011785 increased proportionally with dose and were consistent with the global Phase I study. Single doses of RO7020531 at 100 mg induced increases in serum IFN-α, IL-10, IP-10 and neopterin, as well as in mRNA species including ISG-15, OAS-1 and MX1.
Conclusions: RO7020531 was safe and well tolerated in Chinese HVs following single doses. The PK exposure to the active TLR7 agonist, RO7011785 increased proportionally with dose and correlated with an increase in biomarkers of TLR7 pathway activation.

Abstract #197

No difference in Efficacy of NA therapy in HBeAg negative Chronic Hepatitis B Patients with and without Nonalcoholic Fatty Liver Disease

Chong Jie Gan[1], Ming Xing Huang[1], Peng Yuan He[1], Ruo Man Ke[1], Jin Yu Xia[1]

[1]The Fifth Affiliated Hospstial of Sun Yat-Sen University

The coexistence of nonalcoholic fatty liver disease (NAFLD) and HBV infection becomes a common characteristic of liver disease in China. However, there is still limited data to show their bilateral influence in both disease development and therapeutic response. We sought to compare antiviral efficacy of HBeAg negative (-) chronic hepatitis B patients (CHB) with and without NAFLD through a follow-up study in our hospital. A total of 122 HBeAg (-) CHB patients were evaluated in this study with 62 with NAFLD group and another 60 patients without NAFLD for up to 288 weeks. There were no significant differences at virological response (VR) rates either at the beginning or end of treatment, 3.2% vs 1.7% (P = 0.578) at week 4, 6.5%vs 8.3% (P = 0.691) at week 12 and 98.4% vs 1 (P = 0.323) at week 96. However, VRrates of patients in the CHB without NAFLD group were significantly higher at week 36 than the CHB with NAFLD group (66.7% vs 48.3% respectively, P = 0.041). And at the beginning and end of treatment, ALT normalization rates of the two groups was not statistically different. And there were significantly higher in the without NAFLD group than with NAFLD group from week 36 to 72 (73.3% vs 46.8% respectively, P = 0.003 at week 36, 83.3% vs. 59.7% respectively, P = 0.004 at week 48; 95.5% vs. 80.6% respectively, P = 0.016 at week 72). In summary, HBeAg negative CHB with NAFLD does not affect virological and biochemical responses in the treatment of nucleoside analogs.

Abstract #214

The Use of Tenofovir Disoproxil Fumarate (TDF) in the Management of Patients with Inactive Chronic Hepatitis B (CHB) Infection

Nishita Jagarlamudi[1], Melissa Reyes[1], Florence Wong[1]

[1]Toronto General Hospital

Chronic hepatitis B (CHB) infection is common worldwide with approximately 400 million patients affected. Patients with inactive CHB can undergo spontaneous reactivation and progression of fibrosis. They also carry a risk of developing hepatocellular carcinoma (HCC) despite their inactive carrier state.
Aim: To assess the impact of HBV treatment with TDF on its ability to induce HBsAg seroconversion, thus decreasing their risk of HBV flares and HCC.
Methods: Patients with chronic inactive HBV infection, defined as persistently low HBV DNA of ≤ 3 logs, eAb +, sAg + and normal liver enzymes for > 6 months were prospectively recruited. Patients were given TDF 300 mg daily after baseline liver blood enzymes, liver function tests, HBV DNA, HBV serology, liver ultrasound, fibroscan and fibrotest, and reviewed 6 monthly at which time all blood works were repeated. Liver ultrasound, fibroscan and fibrotest were repeated annually. Patients were monitored for HBV flares, progression of fibrosis, development of HCC and possible sAg seroconversion.
Results: Results of 25 non-cirrhotic patients who completed 24 months follow-up of this ongoing study are presented. These were 9 males and 16 females, mean age 48.2 ± 8.9 years, 20 Asians, 3 Caucasians and 2 Africans. 2 patients withdrew, one due to unplanned pregnancy, 1 because of sAg seroconversion at 6 months. The sAg conversion rate was 4% at 12 months compared to spontaneous loss at 1 year of 1–1.9% (1). No patient had HBV flares and there were no HCC. No patient had any side effects.
References: 1) Invernizzi F, et al. Liver Int. 2016 Jan;36 Suppl1: 100–4.

	ALT (IU/ml)	Creatinine (μmol/L)	DNA (X1000 IU/ml)	sAg (IU/ml)	Fibroscan Score (kPa)	Fibrotest
Baseline	20±8	70±11	2.737±2.778	4082±5679	5.6±1.7	0.19±0.11
M12	23±9	72±13	0.005±0.008*	4706±7003	4.9±1.3	0.25±0.12
M24	23±8	73±11	0.004±0.008*	4316±5867	4.5±1.0*	0.28±0.16

* p<0.05 compared to baseline. 15 patients had negative HBV DNA at 12 months, and 16 at 24 months. Conclusions: The use of TDF in patients with inactive CHB led to a significant reduction of HBV DNA, associated with a significant reduction in fibrosis score. Longer term follow-up is needed to determine whether its use will positively impact the prognosis of these patients.

Abstract #231

Continuing Besifovir Depivoxil Maleate Versus Switching from Tenofovir Disoproxil Fumarate for Treatment of Chronic Hepatitis B: 144 weeks Results of Phase 3 Trial

Hyung Joon Yim[1], Sang Hoon Ahn[2], Won Kim[3], Jin Mo Yang[4], Jae Young Jang[5], Yong Oh Kweon[6], Yong Kyun Cho[7], Yoon Jun Kim[8], Gun Young Hong[9], Dong Joon Kim[10], Soon Ho Um[11], Joo Hyun Sohn[12], Jin Woo Lee[13], Sung Jae Park[14], Byung Seok Lee[15], Ju Hyun Kim[16], Hong Soo Kim[17], Seung Kew Yoon[18], Moon Young Kim[19], Kwan Sik Lee[20], Young Suk Lim[21], Wan Sik Lee[22], Kwang-Hyub Han[23]

[1]Korea University College of Medicine, [2]Yonsei University College of Medicine, [3]Seoul National University College of Medicine, [4]Catholic University Medical College St. Vincent's Hospital, [5]College of Medicine, Soonchunhyang University, [6]Kyungpook National University College of Medicine, [7]Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, [8]Seoul National University College of Medicine, [9]Kwangju Christian Hospital, [10]Hallym University College of Medicine, [11]Korea University College of Medicine, [12]Hanyang University College of Medicine, [13]Inha University College of Medicine, [14]Paik Hospital, Inje University, [15]Chungnam National University School Of Medicine, [16]Gacheon University College Of Medicine, [17]Soonchunhyang University College of Medicine, [18]Catholic University of Korea, [19]Yonsei University Wonju College of Medicine, [20]Yonsei University College of Medicine, [21]Asan Medical Center, University of Ulsan College of Medicine, [22]Chonnam University Medical School, [23]Yonsei University College of Medicine

Background/Aims: Besifovir dipivoxil maleate (BSV) is an acyclic nucleotide phosphonate with a potent antiviral activity against hepatitis B virus (HBV). An antiviral efficacy of BSV for forty-eight week was shown to be comparable to tenofovir disoproxil fumarate (TDF) with improved renal and bone safety. We evaluated the efficacy and safety of BSV in treatment-naïve chronic hepatitis B patients in 144 weeks follow-up study.
Methods: After 48 weeks of double-blind comparison of BSV to TDF, patients continued to participate in the open-label BSV study. We evaluated antiviral efficacy and drug safety for both BSV group (BSV-BSV) and the group switched from TDF to BSV (TDF-BSV) up to 144 weeks. The primary endpoint was the proportion with HBV DNA < 400 copies/mL (virological response).
Results: Among 197 patients who received randomized treatments, 170 (87%) patients entered the open-label phase, and 153 (78%) completed 144 weeks of the study. The virological response rate of those who have taken BSV over 144 weeks is 87.65% while 92.11% of patients who switched the treatment from TDF were respondent (p = 0.36). HBeAg seroconversion and ALT normalization rates were similar between the groups. There were no drug resistant mutations to BSV and no adverse events related to bone mineral density or renal function.
Conclusions: BSV maintained efficacy in both suppression of HBV DNA and ALT normalization over 144 weeks without any evidence of resistance to BSV. Also, BSV is safe, well tolerated, and effective for those who have switched to BSV from TDF.

Abstract #263

Long-term renal and bone safety of tenofovir disoproxil fumarate in chronic hepatitis B patients with cirrhosis

Ken Liu[1], Jonggi Choi[2], An Le[3], Vincent Wai-Sun Wong[4], Stephen Lam Chan[5], Mindie H Nguyen[6], Young-Suk Lim[7], Grace Lai-Hung Wong[8]

[1]AW Morrow Gastroenterology And Liver Centre, Royal Prince Alfred Hospital, Sydney, Australia & Sydney Medical School, Sydney, Australia, [2]Department of Gastroenterology, Asan Medical Centre, University of Ulsan, [3]Division of Gastroenterology and Hepatology, Stanford University School of Medicine, [4]Department of Medicine And Therapeutics, The Chinese University of Hong Kong, Hong Kong & State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong & Institute of Digestive Disease, The Chinese University Of Hong Kong, Hong Kong, [5]Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong, [6]division of Gastroenterology and Hepatology, Stanford University School of Medicine, [7]Department Of Gastroenterology, Asan Medical Centre, University of Ulsan, [8]Department of Medicine And Therapeutics, The Chinese University of Hong Kong, Hong Kong & State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong & Institute of Digestive Disease, The Chinese University of Hong Kong, Hong Kong

Introduction: Although real-life data suggests that TDF is generally safe, there are renal and bone safety concerns. Long-term data in patients with cirrhosis is limited. We aimed to investigate long-term renal and bone toxicity of TDF therapy in chronic hepatitis B (CHB) patients with cirrhosis.
Methods: We studied two CHB cirrhotic cohorts: one treated with TDF and one untreated historical control group. Cirrhosis was defined by liver histology, thrombocytopenia ($< 150 \times 10^9$/L) and/or features of portal hypertension clinically or on imaging. TDF cohort included consecutive patients from 3 tertiary centres who received TDF 300 mg/day for ≥ 12 months. Estimated glomerular filtration rate (eGFR) and 5-year cumulative probabilities of chronic kidney disease (CKD) progression ≥ 1 stage and fracture were compared.
Results: For renal outcomes, we analysed 935 TDF-treated (baseline mean eGFR 92 mL/min/1.73m2) and 69 untreated cirrhotics (baseline mean eGFR 85 mL/min/1.73m2). At 5-year follow-up, there was less eGFR decline in TDF-treated patients vs. controls (− 5 mL/min/1.73m2 vs. − 13 mL/min/1.73m2, $P < 0.001$) (Figure 1). 5-year probability of CKD progression was lower in TDF-treated patients vs. controls (19% vs. 42%, $P < 0.001$). TDF treatment was associated with less CKD progression (hazard ratio 0.4, $P < 0.001$) even after adjusting for age and baseline eGFR. For bone outcomes, we analysed 443 TDF-treated and 291 untreated cirrhotic patients and found similar 5-year probability of fracture in TDF-treated patients vs. controls (5% vs. 3%, P = 0.174) (Figure 2).

Conclusions: Among CHB patients with cirrhosis, TDF treatment appears safe with no significant increase in eGFR decline, CKD progression, or fracture risk compared to untreated patients.

Figure 1. (A) Change in eGFR in TDF-treated vs. untreated CHB patients with cirrhosis over time (B) Kaplan-Meier analysis of cumulative probability of CKD progression in TDF-treated vs. untreated CHB patients with cirrhosis

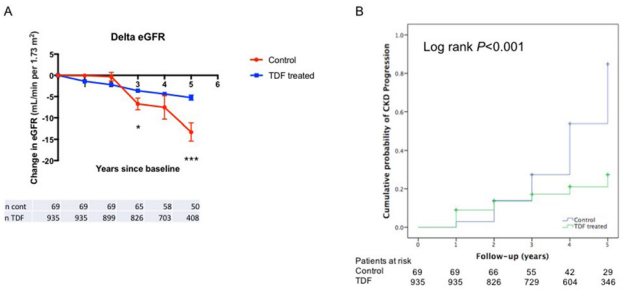
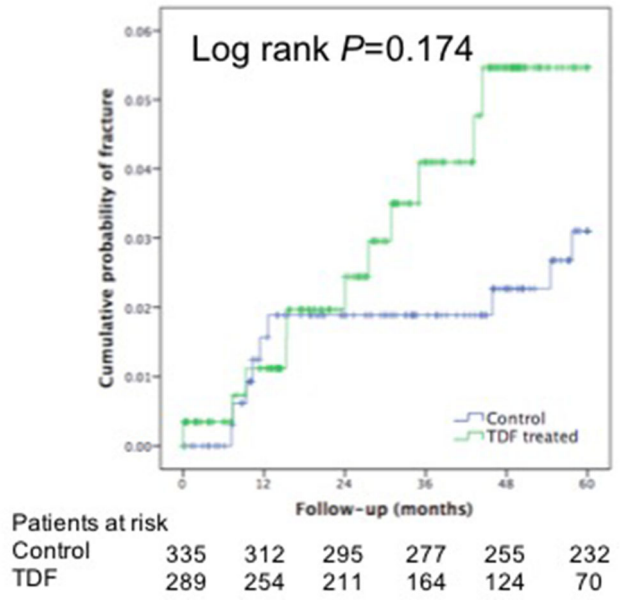


Figure 2. Kaplan-Meier analysis of cumulative probability of fracture in TDF-treated vs. untreated CHB patients with cirrhosis



Abstract #274

No Resistance to Tenofovir Alafenamide (TAF) Detected Through 144 Weeks of Treatment in Patients with Chronic Hepatitis B (CHB)

Young-Suk Lim[1], Yang Liu[2], Bandita Parhy[2], Silvia Chang[2], Ross Martin[2], Becket Feierbach[2], Hongmei Mo[2], Anuj Gaggar[2], John Flaherty[2], Namiki Izumi[3], Henry Lik-Yuen Chan[4]

[1]Asan Medical Center, Seoul, South Korea, [2]Gilead Sciences, [3]Japanese Musashino Red Cross Hospital, Tokyo, Japan, [4]Institute of Digestive Disease and State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong

Aim: Cumulative resistance analyses were performed through Week 144 for 2 Phase 3 studies (GS-US-320-0108, GS-US-320-0110) evaluating TAF or tenofovir disoproxil fumarate (TDF) for the treatment of CHB in HBeAg + and HBeAg- treatment-naïve or treatment-experienced adults.
Methods: Patients were randomized 2:1 to receive TAF or TDF double-blind (DB) treatment for 144 weeks, and were then switched to open-label (OL) TAF. HBV pol/RT deep sequencing was conducted for any patient with $\geq$ 24 weeks of treatment and HBV DNA $\geq$ 69 IU/mL at Week 144 or at early discontinuation. Illumina Mi-Seq deep sequencing was conducted and sequence changes at the consensus sequence level (15%) were reported. In vitro phenotypic analysis using recombinant HBV in HepG2 cells was performed for: VB patients who were adherent to study drug, those with conserved site substitutions, or when polymorphic substitutions emerged in > 1 patient.
Results: 1298 patients were randomized and treated with TAF (n = 866) or TDF (n = 432). Through Week 144, 9.9% (TAF, 10.4%; TDF DB, 11.9%) of enrolled patients qualified for sequencing at their last evaluable visit; Of these 128 patients, 63 had no sequence change from baseline, 22 were unable to sequence, 31 had polymorphic site substitutions, and 12 had conserved site substitutions. Cumulatively, 70 patients qualified for phenotypic analysis and no isolates showed reduction in susceptibility to TAF or tenofovir (TAF: n = 54, mean fold change EC50 0.99, range 0.32–1.68; tenofovir: n = 16, mean fold change EC50 0.92, range 0.33–1.45).
Conclusion: No substitutions associated with resistance to TAF were detected through 144 weeks of treatment.

Abstract #279

Prognostic value of various liver scoring systems in chronic hepatitis B patients with cirrhosis and the effect of treatment with tenofovir disoproxil fumarate

Jonggi Choi[1], Ken Liu[2], An Le[3], Vincent Wai-Sun Wong[4], Stephen Lam Chan[5], Mindie H Nguyen[6], Young-Suk Lim[7], Grace Lai-Hung Wong[8]

[1]Department of Gastroenterology, Asan Medical Centre, University of Ulsan, [2]AW Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital, Sydney, Australia & Sydney Medical School, Sydney, Australia, [3]Division of Gastroenterology and Hepatology, Stanford University School of Medicine, [4]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong & State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong & Institute of Digestive Disease, The Chinese University of Hong Kong, Hong Kong, [5]Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong, [6]Division of Gastroenterology and Hepatology, Stanford University School of Medicine, [7]Department of Gastroenterology, Asan Medical Centre, University of Ulsan, [8]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong & State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong & Institute of Digestive Disease, The Chinese University of Hong Kong, Hong Kong

Introduction: Various scoring systems predict risk of decompensating events and deaths (Child-Pugh, model for end-stage liver disease [MELD]) and chronic hepatitis B (CHB)-related hepatocellular carcinoma (CU-HCC, REACH-B, PAGE-B). The performance of these scores in CHB patients with cirrhosis treated with tenofovir disoproxil fumarate (TDF) is unclear. We aimed to investigate the predictive

value of these scores for hepatic decompensation, hepatocellular carcinoma (HCC) and death.

Methods: Two CHB cirrhotic cohorts were retrospectively studied. Cirrhosis was defined by liver histology, thrombocytopenia ($< 150 \times 10^9$/L) and/or features of portal hypertension on imaging. TDF cohort included consecutive patients from three centres who received TDF 300 mg/day for $\geq$ 12 months. Control cohort included historical untreated patients.

Results: 808 TDF-treated and 291 control patients were studied. There were 72 decompensating events, 113 HCC and 41 deaths at 5-years follow-up. Among untreated controls, baseline Child-Pugh and MELD scores were predictive for decompensation, HCC and death at 5 years (Table 1). REACH-B and CU-HCC scores were predictive for HCC. Areas under receiver operator characteristics curve were best for Child-Pugh and CU-HCC scores. Scores lost their predictive value for events in the TDF-treated cohort, except Child-Pugh, CU-HCC and PAGE-B were predictive for HCC. TDF treatment led to significant improvements in all scores except PAGE-B after 1-year follow-up compared to baseline, which were sustained at 5-years follow-up (Figure 1).

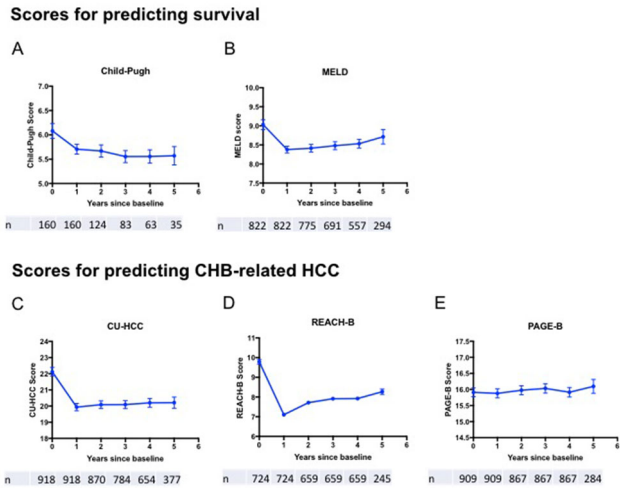
Conclusions: Baseline liver prognostic scores have predictive value for liver events and deaths in untreated but not TDF-treated CHB patients with cirrhosis. TDF treatment led to sustained improvements in prognostic scores.

Table 1. Predictive value of each scoring system based on univariate Cox regression model for liver events and deaths at 5-years follow-up

SCORE	UNTREATED PATIENTS			TDF-TREATED PATIENTS		
Decompensation	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
Child-Pugh (per point increase)	2.32	1.76-3.05	**<0.001**	1.25	0.39-4.00	0.712
MELD (per point increase)	1.22	1.13-1.31	**<0.001**	1.10	0.92-1.30	0.288
HCC	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
Child-Pugh (per point increase)	1.84	1.38-2.45	**<0.001**	1.37	1.03-1.82	**0.032**
MELD (per point increase)	1.16	1.04-1.29	**0.008**	1.02	0.93-1.11	0.696
CU-HCC (per point increase)	1.09	1.03-1.15	**0.002**	1.05	1.02-1.08	**<0.001**
REACH-B (per point increase)	1.31	1.04-1.64	**0.021**	1.04	0.96-1.12	0.393
PAGE-B (per point increase)	1.03	0.93-1.15	0.556	1.09	1.03-1.16	**0.007**
Death	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
Child-Pugh (per point increase)	2.18	1.54-3.09	**<0.001**	0.85	0.18-4.00	0.832
MELD (per point increase)	1.35	1.19-1.52	**<0.001**	0.97	0.69-1.38	0.883

HR = hazard ratio, CI = confidence interval, HCC = hepatocellular carcinoma, MELD = model for end-stage liver disease, TDF = tenofovir disoproxil fumarate

Figure 1. Trend of various liver scores over time in TDF-treated CHB patients with cirrhosis. (A) Child-Pugh and (B) MELD for predicting survival and (C) CU-HCC, (D) REACH-B and (E) PAGE-B scores for predicting HCC.



Abstract #309

Paired liver biopsies in combination with serial liver stiffness measurements in monitoring histological improvement among CHB patients with long-term nucleos(t)ide analogue therapy

Rong Fan[1], Junqi Niu[2], Qing Xie[3], Shijun Chen[4], Guangfeng Shi[5], Hao Wang[6], Xiaoguang Dou[7], Deming Tan[8], Min Xu[9], Yanyan Yu[10], Jun Cheng[11], Hongfei Zhang[12], Xinyue Chen[13], Jinlin Hou[14], Effort Study Group[15]

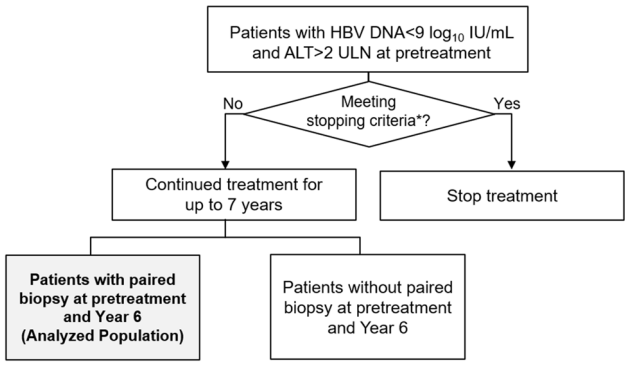
[1]Hepatology Unit, Nanfang Hospital, Southern Medical University, Guangzhou, [2]Hepatology Unit, No. 1 Hospital Affiliated to Jilin University, Changchun, [3]Department of Infectious Diseases, Ruijin Hospital, Shanghai, [4]Ji'nan Infectious Diseases Hospital, Ji'nan, [5]Department of Infectious Diseases, Huashan Hospital, Fudan University, Shanghai, [6]Hepatology Unit, Peking University People's Hospital, Beijing, [7]Department of Infectious Diseases, Shengjing Hospital of China Medical University, Shenyang, [8]Department of Infectious Diseases, Xiangya Hospital, Central South University, Changsha, [9]8th People's Hospital, Guangzhou, [10]Department of Infectious Diseases, First Hospital of Peking University, Beijing, [11]Beijing Ditan Hospital, Beijing, [12]302nd Pla Hospital, Beijing, [13]Beijing Youan Hospital, Beijing, [14]Hepatology Unit, Nanfang Hospital, Southern Medical University, Guangzhou

Background: Two-year telbivudine optimization strategy based on "ROADMAP CONCEPT" in nucleos(t)ide-naïve patients with HBeAg-positive chronic hepatitis B (CHB) resulted in significantly improved liver histology (EFFORT Study). Patients who received long-term optimization strategy were evaluated further for improvements in liver histology.

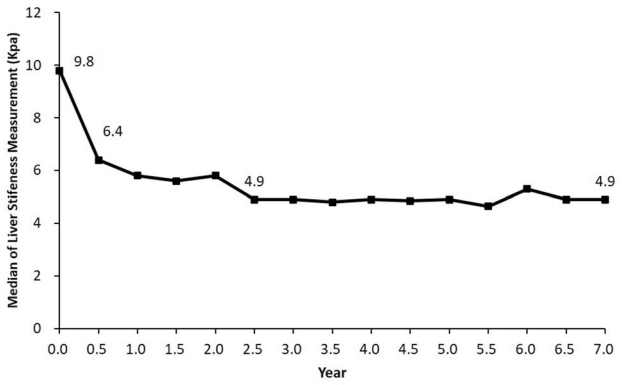
Methods: Patients in EFFORT study with pretreatment HBV DNA $<$ 9 log10 copies/mL and ALT $>$ 2 ULN, who did not meet APASL guideline recommended stopping criteria within 5 years, continued to be treated with telbivudine with/without adefovir for further 2 years (total 7 years), and underwent liver biopsy at year 6 (Figure 1). Liver stiffness measurement (LSM) was performed by Fibroscan® every 6 months.

Results: Histological improvement was analyzed for 56 patients (87.5% male, 32.3 year of mean age) who had adequate pretreatment and 6-year biopsy samples. The median of Knodell necroinflammatory and Ishak fibrosis scores were 5 (2–11) and 2 (1–5) at pretreatment, respectively. At year 6, 82.1% (46/56), 41.1% (23/56) and 80.4% (45/56) patients achieved HBV DNA $<$ 20 IU/mL, HBeAg loss and normalized ALT, respectively. Histological improvement (defined as $\geq$ 2-point decrease in Knodell necroinflammatory score and no worsening of Ishak fibrosis score) was observed in 64.3% (36/56) of patients, and $\geq$ 1-point improvement in Ishak fibrosis score was found in 44.6% (25/56) of patients. LSM decreased rapidly before Year 0.5, and then decreased slowly until Year 2.5, and then remained relatively stable (Figure 2).

Conclusion: The long-term antiviral treatment could result in continued histological improvement with later-stage stable LSM level among HBeAg-positive naïve CHB patients.



* stopping criteria was defined as HBeAg seroconversion and HBV DNA <300 copies/mL for at least 48 weeks within 5 years.



Abstract #323

Long-term Clinical Outcome Of Entecavir Therapy In Patients With Chronic Hepatitis B

Hee Jeong Jeon[1], Seung Bum Lee[1], Neung Hwa Park[1], Jung Woo Shin[1]

[1]Department of Internal Medicine, University of Ulsan College of Medicine, Ulsan University Hospital, Ulsan, Republic of Korea

Introduction and Objectives: little large long-term follow-up study has investigated the effect of ETV treatment on specific liver-related events (LREs), namely, hepatocellular carcinoma (HCC), cirrhotic complications and mortality in Korea.
Methodology: This was a 10-year longitudinal observational study of treatment-naïve patients with CHB who received ETV treatment. The primary outcome was the cumulative probability of LREs. LREs were defined as cirrhotic complications (ascites, variceal bleeding, spontaneous bacterial peritonitis (SBP), hepatic encephalopathy (HE), hepatorenal syndrome (HRS) and LT (liver transplantation)), HCC, and liver-related mortality.
Results: Data from 1,288 treatment-naïve CHB patients who received ETV were analyzed. The median follow-up period during ETV therapy was 5.4 years (interquartile range [IQR], 3.1–7.6 years). A total of 649 patients (50.4%) had cirrhosis. During follow-up, virologic response (VR) was observed in 1096 patients (85.4%). One hundred sixty-nine (13.1%) patients experienced virologic breakthrough (VBT), of whom 29 (2.9%) developed ETV-resistant mutations. During the median 5.4-year follow-up period (range, 1.0–10.0 years), 99 patients (7.7%) developed HCC, the majority of whom (96/99, 97.0%) had cirrhosis at baseline. Overall, 17 patients (1.3%) died during the study period. During follow-up, 165 patients (12.8%) developed cirrhotic complications, of which the most commonly encountered were HCC, followed by ascites (n = 84), variceal bleeding (n = 29), HE (n = 21), SBP (n = 21) and HRS (n = 3).
Conclusion: The effective suppression of HBV replication cannot completely eliminate the risk of HCC and cirrhotic complications, particularly in those with cirrhosis. Therefore, regular LREs surveillance is still needed even if undetectable HBV DNA is achieved.

Abstract #324

Long-term Cinical Outcome Of Tenofovir Therapy In Patients With Chronic Hepatitis B

Hee Jeong Jeon[1], Seung Bum Lee[1], Neung Hwa Park[1], Jung Woo Shin[1]

[1]Department of Internal Medicine, University of Ulsan College of Medicine, Ulsan University Hospital, Ulsan, Republic of Korea

Introduction and Objectives: With the availability of potent tenofovir (TDF) therapy, the natural course of chronic hepatitis B has now changed and the risk of liver disease progression has been reduced, slowed down or even reversed. However, little large long-term follow-up study has investigated the effect of TDF treatment on specific liver-related events (LREs), namely, hepatocellular carcinoma (HCC), cirrhotic complications and mortality in Korea.
Methodology: The primary outcome was the cumulative probability of LREs. LREs were defined as cirrhotic complications (ascites, variceal bleeding, spontaneous bacterial peritonitis (SBP), hepatic encephalopathy (HE), hepatorenal syndrome (HRS) and LT (liver transplantation)), HCC, and liver-related mortality.
Results: Data from 900 treatment-naïve CHB patients who received TDF for more than 12 months were analyzed. The median follow-up period during TDF therapy was 34 months (interquartile range [IQR], 21–47 months). The mean age was 50.8 ± 11.2 years, and patients were predominantly male (n = 571 [63.4%]). A total of 421 patients (46.8%) had cirrhosis. During follow-up, VR was observed in 795 patients (88.3%). Eighty-nine (9.9%) patients experienced VBT. During treatment period, 20 patients (2.2%) developed HCC, all of whom (20/20, 100%) had cirrhosis at baseline. Overall, 8 patients (0.9%) died during the study period. During follow-up, 27 patients (3.0%) developed cirrhotic complications, of which the most commonly encountered were HCC, followed by ascites (n = 8), variceal bleeding (n = 6), SBP (n = 5), HE (n = 4) and HRS (n = 2).
Conclusions: The effective suppression of HBV replication cannot completely eliminate the risk of HCC and cirrhotic complications, particularly in those with cirrhosis.

Abstract #325

Association of adherence to entecavir or tenofovir therapy with cirrhotic complications in chronic hepatitis B patients with continuous virologic response

Hee Jeong Jeon[1], Seung Bum Lee[1], Neung Hwa Park[1], Jung Woo Shin[1]

[1]Department of Internal Medicine, University of Ulsan College of Medicine, Ulsan University Hospital, Ulsan, Republic of Korea

Introduction and Objectives: Treatment of chronic hepatitis B (CHB) with oral antiviral agents, especially the first line ones entecavir (ETV) and tenofovir (TDF), reduces the incidence of liver-related events (LREs), namely, hepatocellular carcinoma (HCC), cirrhotic complications and mortality. The aim of this study was to investigate risk predictors for development of LREs in patients with continuous virologic response (CVR).
Methodology: We performed a retrospective analysis of data from 1362 CHB patients with CVR, treated with ETV (n = 717) or TDF (n = 645) therapy for > 1 year. CVR was defined as having HBV DNA persistently undetectable throughout the treatment period, after achieving a virologic response (HBV DNA < 12 IU/mL). The cumulative level of adherence to medication was categorized as good (≥ 90%) or poor (< 90%).
Results: During the median 3.7-year follow-up period (range, 1.0–10.0 years), 67 patients (4.9%) developed HCC, 14 patients (1.0%) died, and 88 patients (6.5%) developed cirrhotic complications. Multivariate analyses showed that cirrhosis at baseline, male, age, adherence rate and albumin level were significantly factors for LREs. Patients with poor adherence increased their risk of developing HCC by 2.5-fold (95% CI, 1.507–4.386; P < 0.001) and cirrhotic complications by 2.6-fold (95% CI, 1.603–4.055; P < 0.001).
Conclusion: In addition to known risk factors (e.g. cirrhosis, age and sex), adherence was strong predictive factor for HCC and cirrhotic complications. Our study raises important clinical implications, emphasizing the benefits of adherence and the substantial harm of nonadherence to ETV or TDF therapy for patients with CHB.

Abstract #326

Association Of Low-level Viremia With Cirrhotic Complications In Chronic Hepatitis B Patients With Good Adherence To Entecavir Or Tenofovir Therapy

Hee Jeong Jeon[1], Seung Bum Lee[1], Neung Hwa Park[1], Jung Woo Shin[1]

[1]Department of Internal Medicine, University of Ulsan College of Medicine, Ulsan University Hospital, Ulsan, Republic of Korea

Introduction and Objectives: Recently, low-level viremia (LLV) during antiviral therapy was associated with an increased risk of HCC, especially in patients with cirrhosis. However, detailed information on adherence was lacking. The objectives of this study were, therefore, to evaluate the effect of LLV to entecavir (ETV) or tenofovir (TDF) treatment on cirrhotic complications and HCC development in chronic hepatitis B (CHB) patients with good adherence.
Methodology: We performed a retrospective analysis of data from 1336 CHB patients with good adherence, treated with ETV (n = 617) or TDF (n = 719) therapy for > 1 year. Good adherence to medication was defined as a cumulative adherence ≥ 90% per study period among patients who were prescribed ETV or TDF in a given period. LLV was defined by either persistent or intermittent episodes of < 2,000 IU/mL detectable HBV DNA.
Results: During the median 3.7-year follow-up period (range, 1.0–10.0 years), 45 patients (3.4%) developed HCC, 9 patients (0.7%) died, and 60 patients (4.5%) developed cirrhotic complications. LLV was observed for 102 patients (7.6%). Multivariate analyses showed that cirrhosis at baseline, male, age and albumin level were significantly factors for HCC and cirrhotic complications. However, LLV was not an independent risk factor for HCC and cirrhotic complications, regardless of cirrhosis.
Conclusion: In CHB patients with good adherence to ETV or TDF treatment, low-level viremia during treatment was not predictive factor for HCC and cirrhotic complications, even if cirrhosis. Therefore, for patients with LLV, adjustment of ETV or TDF therapy is unnecessary.

Abstract #330

Complication is a major risk factor for mortality of cirrhotic hepatitis B virus-related acute-on-chronic liver failure patients: a multi-national study from Asian-Pacific region

Tao Chen[1], Zhongyuan Yang[2], Jun Li[3], Yu Chen[4], Tao Han[5], Jinhua Hu[6], Shaojie Xin[7], Ashok Kumar Choudhury[8], Mamun Al Mahtab[9], Yuemin Nan[10], Seok Siam Tan[11], Amna Butt[12], Lee Guan Huei[13], Hasmik Ghazinian[14], Yogesh Chawla[15], Jidong Jia[16], Zaigham Abbas[17], Harshad Devarbhavi1[18], A K Dokmeci[19], Deepak Amarapurkar[20], Manoj Sahu[21], Laurentius Lesmama[22], George Lau[23], Osamu Yokosuka[24], Zhongping Duan[25], Wei Guo[26], Ke Ma[27], Zhongwei Zhang[28], Shiv Kumar Sarin[29], Qin Ning[30]

[1]Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, [2]Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, [3]Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [4]Youan Hospital, Capital Medical University, [5]Department of Gastroenterology, Third Central Hospital, [6]Liver Failure Treatment And Research Center, 302 Military Hospital, Peking University Health Science Center, [7]Liver Failure Treatment And Research Center, 302 Military Hospital, Peking University Health Science Center, [8]Departments of Hepatology And Transplant, Institute Of Liver And Biliary Sciences, [9]Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, [10]Department of Hepatology, Hebei Medical University, [11]Department of Gastroenterology And Hepatology, Selayang Hospital, [12]10 Department Of Medicine, Aga Khan University Hospital, [13]Department of Gastroenterology, National University of Health System, [14]Department of Hepatology, Nork Clinical Hospital of Infectious Diseases, [15]Department of Hepatology, Post Graduate Institute of Medical Education and Research, [16]liver Research Center, Beijing Friendship Hospital, [17]Department of Hepatogastroenterology, Ziauddin University, [18]Department of Gastroenterology and Hepatology, St John Medical College, [19]Department of Gastroenterology, Ankara University School of Medicine, [20]Department of Gastroenterology and Hepatology, Bombay Hospital and Medical Research Centre, [21]Department of Gastroenterology And Hepatology, Ims &Sum Hospital, [22]Digestive Disease & Oncology Centers, Medistra Hospital, [23]Humanity and Health Research Centre, [24]Departments of Gastroenterology And Nephrology, Graduate School of Medicine, Chiba University, [25]youan Hospital, Capital Medical University, [26]Tongji Hospital, Tongji Medical College, Huazhong University Of Science And Technology, [27]Tongji Hospital, Tongji Medical College, Huazhong University Of Science And Technology, [28]Tongji Hospital, Tongji Medical College, Huazhong University of Science And Technology, [29]Institute of Liver And Biliary Sciences, [30]Tongji Hospital, Tongji Medical College, Huazhong University Of Science And Technology

Background and Aims: Cirrhosis is a unique entity of chronic liver disease which is still a controversial determinant to mortality of hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF).
Methods: In this prospective-retrospective study, 709 patients with HBV-ACLF defined by the Asian Pacific Association for the Study of Liver ACLF Research Consortium (AARC) criteria were enrolled from 12 Asian-Pacific countries. Cirrhosis were evaluated as a risk factor intervening short-term mortality. Meanwhile, Current main prognostic models Tongji prognostic predictor model score (TPPMs), Chinese Group on the Study of Severe Hepatitis B-ACLF score (COSSH-ACLFs), CLIF consortium organ failure score (CLIF-C

OFs), CLIF-C ACLFs, MELDs and MELD-Nas were measured for predicting ability of mortality with area under the receiver operating characteristic curves.
Results: Among 709 patients, cirrhotic group showed significantly higher mortality and complications. Only 36.1% and 40.1% of patients met CLIF-C criteria in non-cirrhotic and cirrhotic group respectively, who showed significantly higher mortality and complications than those who did not satisfy the CLIF-C criteria. Furthermore, in patients who did not meet CLIF-C criteria, cirrhotic group exhibited higher mortality and complication occurrence than non-cirrhotic group, without significant difference of organ failures. TPPMs showed prior ability than COSSH-ACLFs, CLIF-Cs, CLIF-OFs, MELDs and MELD-Nas in cirrhotic patients. Number of complications more than 1 was an independent risk factor in cirrhotic HBV-ACLF patients.
Conclusions: Cirrhosis has its advantages in HBV-ACLF risk stratification. TPPMs possess high predicting ability in cirrhotic HBV-ACLF patients. Complication other than organ failure is the major risk factor for mortality of cirrhotic HBV-ACLF patients.

Abstract #343

Predictors of Inarigivir dose response in HBV Treatment-Naïve Patients: Role of HBeAg Status and Baseline HBsAg in Anti-Viral Response

Man Fung Yuen[1], Carla S Coffin[2], Magdy Elkhashab[3], Alnoor Ramji[4], Scott Fung[5], Susan Greenbloom[6], Chi Yi Chen[7], Wen Juei Jeng[8], Yung Fa Chen[9], Chun Jen Liu[10], Kwan Sik Lee[11], Yoon Jun Kim[12], Won Kim[13], Jeong Won Jang[14], Doon Joon Kim [15], Radhakrishnan Iyer[16], Chelsea Macfarlane[17], Kathy Jackson[18], Stephen Locarnini[19], Nezam Afdhal[20], Henry Ly Chan[21]

[1]Queen Mary Hospital & University of Hong Kong, [2]University of Calgary, [3]Toronto Liver Centre, [4]Gastrointestinal Research Institute, [5]Toronto General Hospital & United Health Network, [6]Toronto Digestive Disease Associates, [7]Chia-Yi Christian Hospital, Chia Yi, Taiwan, [8]Chang Gung Memorial Hospital & Chang Gung University, [9]Taipei Medical University-Wan Fang Hospital, [10]National Taiwan University & National Taiwan University Hospital, [11]Gangnam Severance Hospital & Yonsei University Health System, [12]Seoul National University, [13]Borame Hospital Seoul, [14]The Catholic University Of Korea, [15]Hallym University Medical Center, [16]Spring Bank Pharmaceuticals, [17]Spring Bank Pharmaceuticals, [18]Vidrl, [19]Vidrl, [20]Spring Bank Pharmaceuticals, [21]Prince Of Wales Hospital & Chinese University Of Hong Kong

Background: Inarigivir soproxil is an oral RIG-1 agonist with antiviral activity against HBV. The ACHIEVE trial is evaluating 5 ascending dose cohorts of inarigivir monotherapy versus placebo for 12 weeks followed by a switch to tenofovir 300 mg daily in treatment-naïve HBV patients.
Methods: 3 cohorts each of 20 patients (active 16: placebo 4) have completed treatment in the 25 mg, 50 mg and 100 mg dose groups. Demographic and baseline virological data is given in the table
Results: HBV DNA was significantly reduced compared to placebo (ANOVA $p < 0.0001$) in all 3 groups with a clear dose response especially in HBeAg -ve patients where mean reduction was − 2.26log10 in the 100 mg group. Serum HBV RNA was also reduced in all HBeAg-ve inarigivir patients (mean − 1.7 log10) compared to HBeAg-ve placebo (+0.84 log10; t-test, $P < 0.02$), but only for the 100 mg group in HBeAg + ve patients (− 0.57 log10) compared to HBeAg + ve placebo (− 0.16 log10; t-test, $p < 0.05$). 26 patients (12 HBeAg + ve) had baseline of HBsAg of < 4 log10 and when compared to the 20 patients with HBsAg > 4 log10 there was a significant difference in response for both HBV DNA (− 1.061 log10 versus − 0.37 log10; $p < 0.002$) and HBV RNA (− 1.281 log10 versus − 0.33 log10; $p < 0.007$). Safety profile was favorable across all cohorts with no SAE's or significant laboratory TEAEs.
Conclusion: Inarigivir monotherapy is safe and effective as an antiviral agent in HBV patients. Baseline HBsAg is an important response predictor and may reflect the effect of viral proteins on inhibition of RIG-I activation.

BASELINE DEMOGRAPHICS COHORT 1, 2 and 3

	Placebo	25mg HBeAg +ve	25mg HBeAg-ve	50mg HBeAg +ve	50mg HBeAg -ve	100mg HBeAg+ve	100mg HBeAg-ve
Number	11	9	7	11	5	13	4
Age	40	37	43	36	47	34	46
Gender M:F	7:4	5 : 5	3 : 3	9 : 2	5:0	7:6	3:1
Baseline ALT	69	82	75	75	65	75	90
Baseline HBV DNA log_{10}	6.20	7.86	5.69	7.79	4.55	8.20	5.95
Genotype A	1		1				
B	6	4	3	3	3	4	3
C	4	5	1	7	1	8	1
D			2	1		1	

Abstract #395

Safety and Antiviral Activity of a Novel Hepatitis B Virus Capsid Assembly Modulator, JNJ-56136379, in Asian and non-Asian Patients with Chronic Hepatitis B

J. Z. Yogaratnam[1], F Zoulim[2], J. Vandenbossche[3], O. Lenz[4], W. Talloen[5], I. Moscalu[6], M. Rosmawati[7], A. Streinu-Cercel[8], Wl Chuang[9], S. Bourgeois[10], Ss. Yang[11], M. Buti[12], J. Crespo[13], Yc. Chen[14], J. M. Pascasio[15], C. Sarrazin[16], T. Vanwolleghem[17], U. Shukla[18], J. Fry[19]

[1]Janssen Biopharma Inc, [2]Croix Rousse Hospital, Hospices Civils De Lyon, [3]Janssen Pharmaceutica Nv, [4]janssen Pharmaceutica Nv, [5]Janssen Pharmaceutica Nv, [6]Spitalul Clinic Republican, [7]University Malaya Medical Centre, [8]National Institute for Infectious Diseases "Prof. Dr. Matei Bals", Carol Davila University of Medicine And Pharmacy, [9]Koahsiung Medical University Hospital, [10]ZNA Jan Palfijn, Cpu, [11]Taichung Veterans General Hospital, [12]Hospital Universitario Vall D'hebrón, [13]Hospital Universitario Marques De Valdecilla, [14]chang Gang Memorial Hospital Linkou, [15]Hospital Universitario Virgen Del Rocio, [16]medizinische Klinik Ii, St. Josefs-Hospital, [17]Erasmus Mc, University Medical Center, [18]Janssen Pharmaceuticals R&D, [19]Janssen Biopharma Inc.

Introduction: The capsid assembly modulator, JNJ-56136379 (JNJ-6379), was well tolerated in healthy volunteers and patients with chronic hepatitis B (CHB) in a first-in-human study. Significant antiviral activity was observed in patients with CHB at doses of 25 mg to 250 mg QD (NCT02662712).
Objectives: To compare safety and antiviral activity of 75 mg JNJ-6379 in Asian and non-Asian patients with CHB.
Methodology: Non-cirrhotic, treatment-naïve, HBeAg-positive or -negative patients with CHB were enrolled to receive JNJ-6379 or placebo QD for 4 weeks (+8 weeks follow-up). Two groups were administered JNJ6379 at a dose of 75 mg; twelve patients (8 JNJ-6379:4 placebo) in European sites, and 9 patients (7:2) in Asian sites.
Results: All patients were Caucasian in the European group, and Asian in the Asian group. There were 6 HBeAg-positive patients in the European group, and 4 in the Asian group. In patients treated with JNJ-6379, 57% in the Asian group and 50% in the European group

reported any AE. No serious AEs or deaths occurred. HBV DNA and HBV RNA decreases were comparable in both groups (see Table).
Conclusion: JNJ-6379 at a dose of 75 mg was well tolerated, and resulted in similar antiviral effects, in Asian and non-Asian patients with CHB. This data supports further examination of any differences in these populations through evaluating the same dose of JNJ-6379 ± nucleos(t)ide analogs in a larger cohort of patients at European and Asian sites in an international Phase 2a study (NCT03361956).

Abstract #412

Safety, Pharmacokinetics and Antiviral Activity of a Novel Hepatitis B Virus Capsid Assembly Modulator, JNJ-56136379, in Patients with Chronic Hepatitis B

F. Zoulim[1], J. Z. Yogaratnam[2], J. J. Vandenbossche[3], I. Moscalu[4], A. Streinu-Cercel[5], O. Lenz[6], S. Bourgeois[7], M. Buti[8], W. Talloen [9], J. Crespo [10], J. M. Pascasio[11], C. Sarrazin[12], T. Vanwolleghem[13], U. Shukla[14], J. Fry[15]

[1]Croix Rousse Hospital, Hospices Civils De Lyon & Inserm U1052-Cancer Research Institute of Lyon, [2]Janssen Biopharma, [3]Janssen Pharmaceuticals Bv, [4]Spitalul Clinic Republican, [5]National Institute For Infectious Diseases "Prof. Dr. Matei Bals", Carol Davila University of Medicine And Pharmacy, [6]Janssen Pharmaceuticals Bv, [7]ZNA Jan Palfijn, CPU, [8]Hospital Universitario Vall D'hebrón, [9]Janssen Pharmaceuticals Bv, [10]Hospital Universitario Marques De Valdecilla, [11]Hospital Universitario Virgen Del Rocio, [12]medizinische Klinik Ii, St. Josefs-Hospital, [13]Erasmus Mc, University Medical Center & Antwerp University Hospital, [14]Janssen Pharmaceuticals R&D, [15]Janssen Biopharma

Introduction: JNJ-56136379 (JNJ-6379) is a capsid assembly modulator that blocks hepatitis B virus (HBV) replication. JNJ-6379 (single and multiple doses) was well tolerated and demonstrated dose-proportional pharmacokinetics in healthy subjects in Part 1 of a first-in-man study (NCT02662712).
Objectives: To evaluate the safety, pharmacokinetics and antiviral activity of JNJ-6379 during 4-week treatment at different doses in patients with chronic hepatitis B (CHB) in Part 2 of the study.
Methodology: Non-cirrhotic, treatment-naïve, HBeAg-positive or -negative patients with CHB were randomized to receive JNJ-6379 or placebo once daily for 4 weeks with another 8 weeks follow-up. There were 4 groups, each with 12 patients: 25 mg (100 mg loading dose) (n = 8 JNJ-6379: n = 4 placebo); 75 mg (n = 8:4); 150 mg (n = 9:3); and 250 mg (n = 9:3).
Results: Patients were 21–58 years. 19/34 (56%) patients receiving JNJ-6379 experienced ≥ 1 adverse events (AE) versus 9/14 (64%) receiving placebo. No dose-related or serious AEs were reported. 3 (9%) patients receiving JNJ-6379 had Grade 3 AEs of which 1 (150 mg) had ALT increase to Grade 4 and was discontinued from treatment. After repeated administration, JNJ-6379 exposure increased dose dependently with no change in apparent clearance over time. HBV DNA (Figure) and HBV RNA (not shown) reduced substantially at all doses. During follow-up, HBV DNA levels generally rebounded more slowly at higher doses.
Conclusion: At all evaluated doses, JNJ-6379 was generally well tolerated, demonstrated dose-dependent pharmacokinetics, and exhibited potent antiviral activity in patients with CHB. A Phase 2a study is evaluating JNJ-6379 ± nucleos(t)ide analogs in patients with CHB (NCT03361956).

Abstract #418

Three Year Efficacy and Safety of Tenofovir Alafenamide (TAF) Compared to Tenofovir Disoproxil Fumarate (TDF) in HBeAg-negative and HBeAg-positive Patients with Chronic Hepatitis B

Henry Lik-Yuen Chan[1], Young-Suk Lim[2], Wai Kay Walter Seto[3], Harry L.A. Janssen[4], Owen Tsang[5], Hiroshi Yatsuhashi[6], Won Young Tak[7], Chi-Yi Chen[8], Vithika Suri[9], John Flaherty[10], Lanjia Lin[11], Anuj Gaggar[12], Calvin Pan[13], - Shalimar[14], Maria Buti[15]

[1]Chinese University Of Hong Kong, [2]Asan Medical Center, [3]Queen Mary Hospital, [4]Toronto Centre For Liver Disease, [5]Princess Margaret Hospital, [6]National Hospital Organization Nagasaki Medical Center, [7]Kyungpook National University School Of Medicine, [8]Chia-Yi Christian Hospital, [9]Gilead Sciences, [10]Gilead Sciences, [11]Gilead Sciences, [12]Gilead Sciences, [13]Nyu Langone Medical Center, [14]All India Institute of Medical Sciences, [15]Vall D'hebron Barcelona Campus Hospitalari

Background and Aims: In 2 identically-designed double-blind, randomized (2:1), Phase 3 studies, the safety and efficacy of TAF vs TDF was evaluated in subjects treated for 3 years.
Methods: 1298 HBeAg-negative and HBeAg-positive CHB patients were randomized and treated with TAF 25 mg or TDF 300 mg QD. Included in this analysis, were 1118 patients (759 HBeAg-positive and 359 HBeAg-negative); 866 of whom received TAF and 252 who received TDF for 3 years. Efficacy analyses included virologic, biochemical, and serologic responses, and pooled safety assessments included changes in bone mineral density (BMD), serum creatinine, and estimated GFR by Cockcroft- Gault method (eGFRCG).
Results: Baseline characteristics were similar between groups; mean age 39 years, 63% males, 78% Asian, mostly genotypes C (48%) and D (26%); mean HBV DNA was 7.0 log10 IU/mL (34% had HBV DNA ≥ 8 log10 IU/mL), and 25% previously treated with nucleos(-t)ides. At Week 144, high rates of virologic control were maintained in TAF vs. TDF subjects; a greater proportion of TAF vs TDF patients achieved ALT normalization (Table). Overall, adverse events (AEs) and serious AEs were similar between groups. At Week 144, greater median declines in eGFRCG were observed with TDF treatment; similarly, hip and spine BMD declines in the TDF group were larger than in the TAF group (Table).
Conclusion: After three years of treatment, high and similar rates of virologic suppression were achieved and maintained, and continued improvements in renal and bone safety were observed in patients receiving TAF compared to TDF.

Abstract #419

Bone and Renal Safety Are Improved in Chronic HBV Patients 1 Year after Switching to Tenofovir Alafenamide (TAF) from Tenofovir Disoproxil Fumarate (TDF)

Wai Kay Walter Seto[1], Namiki Izumi[2], Young-Suk Lim[3], Jia-Horng Kao[4], Vithika Suri[5], John Flaherty[6], Audrey Lau[7], Anuj Gaggar[8], Shuyuan Mo[9], Abhijit Chowdhury[10], Scott Fung[11], Wan-Long Chuang[12], Edward Gane[13]

[1]Queen Mary Hospital, Hong Kong, [2]Japanese Red Cross Musashino Hospital, Tokyo, Japan, [3]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea, [4]Graduate Institute Of Clinical Medicine, National Taiwan University Hospital, Taipei, Taiwan, [5]Gilead Sciences, [6]Gilead Sciences, [7]Gilead Sciences, [8]Gilead Sciences, [9]Gilead Sciences, [10]School of Digestive And Liver Diseases, Institute Of Post Graduate Medical Education

And Research, Kolkata, India, [11]University of Toronto, Ontario, Canada, [12]Kaohshiug Medical University Chung-Ho Memorial Hospital, Kaohsiung, Taiwan, [13]Auckland Clinical Studies, Auckland, New Zealand

Objectives: Following a protocol amendment to extend double blind (DB) treatment for an additional year, 50% of patients continued on DB treatment, while the remainder rolled-over to open-label (OL) TAF at Week 96. The efficacy and safety from Week 96–144 was evaluated in patients randomized to TDF, who either continued on TDF or switched to TAF at Week 96.
Methods: In 2 identically-designed studies, 1298 HBeAg-negative and HBeAg-positive CHB patients (866 TAF, 432 TDF) were randomized and treated. In the TDF group, 211 remained on TDF (DB TDF) while 180 patients switched to OL TAF (TDF → TAF) at Week 96. Assessments including changes in BMD, renal (CrCl by Cockcroft-Gault [eGFRCG], serum creatinine) parameters, viral suppression, and biochemical responses were evaluated from Week 96–144.
Results: Patient characteristics were similar between those who continued TDF and the TDF → TAF group. In the TDF → TAF group, eGFRCG improved while those remaining on TDF showed a continued decrease in eGFRCG at Week 144 (Table). Similarly, significant improvements in hip and spine BMD were seen over 1 year in TDF → TAF patients compared to those remaining on TDF (Table). High rates of virologic suppression were maintained in both groups (TDF → TAF 84%; DB TDF 88%; M = F), while a greater rate of ALT normalization (2018 AASLD criteria) was seen in TDF → TAF patients 1 year following switch (45% vs 29%; M = F).
Conclusions: 1 year after switching to TAF, virologic control was maintained, ALT normalization rates were higher, and patients had improved bone and renal safety compared to those remaining on TDF.

Abstract #438

Long-term Tenofovir Treatment for Nuclos(t)ides-Naïve Chronic Hepatitis B Patients in Real World: Adaptation Is Not Necessary for Patients with Partial Virologic Response

Jeong Eun Song[1], Chang Hyeong Lee[1], Byung Seok Kim[1]

[1]Department of Internal Medicine, Daegu Catholic University School of Medicine

Background and Aims: The aim of this study was to evaluate the long-term efficacy of prolonged TDF therapy in treatment-naïve CHB patients with PVR to TDF therapy.
Method: We retrospectively investigated the efficacy of prolonged TDF therapy in treatment-naïve CHB patients with PVR to TDF. PVR was defined as a decrease in serum hepatitis B virus (HBV) DNA of more than 2 log10 IU/mL from baseline but with detectable HBV DNA by real-time polymerase chain reaction (PCR) assay at week 48. Complete virologic response (CVR) was defined as undetectable HBV DNA by real-time PCR at week 48.
Results: This study included 232 patients treated with TDF therapy for more than 48 weeks. Forty-two (18.1%) of 232 patients showed PVR. In multivariate analysis, HBeAg positivity and high levels of serum HBV DNA at baseline and week 12 were independent predictive factors for PVR during TDF therapy. Among 42 patients with PVR, 39 (92.9%) patients achieved virologic response (VR) during continuous TDF treatment. Of 31 patients with HBV DNA < 100 IU/mL at week 48, VR within additional 12 months of therapy was achieved in 28 (90.3%) patients, compared to 5 of 11 (45.5%) patients with HBV DNA ≥ 100 IU/mL.
Conclusion: The great majority of patients achieved a VR through prolonged TDF therapy, thus TDF treatment can be maintained in nucleos(t)ides-naïve patients with PVR at week 48, especially in those having low viremia.

Abstract #482

Two-center, 24-months result of switching to tenofovir-monotherapy in multi-drug experienced CHB patients

Jeong Han Kim[1], Eileen L Yoon[2]

[1]Konkuk University School of Medicine, [2]Sanggye Paik Hospital Inje University

Background/Aims: Chronic hepatitis B(CHB) patients with multi-drug experience are frequently switched to tenofovir-monotherapy, recently in Korea. We aimed to evaluate safety and efficacy of switching to tenofovir-monotherapy from tenofovir-based combination therapy upto 24 months.
Methods: This is a retrospective study of multi-drug experienced CHB patients who have switched from tenofovir-based combination therapy to tenofovir-monotherapy after achievement of virologic response (VR, less than 20 IU/mL) in two centers from 2013 to 2018.
Results: A total of 40 patients were included. Median age was 52 years old. Twenty nine patients were male (74.4%). HBeAg positive patients were 32 (82.1%). Twenty one patients had experienced multi-drug resistance to both nucleoside and nucleotide analogues. Median duration of VR before switching to monotherapy was 16.3 months and median duration of monotherapy was 31.6 months (range, 3–60). VR at 12 and 24 months were achieved in 36 patients. One patient lost to follow-up after 12 months of monotherapy without non VR. Two patients experienced virologic breakthrough during 24 months of tenofovir-monotherapy. All the 5 patients who experienced non VR easily achieved VR within 3 months with tenofovir-monotherapy, but all of them had experienced adefovir previously. Duration of consolidation with combination therapy after VR were less than 6 months in 4 out 5 patients who showed non-VR during 24 months of tenofovir-monotherapy.
Conclusions: Switching to tenofovir-monotherapy in multi-drug experienced patients is generally safe and effective upto 24 months. Constant monitoring of virus may be required in patients with previous adefovir-exposure and short duration of consolidation after VR achievement.

Abstract #491

Comprehensive Analysis for the Impact of On-Treatment Intermediate Endpoints on Outcomes of HBeAg (+) Chronic Hepatitis B

Jonggi Choi[1], Young-Suk Lim[1], Gi-Ae Kim[1], Ju Hyun Shim[1], Kang Mo Kim[1], Han Chu Lee[1], Yung Sang Lee[1]

[1]Asan Medical Center, University Of Ulsan College Of Medicine

Backgrounds: Alanine aminotransferase (ALT) normalization, virological response (VR), and HBeAg seroclearance are intermediate surrogate endpoints that are commonly used to monitor treatment responses in HBeAg-positive chronic hepatitis B (CHB) patients.
Methods: We included a total of 2,630 HBeAg-positive CHB patients who initiated treatment with entecavir or tenofovir disoproxil fumarate at a tertiary hospital in Korea between 2007 and 2016, and analyzed the risk of hepatocellular carcinoma (HCC) and death/transplantation. Normal ALT was defined as ≤ 25 U/L for female and ≤ 35 for male. We defined VR as serum HBV DNA $<$ 15 IU/mL.

Results: The mean age of the patients was 45.1 years, 65.1% were male, and 38.7% had cirrhosis. During median follow-up period of 5.1 years, 216 patients developed HCC and 107 died or received liver transplants. ALT normalization was associated with a significantly lower risk of HCC and death/transplantation by landmark analyses at 1-year and 2-years of treatment ($P < 0.001$ for all). By 2-year landmark analysis, VR was associated with a significantly lower risk of death/transplantation ($P = 0.003$) but not with the risk of HCC ($P = 0.97$), while HBeAg seroclearance was not associated with the risk of HCC ($P = 0.13$) or death/transplantation ($P = 0.34$). On-treatment ALT normalization was independently associated with significantly lower risk of HCC (adjusted hazard ratio [aHR] = 0.44) and death/transplantation (aHR = 0.47) by multivariable time-dependent Cox analysis. **Conclusions:** In HBeAg-positive CHB patients under treatment with highly-potent antiviral agents, ALT normalization was the sole on-treatment surrogate endpoint that was independently associated with lower risk of HCC and death/transplantation.

Abstract #492

Monotherapy with Tenofovir Disoproxil Fumarate for Multiple Drug-Resistant Chronic Hepatitis B: Results of 5-Year Clinical Trials

Jonggi Choi[1], Young-Suk Lim[1], Gi-Ae Kim[1], Yung Sang Lee[1], Han Chu Lee[1], Geum-Youn Gwak[2], Kwan Soo Byun[3], Yoon Jun Kim[4], Byung Chul Yoo[5], So Young Kwon[5]

[1]Asan Medical Center, University of Ulsan College of Medicine, [2]Samsung Medical Center, Sungkyunkwan University School Of Medicine, [3]Korea University College of Medicine, [4]Seoul National University College of Medicine, [5]Konkuk University School of Medicine

Background and Aims: Monotherapy with tenofovir disoproxil fumarate (TDF) has displayed non-inferior efficacy to TDF plus entecavir (ETV) combination therapy in patients with hepatitis B virus (HBV) resistant to ETV and/or adefovir (ADV). Nonetheless, the rate of virologic response was suboptimal up to 144 weeks of TDF monotherapy with uncertain long-term safety.
Methods: One trial enrolled patients with ETV-resistance without ADV-resistance (ETV-resistance group; n = 90), and the other patients with ADV-resistance (ADV-resistance group; n = 102). Patients were randomized 1:1 to receive TDF monotherapy or TDF + ETV combination therapy for 48 weeks, and then to receive TDF monotherapy until 240 weeks.
Results: At week 240, the proportion of patients with serum HBV DNA < 15 IU/mL was not significantly different between the ETV-resistance and ADV-resistance groups in the full analysis set (84.4% vs. 73.5%; $P = 0.07$), which was significantly different by on-treatment analysis (92.7% vs. 79.8%; $P = 0.02$). Transient virologic breakthrough occurred in 7 patients throughout the 240 weeks associated with poor medication adherence. None developed additional HBV resistance mutations throughout study period. Among 170 HBeAg-positive patients at baseline, HBeAg seroconversion was achieved in 12 (7.1%) at week 240. None achieved HBsAg seroclearance. There was a significant decrease at week 240 from baseline in estimated GFR (− 3.21 mL/min/1.73 m2 by CKD-EPI equation, $P < 0.001$) and bone mineral density (g/cm^2) at femur (− 2.48%, $P < 0.001$).
Conclusions: TDF monotherapy provided an increasing rate of virologic response for up to 240 weeks in heavily pretreated patients with HBV resistant to ETV and/or ADV. However, it was associated with poor serologic responses, and decreasing renal function and bone mineral density.

Abstract #493

A Prospective, Open-label, Dose-escalation, Single-center, Phase 1 study for Lenvervimab (GC1102), a new and safe human monoclonal antibody drug for chronic hepatitis B patients

Hye Won Lee[1], Jun Yong Park[1], Taegon Hong[2], Min Soo Park[3], Sang Hoon Ahn[1]

[1]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea & Yonsei Liver Center, Severance Hospital, Seoul, Korea, [2]Department of Clinical Pharmacology, Yonsei University College of Medicine, Seoul Korea, [3]Department of Pediatrics, Yonsei University College of Medicine, Seoul, Korea

Background/Aim: Lenvervimab (GC1102) is a recombinant hepatitis B human immunoglobulin and is expected to boost therapeutic effects by improving the sustained virological response from reducing the blood HBsAg level. This study aimed to evaluate the safety and efficacy of lenvervimab with single and multiple intravenous administrations in patients with chronic hepatitis B (CHB).
Methods: This study was designed as a prospective, open-label, sequential group dose-escalation, and single-center study in treatment groups. There were two groups with single administration of lenvervimab (Part A, n = 24) and multiple administrations (Part B, n = 29) of 80,000 IU, 120,000 IU, 180,000 IU, and 240,000 IU to CHB patients who had ≤ 1,000 IU/mL of serum HBsAg.
Results: According to the result of analysis on safety and tolerability, no dose limiting toxicity has occurred at all doses so it is considered favorable. No adverse drug reaction was observed up to the 120,000 IU group of both Part A and B. However, in the 240,000 IU group, the frequency of the mild adverse events (flushing, nausea, and dizziness) which seemed to have occurred due to the administration rate of lenvervimab. Maximum change of the log-transformed HBsAg from the baseline was observed to increase with increasing dose, except 240,000 IU, and appeared 2–24 hours after the last dosing in all dose groups.
Conclusions: The tolerability and safety of lenvervimab are considered favorable in patients with CHB when using single and multiple administration of lenvervimab.

Abstract #536

Long-Term Follow-up of Treated Patients with Chronic Hepatitis B Infection: Patient-Reported Outcomes

Zobair Younossi[1], Maria Stepanova[2], Issah Younossi[3], Calvin Q. Pan[4], Harry L. A. Janssen[5], George Papatheodoridis[6], Sang Hoon Ahn[7], Young-Suk Lim[8], Anuj Gaggar[9], Fatema Nader[10]

[1]Center for Liver Diseases, Department of Medicine, Inova Fairfax Hospital & Betty and Guy Beatty Center for Integrated Research, Inova Health System, [2]Center for Outcomes Research in Liver Disease, [3]Center for Outcomes Research in Liver Disease, [4]Nyu Langone Health, Nyu School of Medicine, [5]toronto Centre For Liver Disease, University Health Network, [6]Medical School of National & Kapodistrian University of Athens, [7]College of Medicine, Yonsei University, [8]Asan Medical Center, University of Ulsan College of Medicine, [9]Gilead Sciences, [10]Center for Outcomes Research in Liver Disease

Background: Chronic hepatitis B (CHB) is an important cause of chronic liver disease worldwide. It negatively impacts both clinical and patient-reported outcomes (PROs).

Aim: To assess long-term trends in PROs in CHB patients receiving anti-viral treatment in a registry.
Methods: Patients with CHB without significant fibrosis or cirrhosis (Metavir stages 0–2) who had completed treatment with an approved or investigational agent in a clinical trial were prospectively enrolled in a long-term registry (clinicaltrials.gov #NCT02258581). PROs were collected every 24 weeks using Short Form-36 (SF-36), Chronic Liver Disease Questionnaire (CLDQ), and Work Productivity and Activity Impairment (WPAI:SHP).
Results: There were 229 CHB patients with viral suppression (48.6 ± 10.4 years old, 71% male, 75% Asian, 62% enrolled in the U.S, HBV DNA < 5,000 IU/mL); the patients were followed for 2 years. Baseline registry PROs were similar or higher than general population norms: mean Physical Component Summary 53.0 vs. 50.0, mean Mental Component Summary 52.7 vs. 50.0 ($p < 0.05$ for all but one domains of SF-36), mean total CLDQ: 6.0 vs. 6.0 ($p > 0.05$). Despite this, CHB patients still had a statistically significant work productivity impairment due to presenteeism: mean 0.07 ($p < 0.0001$). Over the duration of registry, there were no significant changes in PROs of patients with CHB up to 96 weeks from enrollment ($p > 0.05$).
Conclusion: Patients with CHB and early liver disease and viral suppression maintain good PROs with some impairment of work productivity. Patient-reported outcomes should complement other clinical outcomes to provide a comprehensive assessment of the impact of CHB on patients' well-being.

Abstract #537

Assessment of liver stiffness change by transient shear wave elastography in tenofovir-naïve patients with chronic hepatitis B : three-years follow up

Byung Ik Kim[1], Kyungjin Ko[1]

[1]Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea

Introduction: Several longitudinal studies have demonstrated that elastography could be a useful tool for monitoring of liver fibrosis during the treatment of chronic hepatitis B. However, studies assessing regression of liver fibrosis by elastography are rare. Therefore, the purpose of this study was to evaluate the liver stiffness before and during the treatment and access the usefulness of the presented non-invasive modality in nucleotide-naïve patients with CHB.
Methods: One hundred twenty-seven treatment-naïve patients started treatment with tenofovir. Measurement of liver stiffness by a transient elastography was performed at baseline, after 6, 12, 18, 24, 30, 36 and 42 months. The difference in results between baseline and each month of elastography were compared respectively by paired t-test method.
Result: Typically, 103, 106, 98, 88, 76, 78 and 61 patients underwent elastography at 6, 12, 18, 24, 30, 36 and 42 months after tenofovir medication, respectively. Median liver stiffness values were decreased from 7.36 kPa (95% CI, 8.33–6.38) at baseline to 5.83 (95% CI, 6.55–5.10), 5.45 (95% CI, 4.78–6.12), 5.16 (95% CI, 4.39–5.93), 4.93 (95% CI, 5.79–4.06), 4.95 (95% CI, 5.58–4.31), 4.58 (95% CI, 4.13–5.03) and 4.14 (95% CI, 3.79–4.49) kPa at 6, 12, 18, 24, 30, 36 and 42 months after tenofovir medication.
Conclusion: A significant improvement in liver stiffness was observed in chronic hepatitis B patients during 42 months of tenofovir treatment.

Abstract #546

One-Year Effect of Tenofovir Alafenamide (TAF) on Alanine Aminotransferase (ALT) Levels and Renal Safety in Post Liver Transplant Chronic Hepatitis B Patients

Pimsiri Sripongpun[1], Ajitha Mannalithara[2], Paul Y. Kwo[2], W. Ray Kim[2]

[1]Stanford University & Prince Of Songkla University, [2]Stanford University

Background and Aim: Tenofovir Alafenamide (TAF) showed better renal safety and comparable efficacy compared to tenofovir disoproxil fumarate (TDF) in general chronic hepatitis B (CHB) patients. Nonetheless, data regarding TAF effect in liver transplantation (LTx) recipients are scarce. This study aimed to determine the effect of switching from other nucleot(s)ide analogs (NA) to TAF on alanine aminotransferase (ALT) level and glomerular filtration rate (GFR, CKD-EPI) in LTx CHB patients.
Method: This is a retrospective study, we included all adult LTx CHB patients who had been treated with NA for >/=48 weeks before switched to TAF in November 2016–17, and continued TAF >/=48 weeks. Exclusion criteria were HIV/HCV/HDV co-infection, coexisting liver tumor, and simultaneously TAF 1st prescription at the time of LTx. Demographic and laboratory data were retrieved from the Stanford Health Care database. Change in ALT and GFR between the time of TAF initiation (baseline) and at 48 weeks post TAF were analyzed.
Results: Eleven patients were eligible, 72.7% were male, 90.9% were Asian, with a mean age of 61.6 years. The mean interval since LTx to TAF was 5.7 years. At baseline, the mean ALT was 41.2 U/L, and GFR was 63.9 ml/min/1.73m2, 54.5% coexisted with diabetes/hypertension/dyslipidemia. At 48 weeks post TAF, the median change in ALT was − 6 U/L compared to baseline ($p = 0.041$) with 100% unquantifiable HBV DNA, and 72.7% improved in GFR, the median GFR change was + 2.46 ml/min/1.73m2 ($p = 0.24$).
Conclusion: Switching from other NA to TAF demonstrated favorable efficacy and renal safety profiles LTx CHB patients.

Abstract #572

Artificial liver support system improves survival of patients with hepatitis B virus-related acute-on-chronic liver failure: A propensity-score matched analysis

Lingling Yang[1], Tianzhou Wu[2], Jiang Li[3], Jing Jiang[4], Jiaojiao Xin[5], Dongyan Shi[6], Yinyun Lu[7], Xingping Zhou[8], Jiaxian Chen[9], Jiaqi Li[10], Jianing Zhang[11], Keke Ren[12], Beibei Guo[13], Tan Li[14], Xiaowei Xu[15], Xin Chen[16], Jun Li[17]

[1]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School Of Medicine, [2]The Infectious Disease Department, The First People's Hospital of Wenling, [3]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School Of Medicine, [4]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School Of Medicine, [5]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [6]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [7]State Key Laboratory for Diagnosis and Treatment Of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School Of Medicine, [8]State Key Laboratory for

Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [9]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School Of Medicine, [10]State Key Laboratory For Diagnosis And Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School Of Medicine, [11]Institute of Pharmaceutical Biotechnology, Zhejiang University School of Medicine, [12]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [13]State Key Laboratory For Diagnosis And Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School Of Medicine, [14]State Key Laboratory for Diagnosis And Treatment Of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, [15]The Infectious Disease Department, The First Affiliated Hospital, Zhejiang University School Of Medicine, [16]Institute Of Pharmaceutical Biotechnology, Zhejiang University School of Medicine, [17]State Key Laboratory for Diagnosis And Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine

Introduction: Artificial liver support system (ALSS) is recognized as an alternative to liver transplantation for treatment of hepatitis B virus-related ACLF (HBV-ACLF). However, its survival impact is unknown.
Objectives: To determine the efficacy of ALSS in patients with HBV-ACLF.
Methodology: The clinical data of HBV-ACLF patients receiving ALSS (n = 507) and standard medical treatment (SMT, n = 417) from Chinese Group on the Study of Severe Hepatitis B ACLF (COSSH-ACLF) cohort were used to evaluate the short-term mortality and cumulative survival rate using propensity-score matched analysis.
Results: Among the patients assessed using the COSSH-ACLF criteria, the short-term (day 7, 14, 21, 28) mortality rate in ALSS group was significantly lower ($p < 0.001$) than those in SMT group. The cumulative survival rate of 90-days was also higher in ALSS group ($p < 0.001$) than that in SMT group. In the propensity-score matched cohort (294 pairs), the short-term mortality rate was significantly lower in ALSS group compared to SMT group (12.9-, 21.6-, 26.2-, 31.0% vs 22.6-, 34.7-, 42.5-, 45.2% at day 7, 14, 21 and 28, respectively), especially in ACLF-1 ($p < 0.01$) and -2 ($p < 0.05$). There was no significant difference in short-term mortality rate of ACLF-3 patients ($p > 0.05$), but a beneficial effect on cumulative survival of ALSS therapy was observed at day 7, 14, 21 and 28, respectively.
Conclusions: ALSS can improve short-term survival in patients with HBV-ACLF, especially in ACLF-1 and -2, which may serve as a bridge to liver transplantation.

Abstract #578

Monitoring of serum hepatitis B virus (HBV) RNA, HBcrAg, HBsAg, and anti-HBc levels in patients during long-term nucleoside/nucleotide analog therapy

Liao Hao[1], Liu Yan[2], Li Xiaodong[3], Wang Jie[4], Chen Xiangmei[5], Zou Jun[6], Li Qi[7], Liu Lujie[8], Wang Jun[9], Huang Bixia[10], Lu Fengmin[11], Xu Dongping[12]

[1]Department of Microbiology & Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing, China, [2]Institute of Infectious Diseases, Beijing 302 Hospital (The 5th Medical Center of General Hospital of PLA), [3]Institute of Infectious Diseases, Beijing 302 Hospital, [4]Department of Microbiology & Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing, China, [5]Department of Microbiology & Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing, China, [6]Department of Microbiology & Infectious Disease Center, School Of Basic Medical Sciences, Peking University Health Science Center, Beijing, China, [7]Institute of Infectious Diseases, Beijing 302 Hospital, [8]Institute of Infectious Diseases, Beijing 302 Hospital, [9]Institute of Infectious Diseases, Beijing 302 Hospital, [10]Institute of Infectious Diseases, Beijing 302 Hospital, [11]Department of Microbiology & Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing, China, [12]Institute of Infectious Diseases, Beijing 302 Hospital

Introduction: It is a hot topic to study hepatitis B virus (HBV) serum markers for indicating intrahepatic viral replicative activity.
Objectives: This study was aimed at evaluating the clinical significance of serum HBV RNA, HBcrAg, and anti-HBc levels in chronic hepatitis B patients with undetectable HBV DNA during nucleoside/nucleotide analog (NA) treatment.
Methodology: Fifty-seven patients who received NA treatment of median 5.83 (4.67, 7.75) years were enrolled, and 285 serum samples at five time points for each patient were quantitatively analyzed for the serum markers.
Results: The HBV RNA level significantly correlated with HBcrAg ($r = 0.629$, $P < 0.001$) but not HBsAg levels. Nonetheless, the HBcrAg level significantly correlated with the HBsAg level ($r = 0.469$, $P < 0.001$). HBeAg-positive samples showed higher HBV RNA, HBcrAg, and HBsAg levels than HBeAg-negative samples did (all $P < 0.05$). Nine patients with HBeAg loss manifested a significantly greater decline in HBV RNA and HBcrAg levels [1.84 (0.2, 3.19) log10 copies/mL, 1.14 (0.21, 2.76) log10 U/mL, respectively] compared to those in seven patients without HBeAg loss [0.74 (0.03, 1.34) log10 copies/mL and 0.41 (0.18, 0.73) log10 U/mL, respectively]. Overall, serum HBV RNA, HBcrAg, HBsAg, and anti-HBc levels gradually decreased with time during NA treatment. At the end of observation, HBV RNA and HBcrAg reached an undetectable level in 26 and six (46% and 11%) patients, respectively.
Conclusions: Monitoring of HBV RNA and HBcrAg levels is useful for NA-treated patients with undetectable HBV DNA. The attainment of HBV RNA undetectability usually occurs prior to HBcrAg undetectability.

Abstract #582

TDF: The role of tenofovir in prevention of perinatal transmission of HBV from mother to child: Systematic review with meta-analysis

Minjin Lee[1], Youngsun Lee[1], Chanuk Lee[1], Sehwa Kim[1], Haein Bak[1], Haseok Lee[1], Sangjun Suh[1], Youngkul Jung[1], Jihoon Kim[1], Yeonseok Seo[1], Hyungjoon Yim[11], Jongeun Yeon[1], Kwansoo Byun[1]

[1]Department of Internal Medicine, Korea University College of Medicine, Seoul, South Korea

Background and Aims: To prevent the vertical transmission of Hepatitis B virus (HBV) from the mother to the child, administration of an antiviral agent, tenofovir disoproxila fumarate (TDF), during pregnancy has been tried in women who are either HBeAg positive or have a high viral load. In this systematic review and meta-analysis, we analyzed the efficacy and safety of TDF in preventing the vertical transmission of HBV in pregnant women with a high risk of vertical transmission including only RCTs.

Method: Multiple comprehensive databases (PubMed, EMBASE, and Cochrane databases) were searched for studies evaluating the efficacy of TDF for the prevention of vertical transmission of HBV.
Results: Two studies (1 open label study and 1 double blind study) were included and analyzed. Intention to treat analysis (527 pregnancies) showed that the preventive effect of TDF was not significant (OR = 0.53, 95% CI = 0.13–2.17, P = 0.38, I^2 = 81%). However, the per-protocol analysis showed that TDF significantly reduced vertical transmission (OR = 0.10, 95% CI = 0.01–0.77, P = 0.03, I^2 = 0%). There was no significant difference between the TDF group and the control group with respect to maternal and fetal safety outcomes.
Conclusion: In pregnant women who are HBeAg-positive or have high HBV DNA titers, TDF can reduce the vertical transmission from the mother to the child without significant adverse events.

Abstract #625

Dynamic changes of serum HBV pgRNA levels in patients with chronic hepatitis B treated with entecavir of peg-interferon

Xiaoqi Yu[1], Xinxin Zhang[2], Peizhan Chen[3], Qiming Gong[4], Demin Yu[5]

[1]Research Laboratory of Clinical Virology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, [2]Research Laboratory of Clinical Virology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine & Translational Medicine Research Center, Ruijin Hospital North, Shanghai Jiao Tong University School Of Medicine, [3]Translational Medicine Research Center, Ruijin Hospital North, Shanghai Jiao Tong University School of Medicine, [4]Department of Infectious Diseases, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, [5]Research Laboratory of Clinical Virology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine

Introduction: Serum hepatitis B virus (HBV) pregenome RNA (pgRNA) levels may predict virological and serological response during antiviral therapy.
Objectives: To find the correlation between serum HBV pgRNA levels and other biomarkers, further investigate the dynamic changes of serum HBV pgRNA levels and its clinical significance during treatment.
Methodology: A real-time polymerase chain reaction was developed for quantification. HBV pgRNA levels were retrospectively determined in serial serum samples from 136 chronic hepatitis B patients who received entecavir or peg-interferon treatment. Receiver operating characteristics (ROC) analysis was performed to evaluate the prediction value in HBeAg seroconversion.
Results: The mean serum HBV pgRNA level was 6.41 [1.94] copies/ml at baseline, which was higher in HBeAg-positive patients of 7.20 [1.54] copies/ml than in HBeAg-negative patients of 4.60 [1.51] copies/ml ($p < 0.001$). Baseline HBV pgRNA levels correlate strongly with HBV DNA levels ($r = 0.82$, $p < 0.001$), moderately with HBsAg levels ($r = 0.69$, $p < 0.001$), weakly with serum alanine aminotransferase ($r = 0.28$, $p < 0.05$). Peg-interferon treatment induced a stronger decline in HBV pgRNA level from baseline to week 4, 24 and 48 in comparison to entecavir monotherapy ($p < 0.05$). Entecavir treated patients with HBeAg seroconversion showed a stronger decline in HBV pgRNA level during treatment. During treatment, the best prediction of HBeAg seroconversion was HBV pgRNA at week 4 (AUC = 0.71) in entecavir treated patients and HBV pgRNA level at week 24 in peg-interferon treated patients (AUC = 0.70).
Conclusion: Serum HBV pgRNA levels may serve as a brand new biomarker in the evaluation of patients with chronic HBV infection during antiviral therapy.

Abstract #627

Effectiveness and safety with tenofovir alafenamide (TAF) for Hepatitis B in patients of Asian race in US clinical practice

K. Rajender Reddy[1], Michael Curry[2], Ho Bae[3], Douglas Dieterich[4], Victor Ankoma-Sey[5], Calvin Pan[6], Myron Tong[7], Hie-Won Hann[8], W. Ray Kim[9], Paul Kwo[10], Lynn Frazier[11], Scott Milligan[12], Nezam Afdhal[13]

[1]University of Pennsylvania, [2]Beth Israel Deaconess Medical Center, [3]st. Vincent Medical Center, Asian Pacific Liver Center, [4]Mount Sinai School of Medicine, [5]Liver Associates Of Texas, P.A, [6]Nyu Langone Health, Nyu School of Medicine, [7]Huntington Medical Research Institute Liver Center, [8]Thomas Jefferson University Hospital, [9]Stanford University School of Medicine, [10]Stanford University School of Medicine, [11]Liver Wellness Center, [12]Trio Health Analytics, [13]Beth Israel Deaconess Medical Center

Introduction: TAF is a new prodrug of tenofovir with improved safety profile compared to tenofovir disoproxil fumarate (TDF).
Objective: To assess real-world experience with TAF for HBV patients of Asian race in US Clinical Practice.
Methodology: This study includes 212 of 1078 TRIO HBV registry patients in care at 10 centers and representing 17 US states. Patients were self-reported Asian race, initiated TAF after Nov 2016, and received $\geq$ 6 months TAF with follow up to 18 months.
Results: Population characteristics. Country of origin 49% China, 27% South Korea, 7% Viet Nam, 17% from 13 other Asian countries, median age 53 years, BMI 24.0 kg/m2, 58% male, 23% HBeAg positive, 18% osteopenia/osteoporosis, and 6% FIB-4 > 3.25. 200/212 (94%) TAF patients switched from TDF (182/200, 91%), entecavir (15/200, 8%), or other therapies (3/200, 2%). Median TAF duration was 12 months as of data collection.
Paired comparisons. HBV DNA suppression (< 2000 IU/ml) increased from 94% patients at baseline to 99% after 6 or 12 months TAF (n = 206, p = 0.006). Mean eGFR increased 4% from baseline 86.5 to 90.1 ml/min after 6 months TAF (n = 179, $p < 0.001$) and 5% from 86.2 to 90.6 ml/min after 12 months TAF (n = 120, $p < 0.001$). Normal ALT ($\leq$ 29 U/L females, $\leq$ 35 U/L males) increased from 73% patients at baseline to 86% after 6 months TAF (n = 185, p = 0.002) and from 70% at baseline to 87% after 12 months TAF (n = 126, p = 0.001).
Conclusion: In US, clinical experience with TAF for Asian patients indicates effective HBV suppression and improved renal function and ALT normalization.

Abstract #633

Anluohuaxian capsule combined with entecavir in a cohort of Chinese patients with chronic hepatitis B after 78 Week treatment: A multicentre,

Liang Miao[1], Na Wan Yang[2], Qing Xiao Dong[2], Hong Zhao[2], Qiang Gui Wang[2]

[1]Peking University First Hospital & The Third Hospital Of Qinhuangdao, [2]Peking University First Hospital

Introduction: Hepatitis B virus (HBV) infection remains a serious global health problem, which leads to chronic liver diseases such as cirrhosis and hepatocellular carcinoma (HCC). The accumulation of hepatic fibrosis leads to the development of cirrhosis and its life-threatening complications. It is critically important to screen patients who would benefit from antiviral and antifibrosis treatment. The aims of the current study were to evaluate the association between anluohuaxian capsule plus entecavir and entecavir. Methods: From October 2013 to August 2015, a total of 193 chronic hepatitis B (CHB) patients with paired liver biopsy before and after treatment in 24 teaching hospitals located in mainland China were recruited into this study and staging based on the Ishak system. Ishak histological scores of fibrosis was assessed (F0-1 no/mild fibrosis, F2 moderate fibrosis, F3 significant fibrosis, F4 advanced fibrosis and F $\geq$ 5 cirrhosis). At the time of liver biopsy, biochemical tests, blood cell and coagulation tests were performed using routine automated analyzers.
Conclusion: In this study, F $\geq$ 3 of pre-treatment patients, reverse of anluohuaxian capsule combined with entecavir group is more significant than entecavir group.

Abstract #638

RNA interference (RNAi) in chronic hepatitis B (CHB): Data from Phase 2 study with JNJ-3989

Edward Gane[1], Stephen A Locarnini[2], Tien Huey Lim[3], Simone Strasser[4], William Sievert[5], Wendy Cheng[6], Alexander Thompson[7], Bruce Given[8], Thomas Schluep[9], James Hamilton[10], Gavin Cloherty[11], Danny Wong[12], Christian Schwabe[13], Kathy Jackson[14], Carlo Ferrari[15], Ching-Lung Lai[16], Robert G Gish[17], Man-Fung Yuen[18]

[1]Auckland Clinical Studies, [2]Victorian Infectious Disease Reference Laboratory, [3]Middlemore Hospital, [4]Royal Prince Alfred Hospital, [5]Monash University Hospital, [6]Royal Perth Hospital, [7]St. Vincent's Hospital, [8]Arrowhead Pharmaceuticals, [9]Arrowhead Pharmaceuticals, [10]Arrowhead Pharmaceuticals, [11]Abbott Diagnostics, [12]The University Of Hong Kong, [13]Auckland Clinical Studies, [14]Victorian Infectious Disease Reference Laboratory, [15]University Of Parma, [16]The University Of Hong Kong, [17]Stanford University & The Hepatitis B Foundation, [18]The University Of Hong Kong

Introduction: RNAi with JNJ-3989 (formerly ARO-HBV) shows promise in CHB by silencing HBV RNA from cccDNA and integrated HBV DNA, reducing all viral products, including HBsAg (AASLD 2018). Herein we update those findings.
Objectives: To assess the activity of JNJ-3989 on circulating viral products.
Methodology: CHB cohorts 2b-5b (n = 4 each, HBeAg pos or neg, NUC treated or not) received 3 monthly doses of 100, 200, 300 or 400 mg. HBeAg pos NUC naïve and experienced CHB (cohorts 8, 9, n = 4 each) received 300 mg monthly $\times$ 3. NUC untreated received NUCs from day1 and continued NUCs after the last dose of JNJ-3989.
Results: Adverse events were mild and similar in occurrence for active or placebo. Injection site AEs (all mild) occur in $\sim$ 12% of injections. In CHB, mean (max) log10 reductions in HBsAg were: 100 mg 1.9 (2.5), 200 mg 1.8 (2.4), 300 mg 1.7 (2.1) and 400 mg 1.9 (2.5) through day 113 (56 days after 3rd dose, cohorts 2b–5b) and 2.0 (3.7) in cohort 8 through day 85 (28 days after 3rd dose) and 2.0 (2.7) through day 57 (day of 3rd dose) in cohort 9. All patients reaching day 85 reduced HBsAg $>$ 1.0 log, with nadir at day 113 in many. In CHB patients, all viral parameters above LLOQ at baseline improved following JNJ-3989.
Conclusions: JNJ-3989 was well tolerated. Monthly RNAi effectively reduced all measurable viral products, including HBsAg. JNJ-3989 has characteristics desirable for RNAi as a cornerstone therapy in finite regimens aimed at HBsAg clearance.

Abstract #639

Cost-effectiveness analysis (CEA) of nucleos(t)ide analogs (NAs) for chronic hepatitis B (CHB) patients in China: A literature review

Guiqiang Wang[1], Jianwei Xuan[2], Ying Han[3], Si Xuan[4], Gabriel Wong[5], Ming Hu[6], Yida Yang [7], Lei Wang[8], Fengqin Hou[9], Dongying Xie[10], Luwen Shi[11]

[1]Peking University First Hospital, [2]pharmacoeconomics Research Centre, Sun Yat-Sen University, [3]Xijing Hospital Of The 4th Military Medical University, [4]Leonard D. Schaeffer Center For Health Policy and Economics, University of Southern California, Los Angeles, CA, USA, [5]Gilead Sciences Inc, Foster City, CA, USA, [6]Huaxi Healthcare Policy And Pharmacoeconomics Research Centre, Sichuan University, [7]The 1st Affiliated Hospital of Zhejiang University, [8]The 2nd Hospital of Shandong University, [9]Peking University First Hospital, [10]The 3rd Affiliated Hospital of Sun Yat-Sen University, [11]Medical Faculty of Peking University

Introduction/Objectives: As CHB patients are aging with increasing comorbidities, current guidelines have recommended that treatment switches should be considered for patients presenting with renal or bone comorbidities to avoid exacerbating current health. Cross-resistance for low genetic barrier NAs is another concern due to lifelong treatment required for NAs. The objective of this study is to systematically assess CEAs of NAs for CHB treatment in China that have been published in recent years and identify potential modelling gaps
Methods: We performed a comprehensive literature review of CHB burden in China including CEAs of NAs. PubMed was searched using MeSH terms chronic hepatitis B virus or CHB or HBV and China from 2008 to 2018. Two reviewers independently screened a total of 6,942 studies. Inclusion criteria were 1) China based; 2) CHB study population; 3) NA interventions; and 4) CEA study type. Burden-of-illness studies and cost analyses were excluded.
Results: A total of 8 studies were included. All studies utilized a cohort Markov model with lifetime horizon and applied a willingness-to-pay threshold of 3 times GDP-per-capita. Overall, the most influential parameters were utility values and costs related to treatment. However, no study considered costs and disutility due to adverse events or modelled subsequent lines of treatment after development of resistance.
Conclusion: Given the aging Chinese CHB populations with increasing comorbidities and lifelong treatment often required, future models should incorporate adverse events and model clinical outcomes after resistance.

Abstract #644

A Randomized, Placebo-controlled, Blinded Phase 1b Study Evaluating the Oral TLR8 Agonist GS-9688 in Patients with Chronic Hepatitis B (CHB)

Edward J. Gane[1], Hyung Joon Kim[2], Kumar Visvanathan[3], Yoon Jun Kim[4], Anh-Hoa Nguyen[5], Maribel Reyes[6], Audrey Lau[7], Anuj Gaggar[8], G. Mani Subramanian[9], Stuart K. Roberts[10], Young-Suk Lim[11]

[1]Department of Gastroenterology and Hepatology, Auckland City Hospital, Auckland, New Zealand, [2]Department of Internal Medicine, Chung-Ang University Hospital, Seoul, South Korea, [3]Department of Medicine, St. Vincent's Hospital, Melbourne, Australia, [4]Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea, [5]Gilead Sciences, Inc, Foster City, CA, United States, [6]Gilead Sciences, Inc, Foster City, CA, United States, [7]Gilead Sciences, Inc, Foster City, CA, United States, [8]gilead Sciences, Inc, Foster City, CA, United States, [9]gilead Sciences, Inc, Foster City, CA, United States, [10]Department of Gastroenterology, Alfred Hospital, Melbourne, Australia, [11]Department of Gastroenterology, Asan Medical Center, Seoul, South Korea

Introduction: GS-9688 is an oral selective small molecule agonist of Toll-like receptor 8 in clinical development for the treatment of chronic hepatitis B (CHB). GS-9688 was previously shown to induce cytokine production, activate human immune effector cells in vitro, and demonstrate sustained efficacy in the woodchuck model of CHB.
Objectives: To evaluate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of GS-9688 in CHB patients.
Methods: In this randomized, blinded, placebo-controlled phase 1b study, 38 patients were enrolled in 4 cohorts evaluating 2 or 4 weekly doses. Virally suppressed patients received doses of 1.5 mg or 3 mg and untreated viremic patients received doses of 3 mg (Table). Periodic evaluation of safety assessments (e.g. adverse events [AEs] and laboratory abnormalities), PK, viral parameters, and PD (IL-12p40 and IL-1RA) response was performed.
Results: Baseline demographics are summarized in the table. GS-9688 was well tolerated in patients with no serious AEs, Grade $\geq$ 3 AEs or laboratory AEs, and no study drug discontinuations. The most common AEs were headache and nausea. PK was similar in virally suppressed and viremic patients. Dose-dependent induction of serum PD biomarkers was observed with no evidence of tachyphylaxis through 4 doses.
Conclusions: Oral administration of GS-9688 is safe and well-tolerated in CHB patients and induces PD response. Based on the encouraging data in this study, GS-9688 is now being evaluated in two Phase 2 clinical trials. These longer duration studies are designed to evaluate the antiviral efficacy of GS-9688 in virally suppressed and untreated viremic CHB patients.

Abstract #656

Efficacy and safety of tenofovir with and without UDCA in chronic hepatitis B: Interim analysis of phase 2 randomized, double-blinded, placebo-controlled study

Hee Yeon Kim[1], Chang Wook Kim[2], Sung Geun Kim[3], Seung Up Kim[4], Jung Hyun Kwon[5], Joo Ho Lee[6], Hyung Jun Yim[7], Jae Youn Cheong[8]

[1]Department of Internal Medicine, The Catholic University of Korea College of Medicine, [2]Department of Internal Medicine, The Catholic University of Korea College of Medicine, [3]Department of Internal Medicine, The Catholic University of Korea College of Medicine, [4]Department of Internal Medicine, Yonsei University College of Medicine, [5]Department of Internal Medicine, The Catholic University of Korea College of Medicine, [6]Department of Internal Medicine, Cha University Cha Bundang Medical Center, [7]Department of Internal Medicine, Korea University College of Medicine, [8]Department of Internal Medicine, Ajou University School of Medicine

Background: This study aimed to assess the effect of ursodeoxycholic acid (UDCA) in improving liver inflammation in alanine aminotransferase (ALT) elevated chronic hepatitis B (CHB) patients who commence tenofovir therapy.
Methods: Eighty-nine tenofovir-naïve patients with CHB were enrolled from 6 centers. Patients were randomly assigned into 3 groups; tenofovir combined with placebo, tenofovir combined with UDCA 600 mg, and tenofovir combined with UDCA 1000 mg groups. Serum ALT, HBV DNA, ELF score as fibrosis state, inhibitory molecules of T cell such as PD-1, CTLA-4 and FoxP3, superoxide dismutase, malondialdehyde and TNF-alpha were checked longitudinally.
Results: Out of 89 patients, 8 patients dropped out, 58 patients completed 1-year follow-up, and follow-up of remaining patients is ongoing. ALT normalization rates based on AASLD criteria at week 4 were not statistically different between 3 groups. However, ALT normalization rates were higher in UDCA combination groups than those in tenofovir monotherapy group at week 24, 36 and 48 ($P < 0.05$). Improvement of liver fibrosis measured by enhanced liver fibrosis score at week 48 was not different between groups ($P = 0.66$). Inhibitory molecules of T cell such as PD-1, CTLA-4 and FoxP3, superoxide dismutase, malondialdehyde and TNF-alpha were checked longitudinally, however, there were no significant differences among these three groups ($P > 0.05$).
Conclusions: Combination treatment of UDCA with tenofovir can improve ALT normalization rate based on AASLD criteria in ALT elevated CHB patients.

Abstract #679

Projection of health outcomes over 5-year and 10-year period using tenofovir alafenamide (TAF) for the management of chronic hepatitis B (CHB) in China

Ying Han [1], Bin Wu [2], Ming Hu [3], Fengqin Hou[4], Yida Yang [5], Lei Wang [6]

[1]Xijing Hospital of the 4th Military Medical University, [2]Renji Hospital of Shanghai Jiaotong University, [3]Huaxi Healthcare Policy and Pharmacoeconomics Research Centre, Sichuan University, [4]The 1st Hospital of Peking University, [5]The 1st Affiliated Hospital of Zhejiang University, [6]The 2nd Hospital of Shandong University

Introduction/objectives: The burden of CHB infection in China is high, with an estimated 96 million patients. The goal of therapy is to suppress viral replication and achieve normalization of alanine aminotransferase (ALT) levels to reduce related liver complications such as compensated cirrhosis (CC), decompensated cirrhosis (DC), and hepatocellular carcinoma (HCC). In this study, we simulated the health consequences of nuecleos(t)ide analog (NA) therapies on 100,000 Chinese CHB patients comparing TAF to tenofovir disoproxil fumarate (TDF) and entecavir (ETV).
Methodology: A health outcomes model was developed using an individual patient simulation framework. Model inputs were sourced from randomized controlled trials and peer-reviewed Chinese literature and validated by a panel of Chinese hepatologists. The model assumed that 90% of patients in the overall population were treatment-experienced (TE), of which 27% were assumed to have

lamivudine (LAM) experience. The 5-year and 10-year risks for developing CC and HCC were calculated based on REVEAL score, taking into account early ALT normalization.
Results: Over the 5-year and 10-year period, patients treated with TAF were expected to experience less liver complications including CC, DCC, and HCC compared to TDF and ETV (Table 1). Specifically, compared to TDF and ETV, with TAF the rates of HCC were reduced by 13% and 31% over the 5-year projection.
Conclusions: TAF is projected to have fewer hepatic complications when compared to TDF and ETV over 5-year and 10-year time period, driven by its favorable efficacy and resistance profile.

Abstract #684

PEG-IFNa add-on Entecavir achieved more HBsAg clearance compared to ETV monotherapy and PEG-IFNa based therapy

Xiaoyu Fu[1], Yi Ouyang[2], Lei Fu[3], Shifang Peng[4], Deming Tan[5]

[1]Department of Infectious Diseases, Xiangya Hospital, Central South University

Objectives: To evaluate the HBsAg clearance by different therapy in naïve HBeAg positive CHB patients.
Methods: In total, 162 patients were included of which were divided into three groups. 1) ETV: 65 were treated with 48 weeks, and 31%(20/65) was completed 96 weeks; 2) PEG-IFNa add-on: 62 were treated for more than 24 weeks with ETV (different duration from 24 to 96 weeks) + 48 weeks PEG-IFNa add-on, and 35.5%(22/62) received 96 weeks with PEG-IFNa add-on; 3) 35 received 48 weeks with PEG-IFNa based therapy (PEG-IFNa and NAs combination therapy or PEG-IFNa monotherapy). HBsAg level was assessed at different points.
Results: 1) For add-on, PEG-IFNa based and ETV, the mean HBsAg-level change at 48 weeks was 1.51, 0.69 and 0.26 log10 IU/mL, respectively (P<0.01), HBeAg clearance at 48 weeks was 38.2%, 31.7% and 25.4%, respectively (P<0.05). At 48 weeks, the HBsAg clearance/HBsAg seroconversion rate was more frequently achieved for patients in the add-on therapy (10/62 = 16.13%, 5/62 = 8.06%), compared to PEG-IFN based (2/35 = 5.7%, 1/35 = 2.86%) or ETV (1/65 = 1.54%, 1/65 = 1.54%) (P<0.01) therapy. 2) At 96 weeks, there were significant differences on both HBsAg<100 IU/ml and HBsAg clearance rate (15/22 = 68.18%, 8/22 = 36.36%; and 3/20 = 15%, 1/20 = 5%, respectively) between PEG-IFNa add-on and ETV. 3) The HBsAg level change $\geq$ 0.5log10 IU/ml at 24 weeks have higher HBsAg clearance rate than that at 12 weeks (P<0.05).
Conclusion: PEG-IFNa add-on for 48 weeks results in more HBsAg decline and HBsAg clearance than does 48 weeks of ETV or PEG-IFN based therapy. Prolong the duration of PEG-IFNa add-on to 96 weeks could achieve higher HBsAg clearance rate.

Abstract #711

Five year renal outcome in Korean chronic hepatitis B patients treated with tenofovir disoproxil fumarate

Tae Seop Lim[1], Beom Kyung Kim[2], Hye Won Lee[3], Mi Young Jeon[4], Seung Up Kim[5], Jun Yong Park[6], Do Young Kim[7], Kwang-Hyub Han[8], Sang Hoon Ahn[9]

[1]Yonsei University College of Medicine & Yonsei Liver Center, Severance Hostpital, [2]Yonsei University College of Medicine & Yonsei Liver Center, Severance Hostpital, [3]Yonsei University College Of Medicine & Yonsei Liver Center, Severance Hostpital, [4]Yonsei University College of Medicine & Yonsei Liver Center, Severance Hostpital, [5]Yonsei University College of Medicine & Yonsei Liver Center, Severance Hostpital, [6]Yonsei University College of Medicine & Yonsei Liver Center, Severance Hostpital, [7]Yonsei University College Of Medicine & Yonsei Liver Center, Severance Hostpital, [8]Yonsei University College of Medicine & Yonsei Liver Center, Severance Hostpital, [9]Yonsei University College of Medicine & Yonsei Liver Center, Severance Hostpital

Introduction: Tenofovir disoproxil fumarate (TDF) is known to be an effective antiviral agent for chronic hepatitis B (CHB). However, its long-term effects on renal function have been controversial.
Objectives: This study aimed to analyze the real-world long-term effects of TDF on renal function in Korean patients with CHB.
Methodology: We analyzed a cohort of consecutive treatment-naïve patients with CHB who were treated with TDF between May 2012 and December 2015 at Severance Hospital, Seoul, Republic of Korea. Estimated glomerular filtration rate (eGFR) was calculated with Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI).
Results: A total of 640 patients were analyzed. The mean age was 48.3 years old, and 59.5% were male. During the 5 year follow up, using linear mixed model, serum creatinine increased from 0.77 $\pm$ 0.01 mg/dL to 0.85 $\pm$ 0.02 mg/dL ($P < 0.001$), and eGFR decreased from 102.6 $\pm$ 0.6 mL/min/1.73m2 to 93.4 $\pm$ 1.4 mL/min/1.73m2 ($P < 0.001$). In subgroup analysis, eGFR was statistically more decreased in patients with age > 60 than $\leqq$ 60 ($P = 0.027$), and in patients with using diuretics than without using diuretics ($P = 0.008$). In multivariate analysis, the independent risk factors for eGFR decrease more than 20% were baseline eGFR < 60 mL/min/1.73m2 ($P = 0.047$) and use of diuretics ($P < 0.001$).
Conclusion: Renal function was more decreased in patients with age > 60 and in group using diuretics, and baseline eGFR < 60 mL/min/1.73m2 and use of diuretics were independent risk factors of eGFR decline more than 20% on TDF therapy.

Abstract #730

Reduction serum HBsAg level in patients with chronic hepatitis B infected induced by (pegylated) interferon alfa-2a

Jacobus Albertus Auwyang[1], Priska Harsanti Devi[2]

[1]tugurejo General Hospital & Mitrakita Clinic, [2]mitrakita Clinic

Background: A recent study suggested that on-treatment HBsAg quantification may provide clues about the likelihood of subsequent HBsAg clearance.
Study Aim: To quantify serum HBsAg in patients with CHB who were treated with peginterferon alfa-2a.
Methods: We enrolled 98 patients (median age 34 years, range 18–56 years; 54 males, 44 females) with chronic hepatitis B. 91 patients received in peginterferon alfa-2a monotherapy for 48 weeks, 7 pts received peginterferon alfa-2a + Tenovofir (TDF) in combination for 24 weeks. HBsAg was measured every 6 months during treatment. HBV DNA was measured before and the end of treatment.
Results: During treatment peginterferon alfa-2a + Tenovofir (TDF) in combination for 24 weeks 7/7 patients (100%) achieved a complete inhibition of viral replication while in therapy with peginterferon alfa-2a alone 80 of these 91 pts (81.6%) had a response at the end of treatment. Reductions in HBsAg levels from baseline to last observation : > 1500 IU/ml : 22/88 pts (22.4%); < 1500 : 28/88 pts (28.5%); < 100 : 25/88 pts (25.5%); < 10 : 13/88 pts (13.3%) and 10 of these 98 pts (10.2%) cleared HBsAg (seroconevrsion). Safety Assessment alopecia was another frequent side-effect identified at 38.7%. Other adverse effects included myalgia, headache and dose modification (12.2%).

Conclusion: peginterferon alfa-2a -based therapy most effective in reducing levels of serum HBsAg independent of baseline host and virologic features. Yearly quantification of serum HBsAg could provide a useful tool to predict the long-term outcome of IFN-based therapy.

Abstract #762

Fibrosis Change with Transient Elastography in Chronic Hepatitis B Virus Treatment with Tenofovir

Luciana Sophie Mariana Rotty[1], Bradley Jimmy Waleleng[1]

[1]Gastroenterohepatology, Department Of Internal Medicine, Sam Ratulangi University/R. D. Kandou Hospital, Manado, Indonesia

Introduction: Hepatitis B virus infection are a major global health problem that can result in cirrhosis, liver failure, and hepatocellular carcinoma. The current antiviral used to decrease viremia, inflammation and the growth of liver fibrosis. We investigate the change in liver fibrosis using transient elastography under tenofovir treatment.
Objective: Fibrosis change under Tenofovir treatment in chronic hepatitis b infection.
Methodology: From January 2017 to December 2018, all consecutive patients with chronic hepatitis b infection who receive tenofovir treatment enrolled. Liver fibrosis was assessed before treatment using transient elastography and during treatment.
Result: 70 patients with chronic hepatitis B virus treated with tenofovir was enrolled. Liver fibrosis assessed using transient elastography. Age between 20–75 with average age 48.08 years with SD $\pm$ 15.37 years. Gender was 19 (27.14%) female and 51 (72.86%) male. Liver fibrosis significantly decrease during the treatment (21.44 kPa [2.8– 75] vs 15.63 kPa [4–68]; $p < 0.001$).
Conclusion: Suppression hepatitis virus with antiviral treatment leads to reduction in necroinflammatory activity and improvement in staging of liver fibrosis. Treatment with tenofovir improved significantly reduce liver stiffnes measured with transient elastography in this study. Antivirals in clinical use for treatment chronic hepatitis b infection lead to reduction of liver stiffness.

Abstract #770

Providing Tenofovir in Primary Care Setting for Prevention of Mother-to-Child Transmission of Hepatitis B (PMTCT of HBV) in Peri-urban Yangon, Myanmar: A Mixed-methods Study Protocol

Khin Pyone Kyi[1], Win Win Swe[2], Adam Richards[3], Myat Sandi Min[4], Win Naing[5], Rachel Whelan[6], Hnin Nandar Htut[7], Eindra Htoo[8], Htun Aung Shein[9]

[1]Myanmar Liver Foundation, [2]Department of Hepatology, North Okkalapa General Hospital, [3]Department of Medicine, University Of California, [4]Community Partners International, [5]Department of Hepatology, 500-Bedded Specialist Hospital, [6]Community Partners International, [7]B.K.Kee Foundation, [8]Community Partners International, [9]B.K.Kee Foundation

Introduction: Mother-to-child transmission accounts for the majority of chronic hepatitis B infections in Southeast Asia. Because evidence is lacking for feasible implementation strategies for PMTCT of HBV in resource-limited settings, this study aims to develop and implement a community-oriented primary care (COPC) model for PMTCT of HBV.
Methods: 110 HBsAg-positive pregnant women are being recruited from first trimester of pregnancy through hospital-based and antenatal care clinic-based HBV screening, community-based pregnancy surveillance and community-based HBV education sessions. Women who are eligible for treatment according to WHO criteria or with viral load (VL) > 200,000 IU/mL at baseline receive Tenofovir from Antenatal Care Clinic, from 20 weeks gestation until 4 weeks after delivery. All newborns receive the HBV birth-dose vaccine, and newborns of Tenofovir-treated mothers receive Immunoglobulin within 24 hours after delivery. Maternal VL is tested at delivery, and infant infection status and VL are tested at 24–28 weeks after delivery. In-depth-interviews with pregnant women are conducted to explore barriers and facilitators in accessing HBV-related services. Research implementation is guided by a Community Advisory Committee in community-based participatory research approach.
Results: In the first 5 months of this 2-year project (July-November 2018), 1267 pregnant women were screened, 4.3% were HBsAg-positive and two were eligible for Tenofovir. As a case-study, VL of a HBsAg-positive woman reduced from 7,056,370 IU/mL at baseline (24 gestational weeks) to 270 IU/mL at delivery after taking Tenofovir for 12 weeks.
Conclusion: Results will inform Myanmar's National Hepatitis Control Program to develop a cost-effective, COPC model using evidence-based treatment protocols for PMTCT of HBV.

Abstract #788

First line nucleos(t)ide analogue monotherapy is more cost-effective than combination approaches in HBeAg-positive chronic hepatitis B patients in terms of functional cure

Xueru Yin[1], Zhihong Liu[2], Jing Liu[3], Yuanyuan Liu[4], Li Xie[5], Libo Tao[6], Jidong Jia[7], Fuqiang Cui[8], Jinlin Hou[9]

[1]Hepatology Unit, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, [2]Hepatology Unit, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, [3]School of Pharmaceutical Sciences, Sun Yat-Sen University, [4]Hepatology Unit, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, [5]Department of Epidemiology And Biostatistics, School of Public Health, Xi'an Jiaotong University Health Science Center, [6]School of Pharmaceutical Sciences, Sun Yat-Sen University, [7]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, [8]School of Public Health, Peking University, [9]Hepatology Unit, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University

Introduction: Nucleos(t)ide analogue (NA) combined with peginterferon (PegIFN) therapy in patients with hepatitis B e antigen (HBeAg) positive chronic hepatitis B (CHB) shows superiority in hepatitis B surface antigen loss termed 'functional cure', compared with monotherapy. However, it is unknown the cost-effectiveness of these treatment approaches in terms of functional cure.
Objectives: The aim of this study is to analyse the cost-effectiveness of monotherapy and combination approaches for the treatment of HBeAg positive CHB patients in China aiming for functional cure.
Methodology: We developed a Markov model with six states, CHB, functional cure, compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma and death, to access the cost-effectiveness of eight representative treatment strategies in HBeAg positive CHB patients in China.
Results: In the base-case analysis, compared with no treatment, entecavir (ETV) monotherapy yielded the lowest ICER of $6,975 per QALY, following by strategy NA switching to PegIFN, tenofovir, and

ETV adding on PegIFN with $7,415/QALY, $12,042/QALY, and $25,146/QALY respectively. ETV generated the highest costs with $44,341, the highest QALYs with 16.75 years and life expectancy with 17.03 years. The least costs with $33,004 and QALYs with 13.55 years were obtained with PegIFN. Both one-way sensitivity analysis and probabilistic sensitivity analysis confirmed the robustness of the results and strategy ETV was the preferred option at a threshold of $26,517/QALY.
Conclusion: Among eight treatment strategies, compared with no treatment, NA monotherapy (ETV) is more cost-effective than combination approaches for HBeAg positive CHB patients in China.

Abstract #809

Fibrosis Change with Transient Elastography in chronic hepatitis B virus treatment with Tenofovir

Luciana Rotty[1], Fandy Gosal[1], Bradley Jimmy Waleleng[1], Andrew Piere Waleleng[1], Andrew Piere Waleleng[1]

[1]Internal Medicine Samratulangi University

Introduction: Hepatitis B virus infection are a major global health problem that can result in cirrhosis, liver failure, and hepatocellular carcinoma. The current antiviral used to decrease viremia, inflammation and the growth of liver fibrosis. We investigate the change in liver fibrosis using transient elastography under tenofovir treatment.
Objective: Fibrosis change under Tenofovir treatment in chronic hepatitis b infection.
Methodology: From January 2017 to December 2018, all consecutive patients with chronic hepatitis b infection who receive tenofovir treatment enrolled. Liver fibrosis was assessed before treatment using transient elastography and during treatment.
Result: 70 patients with chronic hepatitis B virus treated with tenofovir was enrolled. Liver fibrosis assessed using transient elastography. Age between 20–75 with average age 48.08 years with SD $\pm$ 15.37 years. Gender was 19 (27.14%) female and 51 (72.86%) male. Liver fibrosis significantly decrease during the treatment (21.44 kPa [2.8 – 75] vs 15.63 kPa [4–68]; $p < 0.001$).
Conclusion: Suppression hepatitis virus with antiviral treatment leads to reduction in necroinflammatory activity and improvement in staging of liver fibrosis. Treatment with tenofovir improved significantly reduce liver stiffnes measured with transient elastography in this study. Antivirals in clinical use for treatment chronic hepatitis b infection lead to reduction of liver stiffness.

Abstract #811

Non invasive evaluation on fibrosis change in chronic hepatitis B virus after 6 month treatment with Tenofovir

Rendy Suherman Sidik[1], Luciana Rotty[2], Jeane Winarta[3], Fandy Gosal[4], Bradley Jimmy Waleleng[5], Bradley Jimmy Waleleng[6]

[1]Internal Medicine Samratulangi University

Introduction : Hepatitis B virus is a leading cause of chronic liver disease and current treatment strategies is to prevent liver fibrosis by eradicating the virus. Use Tenovofir antivirals has been used in worldwide and this study reports outcome of liver fibrosis after 6 month chronic hepatitis b treatment with Tenofovir.
Objective : to evaluate changes in liver fibrosis after 6 month Tenofovir treatment in chronic hepatitis b infection.
Methodology : From January 2017 to December 2018, all consecutive patients with liver fibrosis with chronic hepatitis b infection who receive tenofovir treatment enrolled. Liver fibrosis was assessed through AST/Platelet Ratio Index (APRI score) before and during the treatment.
Result: 85 patients with chronic hepatitis B virus treated with tenofovir was enrolled. Virological response was achieved in all patient with tenofovir. Age between 20–75 with average age 47.22 years with SD $\pm$ 14.81 years. Gender was 22 (25.8%) female and 63 (74.2%) male. The APRI score values significantly decrease after treatment (2.38 [2.080–3.450] vs 2.25 [2–3.23]; $p < 0.05$).
Conclusion: Achievement of virological response after 6 month treatment with tenofovir improved liver function and significantly reduce liver fibrosis measured with APRI score in this study but need further time to followup this condition to evaluate incidence of decompensation or even hepatocellular carcinoma.

Abstract #822

Precise activation of APOBEC/AID transcription in HBV-infected cells: efficacy and safety in cell culture systems

Anastasiya Pavlovna Kostyusheva[1], Sergey Alexeyevich Brezgin[2], Elena Vasil'evna Volchkova[3], Dmitrii Sergeyevich Kostiushev[4], Vladimir Petrovich Chulanov[5]

[1]CRIE, [2]CRIE, [3]Sechenov University, [4]CRIE, [5]CRIE

Introduction: dCas9-activation tools allow precisely activating transcription of the host genes. APOBEC/AID deaminases have been shown to directly deaminate HBV cccDNA and can potentially be used for developing anti-HBV therapeutics, but stimulation of APOBEC/AID transcription remains challenging.
Objective: Achieve high-level activation of APOBEC/AID transcription using dCas9-activation tools to clear HBV infection and perform comprehensive analysis of the safety of this approach.
Methodology: Transcription of APOBEC3A, APOBEC3B, APOBEC3G, AID and UNG was activated by dCas9-p300 or dCas9-VP64 using a single sgRNA targeting promoters of these genes. Activation of transcription was monitored by measuring relative levels of mRNA and acetylation of target genes' promoters by ChIP-PCR. Antiviral activity was analyzed in four different HepG2 cell culture systems. Potential off-target activity of activated APOBEC/AID was investigated in a comprehensive manner, using cyto- and genotoxicity assays and NGS sequencing.
Results: dCas9-activation tools achieve 6–3,500-fold activation of APOBEC/AID transcription in various cell systems leading to 80–95% suppression of HBV transcription, deamination and degradation of cccDNA. Safety tests identified potential toxicity of AID and UNG. Activation of APOBEC3A, APOBEC3B and APOBEC3G does not exhibit measurable toxicity.
Conclusion: Activation of APOBEC deaminases by dCas9-activation tools is a safe approach to efficiently suppress HBV and destroy cccDNA.

Abstract #848

Development of lentiviral vectors for inhibition of hepatitis B virus, via interfering RNAi

Barbara Vieira Do Lago[1], Nayhanne De Paula Tizzo[2], Francisco Campello Do Amaral Mello[3], Vanessa Salete De Paula[4], Maryrose Fernandes Lavatori[5], Elisabeth Lampe[6]

[1]Instituto Oswaldo Cruz, Fiocruz, Rio De Janeiro, Brazil. & Bio-Manguinhos, Fiocruz, Rio De Janeiro, Brazil, [2]Bio-Manguinhos, Fiocruz, Rio De Janeiro, Brazil. & Empresa Brasileira Em Pesquisa Agropecuária – Embrapa, Federal District, Brazil, [3]Instituto Oswaldo Cruz, Fiocruz, Rio De Janeiro, Brazil, [4]Instituto Oswaldo Cruz, Fiocruz, Rio De Janeiro, Brazil, [5]Instituto Oswaldo Cruz, Fiocruz, Rio De Janeiro, Brazil, [6]Instituto Oswaldo Cruz, Fiocruz, Rio De Janeiro, Brazil.

Introduction: It is estimated that chronic hepatitis B virus (HBV) infection accounts for one million deaths/year. Currently, several drugs are used in the treatment of HBV, however, complete cure is still controversial. The major challenge is the persistence of viral covalently closed circular DNA (cccDNA), as well as the ability of HBV to integrate into the host genome, which enables the infection's reactivation. Interfering RNA (RNAi) is a post-transcriptional mechanism of gene silencing and is a promising alternative as HBV therapy.

Objectives: To obtain an effective lentiviral plasmid in the silencing of HBV proteins, via RNAi.

Methodology: Three silencing vectors candidates were obtained and tested in silico to prevent off-target effects. Such molecules targets overlapped Open Reading Frames (ORFs), allowing different viral proteins and the pre-genomic RNA to be silenced with a single RNAi. The efficiency of silencing by lentiviral vectors candidates, used individually or in combination, have been assessed by quantification of HBV proteins by immunoassay and quantification of HBV DNA during the post-transfection period.

Results: Huh7 cells were transfected with HBV DNA and 3 days later, infected with the first lentiviral candidate, targeting S/Pol genes of HBV. From the third day post-infection, HBsAg became undetectable on cells treated with the construct, while untreated controls maintained viral protein expression. HBV DNA were also undetectable by PCR.

Conclusions: The first lentiviral candidate was able to silence HBV in vitro. This approach allows long-term, sustained knockdown of HBV replication and gene expression, which can effectively eliminate HBV from chronic carriers.

Abstract #907

Treatment Eligibility Of Hepatitis B Patients On The Index Hepatology Visit According To APASL 2015 And EASL 2017 Criteria

Maria Aloiza Joven Hadloc[1], Stephen Ng Wong[1]

[1]Section of Gastroenterology Chinese General Hospital

Introduction: Recent European Association for Study of Liver (EASL) criteria for chronic hepatitisB (CHB) treatment differs from Asia Pacific Association for Study of Liver (APASL) in that thresholds been lowered.

Objectives: We aimed to determine CHB patients who meet APASL/EASL treatment criteria on initial hepatologist consult, to determine prescription patterns, and identify factors for discordance in treatment eligibility&medications.

Methodology: CHB patients in single hepatology clinic February 2007-October 2017 were included. Demographics, laboratories, treatment eligibility according to APASL 2015and EASL 2017guidelines, and treatment were recorded.

Results: 501 patients (24.3%HBeAg-positivevs.75.7% HBeAg-negative) were included, of which38.7% HBeAg-positive and 37%HBeAg-negative met APASL treatment criteria. Patients meeting APASL treatment criteria were likely with significant alcohol intake (33% vs. 14.3%; $p < 0.001$), male (77.7% vs. 53.3%; $p < 0.001$), older (52.5 + 28.6 vs. 38.1 + 28.3; $p < 0.001$), with lower albumin (36.7 + 9.5 vs. 43.4 + 5.1; $p < 0.001$) and platelets (207.9 + 95.8 vs. 238 + 80.9; $p < 0.001$), higher INR (1.3 + 0.6 vs. 1 + 0.2; $p < 0.001$) and AST (115.5 + 144.1 vs. 60.2 + 180.5; $p = 0.001$) levels. While 97.1%with hepatocellular carcinoma (HCC)/cirrhosis met treatment criteria, only 7.3%without complications met criteria ($p < 0.001$). Among 193 who met APASL criteria, 65.8% had treatment. The most common treatment after hepatologist consult were entecavir (70.1%) and tenofovir (12%), while lamivudine (30.2%) and entecavir (28.1%) were commonly prescribed before seeing a hepatologist. Reasons for not starting treatment in 66 patients were loss tofollow-up (62.1%) and patient/doctor decision (37.9%). The 84 patients treated despite not meeting APASL criteria were likely > 40 y/o (56% vs. 44%) and started on treatment before hepatologist consult (61.4% vs. 38.6%). Applying EASL criteria to same cohort resulted in additional 44 (8.7%) who meet treatment thresholds, all from subgroup without complications (n = 39) and those with jaundice/ALT flares (n = 5).

Conclusions: CHB patients who meet treatment criteria be skewed towards treatment because of high number cirrhotic/HCC patients included, and be closer to the7.3%patients without complications in typical gastroenterology clinic. Although lowering treatment threshold increases patients needing treatment, its influence on development of liver complications has yet be proven.

Abstract #911

Establishment of High Rates of Functional cure of HBeAg negative chronic HBV with REP 2139-Mg Based Combination Therapy

Michel Bazinet[1], Victor Pantea[2], Gheorge Placinta[3], Iurie Moscalu[4], Valentin Cebotarescu[5], Lilia Cojuhari[6], Pavlina Jimbei[3], Liviu Iarovoi[3], Valentina Smesnoi[3], Tatiana Musteata[3], Alina Jucov[7], Adalbert Krawczyk[8], Andrew Vaillant[1]

[1]Replicor INC, Montreal, Canada, [2]nicolae Testemiţanu State University, Chişinău, Moldova Of Medicine And Pharmacy, [3]Nicolae Testemiţanu State University, Chişinău, Moldova Of Medicine And Pharmacy, [4]Arensia Exploratory Medicine, Chişinău, Moldova, [5]Nicolae Testemiţanu State University, Chişinău, Moldova Of Medicine And Pharmacy, [6]Nicolae Testemiţanu State University Of Medicine And Pharmacy, Chişinău, Moldova, [7]Nicolae Testemiţanu State University Of Medicine And Pharmacy, Chişinău, Moldova & Arensia Exploratory Medicine, Chişinău, Moldova, [8]Universitätsklinikum Essen, Essen, Germany

Introduction: The REP 401 study (NCT02565719) is assessing the safety and efficacy of REP 2139-Mg (clinical lead) or REP 2165-Mg combined with TDF and pegIFN in HBeAg negative chronic HBV infection.

Methods: Following lead-in TDF, 40 patients were randomized into experimental (TDF, pegIFN and REP 2139-Mg or REP 2165-Mg) or control groups (TDF and pegIFN). Following futility at 24 weeks, all control patients crossed over to experimental therapy for 48 weeks.

Initial follow-up is for 48 weeks. Viremia is monitored on the Abbott Architect and Realtime platforms.
Results: Following introduction of REP 2139-Mg or REP 2165-Mg, HBsAg reduction was > 1 log in 36/40 and became < 1 IU/mL in 28/40 and < 0.05 IU/mL in 24/40 participants. Transaminase flares (otherwise asymptomatic) occurred in 38/40 patients, correlated with reductions in HBsAg and HBsAg seroconversion and self-resolved during therapy and follow-up.
Follow-up is ≥ 24 weeks in 34 patients completing treatment. Inactive chronic HBV (HBV DNA < 2000 IU/mL, normal ALT) is present in 15/34 (44%) of participants. Functional cure (undetectable HBV DNA and HBsAg) is present in an additional 14/34 (41%) of participants. Liver function has normalized in 94% of patients (47% at baseline) and median hepatic stiffness consistent with F0 (≤ 7 kPa) is present in 81% of patients (52% at baseline).
Conclusion: A finite REP 2139-Mg based therapy with TDF and pegIFN is well tolerated and restores control of infection requiring no further treatment in 85% of patients and is accompanied by normalization of liver function and reversal of liver inflammation.

Abstract #912

Development of a Nasal Therapeutic Vaccine Against Chronic Hepatitis B

Gerardo Guillen[1], Julio Cesar Aguilar[1], Yadira Lobaina[1], Eduardo Penton[1], Verena Muzio[1], Mamun Al Mahtab[2], Sheikh Mohammad Fazle Akbar[3]

[1]Center For Genetic Engineering and Biotechnology, [2]Bangabundhu Sheikh Mujib Medical University, [3]Department of Pathology, Ehime University, Graduate School of Medicine

Introduction: Despite the existence of effective prophylactic vaccines, hepatitis B virus (HBV) infections remain a major public health problem. About 370 million people are chronically infected worldwide. Chronic hepatitis b (CHB) infection also increases the risk of liver diseases such as cirrhosis and hepatocellular carcinoma.
Current antiviral therapies fail to control viral replication in the long term in most patients. As HBV persistence has been associated with a defect in the development of HBV-specific cellular immunity, therapeutic vaccination has been extensively studied in CHB.
Materials and Methods: HeberNasvac is a novel vaccine containing HBcAg expressed in E. coli and HBsAg expressed in Pichia pastoris in phosphate buffer administered by the intra nasal (IN) and subcutaneous (SC) routes. The vaccine induces B and T cell functional response in mice and randomized double blinded and controlled trials. Patients from Phase I and III trials were followed for 5 and 3 years after treatment, respectively. Clinical efficacy was monitored by assessing the levels of DNA, ALT, HBeAg to anti-HBeAg seroconversion, comparing HeberNasvac vs PEgIFN.
Results: The pharmacological results and clinical data support the rationality of the IN administration. The HeberNasvac immunized subjects account for a higher proportion of patients with < 250 c/mL and also with < 10 000 copies/mL compared to PegIFN and support the benign nature of the transient ALT flares at week 12, associated to HBV control.
Conclusion: HeberNasvac induced an antiviral effect associated to a Th1 response. This antiviral response was more sustained in vaccinated than PegIFNα treated patients.

Abstract #924

Cytomegalovirus-based HBsAg vaccine induces robust T cell responses and results in viral clearance in HBV persistent mice

Hongming Huang[1], Dongliang Yang[1], Jia Liu[1]

[1]Department of Infectious Disease, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Curative approaches for chronic hepatitis B (CHB) are urgently needed. Cytomegalovirus (CMV) can elicit a remarkable impact on the immune system of their hosts. CMV-based vaccines are currently in the spot-light as they showed superb control of chronic viral infections and tumors growth in animal models. In this study, we examined the potential of using CMV as vectors for generating HBV vaccines. To test the ability of MCMV-based HBV vaccines against HBV, C57BL/6 mice were vaccinated either with MCMV-HBsAg or Δm27 -HBsAg (MCMV replication deficiency strain), and were challenged with HBV through hydrodynamic injection. Compared to untreated or MCMV-vaccinated control mice, mice vaccinated with MCMV-HBsAg or Δm27 -HBsAg showed significantly accelerated HBV clearance in the serum and liver. A rapid development of serum HBsAb after HBV challenge was detected in MCMV-HBsAg vaccinated mice but not control mice. And significantly increased numbers of HBsAg-specific CD8 + T cells in the liver was only observed in MCVM-HBsAg but not MCMV vaccinated mice. A rapid development of robust HBsAg and HBcAg specific CD8 + T cell responses was also observed in the liver of MCMV-HBsAg vaccinated mice compared to control mice. Moreover, we also explored the therapeutic effect of MCMV-HBsAg vaccines in HBV persistent replication mice. Both Δm27- HBsAg and MCMV-HBsAg vaccination resulted in significant HBV suppression. In conclusion, our results demonstrated that MCMV-HBsAg vaccine could elicit robust anti-HBV immune responses and mediate HBV clearance in mice.

Abstract #1006

Histological Improvement In Chronic Hepatitis B Patients Treated With Bicyclol: Real World Experience

Xiaoling Chi[1], Huanming Xiao[1], Meijie Shi[1], Gaoshu Cai[1], Yubao Xie[1], Junmin Jiang[1], Guangjun Tian[1], Shuduo Wu[1], Chaozhen Zhang[1], Pengtao Zhao[1], Jiezhen Chen[1]

[1]Guangdong Provincial Hospital Of Chinese Medicine

Background: Data on histological changes after bicyclol treatment in these patients is scarce. Therefore, this study was conducted to find out whether bicyclol has good benefits of histological improvement in CHB patients who refused antiviral agents.
Methods: The demographic, clinical, and pathological data were collected from CHB patients who received bicyclol from January 2010 to June 2016. The biochemical, virological parameters as well as the pathological changes of liver were assessed after bicyclol treatment. Improvement in liver inflammation or fibrosis was defined as at least one-grade or one-stage decrease as measured by the Scheuer scoring system.
Results: A total of 123 patients with CHB treated with bicyclol were included in this study. Paired liver biopsies were performed in 70 patients. Inter-biopsy interval was 17.44 ± 8.90 months (12–60 months). It showed that 41.4% patients achieved liver inflammation improvement, while only 10.0% patients showed liver inflammation progression after bicyclol treatment. Regarding to living fibrosis, it showed 28.6% patients achieved fibrosis improvement.

Most of patients (82.4%) with elevated baseline ALT had become normal after bicyclol treatment. More importantly, the multivariate analysis showed that the treatment course of bicyclol was an independent factor for liver inflammation improvement. After adjusting for the HBeAg status, ALT and HBV-DNA quantity, the odds ratio (95% confidence interval) of patients with ≥ 48-week treatment was 5.756 (1.893, 17.500) when compared with patients with < 48-week treatment.
Conclusion: Bicyclol could improve liver inflammation and the ALT normalization rate of CHB patients, especially when prolonging the treatment course.

Abstract #1017

Efficacy of entecavir treatment for up to 6 years in chronic hepatitis B patients in Turkey; real life data

Mehmet Demir[1]

[1]mustafa Kemal University

Background: The aim of this study was to determine the efficacy and safety of long term entecavir monotherapy in chronic hepatitis B (CHB) patients.
Methods: We performed a retrospective analysis of data from 176 adult patients with CHB, beginning in 2012, at single center throughout Turkey. Baseline demographic characteristics, laboratory and clinical outcomes were recorded at yearly intervals. Patients with cirrhosis, hepatocellular carcinoma, pregnant or in lactation, and co-infected with hepatitis C, D or human immunodeficiency virus were excluded. Baseline liver biopsy was performed in 81% of the patients.
Results: In this study, 176 CHB patients from four centers receiving entecavir therapy were included. Average age was 46 ± 8 years, 94% of patients were naive, 32.1% of patients were HBeAg positive and 59.5% were male. Mean follow-up was 42 ± 13 months. Mean histopathologic activity index were 8 and fibrosis scores were 2.1. Baseline mean ALT and HBV DNA levels were 92 U/L and 8.1 log10 copies/mL, respectively. At the end of the 1st, 2nd, 3rd, 4th, 5th and 6th years of therapy, HBV DNA < 400 copies/mL was 90.4, 94.1, 95.8, 99.4 and 100%; ALT normalization was 82.1, 88.6, 89.2, 91.1, 93.2 and 94.3%; HBeAg loss/seroconversion was 11.1, 20.4, 35.1, 44.4, 54.3 and 59.3%, respectively. HBsAg loss and HBsAg seroconversion were detected in 3 patients. No adverse effects were determined for withdrawal of durg. Age, sex, baseline serum ALT, HBV DNA levels and HBeAg positivity were not associated with maintained virological suppression.
Conclusion: Entecavir is effective and safe for long-term use in patients with CHB patients in Turkey.

Abstract #1021

Efficacy of tenofovir treatment for up to 8 years in chronic hepatitis B patients in real life data from Turkey.

Mehmet Demir[1]

[1]Mustafa Kemal University

Background: The aim of this study was to determine the efficacy and safety of long term tenofovir monotherapy in chronic hepatitis B (CHB) patients in Turkey.
Methods: We performed a retrospective analysis of data from 265 adult patients with CHB, beginning in 2010, at single center. Baseline demographic characteristics, laboratory and clinical outcomes were recorded at yearly intervals. Patients with cirrhosis, hepatocellular carcinoma, pregnant or in lactation, and co-infected with hepatitis C, D or human immunodeficiency virus were excluded. Baseline liver biopsy was performed in 81% of the patients.
Results: In this study, 265 CHB patients from two centers receiving tenofovir therapy were included. Average age was 41 ± 28 years, 69% of patients were naive, 20% of patients were HBeAg positive and 61% were male. Mean follow-up was 48 ± 15 months. Mean histopathologic activity index were 9 and fibrosis scores were 2.1. Baseline mean ALT and HBV DNA levels were 76 U/L and 6.3 log10 copies/mL, respectively. At the end of the 1st, 2nd, 3rd, 4th, 5th, 6th, 7th and 8th years of therapy, HBV DNA < 400 copies/mL was 92.4, 95.1, 98.2, 99.3, 100, 100, 100 and 100%; ALT normalization was 73.4, 84.7, 88.8, 90.1, 94.3, 96.8, 97.4 and 98.3%; HBeAg loss/seroconversion was 9.2, 16.3, 25.4, 39.5, 45.4, 49.1, 53.5 and 59.6% respectively. HBsAg loss and HBsAg seroconversion were detected in 5 patients. No adverse effects were determined for withdrawal of durg. Age, sex, baseline serum ALT, HBV DNA levels and HBeAg positivity were not associated with maintained virological suppression.
Conclusion: Tenofovir is effective and safe for long-term use in patients with CHB patients in Turkey.

Abstract #1088

Adverse events during HBV treatment with Tenofovir Disoproxil Fumarate (TDF) in 542 chronic HBV patients in Mongolia

Chantsalsuren Sukhsuren[2], Namuuntsetseg Gankhuyag[1], Budmaa Dashlkhundev[1], Zolzaya Sumiyajav[1], Nasanbayar Tumurbaatar[1], Ankhbayar Bat-Ochir[2], Choijamts Nagir[3], Erdenebayar Gonchig[2], Baatarkhuu Oldov[2], Bold Manaljav[1], Amarsanaa Jazag[3]

[1]Etugen University, [2]Happy Veritas Hospital, [3]Mongolian Association for the Study of Liver (MASLD)

Background: Mongolia is country with high prevalence HBV infection. Approximately 10% of apparently healthy population is infected with HBV. HBV is one of main causes of liver cirrhosis and HCC in our country. As a result Mongolia has the highest prevalence of HCC and HCC related mortality in the world. About 723 people die each year due to liver cirrhosis. The study analized real-life experience of 542 patients who had treatment for chronic hepatitis B.
Method: 542 patients were administered daily dose of 300 mg of TDF (both brand and generic verstions of the drug, there was no difference between generic /Mylan/and brand/Gilead Sciences/versions in terms of toxicity and side effects) in chronic HBV patients for 6–24 months. Retrospective analysis of doctor's examination sheet and survey questionnaire was performed.
Result: Out of 542 patients, adverse events were observed in 63.3% (n = 343), adverse events were not observedin36.7% (n = 199). 53.3% of patients with adverse events were male, and 46.7% female. 44% of those had twoadverse events, 40.5% single adverse event, 14.5% had more three adverse events respectively. Out of 42 adverse events observed during the course of treatment, the most common adverse events were back pain 28%, headache 12%, fatigue 9%, nausea 7.7%, stomach pain 6%, hair loss 4.8%.
Conclusion: Though considered relatively safe, 63% of patients had certain adverse events during the course of treatment of Tenofovir 300 mg per day. There is no difference in adverse events between the sexes. TAF (Tenofovir alafenamide) is considered to have less adverse events and it is available in Mongolia. We need to compare TDF and TAF in Mongolian HBV patients in near future.

HEPATITIS C

C01 - Epidemiology and Natural history

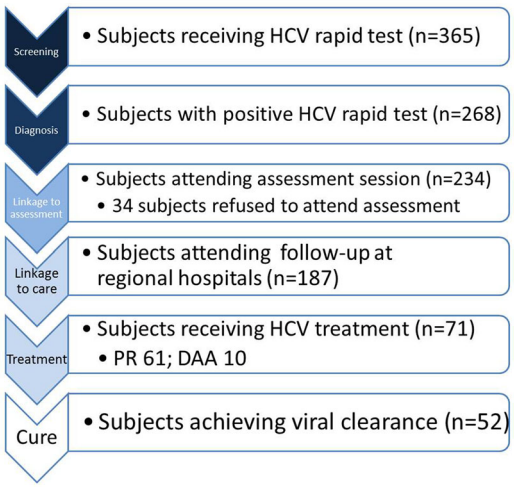
Abstract #136

Change in treatment paradigm in ex-people who inject drugs with chronic HCV in the era of direct-acting antiviral (DAA) therapy – a 9-year screening program

Grace Lai-Hung Wong[1], Yee-Tak Yui[2], Henry Lik-Yuen Chan[3], Ching-Kong Loo[4], James Yy Fung[5], Vincent Wai-Sun Wong[6]

[1]9/F, Lui Che Woo Clinical Sciences Building, & Prince Of Wales Hospital, Shatin, [2]QEH, Kowloon, [3]Lui Che Woo Clinical Sciences Building, Prince of Wales Hospital, [4]KWH, Kowloon, [5]QMH, Hong Kong Island, [6]Lui Che Woo Clinical Sciences Building, Prince of Wales Hospital

Background: Chronic hepatitis C virus (HCV) infection is highly prevalent among people who inject drugs (PWID) but is often undiagnosed because they represent an underprivileged group that faces multiple barriers to medical care. We report the data in a 9-year targeted screening program in ex-PWID. We aimed to evaluate the change in treatment paradigm of ex- PWID in Hong Kong before and after the availability of direct-acting antiviral (DAA).
Method: Consecutive ex- PWID referred from various non-government organizations attended education talks and then received point-of-care rapid test for anti-HCV. Subjects tested positive for anti-HCV were invited to undergo further assessment within 2 months.
Results: 365 ex- PWID received HCV rapid test; 268 (73.4%) were found to be anti-HCV positive. Among these 268 HCV + ex- PWID, 234 (87.3%) attended the assessment session (mean age 52 years, 90.2% male, 45.5% genotype 1b, 41.1% genotype 6a, median liver stiffness 5.9 kPa); 187 (69.8%) attended follow-up visits at regional hospitals. 71 patients received antiviral treatment for HCV; 69 first received peginterferon and ribavirin (PR), whereas 10 patients (8 PR-treated) patients received DAA treatment. 52 patients achieved sustained virologic response at 12 or 24 weeks (Figure 1). Treatment uptake rates of PR and DAA treatment in the pre- vs. post-DAA era were 22.3% vs. 48.5% and 0% vs. 15.6% respectively.
Conclusion: Targeted screening in ex- PWID is effective in identifying patients with HCV infection in the community. To improve treatment uptake, further improvements in the referral system and treatment regimens are needed.



Abstract #145

Genetic variants of TLL1 gene and associated risk of hepatocellular carcinoma among chronic hepatitis C patients

Yu-Han Huang[1], Yu-Ju Lin[2], Bo-Jun Liu[3], Chin-Lan Jen[4], Sheng-Nan Lu[5], Yasuhito Tanaka[6], Chien-Jen Chen[7], Hwai-I Yang[8], Mei-Hsuan Lee[9]

[1]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [2]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [3]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan & Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan, [4]Genomics Research Center, Academia Sinica, Taipei, Taiwan, [5]Department of Gastroenterology, Chang-Gung Memorial Hospital, Kaohsiung, Taiwan, [6]Department of Virology and Liver Unit, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan, [7]Academia Sinica, Taipei, Taiwan, [8]Genomics Research Center, Academia Sinica, Taipei, Taiwan, [9]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan

Introduction: A Japanese genome-wide association study identified rs17047200 on Tolloid-like 1 gene (TLL1) was associated with hepatocellular carcinoma (HCC) among hepatitis C virus (HCV) infected patients with sustained virological response.
Objective: The study aimed to validate rs17047200 on TLL1 gene and explore genetic variations expanding TLL1 by fine mapping.
Methodology: The R.E.V.E.A.L-HCV cohort enrolled participants seropositive for antibodies against HCV but seronegative for hepatitis B surface antigen in community. All of the participants have been examined for whole-genome SNP typing by Axiom Genome-Wide CHB Array. The rs17047200 was additionally tested through TaqMan genotyping assay. In total, 141 HCC cases and 848 non-HCC cases were included in the subsequent analyses. By using the Han Chinese population in 1000 genome project as a reference, imputation algorithm was performed to expand the genetic information from Chr4: 162,000,000 to 168,000,000 in human genome for analyses. Cox's proportional hazards models were used to evaluate the associations between genetic variants and HCC risk.
Results: Participants with increasing number of risk alleles for rs17047200 showed higher risks of developing HCC. The multivariate-adjusted HRs was 1.01 (95% CI: 0.63–1.63, p = 0.9602) and 3.61 (95% CI: 1.43–9.17, p = 0.0068) for AT and TT genotype, respectively, by taking AA genotype as a reference group. A total of 184,942 SNPs were further obtained after imputation, with 601, 754, 180 and 193 SNPs found to be associated with HCC based on allelic, dominant, recessive and genotypic models, correspondingly ($p < 0.05$).
Conclusion: The study validated rs17047200 and identified numerous SNPs near TLL1 associated with HCV-related HCC.

Abstract #227

Impact of mixed cryoglobulinemia on patients with spontaneous HCV clearance : A 13-year prospective cohort study

Kuan Chieh Lee[1], Ming Ling Chang[1]

[1]Liver Research Center, Division of Gastroenterology, Department of Gastroenterology and Hepatology, Chang Gung Memorial Hospital, Taoyuan, Taiwan

Background & Aim: The prevalence and associations of mixed cryoglobulinemia (MC) in patients with spontaneous clearance of hepatitis C virus (HCV) remain elusive.

Methods: A 13-year prospective cohort study of anti-HCV treatment naive patients with spontaneous HCV clearance was conducted in a tertiary care center. Baseline characteristics, incident cardiovascular and neurologic events and cancers were analyzed.
Results: Of 104 consecutive patients [mean age: 54.08 yrs; females: 71 (68%)], 37 (34.6%) had MC and 6 (5.8%) had cirrhosis. MC (+) patients were female dominant, had higher rate of cirrhosis, levels of Immunoglobulin G (IgG), IgM, and fibrosis-4 (FIB-4), but lower levels of complement C4 than the MC (-) patients. Female gender (95% confidence interval of odds ratio: 1.402 ~ 26.715), levels of IgG (1.000 ~ 1.004), IgM (1.009 ~ 1.037), and FIB-4 (1.217 ~ 3.966) were independently associated with MC. During the follow-up, 1 MC (+) (acute myeloid leukemia) and 3 MC (-) non-cirrhotic patients (hepatocellular carcinoma, prostate and colon cancers) developed cancers. Baseline rheumatoid factor (RF) levels were independently associated with incident cancer. With a cut-off value of 11.25 IU/mL, RF levels significantly determined incident cancer ($p = 0.002$). No different cumulative incidences of cardiovascular and neurologic events, cancer or mortality were identified between MC (+) and MC (-) patient.
Conclusions: Approximate 1/3 of patients with spontaneous HCV clearance yielded MC, which harbored similar characteristics of MC in chronic hepatitis C. Despite the negligible role of MC in the prognosis of patients with spontaneous HCV clearance, the connection between RF and incident cancer demands further investigation.

Abstract #268

Comparison of the Clinical Characteristics and Outcomes between Leprosy-affected Persons in Sorokdo and the General Population Affected by Chronic Hepatitis C in Korea

Sung Bum Cho[1], Sung Kyu Choi[2]

[1]Chonnam National University Medical School

Background/Aims: Although patients with Hansen's disease are the most vulnerable group to hepatitis C, there are no data on the treatment efficacy of direct acting antiviral agents (DAA) in this group. Therefore, we elucidated the prevalence and clinical outcomes of hepatitis C in persons affected by leprosy in Sorokdo, Jeollanamdo, Korea.
Methods: We retrospectively included 50 leprosy patients with positive hepatitis C virus (HCV) RNA test results (group A), from May 2016 to March 2018 hospitalized at Sorokdo National Hospital and 73 patients with chronic hepatitis C who were treated with DAA at Chonnam National University Hospital (group B) from May 2016 to December 2017.
Results: Overall, at Sorokdo National Hospital, positive HCV antibody and HCV RNA rates were 18.4% and 11%, respectively. The mean study participants' age was 76.5 ± 7 years, and 58% participants were males. Of the 50 patients, 22 (44%) had genotype 1b and 28 (56%) had genotype 2. Sustained virologic response was achieved at a rate of 95.5% (21/22) in genotype 1b and 92.9% (26/28) in genotype 2. Hemolytic anemia due to ribavirin was experienced in 57.1% (16/28) of patients with genotype 2. Among these, 28.5% (8/28) received blood transfusions.
Conclusions: Treatment efficacy was not different between leprosy-affected population and the general population. However, ribavirin-induced severe hemolytic anemia requiring transfusion was 28.5% in genotype 2 patients. Therefore, we suggest ribavirin-free DAAs for the treatment of genotype 2 hepatitis C in leprosy affected persons in the future.

Abstract #287

Changes of HCV patients profile and treatment effectiveness at the beginning of the interferon-free era based on the large european real world experience study

Robert Flisiak[1], Beata Lorenc[2], Jakub Klapaczyński[3], Ewa Janczewska[4], Włodzimierz Mazur[5], Dorota Zarębska-Michaluk[6], Krzysztof Tomasiewicz[7], Waldemar Halota[8], Aleksander Garlicki[9], Krzysztof Simon[10], Barbara Baka-Ćwierz[11], Hanna Berak[12], Jerzy Jaroszewicz[13], Anna Piekarska[14], Marta Wawrzynowicz-Syczewska[15]

[1]Department of Infectious Diseases And Hepatology, Medical University Of Białystok, Białystok, Poland, [2]Pomeranian Center Of Infectious Diseases, Department Of Infectious Diseases, Medical University of Gdańsk, Gdańsk, Poland, [3]Department Of Internal Medicine And Hepatology, Central Clinical Hospital Of The Ministry Of Internal Affairs And Administration, Warsaw, Poland, [4]Department Of Basic Medical Sciences In Bytom, Medical University Of Silesia, Katowice, Poland, [5]Clinical Department Of Infectious Diseases In Chorzów, Medical University Of Silesia, Katowice, Poland, [6]Department Of Infectious Diseases, Voivodship Hospital And Jan Kochanowski University, Kielce, Poland, [7]department Of Infectious Diseases And Hepatology, Medical University Of Lublin, Lublin, Poland, [8]Department of Infectious Diseases And Hepatology, Collegium Medicum of Nicolaus Copernicus University, Bydgoszcz, Poland, [9]Department of Infectious And Tropical Diseases, Jagiellonian University Collegium Medicum, Kraków, Poland, [10]Department Of Infectious Diseases and Hepatology, Wrocław Medical University, Wrocław, Poland, [11]Regional Center For Diagnosis And Treatment Of Viral Hepatitis And Hepatology, John Paul Ii Hospital, Kraków, Poland, [12]Hospital For Infectious Diseases, Warsaw, Poland, [13]Department Of Infectious Diseases In Bytom, Medical University Of Silesia, Katowice, Poland, [14]Department Of Infectious Diseases And Hepatology, Medical University Of Łódź, Łódź, Poland, [15]Department Of Infectious Diseases, Hepatology And Liver Transplantation, Pomeranian Medical University, Szczecin, Poland

Introduction: Interferon-free regimens became available recently and changed landscape of chronic hepatitis C (CHC) treatment.
Objectives: To follow profile of CHC patients treated in central-european setting at the beginning of the interferon-free era.
Methodology: Analysis included 8328 patients treated in 22 centers of Poland in three periods A: 2015–2016 (n = 2879), B: 2017 (n = 3349), C: 2018 (n = 2100), which were registered in the EpiTer-2 database. Baseline characteristics of this real world experience (RWE) population was published recently (J. Viral. Hepat.2018;25:661).
Results: We observed significant reduction of age (A: 55 ± 13, B: 53 ± 15, C: 50 ± 15), proportion of overweight (BMI > 25) patients (A: 62%, B: 55%, C: 52%), accompanying diseases (A: 69%, B: 67%, C: 40%), concomitant medications (A: 65%, B: 63%, C: 23%). Genotype 1b prevalence decreased from 87% to 78%. Increasing proportion of treatment naïve (A: 47%, B: 66%, C: 84%) and less advenced (F0-F2) fibrosis (A: 35%, B: 53%, C: 76%) was noticed. Reduced number of cirrhotics (A: 44%, B: 26%, C: 15%) was accompanied by less ferquent decompensation history (A: 7.6%, B: 1.6%, C: 0.8%), Child-Pugh B/C (A: 6.0%, B: 3.0%, C: 1.1%), MELD > 15 (A: 4.4%, B: 3.8%, C: 2.2%) and liver transplantation history (A: 3.5%, B: 1.3%, C: 0.1%). During B/C period more HIV coinfected patients received treatment for HCV (3.9%) compared to A period (1.4%). Ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin (OPrDR) was the most frequent regimen untill 2017 (A: 64%, B: 44%, C: 23%), followed by sofosbuvir options (A: 27%, B: 38%, C: 33%), but in 2018 grazoprevir/elbasvir ± ribavirin (GER) (A: 0,

B: 12%, C: 36%) became leading. Effectiveness of OPrDR (n = 3804) was higher (97%) compared to ledipasvir/sofosbuvir ± ribavirin (95%; n = 2294) and GER (95%, n = 1171). Pangenotypic regimens became available in 2018 and data will be available shortly for possible presentation.
Conclusions: Patients treated currently for HCV are younger and demonstrate less advanced liver disease compared to the beginning of interferon-free era. Effectiveness of novel regimens in this large RWE study reached up to 97%.

Abstract #369

Geographical distribution of HCV prevalence among the Nomadic people of central region of Mongolia

Byambatsogt E[1], Naranzul N[2], Ariun-Erdene E[3], Buyankhishig G[4], Gandiimaa R[5], Munkhbayar D[6], Enkhjargal A[7], Amarsanaa J[8], Baatarkhuu O[9]

[1]Health Department, Arkhangai, Mongolia, [2]Department of Infectious Disease, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia & Mongolian Association for the Study of Liver Disease, Ulaanbaatar, Mongolia, [3]Health Department, Arkhangai, Mongolia, [4]Health Department, Arkhangai, Mongolia, [5]Health Department, Arkhangai, Mongolia, [6]Health Department, Arkhangai, Mongolia, [7]Mongolian Academy of Medical Professionals, Ulaanbaatar, Mongolia, [8]Mongolian Association for the Study of Liver Disease, Ulaanbaatar, Mongolia, [9]Department of Infectious Disease, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia

Introduction: Mongolia has a large burden of viral hepatitis, especially chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, which are associated with cancer and cirrhosis. In 2017, one of the central regions of Mongolia, Arkhangai province had the third highest HCV prevalence among the provinces in Mongolia.
Objective: To define geographical distribution of HCV prevalence among the soums (administrative and geographical unit) of Arkhangai province.
Methodology: All persons between the ages of 45 and 60 years old from the 19soums of Arkhangai were eligible for HCV antibody screening by a WHO prequalified rapid diagnostic testing (Cypress Diagnostica). The test results were collected by each of the soum'sphysicians and analyzed by SPSS-21 software by using relevant parametric and non-parametric tests.
Results: A total of 17,601 (81.1% of the eligible population) underwent screening, of which 3,289 (18.68%) were positive for hepatitis C antibodies. Most of screened population was female (9095, 52.0%), mainly herdsman (7206, 40.9%), married (15425, 87.6%), educated to secondary level (11997, 68.2%) and aged 50–54 (9289, 52.8%). The prevalence varied by soums (range: 11.1% in Jargalantsoumto24.9% in Erdenebulgan soum) and was associated with older age; the highest rate of HCV infection was among the 55–59 age group ($p < 0.001$), the median age of HCV seropositive individualswas 52 ± 12.
Conclusion: HCV prevalence in Arkhangai is higher than the country average (16.7%). Our experience in Arkhangai, demonstrates that through commitment of provincial public health departments, massive screening of populations at risk for HCV infection is feasible in resource limited settings.

Abstract #381

Risk Assessment Tool for HCV Screening In Mongolia

Ariun-Erdene E[1], Byambatsogt E[2], Naranzul N[3], Gandiimaa R[4], Amgalan B[5], Buyankhishig G[6], Enkhjargal A[7], Suvd B[8], Amarsanaa J[9], Baatarkhuu O[10]

[1]Health Department, Arkhangai, Mongolia, [2]Health Department, Arkhangai, Mongolia, [3]Department Of Infectious Disease, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia & Mongolian Association for the Study of Liver Disease, Ulaanbaatar, Mongolia, [4]Health Department, Arkhangai, Mongolia, [5]Health Department, Arkhangai, Mongolia, [6]Health Department, Arkhangai, Mongolia, [7]Mongolian Academy of Medical Professionals, Ulaanbaatar, Mongolia, [8]Mongolian Academy of Medical Professionals, Ulaanbaatar, Mongolia, [9]Mongolian Association For The Study of Liver Disease, Ulaanbaatar, Mongolia, [10]Department of Infectious Disease, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia & Mongolian Association for the Study of Liver Disease, Ulaanbaatar, Mongolia

Introduction: Liver cancer is the most common cause of cancer related mortality in Mongolia (44%). Chronic hepatitis B and C infections are responsible for 95% of liver cancers in the country.
Objective: To develop a standardized risk assessment tool for HCV infection to facilitate cost effective, case finding of chronic hepatitis C infection among the general population in the Arkhanghai Province of Mongolia.
Methodology: A risk assessment survey was developed in Mongolian, including 31questions about behavioral and clinical factors relevant to acquisition of HCV infection. Statistical analysis was done using by SPSS-21.
Results: Of 17601 adults between ages of 40 and 65 who completed the assessment survey10524 (59.7%) individuals had > 4 risk factors. The age of individuals was the strongest predictor of HCV infection (age group 40–44 vs. 45–49 (OR = 3.26; CI95% 2.87–3.70), age group 40–44 vs. 50–54 (OR = 3.03; CI95% 2.67–3.45), age group 40–44 vs. 55–59 (OR = 2.45; CI95% 2.15–2.79) and age group 40–44 vs. > 60 (OR = 1.39; CI95% 1.22–1.59). Other predictors included: gender (high among female) (OR = 1.45; CI95%, 1.34–1.58), having any kind of surgery in life time (OR = 1.42; CI95%, 1.302–1.55), history of blood transfusion (OR = 1.69; CI95% 1.48–1.94), bloodletting treatment (OR = 1.17; CI95%, 1.06–1.29), and tattoos (OR = 1.16; CI95% 1.05–1.29).
Conclusion: The tool can be used in resource limited settings to facilitate HCV positive case finding and screening promotion all

around Mongolia. The tool is country specific and the strongest risk factor is the age and followed by risky behaviors for Mongolians.

Abstract #448

Genome-Wide Association Study Identified Loci Influencing Serum Alanine Aminotransferase Concentration Levels among Individuals with Hepatitis C Virus Infection

Po-Chun Liu[1], Yu-Han Huang[2], Yu-Ju Lin[3], Chin-Lan Jen[4], Sheng-Nan Lu[5], Chien-Jen Chen[6], Hwai-I Yang[7], Mei-Hsuan Lee[8]

[1]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan. & Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan, [2]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [3]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [4]Genomics Research Center, Academia Sinica, Taipei, Taiwan, [5]Department of Gastroenterology, Chang-Gung Memorial Hospital, Kaohsiung, Taiwan, [6]Academia Sinica, Taipei, Taiwan, [7]Genomics Research Center, Academia Sinica, Taipei, Taiwan, [8]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan.

Introduction: Serum alanine aminotransferase (ALT) level is an inflammatory marker for patients with HCV infection.
Objectives: We performed a genome-wide association study to discover single nucleotide polymorphisms (SNPs) associated with serum ALT levels.
Methodology: The study included 892 anti-HCV seropositives seronegative for hepatitis B surface antigen in REVEAL-HCV cohort. The serum ALT level was measured at baseline and all of the study participants were free of hepatocellular carcinoma. The AxiomTM Genome-Wide CHB Array was examined for the study participants. The serum level of ALT was served as a quantitative trait in the analyses. All SNPs were located on autosomal regions and SNPs with low call- rate ($< 97\%$), low minor allele frequency (< 0.03), and violation of Hardy-Weinburg equilibrium ($p < 10^{-4}$) were excluded for analyses. External validation was performed on 496 individuals in Taiwan Biobank with same criteria. Logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals of the SNPs associated with ALT (> 45 vs. ≤ 45 U/L).
Results: Among the 826 subjects, 364 (44.1%) with ALT ≤ 15 U/L, 327 (39.6%) 16–45 U/L, and 135 (16.3%) > 45 U/L. The means and standard deviation of the serum ALT levels were 30.1+-38.9. Among 589,653 SNPs included in the analyses, 5 SNPs located in chromosome 2, 9, 11 and 14 were associated with ALT levels. The ORs for these SNPs on the associations with ALT levels ranged from 1.58 to 2.14. There were 2 SNPs remained significant in the validation set.
Conclusion: There were 5 SNPs identified to be associated with ALT levels.

Abstract #495

Associated factors of liver fibrosis among patients received HCV antivirals

Chi Chan[1], Yu-Ju Lin[2], Yu-Han Huang[3], Yu-Chieh Huang[4], Sheng-Nan Lu[5], Chien-Jen Chen[6], Chi-Yi Chen[7], Hwai-I Yang[8], Mei-Hsuan Lee[9]

[1]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [2]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [3]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [4]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [5]Division Of Hepato-Gastroenterology, Department Of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital And Chang Gung University College Of Medicine, Kaohsiung, Taiwan, [6]Academia Sinica, Taipei, Taiwan, [7]Department Of Gastroenterology, Ditmanson Medical Foundation, Chia-Yi Christian Hospital, Chia-Yi, Taiwan, [8]Genomics Research Center, Academia Sinica, Taipei, Taiwan, [9]Institute Of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan.

Introduction: Liver fibrosis was examined by transient elastography, a non-invasive tool with satisfactory accuracy and reproducibility.
Objectives: This study aimed to evaluate lifestyle and clinical associated factors for liver fibrosis among hepatitis C virus (HCV) infected patients experienced antiviral treatment.
Methodology: There were 721 patients with interferon-based antivirals were enrolled. All of the patients were aged 40 years or older. The information of demographic data, lifestyle, and previous diseases were collected by a structured questionnaire. The patients were examined by transient elastography, and the cut-off was 0 to ≤ 5 kPa for F0, 5 to ≤ 7.1 kPa for F1, 7.1 to ≤ 9.5 kPa for F2, 9.5 to ≤ 12.5 kPa for F3, and > 12.5 kPa for F4. The virological, serological and treatment data were collected by standardized clinical chart review sheets. Logistic regression models were performed to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for risk factors associated with liver fibrosis.
Results: In total, the prevalence was 30%, 31%, 15%, 8.7%, and 15.5% for F0, F1, F2, F3, and F4 in correspondingly. We compared the patients with mild (F0-F1) and advanced fibrosis (F2-F4). Patients with BMI > 30, current alcohol drinking, diabetes and cirrhosis were positively associated with advanced fibrosis ($p < 0.05$). Individuals with more tea intake (> 2 cups daily) had inversed association with advanced fibrosis with adjusted OR of 0.55 (0.33–0.91). Elevated ALT, alpha-fetoprotein, alkaline, γ-GT, glucose levels were positively associated with advanced fibrosis ($p < 0.05$).
Conclusion: Patients with positive associated factors needed to monitored regularly.

Abstract #508

Human Leukocyte Antigen Variants and Risk for Liver Cirrhosis among Hepatitis C Virus Infected Patients

Ying-Hsin Shih[1], Yu-Han Huang[2], Yu-Ju Lin[3], Chin-Lan Jen[4], Sheng-Nan Lu[5], Chien-Jen Chen[6], Hwai-I Yang[7], Mei-Hsuan Lee[8]

[1]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [2]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [3]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [4]Genomics Research Center, Academia Sinica, Taipei, Taiwan, [5]Department of Gastroenterology, Chang-Gung Memorial Hospital, Kaohsiung, Taiwan, [6]Academia Sinica, Taipei, Taiwan, [7]Genomics Research Center, Academia Sinica, Taipei, Taiwan, [8]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan

Introduction and Objectives: Human leukocyte antigen (HLA) variants was found to be associated with hepatocellular carcinoma in previous genome-wide association study. This study aimed to examine the associations of HLA-DQB1 and DPB1 variants on the risk for liver cirrhosis.
Methodology: There were 994 participants seropositive for anti-HCV but seronegative for HBsAg in REVEAL-HCV study cohort. All of the study subjects were examined for HLA-DQB1 and HLA-DPB1 direct genotyping. The incidence liver cirrhosis was ascertained

through regular abdominal ultrasound examinations and the computerized data linkage with the national health insurance database during 1991–2010. The national death certification system linkage was performed to assure the vital status of these individuals during follow-up. Cox proportional hazards models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (95% CIs) for associations between HLA genes and the risk of liver cirrhosis.
Results: After follow-up, there were 209 incident liver cirrhosis cases occurred, giving the incidence of 13.25 per 1000 person-years. We found that HLA-DQB1*03:01, DQB1*03:03 and DQB1*05:02 were significantly associated with liver cirrhosis after multiple corrections ($p < 0.05$). The adjusted HR (95% CI) for HLA-DQB1*03:01 and DQB1*03:03 for the risk of cirrhosis was 0.74 (0.54–0.998) and 0.65 (0.47–0.92), respectively. The HLA-DQB1*05:02 showed positive association with liver cirrhosis risk, with the HR (95% CI) of 1.83 (1.32–2.54). There showed no significant associations of HLA-DPB1 on the risk of liver cirrhosis.
Conclusion: Variants on HLA-DQB1 were associated with liver cirrhosis risk.

Abstract #516

Changes in the characteristics of hepatitis C patients treated with direct-acting antivirals from 2014–2016

Amanda W. Singer[1], Naoto Fujiyama[1], Chenyu Wang[1], Krystin Matthews[1], Anu Osinusi[1], Diana M. Brainard[1], Laura Telep[1], Anand P. Chokkalingam[1]

[1]Gilead Sciences

Background: The efficacy and safety of direct-acting antiviral (DAA) therapy have influenced the characteristics of patients who are treated for hepatitis C virus (HCV) infection. The objective of this study was to examine how characteristics of DAA-treated patients have changed in the years.
Methods: Patients included 347,721 adults with chronic HCV and at least one year of prior enrollment in a large US administrative claims database between 2006 and 2016. Diagnoses, medication use, and procedures in the year prior to treatment start were compared for patients initiating DAA treatment in 2014, 2015 and 2016. Changes in the baseline characteristics recorded in the prior year for DAA-treated patients from 2014–2016 were examined by frequency and tested for statistical significance using the Cochran-Armitage trend test.
Results: From 2014–2016, there was a significant increase in the proportion of DAA-treated patients who were female (33.9% to 37.1%) and had baseline diagnoses of substance abuse (8.9% in 2014 to 11.6% in 2016) or mental illness (7.4% to 23.6%). There were also increases in indicators of comorbid cardiovascular disease, including increases in prior diagnoses of essential hypertension (8.9% to 11.3%), overweight/obesity (5.2% to 7.0%), and statin use (2.3% to 3.7%). Conversely, there was a decrease from 2014 to 2016 in the proportion of DAA-treated patients who had diagnoses indicating advanced liver disease (29.3% to 22.9%).
Conclusions: While the proportion of DAA-treated patients with advanced liver disease has decreased, possibly representing increased screening and access to treatment, they still represent a sizeable proportion of the treated population.

Abstract #524

Methods to Assess FIB-4 Score in Patients with Chronic Hepatitis C Using a Real-World Dataset

Craig Brooks-Rooney[1], Lucy Eddowes[1], Gabriel Wong[2], I-Heng Lee[2]

[1]Costello Medical, [2]Gilead Sciences, Inc

Objectives: Liver fibrosis is an important prognostic marker in hepatitis. The FIB-4 score is a non-invasive algorithm for measuring liver fibrosis, calculated from ALT, AST and platelet (PLT) laboratory measurements. Given the potential for bias due to measurement frequency in real-world datasets, this analysis examined two different methods for combining laboratory measures in calculating FIB-4 score.
Methods: We used data from a retrospective cohort study of adult ($\geq$ 18 years old) patients with chronic hepatitis C (CHC, ICD-10 code: B18.2) included in the Medical Datavision Database (MDV). The database contains information from inpatient and outpatient visits at 287 hospitals in Japan from Apr 2008–June 2016. Age and gender were derived based on direct reporting for the most recent CHC visit. Two methods were compared to estimate the FIB-4 score from laboratory measurements: an arithmetic mean approach and a novel time integral approach.
Results: 173,796 patients were included (mean $\pm$ SD age 69 $\pm$ 14, 51.7% male), with a large proportion being over the age of 75 (40.7%). In a sample of 18,451 patients with available laboratory measurements, the two methods of estimating FIB-4 score resulted in similar estimates: mean $\pm$ SD FIB-4 score: 4.20 $\pm$ 6.51 (mean arithmetic) and 4.09 $\pm$ 6.07 (time integral). This similarity is potentially due to evenly-spaced laboratory measurements.
Conclusions: These methods will likely be applicable to calculating the FIB-4 score in other real-world datasets and in other liver diseases, such as Hepatitis B and non-alcoholic steatohepatitis (NASH).

Abstract #525

Detection of residual HCV genome in hepatic tissues from patients who have achieved a sustained virologic respons is associated with persistent histological abnormality

Yijin Wang[1], Huiying Rao[2], Xiumei Chi[3], Boan Li[1], Junqi Niu[3], Lai Wei[2], Jingmin Zhao[1]

[1]The 5th Medical Center, Chinese PLA General Hospital, [2]Peking University People's Hospital, [3]The First Hospital Of Jilin University

Introduction: Whether achieving sustained virological response (SVR) in patients with hepatitis C attains complete elimination of hepatitis C virus (HCV) is unknown, because occult HCV infection (OCI), defined as the detection of HCV RNA in hepatocytes or peripheral blood mononuclear cells (PBMC) in absence of serum HCV RNA, may occur.
Objectives: We investigated the prevalence and clinical relevance of OCI.
Methodology: Subjects from three hospitals who had achieved serum HCV clearance, including 60 of Direct-acting antiviral agents (DAAs) induced SVR, 50 of pegylated interferon plus ribavirin (PR) induced SVR, and 30 of spontaneous recovery, were subjected to detect HCV RNA in hepatocytes and in PBMC. Paired liver biopsies at baseline and post-SVR were analyzed.
Results: OCI was detected in 16 of 140 subjects (11.4%), with 15.0% in DAA-based group, 10.0% in PR group and 6.7% in spontaneously resolved group. The occurrence of OCI is more frequent in patients

with HCV genotype 3. No correlation between baseline viral load, interleukin-28B genotype, baseline transaminases, post-SVR transaminases and OCI were found. However, OCI was significantly linked with poor fibrosis status at post-SVR. In addition, both the magnitude of fibrosis improvement and the frequency of fibrosis regression were significantly lower in patients with OCI than in those without OCI after SVR. Importantly, we found HCV relapse in one of the OCI patients at 48 weeks after the end of PR treatment.
Conclusions: HCV RNA can persist in a certain of immunocompetent patients albeit achieving serum resolution of HCV and associated with persistent pathological abnormality.

Abstract #565

Deletion Mutations in HCV NS5A Persist and Resist to Subsequent Treatment

Hoang Hai[1], Akihiro Tamori[2], Kanako Yoshida[3], Sawako Uchida-Kobayashi[4], Masaru Enomoto[5], Ritsuzo Kozuka[6], Hiroyuki Motoyama[7], Atsushi Hagihara[8], Hiroyasu Morikawa[9], Yoshiki Murakami[10], Le Thi Thanh Thuy[11], Norifumi Kawada[12]

[1]Osaka City University Graduate School of Medicine

Introduction: Dominant resistance-associated substitutions (RASs) in chronic hepatitis C virus (HCV) infected patients who failed in previous asunaprevir/daclatasvir (ASV/DCV) treatment affect to subsequent direct acting antivirals (DAAs) therapies.
Objectives: To evaluate the evolution and effect of RASs in HCV during long-term follow-up until 40 months (40 m) after ASV/DCV failure.
Methodology: RASs and deletions in NS5A from 25 patients who failed ASV/DCV were examined by direct sequencing.
Results: Among 25 patients, nineteen (76%) and 20 (80%) had RASs at L31 and Y93, respectively, and 3 (12%) had P29/P32 deletion. In the patient 1, P29 was deleted and persisted for 17 m, following by intermediate population of P29 for 5 m, then returned to deletion until 34 m. In the patient 2, P32 had been deleted for first 3 m, HCV quasispecies then existed for 13 m before P32 was deleted again and persisted until 40 m. In the patient 3, L31 V substitution and P32 deletion were found, then P32 returned to wild type (WT) and, at the same time, Y93H was emerged. Interestingly, from 27 m upward, P32 again deleted together with L28I and L31F emerged but Y93 returned to WT. While patient 1 is in waiting list, patients 2 and 3 were re-treated with LDV/SOF and both were relapsed. Remaining 22 patients, eleven are re-treated by subsequent DAAs, and 9 are in waiting list.
Conclusion: In patients who failed ASV/DCV therapy, long-term persistent of P29 and P32 deletions are high genetic barrier to DAA re-treatment. The P29/P32 deletion should be screened carefully before starting subsequent DAA therapy.

Abstract #608

Prevalence of Hepatitis C among Type 2 Diabetes Mellitus patients in a Single Center Tertiary Hospital in Quezon City, Philippines

Millette Dela Cruz Castro[1], Erlinda Ventura Valdellon[1]

[1]University of the East Ramon Magsaysay Memorial Medical Center

Introduction: There is a growing body of literature between Hepatitis C virus infection and T2DM on the framework of insulin resistance. However, there are gaps in the literature and data is still inconclusive. No local study on the prevalence of HCV among diabetics is available.
Objectives: This is a pilot study that aims to determine the prevalence of HCV infection among diabetic patients seen at our institution.
Methodology: This is a descriptive cross sectional epidemiological study. Written consent was secured, consecutive sampling of 318 known diabetics was done and data was collected using a checklist. A drop of whole blood was collected by the investigator by finger prick method and tested for HCV antibodies using RAPIDQuick screening test. Frequency and proportion and median and range were used to describe the clinical characteristics of the enrolled subjects. STATA 15.0 was used for data analysis.
Results: 318 diabetic patients were tested for HCV. No HCV seropositivity was noted. The median age was 55 years and half were female. 22% were obese. The following risk factors for HCV were reported: more than half had reported unprotected sex, shares nail-cutters, toothbrush, and razors. 261 (82%) had abnormal FBS and median HbA1c was 7.5%. Similarly, ¾ had abnormal triglyceride levels. On the average, half of the patients are insulin requiring for four years.
Conclusion: Despite a negative study, we like to continue this study to determine the association between the two diseases and in the future can contribute to the local statistics of Hepatitis C.

Abstract #643

Cost-Effectiveness of Simplified Diagnostic Algorithms for Hepatitis C: An Interactive Tool

Jagpreet Chhatwal[1], Yueran Zhuo[2], Sonjelle Shilton[3], Tiannan Zhan[2], Francesco Marinucci[3], Rakesh Aggarwal[4]

[1]Harvard Medical School & Massachusetts General Hospital, [2]Massachusetts General Hospital, [3]Foundation For Innovative New Diagnostics, [4]Sanjay Gandhi Postgraduate Institute Of Medical Sciences

Introduction: To achieve HCV elimination by 2030, innovative, simple and cost-effective strategies are needed to scale-up hepatitis C virus (HCV) care. The cost and effectiveness of strategies can vary by population and individual components. We therefore developed an interactive, Excel-based tool to evaluate the cost-effectiveness of various testing pathways and identify the most efficient strategy for scale-up. Further, we tested our tool using Georgia as an example.
Methods: We constructed a mathematical model that simulates the natural history of HCV infection and can assess the cost-effectiveness of various testing strategies (defined by sequence and type/cost of diagnostic tests, disease prevalence, etc.) for HCV, and used it to compare the current standard-of-care (SoC) pathway and four innovative HCV testing pathways in Georgia (Figure). Individuals diagnosed with HCV were treated with DAAs. We estimated Georgia-specific costs; test, patient/sample transportation, and management of HCV disease, and used these as inputs to find the most cost-effective testing.
Results: Compared with the SoC, all four innovative pathways (P1-P4) resulted in higher HCV diagnosis rates (increasing from 81% to 90%), lower costs and more quality-adjusted life years (QALYs) (Figure). The P1 pathway with on-site RDT and RNA testing, followed by on-site fibroscan resulted in maximum cost savings—USD 812,500 per 10,000 patients tested (compared with SoC).
Conclusion: We have developed an interactive tool that informs the most cost-effective HCV testing pathway under different settings, depending on HCV prevalence, sample/patient transportation cost, cost of RNA vs HCVcAg test, and need for fibroscan for disease staging.

Abstract #669

Large-Scale Phylogeographic Investigation into the History of Hepatitis C Virus Genotypes 1, 2, and 3

Joel O. Wertheim[1], Reilly Hostager[1], Ben Murrell[1], Manon Ragonnet-Cronin[1], Charlotte Hedskog[2], Anuj Gaggar[2], Seng Gee Lim[3], Tetsuo Takehara[4], Dzhamal Abdurakhmanov[5], Wei Lai[6], Konstantin Zhdanov[7], Vasily Isakov[8], Hongmei Mo[2], Evguenia Svarovskaia[2]

[1]Department Of Medicine, University Of California, [2]Gilead Sciences Inc, [3]Div of Gastroenterology and Hepatology, National University Health System, [4]Department of Gastroenterology and Hepatology, Osaka University Graduate School Of Medicine, [5]Sechenov First Moscow State Medical University, [6]Peking University People's Hospital, Peking University Hepatology Institute, [7]Department of Infectious Diseases Of Military Medical Academy Named After S.M. Kirov, [8]Department Of Gastroenterology & Hepatology Of Federal Research Center Of Nutrition, Biotechnology And Food Safety

Introduction: Hepatitis C virus (HCV) is a highly genetic diverse virus. However, where and when the geographic diversity observed in many HCV subtypes arose remains unclear. Here, migration patterns between different geographic locations of HCV subtypes were characterized.
Methods: NS5A and NS5B sequences from patients enrolled in clinical trials (N = 6941) and publically available sequences (N = 2729) from 34 countries were analyzed using maximum likelihood phylogenies using IQTree for 1a, 1b, 2a, 2b, 3a, and 3b subtypes individually. Molecular clock analysis and phylogeographic reconstruction was performed using TreeTime and custom continuous-time Markov-chain approach, respectively.
Results: All six HCV subtypes analyzed have relatively recent times of most recent common ancestor (MRCA) around the start of the 20th century. 1a and 1b have MRCA in the USA. 1a showed robust migrations routes to Canada, France, Germany, and Thailand. 2a has been circulating in South Korea and the USA with frequent migrations from Korea to China and Taiwan. 2b also has MRCA in the USA. 3a has MRCA in South Asia (India/Pakistan) prior to its introduction to North America and Europe; 3a was introduced on two separate occasions into Russia from Europe in the mid-20th century. 3b has MRCA in China and Thailand with migration patterns to other Asian counties.
Conclusion: Prevalent HCV subtypes began diversifying in developed nations around the start of the 20th century. Knowledge about migration patterns and similarity between sequences in different countries may provide insights for treatment management in countries with limited clinical data.

Abstract #808

Prevalance of Hepatitis C Virus Genotype in West Borneo, Indonesia

Michelle Frastica[1], Yustar Mulyadi[1]

[1]Dr Soedarso General District Hospital

Introduction -Hepatitis C Virus (HCV) is divided into 7 genotypes, from 1 to 7. HCV genotyping is essential to determine the disease prognosis, treatment program and duration. In Indonesia studies regarding Hepatitis C genotype are scarce. Specifically, in West Borneo there were no prior studies concerning Hepatitis C genotype before.
Objectives: This study aim to determine the genotype prevalence of HCV in patients from various regions of West Borneo
Methodology: Retrospective cross-sectional study was conducted on all data sampling of total 23 plasma samples of reactive anti HCV serology sent to a centre laboratory in West Borneo for molecular genotype analysis between August 2012 and August 2018 (6 years)
Results: Among Hepatitis C positive samples the majority were genotype 1b (52.2%, n = 12), followed by genotype 1a (13%, n = 3), 1c (13%, n = 3) and genotype 2, 2a, 2c, 3a, 3 k (4.3% n = 1; each group). Genotype 1. Twenty out of 23 samples were from Pontianak City, 88.9% of which were genotype 1 (n = 18)
Conclusion: Genotype 1b is the predominant HCV infection in West Borneo, which has been suggested related more closely with chronic and severe liver disease than other subtypes

Abstract #889

The Study of HCV Genotypes Distribution in IDUs and non-IDUs Populations

Tao Wu[1], Jiao Wang[1], Ming Liu[1], Biao Wu[1], Jun Ge[1], Hui Li[1], Furong Xiao[1], Feng Lin[1]

[1]Department of Infectious Diseases Hainan General Hospital

Background: Blood transmission is one of the important ways of HCV infection. Injecting drug users (IDUs) have always been the high-risk group of HCV infection. The prevalence of HCV in this population is often as high as 50% or more, and co-infection with HIV is also common.
Methods: 473 HCV-RNA positive patients were selected from 6 methadone maintenance clinics in Hainan Province from January 2017 to November 2018. After epidemiological investigation, they were divided into IDUs group (339 cases) and non-IDUs group (134 cases), and their genotypes were detected by fluorescence probe method and direct sequencing method respectively.
Results: In IDUs group, 6a was the most important genotype (58.7%, 199/339), followed by 3 (32.4%, 110/339), 1 (7.3%, 25/339), 2a (0.6%, 2/339), non-6a (0.9%, 3/339), 1b was the most important genotype (29.9%, 40/134), followed by 6a (27.6%, 37/134 cases) and 3 types (15.7%, 21/134 cases), non-6a (14.9%, 20/134 cases), 2a (5.2%, 7/134 cases), 1a (6.7%, 9/134 cases). The Study of HCV Genotypes Distribution is shown in the table.
Conclusion: The main types of chronic HCV infection in Hainan Island are 6a and 3, especially in IDUs, which are 91.1%. This suggests that the rapid transmission of HCV in Hainan Province in recent years may be closely related to IDUs behavior. The prevention, control and treatment of HCV in IDUs population may be the key to achieve the regional elimination of HCV in Hainan Province in the future.

Abstract #913

Performance of a Rapid Diagnostic Test for Screening of Hepatitis C in a Real-life Prison Setting

Heidar Sharafi[1], Hossein Poustchi[2], Fatemeh Azimian[3], Farnaz Hashemi[4], Mahdi Sheikh[5], Seyed Moayed Alavian[6], Shahin Merat[7]

[1]Baqiyatallah Research Center for Gastroenterology and Liver Diseases, Baqiyatallah University of Medical Sciences, Tehran, Ir Iran, [2]Liver and Pancreatobiliary Diseases Research Center, Digestive Disease Research Institute, Tehran University of Medical Sciences, Tehran, IR Iran, [3]Centre for Communicable Diseases Control, Ministry Of Health And Medical Education, Tehran, IR

Iran, [4]Liver and Pancreatobiliary Diseases Research Center, Digestive Disease Research Institute, Tehran University of Medical Sciences, Tehran, IR Iran, [5]Liver and Pancreatobiliary Diseases Research Center, Digestive Disease Research Institute, Tehran University of Medical Sciences, Tehran, IR Iran, [6]Baqiyatallah Research Center for Gastroenterology And Liver Diseases, Baqiyatallah University of Medical Sciences, Tehran, IR Iran, [7]Liver and Pancreatobiliary Diseases Research Center, Digestive Disease Research Institute, Tehran University of Medical Sciences, Tehran, IR Iran

Introduction: Hepatitis C virus (HCV) testing using rapid diagnostic test (RDT) is the solution for feasible, fast and reliable screening of HCV infection. The aim of this study was to evaluate the diagnostic performance of HCV RDT for screening of HCV in real-life prison setting.
Methods: This study was conducted on individuals incarcerated in the Central Prison of Karaj, 2017–2018. For all inmates, anti-HCV testing using a RDT on finger-stick blood in the prison and ELISA at the laboratory were performed. For evaluation of reproducibility, more than 1000 cases were recruited for re-evaluation of the HCV RDT using anticoagulated blood in the laboratory.
Results: Among 1788 participants, 76 (4.25%) and 106 (5.93%) were positive for anti-HCV using RDT and ELISA, respectively. Among 34 cases with discordant results using the RDT and ELISA, 17 were the result of testing error in prison, 7 false positive of ELISA and 10 false negative of RDT in individuals with HCV spontaneous clearance. The sensitivity of the RDT with inclusion of testing error in prison for detection of anti-HCV was 75%. However, with exclusion of testing error in prison and considering HCV RNA as the reference method for diagnosis of current HCV infection the sensitivity reached 100%. The RDT was 100% reproducible using both evaluations in prison and the laboratory.
Conclusion: The RDT is a reliable and feasible method for screening for anti-HCV in settings such as a prison. However, the testing should be performed in a standard procedure to have the optimal diagnostic performance.

Abstract #914

Hepatitis C in Leprosy: Baba Baghi Study

Heidar Sharafi[1], Bita Behnava[2], Seyed Moayed Alavian[3]

[1]Baqiyatallah Research Center for Gastroenterology and Liver Diseases, Baqiyatallah University of Medical Sciences, Tehran, IR Iran

Introduction: with availability of direct-acting antiviral agents, there is great effort to eliminate HCV by 2030 globally. The case-finding is one of the main challenges in elimination of hepatitis C. One of the neglected groups for screening of hepatitis C is the patients with leprosy.
Methods: We conducted a multi-center study for evaluation of hepatitis C epidemiology, molecular epidemiology, natural history, risk factors and treatment response in patients with leprosy in different locations in Iran.
Results: The study showed high prevalence of hepatitis C in patients with leprosy with overall 47.3% HCV seropositivity in all 239 cases studied in Baba Baghi village (main study location), villages of East Azerbaijan, villages of West Azerbaijan and Behkadeh Razavi in North Khorasan with prevalence of 61.5%, 9.1%, 6.7% and 25.5%, respectively. Assessment of HCV transmission risk factors showed that living in Baba Baghi, living with a HCV-infected spouse and having surgery are the main risk factors of HCV transmission in patients with leprosy. The HCV genotype of 69 patients was evaluated with predominance of HCV-1b in 68 (98.5%) patients. In this study, we have started to treat the patients with HCV infection using Sofosbuvir/Ledipasvir or Sofosbuvir + Daclatasvir for 12 weeks. The rapid virologic response and early virologic response rates were both 100% however, one patients relapsed by now resulting in 96% rate of sustained virologic response.
Conclusion: with the current evidences there is great interest to recommend screening of HCV in patients with history of leprosy in Iran and other countries.

Abstract #1081

Nursing Interventions for Hepatitis C Elderly Patients to Reduce the Side Effects of Pegylated Interferon and Ribavirin and Improve their Quality of Life

Raefa Refaat Alam[1], Doaa Elsayed Fadila[2], Gamal Elsayed Shiha[3]

[1]Mansoura University

Side effects from hepatitis C treatment can be uncomfortable, sometimes debilitating and rarely even life-threatening for elderly people. With the right planning and support, many of these side effects can be managed which will help in complying with the treatment and in turn improve the quality of life.
Objective: To identify the effect of nursing intervention for hepatitis C elderly patients to reduce the side effects of pegylated interferon and ribavirin and improve their quality of life.
Setting: The study was carried out at the outpatient clinics of the Specialized Medical Hospital, the General Mansoura Hospital, and the Egyptian Liver Hospital in Dakahlia.
Subjects: The study comprised 66 elderly patients with HCV divided into two equal groups of 33 each.
Tools: Data was collected using six tools.
Results: The main side effects from treatment as reported by the elderly were fatigue, insomnia, bone ache, heart burn, fever, itching and stomatitis respectively. As well significance improvement in the quality of life post 12 week of intervention in study group was observed.
Conclusion: It can be concluded that the side effects and quality of life mean scores improved significantly in the study group compared to control group after 8 and 12 weeks of nursing intervention. Recommendations: Caregivers of elders undergoing hepatitis C treatment should support, motivate and encourage elders to cope with side effects of the hepatitis C therapy.

C02 - Virology, Pathogenesis and Immunology

Abstract #72

Role of plasma Osteopontin level as a predictor of hepatic fibrosis progression and response to treatment in patients with chronic HBV or chronic HCV infection

Ali Ghweil[1], Heba Osman[2], Ashraf Khodery[3]

[1]South Valley University Qena Faculty of Medicine Egypt, [2]Lecturer of Tropical Medicine and Gastroenterology Qena Faculty of Medicine South Valley University, [3]Lecturer of Clinical Pathology Sohag University

Abstract
Background and Aims: The present study aimed to evaluate the efficacy of pretreatment serum osteopentin as predictor of post

treatment hepatic fibrosis regression and virological response in patients with chronic HBV or HCV infection.

Patients and Methods: All patientswith chronic HBV infection were treated with Entecavir 0.5 mg or 1 mg once daily Patients with chronic HCV infection were treated with sofosbuvir 400 mg and daclatasvir 60 mg with or without ribavirin (800–1,200 mg) once daily for 12 weeks. One year post HBeAg seroconversion and 3 months after end of regular antiviral treatment for patients with chronic HBV infection and chronic HCV infection respectively, all patients are reevaluated for improvement in hepatic condition.

Results: In patients with chronic hepatitis B virus infection pre-treatment high serum osteopentin can be used to predict failure of post treatment virological response and failure of achieving hepatic fibrosis regression at a cutoff level of $>$ 115.5 ng/ml, with 90.91% sensitivity, 82.54% specificity, 83.9% PPV and 90.1% NPV. Also pretreatment high degree of liver stiffness value as evaluated by hepatic fibroscan can be used as a marker to predict failure of post treatment failure of hepatic fibrosis regression at a cutoff level of $>$ 8.7, with 81.8% sensitivity, 73% specificity, 75.2% PPV and 80% NPV. However, in patients with chronic HCV infection no role of pretreatment serum osteopentin or liver stiffness to predict post treatment SVR or improvement in hepatic fibrosis.

Abstract #185

Eradication of HCV with direct antiviral agents (DAA) can improve hyperglycemia in Asian patients with Type 2 Diabetics mellitus

Zong-Sian Cai[1], Tsang-En Wang[2], Ming-Jen Chen[3], Cheng-Hsin Chu[4], Ching-Wei Chang[5], Chen-Wang Chang[6], Yi-Hong Zeng[7]

[1]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan & Mackay Junior College of Medicine, Nursing and Management, Taipei, Taiwan & Mackay Medical College, New Taipei, Taiwan, [2]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan & Mackay Junior College of Medicine, Nursing and Management, Taipei, Taiwan & Mackay Medical College, New Taipei, Taiwan, [3]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan & Mackay Junior College of Medicine, Nursing and Management, Taipei, Taiwan & Mackay Medical College, New Taipei, Taiwan, [4]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan & Mackay Junior College of Medicine, Nursing and Management, Taipei, Taiwan & Mackay Medical College, New Taipei, Taiwan, [5]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan & Mackay Junior College of Medicine, Nursing and Management, Taipei, Taiwan & Mackay Medical College, New Taipei, Taiwan, [6]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan & Mackay Junior College of Medicine, Nursing and Management, Taipei, Taiwan & Mackay Medical College, New Taipei, Taiwan, [7]Division of Endocrinology and Metabolism

Introduction: Association between chronic Hepatitis C infection and type 2 diabetes mellitus have been proposed, and previous studies showed improved glycemic control after HCV eradication with interferon and ribavirin. However, the side effects include anemia and body weight loss with HCV therapy has also been challenged. We wonder whether HCV eradication with DAA agents can have similar benefits for metabolic syndrome control.

Objectives: To investigate whether DAA-based regimen for HCV eradication can improve glycemic control in HCV patients with T2DM.

Methodology: From 1 August 2016 to 3 March 2018, we have identified 63 patients with Type 2 DM and HCV coinfection received DAA regimen in Mackay Memorial Hospital, a medical center in Taipei. Sustained virologic response (SVR) defined as undetectable viral load after 12 weeks. We have collect laboratory data, including liver biochemistry and metabolic profile, before and after successfully HCV eradication (SVR-12). The Demographics of patients was demonstrated as Table 1. The stage of liver fibrosis was expressed with FIB-4 score, which was a common non-invasive tool used for calculate the fibrotic level of liver. Metabolic and biochemistry data were collected at least after 3 months of HCV eradication to avoid drug effect.

Results: HbA1c showed improvement: 6.88% (6.61–7.14, 95% CI) to 6.41% (6.16–6.66, 95% CI) in HCV eradicated group with T2DM. However, other metabolic profiles including triglyceride, total cholesterols, Body weight, BMI had showed no significant change after eradication (as Table 2). Further studies and long term follow-up for metabolic profiles should be pursued for these patients to prove the metabolic benefit

	Characteristic of patients (Number=63)
Age, year (mean ± SD)	68.2 ± 1.13
Sex, male	25
Family history of DM	20
Years of DM	8.5 ± 0.65
Treatment for DM	
Oral hypoglycemics	50
Insulin	13
Commorbidity	
Hypertension	44
Hyperlipidemia	25
ChronicHBV hepatitis	5
Fatty liver	21
Alcohol usage	9
Liver cirrhosis	43
Genotype	
1a	3
1b	29
2	31
Viral load (log10)	6.19 ± 0.1
Ribavirin usage	32
Treatment experienced	12
FIB-4 score, mean	5.87 ± 0.62
Child pugh score	
A	59
B	4

	Before HCV eradication	Post HCV eradication
HbA1c (%)	6.88 ± 0.13	6.41 ± 0.12
Fasting glucose	139.56 ± 6.0	128.56 ± 4.78
Triglyceride (mg/dL)	110.53 ± 6.65	128.56 ± 4.78
Total cholesterol (mg/dL)	166.97 ± 35.03	163.22 ± 5.22
Cr (mg/dL)	1.08 ± 0.17	1.08 ± 0.11
eGFR	77.86 ± 3.35	71.41 ± 3.58
GOT (IU/L)	77.03 ± 8.21	33.89 ± 2.79
GPT (IU/L)	75.8 ± 9.25	29.70 ± 3.40
Total bilirubin (mg/dL)	0.92 ± 0.77	0.92 ± 0.54
Albumin (g/dL)	3.96 ± 0.06	4.25 ± 0.06
Platelet (10^3/μL)	136.6 ± 8.28	149.49 ± 7.14
PT (secs)	10.9 ± 0.11	10.97 ± 0.13
INR	1.08 ± 0.01	1.08 ± 0.01
Body weight (kg)	65.1 ± 1.30	64.4 ± 1.31
BMI	25.3 ± 0.46	24.93 ± 0.43

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Abstract #286

The role of determination of IL-2 and IL-10 in the oral fluid in patients with HCV and HBV infection

Vahe Azatyan[1], Hasmik Ghazinyan[2], Lazar Yessayan[3], Melanya Shmavonyan[4], Tsovinar Galstyan[5]

[1]Departaments of Therapeutic Stomatology, [2]NORQ Clinical Hospital of Infectious Diseases, [3]Departaments of Therapeutic Stomatology, [4]NORQ Clinical Hospital of Infectious Diseases, [5]NORQ Clinical Hospital of Infectious Diseases

Background: The oral fluid testing as an alternative to venipuncture is becoming more popular method for identification of cases with hepatitis C virus (HCV) and hepatitis B virus (HBV).
Aim: Of the study is to assess the state of IL-2 and IL-10, y of patients with HCV and HBV-infection.
Materials and methods: The study was conducted in 63 patients with viral hepatitis: 45 patients with HCV, 18 patients with HBV. The control group consisted of 30 patients with inflammatory periodontal disease. The laboratory ELISA assay and photometer registration method was used for cytokine level determination.
Results: Control group consisted of 30 participants (32.2%); 45(48.3%) had HCV and 18 (19.3%) HBV-infection. The average age of patients was 42 (± 14.9). For IL-2 we received significant difference for all groups compared with control − 2.83 (± 5.67); HBV-31.1 (± 23.59) ($p < 0.001$), HCV-25.99 (± 17.86) ($p < 0.001$). For IL-10 the significant difference was observed between control-0.94 (± 1.33) and HCV-25.99 (± 17.86) (p-0.0267), HBV-8.38 (± 15.51) groups ($p < 0.001$). The adjusted analysis where we considering age as a possible confounder revealed that only IL-2 significantly differs for all groups compared with the control group: control vs HCV ($p = 0.001$) and HBV ($p = 0.024$).
Conclusions: HBV and HCV infections are risk factors for increasing of levels of IL-2 and IL-10 in comparison with control groups.
This data can be alternative of serum levels of IL-2 and IL-10 in infected patients.

Abstract #288

The role of Hepatitis C virus (HCV) in Parkinson's disease

Lusine Navoyan[1], Hasmik Ghazinyan[2], Aregnazan Mkhitaryan[3], Anahit Mkrtchyan[4]

[1]Yerevan State Medical University, [2]''NORK'' Infectious Clinical Hospital, [3]''NORK'' Infectious Clinical Hospital, [4]Yerevan State Medical University

Background: Parkinson's disease (PD) is the most common neurodegenerative disorder after Alzheimers disease. As known, the risk of developing PD is multifactorial, and (HCV) infection is one of the risk factors.
Case report: Patient 54 years old male.
Diagnosis: HCV + ethanol liver cirrhosis, decompensated. Child stage B–C.
Complications: portal hypertension, ascites, splenomegaly, hepatic encephalopathy I-II with hands tremor and hiccups.
Investigations: HCV PCR- positive, G1b, PLT—101 × 10^3/μL, bilirubin total-38.5 μmol/L, bilirubin direct—24.7 μmol/L, AsAT—47.4 U/L, ALAT—31.7 U/L, albumin—33.62 g/l, GGT—63.91 U/L, Pt time—20.90 s, INR-2.07 f, AFP—2.80 ng/mL, glucose—15.89 mmol/L.
Due to receiving pathogenetic and symptomatic treatment disease undergone to compensated state, followed by anti-virial treatment in 2017, for 3 months (DAA with SVR). Following up of patient showed aviremia with the normal level of serum amiak, but hands tremor and hiccups are still remain. After the neurogist's consultation he was diagnosed Parkonsin's disease with asymmetrical start. He is getting treatment for Parkinson's disease with improvement of neurological symptoms and compensated liver cirrhosis.
Conclusions: HCV infection is a systemic disease with the hepatic and extrahepatic manifestations, including central nervous system.
HCV-positive patients need regular neurological evaluation to allow for early detection of PD.

Optimal treatment of HCV infection should take into account extrahepatic, including brain, manifestations of HCV infection.

Abstract #301

Prevalence and impact of occult Hepatitis C infection in patients with persistent liver enzymes elevation after achieving 24 weeks sustained virologic response

Anwar A Mohamed[1], M Ashraf M Eljaky[2], Eman M Abdelsameea[3], Tamer R Fouad[4], Hosam El-Din M El-Ezawy[5]

[1]National Liver Institute-Menofia University, [2]National Liver Institute-Menofia University, [3]National Liver Institute-Menofia University, [4]National Liver Institute-Menofia University, [5]National Liver Institute-Menofia University

Introduction: Despite achieving sustained virologic response (SVR) of chronic hepatitis C infection, some treated patients had persistent elevations of transaminases. Occult hepatitis C infection (OCI) could be one of the causes.
Aim: To detect OCI in peripheral blood mononuclear cells (PBMCs) in patients who achieved 24 weeks SVR with persistent elevations of transaminases. Methods: We included 998 naïve HCV patients to our study. Triple PCR for HCV RNA in PBMNs were done for those with persistent elevations of liver enzymes after 24 weeks SVR.
Results: Nine hundred and sixty-five patients achieved 24 weeks SVR (%96.69). Seventy-four patients of them (7.67%) had

persistently elevated enzymes. Cirrhosis and obesity were associated with this enzymes elevation ($p = 0.005$ and < 0.001). OCI was detected in 14/74 (18.9%) patients (group I) and negative in 60 (group II). There was no significant difference between the two groups regarding different biochemical tests. OCI was present in the same frequency in cirrhotic and non cirrhotic patients.
Conclusion: OCI is common in patients with persistent transaminases elevations despite obtaining 24 weeks SVR. It could be, beside cirrhosis and obesity, important causes of this enzymes elevation. OCI has same frequency of occurrence in both cirrhotic and non-cirrhotic patients.

Abstract #479

Test of HCV core Ag as a marker to assess active HCV infection in individuals with genotype 4 HCV in Egypt

Karim Sobhy Elnoemany[1], Mohamed Hassan Elnadry[2]

[1]Egyptian Ministry of Health, [2]Alazhar University

Introduction: Screening for anti-HCV antibody status often facilitates HCV surveillance in the community Although simple, such an assay cannot differentiate between past and present infection and requires supplemental HCV RNA testing to confirm active HCV infection and monitor antiviral treatment. Testing for HCV core antigen presents a more attractive alternative owing to the lower cost and short turnaround time.
Aim: Evaluate the diagnostic utility of HCV Ag as an alternative to HCV RNA to identify active HCV infection in Egypt.
Methods: Individuals with reactive HCV antibodies (N = 367) were tested for liver function tests, kidney function tests, HBsAg, HIV IgM, AFP, Fibroscan, HCV RNA level and HCV Ag level. All patients were of genotype 4.
Results: The lower limit of detection line for HCV RNA was 16 IU/mL. The cutoff line of HCV core Ag was 3 fmol/L. HCV RNA were less than 16 IU/mL in 33 patients and were excluded from the study. Of There were 235 (70.4%) males and 99 (29.6%) females (mean age 55.3 ± 9.2 and 45.4 ± 10.4 years, respectively). Many of the anti-HCV reactive individuals had elevated levels ($\geq$ 32 U/mL) of AST (63.5%), ALT (54.7%) and advanced liver fibrosis (49.1%, Metavir score: F3–F4). Among the anti-HCV reactive individuals, only 8 were found reactive to HBsAg. Of 334 individuals with HCV RNA level more $\geq$ 16, 290 (86.8%) had HCV core Ag $\geq$ 3.
Conclusion: High validity of HCV core Ag as a reliable marker for diagnosis of active HCV infection.

Abstract #559

An update analysis of hepatitis C virus genotype and subtype distribution in Myanmar

Aye Aye Lwin[1], Nan Cho Nwe Mon[2], Kyi May Htwe[3], Si Thura[4], Charles Chasela[5], Kara Chew[6], Yin Min Thaung[7], Sofiane Mohamed[8], Matthieu Barralon[9], Thomas Minior[10], Robert Kelly [11], Ian Sanne[12], Khin Pyone Kyi[13]

[1]Department of Medical Research, Yangon, Myanmar, [2]Department of Medical Research, Yangon, Myanmar, [3]Department of Medical Research, Yangon, Myanmar, [4]community Partners International, Myanmar, [5]Right to Care Equip, [6]David Geffen School of Medicine at University of California Los Angeles, [7]Community Partners International, Yangon, Myanmar, [8]Advanced Biological Laboratories, Luxembourg, [9]Advanced Biological Laboratories, Luxembourg, [10]United States Agency for International Development (Usaid), [11]Usaid, Burma, [12]Right to Care Equip, [13]Myanmar Liver Foundation, Yangon, Myanmar

Introduction: HCV genotyping is used to select the optimal treatment strategy and allows for further analysis of presence of DAA mutations, that may have a negative impact on SVR rates. Objective: We describe the genotypes/subtypes of the HCV-infected patients enrolled into an EQUIP-USAID sponsored treatment programme in Myanmar.
Methodology: A total of 492 HCV seropositive patients recruited for HCV treatment through Myanmar Liver Foundation Charity Clinics in Yangon and Mandalay regions were included in the analysis. Viral RNA was amplified and sequenced with DeepChek® Single round RT-PCR 5′ UTR/NS5B Premium sanger genotyping assay method. The genotype/subtype was analyzed by DeepChek®-HCV software.
Result: HCV RNA was detected in 465 patients and genotyped in 387 patients. Mean $\pm$ standard deviation (SD) age of those patients was 42.2 ± 12.3 years and 67% (258/387) were male. About 85% (329/387) of patients had HCV RNA $\geq$ 106 IU/L. Based on sequencing of the 5′UTR region, HCV genotype 3 (45.2%) was most prevalent, followed by genotype 6 (43.9%) and genotype 1 (8.8%). Among HCV subtypes, 3b (35.1%) was most prevalent, followed by subtype 6n (24.5%), 3a (9.3%), 6xa (6.7%), 6w (4.9%), 1b (4.9%), 6v (4.1%), 1a (3.1%), 6 m (2.3%), 1c, 3 g, 3 k, 6a, 6c, 6xd, 2a, 2b, 2c, 2j, and 2 m.
Conclusion: in this study, in contrast with previous reports, HCV genotype 3 and 6 were almost equally prevalent. Improved characterization of the genotype distribution in Myanmar may facilitate the development of an HCV elimination strategy in Myanmar.

Abstract #654

Decreased PD-1 and CTLA-4, But Sustained FoxP3 During DAA therapy in patients with chronic Hepatitis C

Chang Wook Kim[1], Ji Young Kim[2], Hee Yeon Kim[3], Sung Geun Kim[4], Sung Won Lee[5], Do Seon Song[6], Jong Young Choi[7], Seung Kew Yoon[8]

[1]Department of Internal Medicine, The Catholic University of Korea College of Medicine, [2]Department of Internal Medicine, The Catholic University of Korea College of Medicine, [3]Department of Internal Medicine, The Catholic University of Korea College of Medicine, [4]Department of Internal Medicine, The Catholic University of Korea College of Medicine, [5]Department of Internal Medicine, The Catholic University of Korea College of Medicine, [6]Department of Internal Medicine, The Catholic University of Korea College of Medicine, [7]Department of Internal Medicine, The Catholic University of Korea College of Medicine, [8]Department of Internal Medicine, The Catholic University of Korea College of Medicine

Background: Immune regulatory molecules such as forkhead box P3 (FoxP3), programmed death-1 (PD-1) and cytotoxic T-lymphocyte-associated protein-4 (CTLA-4) are associated with effector T cell dysfunction. These FoxP3, PD-1 and CTLA-4 are known to up-regulated in patients with chronic hepatitis C (CHC) but, there is few reports about the phenotypic changes of these molecules during direct-acting antiviral (DAA) therapy. We investigated the expression of FoxP3, PD-1 and CTLA-4 for 6 months daclatasvir and asunaprevir (DCV + ASV) treatment in 19 patients with genotype 1b CHC.
Methods: Nineteen patients with genotype 1b CHC under DCV + ASV treatment were enrolled. PBMC were isolated from these subjects before treatment (T0), 1 month (T1), 3 month (T3), 6 month (T6) and 9 month (T9) during DCV + ASV treatment. The expressions of FoxP3, PD-1, CTLA-4, CD8, CD4 on T cells were monitored by flow cytometry.

Results: T cells from patients with CHC before DCV + ASV treatment (T0) showed increased expression of FoxP3, PD-1 and CTLA-4 compared to healthy control. However, T cells from patients with CHC under DCV + ASV treatment showed decreased expression of PD1 and CTLA-4 at T6 compared to T0 significantly. Interestingly, the expression of Foxp3 was sustained from T0 through T6.
Conclusions: in CHC, PD-1 and CTLA-4 as inhibitory T cell molecules were down-regulated during 6 months DCV + ASV therapy but, FoxP3 as regulatory T cell marker was sustained during DCV + ASV therapy. This phenomenon suggests that DAA therapy can restore T cell dysfunction, not immediately but slowly.

Abstract #879

Portal hypertensive spleen in hepatitis C virus (HCV) patients with cirrhosis induces immune tolerance by activating PD-1 signaling pathway

Fanpu Ji[1], Rui Zhou[2], Na Huang[3], Wei Wei[4], Baohua Li[5], Haiyan Chen[6], Changyin Tian[7], Hong Deng[8], Jun Yang[9], Zongfang Li[10]

[1]National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University & Shaanxi Provincial Clinical Research Center for Hepatic & Splenic Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University & Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, [2]National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University & Shaanxi Provincial Clinical Research Center for Hepatic & Splenic Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, [3]National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University, [4]National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University, [5]National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University, [6]National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University, [7]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, [8]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, [9]National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University & Shaanxi Provincial Clinical Research Center for Hepatic & Splenic Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, [10]National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University & Shaanxi Provincial Clinical Research Center for Hepatic & Splenic Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University

Background/Aims: The aim of this study was to investigate the immune changes of spleen, and the effect of splenectomy on peripheral blood T lymphocyte in hepatitis C virus (HCV)-infected patients with portal hypertension (PH).
Methods: The expression of programmed death protein 1 (PD-1) and its ligand PD-L1/2 in spleen of 15 HCV cirrhotic patients and 5 traumatic spleen were analyzed by immunohistochemistry. Flow cytometry was used to evaluate the expression of PD-1 on splenic T cells and the effect of splenectomy on peripheral blood T cells.
Results: Compared with the control group, the expression of PD-1 was higher in the spleen in HCV cirrhotic patients ($P = 0.043$); the expression of PD L2 was higher in the cell membrane of the red pulp and fibrous cord areas ($P = 0.013$). PD-1 + CD8 + T and PD-1 + CD4 + T cells in spleen of patients was significantly higher than that of peripheral blood (both $P < 0.05$) and normal control spleen (both $P < 0.05$). Compared with healthy control group, PD-1 + CD4 + T in peripheral blood of patients with chronic hepatitis C (CHC) group ($Z = 2.100$, $P = 0.036$) and liver cirrhosis (LC) group ($Z = 2.941$, $P = 0.003$) increased significantly. PD-1 + CD4 + T in peripheral blood of LC group was higher than that of CHC group ($Z = 2.521$, $P = 0.012$), which decreased significantly after splenectomy ($Z = 2.380$, $P = 0.017$). PD-1 + CD8 + T in peripheral blood of LC group was significantly higher than that of CHC group ($Z = 2.626$, $P = 0.009$) and healthy control group ($Z = 3.046$, $P = 0.002$).
Conclusions: Portal hypertensive spleen in HCV-infected cirrhotic patients induces immune tolerance by activating PD-1 signaling pathway, which can be partly reversed by splenectomy.

Abstract #990

Single-nucleotide polymorphism in promoter region of the osteopontin gene as predicting marker of Hepatitis C pathogenesis and its related hepatocellular carcinoma in Pakistan population

Talat Roome[1], Anam Razzak[2], Syed M Zahid Azam[3], Hafeezullah Shaikh[4]

[1]Molecular Pathology, Department of Pathology, Dow Diagnostic Reference and Research Laboratory, Dow International Medical College, Dow University of Health Sciences Karachi, Pakistan, [2]Molecular Pathology, Department of Pathology, Dow Diagnostic Reference and Research Laboratory, Dow International Medical College, Dow University of Health Sciences Karachi, Pakistan, [3]National Institute of Liver and Gi Diseases, Dow University of Health Sciences Karachi, Pakistan, [4]National Institute of Liver and Gi Diseases, Dow University of Health Sciences Karachi, Pakistan

Introduction: Hepatitis C virus (HCV) infection is a global health problem, 4.5% to 8% Pakistani population. Osteopontin (OPN) a secretory chemokine essential for Th-1 immune response, mainly contributes to the pathogenesis of HCV infection.
Objective: The main objective of the present is to identify the single nucleotide polymorphism (SNP) in OPN promoter region and to correlate the polymorphisms with HCV disease susceptibility and progression of liver deterioration.
Methodology: About 600 study participants were enrolled including i) normal individuals, ii) HCV patients iii) HCC patients with HCV infection. HCV viral load and genotype was evaluated through Real time PCR, SNPs in OPN promoter gene was identified via DNA sequencing. OPN serum levels was estimated by ELISA and OPN expression in liver tissues of HCV induced HCC patients was performed through immunohistochemistry and classified according to the percentage and intensity of staining.
Results: Osteopontin levels were significantly raised in HCV and HCC patients and correlated well with the viral load and severity of liver fibrosis. SNPs in OPN promoter gene was identified at nucleotide (nt) − 155, − 443, − 616, and − 1748 showed 100% linkage disequilibrium with sustained virological response (SVR) found in 69% patients. Significant differences were found in OPN allele and phenotype frequencies between the HCV & HCC patients compared to controls ($p < 0.05$) suggestive of diverse immunological response during HCV pathogenesis.
Conclusion: SNPs in OPN promoter, serum OPN levels and OPN tissues expressions might serve as powerful non-invasive diagnostic

and prognostic biomarker reflecting hepatitis activity in HCV and HCC patients.

Abstract #1035

Seroconversion of Hepatitis C during dialysis in major cities of Pakistan

Talal Khurshid Bhatti[1]

[1]PIMS

Background: Hepatitis C is highly prevalent in Pakistan. Several studies worldwide have shown that patients undergoing hemodialysis are at a risk for developing Hepatitis C. So this study was carried out to determine the proportion of patients undergoing hemodialysis who seroconverted from HCV negative to HCV positive status in our hospitals.
Methods: This descriptive cross-sectional study was conducted at four tertiary care hospitals of Punjab from January 2016 to March 2016 on patients undergoing haemodialysis currently. With the help of WHO Sample Size Calculator, at confidence level 95%, absolute precision 5% and anticipated population proportion 14%, the minimally required sample size was calculated to be 186 patients but we included 190 patients in our study. Sampling technique was stratified random sampling based on hospital and gender. Inclusion criterion was all those patients who were Hepatitis C negative (determined by HCV serology, based on the principle of immunochromatography) at the initiation of dialysis and remained negative for the subsequent six months after the initiation of haemodialysis.
Results: Out of 190 patients who were HCV negative at the initiation of dialysis, 93 (i.e. 48.9%) patients converted to HCV positive status whereas 97 (i.e. 51.05%) patients remained HCV negative throughout the study. The mean time taken for seroconversion was 18.04 months (SD $\pm$ 15.43) months). The median was 12 months, with an inter quartile range of 14 months.
Conclusion: The proportion of HCV seroconversion in our hemodialysis units is very high.

Abstract #1039

Dyspepsia in cirrhotic Hepatitis C patients

Talal Khurshid Bhatti[1]

[1]PIMS

Background: To determine the frequency of patients with dyspepsia, its patterns of presentation and causes along with their associations with gender and age, amongst HCV cirrhotic patients presenting to a tertiary care health facility of Rawalpindi.
Methods: In this cross sectional study 207 HCV cirrhotic patients, above 25 years of age irrespective of gender, were included. Patients receiving prolonged treatment of acid suppression prior to hospitalization were excluded. After taking history and performing thorough physical examination, routine laboratory investigations, abdominal ultrasonography and endoscopies were performed to determine the cause of dyspepsia.
Results: Amongst 207 HCV cirrhotic patients 146 (70.5%) were presented with dyspepsia. Pain in epigastrium 92 (63.0%), heart burn 81 (55.5%) and water brash 65 (44.5%) were most common patterns of presentation of dyspepsia in HCV cirrhotic patients. Portal hypertensive gastropathy 77(52.7%) came out as leading etiology of dyspepsia, followed by gastritis 9(6.2%), ulcer 6(4.1%) and cholelithiasis4(2.7%). Amongst those diagnosed with Dyspepsia, 25(17.1%) patients were found to have functional dyspepsia i.e. no organic cause was found.
Conclusion: Dyspepsia is very frequent phenomenon in HCV cirrhotic patients with most common patterns of presentation as pain in epigastrium and heart burn. The leading cause of dyspepsia was portal hypertensive gastropathy.

Abstract #1086

Analysis of the lipid profile in chronic hepatitis C patients after direct-acting antiviral agent treatment

Yun-Hao Tai[1], Yuan-Lung Cheng[2], Keng-Hsin Lan[3], Yi-Hsiang Huang[4]

[1]Division of Gastroenterology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, [2]Division of Gastroenterology, Department of Medicine, Taipei Municipal Gan-Dau Hospital, Taipei, Taiwan, [3]Division of Gastroenterology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, [4]Division of Gastroenterology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan & Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan

Background: The eradication of chronic hepatitis C (CHC) leading to changes in the lipid profile has been reported in recent years. However, the changes have not been fully elucidated.
Aims: We aimed to analyze the lipid profile in CHC patients before and after direct antiviral agent (DAA) therapy.
Methods: This single-center retrospective study included 261 CHC patients who started to receive DAA from January 2018 through May 2018, focusing on lipid profile changes before and after DAAs. Paired t test was applied to assess the effect on cholesterol and low density lipoprotein (LDL) between baseline and at three months after treatment.
Results: Of the 261 patients, only 38 and 41 patients had complete data for LDL and cholesterol analyses, respectively: the mean cholesterol level increased from 153 to 175 ($p = 0.0001$), and the mean LDL level from 86 to 104 ($p = 0.0001$). After the subjects were divided based on their gender, the mean cholesterol level rose from 161 to 179 ($p = 0.0478$) in men and from 148 to 173 ($p = 0.0005$) in women. The mean LDL level rose by 17 mg/dl ($p = 0.00445$) in men, and by 19 mg/dl ($p = 0.0004$) in women. The baseline characteristics were similar in both genders except men had higher baseline creatinine and LDL levels. No variable was related to the changes in the lipid profile in this study.
Conclusions: In CHC patients, cholesterol and LDL increased after DAA treatment in both men and women. No significant variable associated with the changes in the lipid profile was found in this study.

C03 - Treatment

Abstract #76

Hepatitis B Virus reactivation during successful treatment of Hepatitis C virus with direct acting antiviral treatment

Ali Abdelrahman Ghweil[1], Heba Osman[2]

[1]South Valley University, [2]Lecturer of Gastroentrology South Valley University

Treatment of hepatitis C virus with potent, interferon-free, direct-acting antiviral regimens with no activity against hepatitis B virus (HBV) may increase the risk for HBV reactivation in coinfected patients. We present 2 cases of HBV reactivation during treatment with55 patients treated an all-oral regimen of daclatasvir and sofosbuvir. 2 cases of HBV reactivation were with hbA1c more than 9.

Abstract #86 Patient tolerability of Interferon and Interferon free regimen for hepatitis C infection

Dexton Antony Johns[1]

[1]Zain Clinical Research Center

The treatment goal of Chronic hepatitis C virus (HCV) infection is sustained virological response (SVR) which indicates HCV eradication. Traditionally pegylated-interferon-alpha (PEG-IFN) in combination with ribavirin was used but lately direct-acting antivirals (DAAs) which are specifically designed to target various stages of HCV life cycle.
Objective: To assess the physical and mental health related quality of life (HRQoL) before during and after treatment using EQ-5D-5L instrument.
Methods: 60 patients were included in our study.15 patients received direct acting antiviral agent (DAAs) plus pegylated alpha interferon (Peg–IFN) and the remaining 45 IFN free regimen. The EQ-5D-5L questionnaire and visual analog scale (VAS) were given to calculate coefficient's utility. Utility EQ index was calculated and statistical analysis were performed.
Results: The VAS score was negative in the IFN group indicating a poorer quality of life. The baseline EQ index were comparable however the post treatment EQ index was statistically better in group that received IFN –free therapy.
Interferon and ribavarin treatment showed more adverse effect compared to DAAs. HRQOL had a statistically significant correlation with age, sex, educational level, living type, employment status, monthly income level, and comorbidity status. Sofosbuvir and velpatasvir showed better tolerability among the DAAs.
Conclusions: DAAs are better tolerated by the patients and has a significant improvement in the quality of life.
Education, compassion and health care needs to be tailored to improve the overall well being of patients with HCV.

Abstract #87

Hepatitis C associated Oral lichen planus management using direct-acting antivirals

Dexton Johns[1]

[1]Zain Clinical Research Center

Objectives: Oral Lichen Planus is one of the extraneous manifestation of hepatitis C infection. Traditionally pegylated-interferon-alpha (PEG-IFN) in combination with ribavirin was used but lately direct-acting antivirals (DAAs) which are specifically designed to target various stages of HCV life cycle. The DAAs are well tolerated and with lesser adverse effects.
Methods: Lichen Planus refractory to conventional steroid treatment was considered as an oral manifestation of HCV and it was confirmed by anti-HCV by ELISA (third generation) and reverse transcription polymerase chain reaction (RT-PCR) for HCV-RNA. Nine patients with HCV-related OLP received Ledipasvir/sofosbuvir for 12 weeks. Out of nine, five were males with a mean age of 64. The patient response were assessed before and after treatment.
Results: Sustained virological response was observed in all patients and there was no worsening of lichen planus in any of the treated patients. Clinically refractory lichen planus resolved with DAAs treatment.
Conclusion: We have reported a case series of successful management of interferon free treatment in HCV associated oral lichen planus. Given the strong association, screening for HCV should be considered in patients with oral lichen planus.

Abstract #126

Direct-acting antiviral drugs used in the treatment of HCV increase cholesterol levels

Osman Ozdogan[1], **Serkan Yaras**[2], **Enver Ucbilek**[3], **Fehmi Ates**[4], **Orhan Sezgin**[5], **Engin Altintas**[6]

[1]Mersin University, Faculty of Medicine, Gastroenterology Department, [2]Mersin University, Faculty of Medicine, Gastroenterology Department, [3]Mersin University, Faculty of Medicine, Gastroenterology Department, [4]Mersin University, Faculty of Medicine, Gastroenterology Department, [5]Mersin University, Faculty of Medicine, Gastroenterology Department, [6]Mersin University, Faculty of Medicine, Gastroenterology Department

Aim and background: Aim is to investigate the effects of direct-acting antiviral (DAA) drugs on insulin resistance and lipid parameters in HCV treatment.
Methods: A total of 121 patients were included in the study. Fasting blood glucose (FBG), insulin level (insulin), insulin resistance, total cholesterol, HDL, LDL cholesterol and triglyceride levels were measured at 0, 1, 3, 6 and 12 months.
Results: HCV RNA levels were $3.394 \times 103 \pm 9.419$x103 (min; 1255, max; 82.000 x103) IU/mL. 117 patients were genotype 1. According to months, FBG levels were 96 ± 12, 102 ± 17, 100 ± 15, 100 ± 14, 100 ± 14 mg/dL, and HOMA-IR was 2.93 ± 0.96, 4.73 ± 2.69, 4.6 ± 2.07, 3.38 ± 2.33, 3.17 ± 1.58, respectively. Especially, at the 1st month of the treatment, insulin and HOMA-IR levels were significantly higher than the initiation of treatment ($p < 0.05$). At the third month of treatment, this elevation continued, but it was observed that at the end of the treatment and at the end of the treatment it decreased to the initial values. It was found that total cholesterol and LDL cholesterol levels increased significantly in the first month of treatment ($p < 0.05$) and this elevation persisted as high during the treatment and after the end of the treatment. Slight increase in triglycerides and HDL was not statistically significant ($p > 0.05$).
Conclusion: DAA drugs used in the treatment of HCV infection increased IR, total cholesterol and LDL cholesterol levels during treatment.

Lipid parameters

	Baseline	Mount 1	Mount 3	Mount 6	Mount 12
TRIGLYCERIDE mg/dL	106±42	117±60	114±61	111±54	113±53
TOTAL CHOL. mg/dL	159±30	180±34	188±37	183±35	179±33
LDL CHOL. mg/dL	84±28	100±30	107±36	102±31	100±30
HDL CHOL. mg/dL	55±16	57±16	58±17	59±16	56±15

Abstract #138

Real-world data of daclatasvir plus asunaprevir for patients infected with HCV genotype 1b in China

Jianping Li[1], Zhiwei Xie[2], Yujuan Guan[3]

[1]Department of Hepatology Division, Guangzhou Eighth People's Hospital, Guangzhou Medical University, [2]Department of Hepatology Division, Guangzhou Eighth People's Hospital, Guangzhou Medical University, [3]Department of Hepatology Division, Guangzhou Eighth People's Hospital, Guangzhou Medical University

Background and Aims: The combination of daclatasvir (DCV) and asunaprevir (ASV) has shown good safety profiles and high sustained virologic response (SVR) in patients with chronic hepatitis C virus(CHC) genotype 1b infection in clinical trial. Recently lots of real life data related to this combination have demonstrated the efficacy and safety profile in Japan and Korea. However, the efficacy and safety in real world of Chinese patients have not been investigated and published. The purpose of this study was to confirm the efficacy and safety of DCV plus ASV regimen in Chinese patients with HCV genotype 1b infection in real world.
Methods: We analyzed clinical data from 38 patients infected with HCV genotype 1b, who received DCV 60 mg daily plus ASV 100 mg twice a day for 24 weeks in the Eighth People's hospital of Guangzhou. The primary end point was sustained viral response rates at week 24(SVR24) after treatment and the incidence of adverse events (AEs).
Results: Among 38 patients treated, 20 (52.6%) patients were female, 10 (26.3%) had compensated liver cirrhosis, 1 had primary carcinoma of liver; 13 (34.2%) previously treated with peginterferon and ribavirin therapy. Overall SVR24 rate was 94.7% (36/38), and 100% (10/10) in patients with compensated liver cirrhosis. Four patients (two patients with chronic hepatitis C and two patients with compensated cirrhosis) experienced AEs, including platelet count decrease (n = 1), hemoglobin decrease (n = 1), uric acid elevation(n = 1) and alanine aminotransferase (ALT) elevation (n = 1).
Conclusions: DCV/ASV combination therapy is well tolerated and highly effective for patients with HCV 1b infection with or without compensated cirrhosis.

Abstract #157

Safety and efficacy of Daclatasvir/Sofosbuvir in HCV-infected decompensated cirrhosis patients: a Cambodian retrospective cohort study

Meiwen Zhang[1], Jean-Philippe Dousset[2], San Kimchamroeun[2], Antharo Kien[2], Vithurneat Hang[2], Keoputhika Unn[2], Chhit Dimanche[3], Mickael Le Paih[2], Tonia Marquardt[2], Suna Balkan[2], Anne Loarec[4]

[1]Epicentre, Paris, France, [2]Médecins Sans Frontières- France, Phnom Penh, Cambodia, [3]Hepato-Gastro Department, Preah Kossamak Hospital, [4]Epicentre, Paris, France

Introduction: Sofosbuvir with Daclatasvir (SOF + DAC) is recommended as a pan-genotypic Hepatitis C Virus (HCV) treatment by the World Health Organization's 2018 guidelines. Data on the efficacy and safety of SOF + DAC for decompensated cirrhosis patients is scarce.
Objectives: Médecins Sans Frontières (MSF) conducted a retrospective analysis of a Cambodian HCV cohort in a national hospital to assess the effectiveness in low-resource context.
Methodology: Patients with decompensated cirrhosis (defined as F4 and Child–Pugh B/C) on SOF + DAC; with/without the addition of Ribavirin (RBV) were included. Genotype was not systematically provided. Efficacy was evaluated by sustained viral response at 12 weeks post-treatment (SVR12). Safety was assessed by biological and clinical follow up, and the presence of serious adverse events (SAE) including death.
Results: A majority of patients (N = 107) were Child–Pugh B (n = 93, 86.9%). Median age was 59 years (IQR: 55–65), and 61.7% (n = 66) were female. Patients were on SOF + DAC for 12 (14, 13.1%) or 24 weeks (32, 29.9%) and SOF + DAC + RBV for 12 weeks (43, 40.2%). Among 94 patients with virological outcomes, 89 achieved SVR12 (94.7%, 95% CI: 88.0%-98.3%), SVR12 among all initiated was 83.2% (95% CI: 74.4%-89.7%) with 2 lost-to-follow-up and 11 deaths. The incidence of SAE (including death) was 11.2% (n = 12). Except for 1(9.1%) SAE with unknown cause, 11(91.7%) were due to nature progression of the decompensation. The most common cause was exacerbation or development of severe ascites/pleural effusion (7, 63.6%).
Conclusion: patients treated with SOF + DAC with or without RBV achieved high SVR12 and was well tolerated in this Cambodian cohort of decompensated cirrhosis patients.

Baseline characteristics		Child-Pugh B		Child-Pugh C		Total	
		n	%	n	%	n	%
Baseline sociodemographic characteristics							
Sex	Female	57	61.3%	9	64.3%	66	61.7%
Age (years)		59 (55, 64)		58 (54, 66)		59 (55, 65)	
Body-mass index (BMI) (kg/m^2)	BMI<25	66	71.0%	7	50.0%	73	68.2%
	BMI≥25 & <30	19	20.4%	6	42.9%	25	23.4%
	BMI≥30	8	8.6%	1	7.1%	9	8.4%
Treatment experience							
	DAA	1	1.1%	0	-	1	0.9%
	IFN, pegIFN, RBV	4	4.3%	0	-	4	3.7%
	Naive	88	94.6%	14	100.0%	102	95.3%
Baseline virology and liver stiffness							
Baseline HCV RNA	(1000 IU)	311.0 (74.0, 77.1)		367.5 (11.2,908.0)		311.0 (65.3, 889.0)	
	>=6 million IU	2	2.2%	1	7.1%	3	2.8%
Genotype	1	16	17.2%	2	14.3%	18	16.8%
	2	3	3.2%	0	-	3	2.8%
	6	22	23.7%	5	35.7%	27	25.2%
	Unknown	52	55.9%	7	50.0%	59	55.1%
Liver stiffness (kPa)		42.8 (31.6, 62.7)		49.3 (27.7, 60.4)		44.3 (30.4, 62.7)	
Baseline laboratory tests							
	Bilirubin (mg/dL)	1.3 (0.8, 2)		4.2 (2.8, 5.1)		1.4 (0.9, 2.4)	
	Albumin (g/dL)	2.9 (2.6, 3.2)		2.5 (2.2, 2.6)		2.8 (2.5, 3.2)	
	PT-INR	1.5 (1.3, 1.6)		1.9 (1.6, 2.1)		1.5 (1.3, 1.8)	
Baseline physical examination							
Ascites	Absent	42	45.2%	3	21.4%	45	42.1%
	Slight	29	31.2%	3	21.4%	32	29.9%
	Moderate	19	20.4%	6	42.9%	25	23.4%
	Severe	3	3.2%	2	14.3%	5	4.7%
Encephalopathy	No Encephalopathy	90	96.8%	14	100.0%	104	97.2%
	Grade 1-2	3	3.2%	0	-	3	2.8%
	Grade 3-4	0		0	-	0	-
Comorbidity							
Co-infection	HBV	1	1.1%	0	-	1	0.9%
	HIV	3	3.2%	0	-	3	2.8%
	HIV and HBV	0	-	0	-	0	0.0%
Diabetes	Mono	89	95.7%	14	100.0%	103	96.3%
	No diabetes history and FBS<126mg/dL	57	61.3%	8	57.1%	65	60.8%
	No diabetes history but FBS >=126mg/dL	23	24.7%	4	28.6%	27	25.2%
	Diagnosed diabetes	13	14.0%	2	14.3%	15	14.0%
Total		93	100.0%	14	100.0%	107	100.0%

Table 1. Demographic and baseline characteristics among decompensated patients (Median (IQR) is applied for Age (years), Baseline VL (1000IU), Bilirubin (mg/dL), Albumin (g/dL), PT-INR. IFN=interferon. PegIFN=pegylated interferon. DAAs=direct-acting antivirals. HCV RNA=Hepatitis C Virus ribonucleic acid. HIV=Human Immunodeficiency Virus. HBV=Hepatitis B Virus. FBS=Fasting blood sugar.)

	Regimen	SVR12	
		Among all initiated (N=107)	Among all received virological outcome (N=94)
Child-Pugh B	SOF+DAC 12 weeks	31/33	31/33
		93.9% (79.8, 99.3)	93.9% (79.8, 99.3)
	SOF+DAC 24 weeks	39/47	39/41
		83.0% (69.2, 92.3)	95.1% (83.5, 99.4)
	SOF+DAC+RBV 12 weeks	12/13	12/12
		92.3% (64.0, 99.8)	100% (-)
	Total	82/93	82/85
		88.2 (79.8, 94.0)	95.4% (88.5, 98.7)
Child-Pugh C	SOF+DAC 12 weeks	1/3	1/2
		33.3% (0.8, 90.6)	50.0% (1.3, 98.7)
	SOF+DAC 24 weeks	4/7	4/4
		57.1% (18.4, 90.1)	100% (-)
	SOF+DAC+RBV 12 weeks	2/4	2/2
		50.0% (6.8, 93.2)	100% (-)
	Total	7/14	7/8
		50.0% (23.0, 77.0)	87.5% (47.4, 99.7)
Total	SOF+DAC 12 weeks	32/36	32/35
		88.9% (73.9, 96.9)	91.4% (76.9, 98.2)
	SOF+DAC 24 weeks	43/54	43/45
		79.6% (66.5, 89.4)	95.6% (84.9, 99.5)
	SOF+DAC+RBV 12 weeks	14/17	14/14
		82.4% (56.6, 96.2)	100% (-)
	Total	89/107	89/94
		83.2% (74.7, 89.7)	94.7% (88.0, 98.3)

Table 2. DAA regimen and SVR12 outcomes by Child-Pugh score (Numbers indicate mean (%) and 95% confidence intervals or n/N.)

Abstract #177

Reappearance of HCV infection after kidney transplantation in SVR achieved patient

Sila Akhan[1], Murat Sayan[2], Simge Fidan[3]

[1]Kocaeli University Medical Faculty Infectious Diseases and Clinical Microbiology, [2]Kocaeli University Medical Faculty PCR Unit, [3]Kocaeli University Medical Faculty Infectious Diseases and Clinical Microbiology

Case: 49 years old male patient had the diagnosis chronic renal failure since 1995. He was in periton dialysis 7.5 years and on haemodialysis 10 years before kidney transplantation. In year 2002 he applied to our Infectious Diseases policlinic and got the diagnosis chronic HBV and HCV (genotype 1b) co-infections. Both HBV DNA and HCV RNA were positive. We began reduced dosage pegylated interferon 135microg/week alone because of the kidney. After 48 weeks therapy HBV DNA became negative but HCV RNA become positive again. He followed up until 2012 without treatment. And then pegylated interferon 135 microg/week plus 200 mg daily low dose ribavirin were given to the patient for 48 weeks. With this therapy patient reached the sustained viral response at 24 weeks (SVR24) for HCV infection. Then he underwent kidney transplantation from his HBV and HCV negative relative live donor. Unfortunately HCV appears again after successful transplantion. His status was anti-HBs positive and HVC RNA positive again at this time. After coming the new therapy options we began to this patient ledipasvir/sofosbuvir (LDV/SOF) 90/400 mg with fix therapy dosage in year 2016. He tolerated well all the treatments. After a 12-week course of therapy, weeks 4–12, the patient's HCV viral load was undetectable; SVR12 was noted.

Conclusion: After SVR of HCV infection, reappearance is very unusual despite the use immunosupressive drugs. In this case we could not explain this HCV infection after reaching SVR not much, but cured HBV infection may have a role to sustain HCV.

Abstract #190

Pharmacokinetics, safety and tolerability of Glecaprevir/ Pibrentasvir in healthy mainland Chinese subjects

Hari Varun Kalluri[1], Rajneet Oberoi[2], Qian Chen[3], Qi Jiang[4], Armen Asatryan[5], Chen Yu[6], Wei Liu[7]

[1]Abbvie Inc., [2]Abbvie Inc., [3]Shanghai Xuhui Central Hospital, [4]Abbvie Inc., [5]Abbvie Inc., [6]shanghai Xuhui Central Hospital, [7]abbvie Inc

Introduction/Objective: Glecaprevir/pibrentasvir (GLE/PIB) 300/120 mg once-daily (QD) is an interferon/ribavirin-free, pan-genotypic (GT1–6) fixed-dose combination regimen approved for treating chronic hepatitis-C virus (HCV) infection in many countries including United States, European Union and Japan. To support China clinical development, a Phase-1 study was conducted to evaluate the pharmacokinetics (PK), safety and tolerability of GLE/PIB in healthy Mainland Chinese subjects.

Methods: This multiple-dose study was conducted in 18 healthy adult subjects who received GLE/PIB 300/120 mg QD for 7 days under non-fasting conditions. Intensive PK sampling was performed on Days 1 and 7. Exposures of GLE/PIB at steady-state were estimated and compared to healthy Western subjects across Phase-1 studies. Safety and tolerability was evaluated through assessment of adverse events (AEs), vital signs, electrocardiograms and laboratory tests.

Results: Following QD administration, GLE/PIB reached steady-state by Day 5 with minimal accumulation (< 17%). GLE exposures in Chinese subjects (maximum concentration [C_{max}]: 2370 ng/mL; area under the concentration–time curve [AUC24]: 7530 ng• h/mL) fell within the range of exposures observed in Western subjects (Cmax: 598–3550 ng/mL; AUC24: 2380–12100 ng•hr/mL). PIB exposures in both populations were comparable. GLE/PIB was well tolerated by Chinese subjects. Most AEs were mild in severity. No clinically significant vital signs, electrocardiogram or laboratory abnormalities were observed during the course of the study.

Conclusion: Combined with the global efficacy and safety data in Western and Asian patients, the PK and safety data from the current study supports the use of GLE/PIB 300/120 mg QD in Chinese chronic HCV-infected patients without any dose adjustment.

Abstract #193

Ledipasvir/Sofosbuvir treatment experience in patient with chronic Hepatitis C (CHC) receiving dialysis: a case report

Selcuk Aksoz[1]

[1]Adiyaman Training and Research Hospital, Clinic of Infectious Diseases, Adiyaman, Turkey

Objective: CHC is a liver inflammation caused by a virus in the RNA genotype called hepatitis C virus (HCV). HCV infection is an important cause of morbidity and mortality in patients with chronic renal failure (CRF). The aim of this study is to evaluate the results of the treatment in dialysis patients receiving dialysis for CRF and treated with ledipasvir/sofosbuvir for chronic hepatitis C for 6 months.

Method: Case: In this study, we discussed a 44-year-old patient who was treated for chronic hepatitis C and receiving dialysis 3 days a week for CRF. The patient had HCV genotype 1 and had previously received pegylated interferon + ribavirin + telaprevir treatment for HCV infection. Although the patient responded to treatment and HCV RNA was negative, HCV RNA was again positive (103400 IU/ML) about 3 years after treatment was completed. The patient was then

treated with ledipasvir/sofosbuvir for 6 months. The patient was evaluated meanwhile clinically and laboratory every 15 days.
Findings: The treatment of the patient whose HCV RNA level was negative on the 15th day of the treatment and without any clinical or laboratory serious side effects during the treatment was completed and discontinued at the end of the 6th month and the patient was listed for transplant.
Conclusion: Ledipasvir/sofosbuvir treatment seems to be effective and reliable for the treatment of CHC in dialysis patients with CRF. But it is important to support this study with a larger group of patients.

Abstract #212

An open-label, randomized, active control trial of 8 versus 12 weeks of elbasvir/grazoprevir for treatment-naïve chronic hepatitis C genotype 1b patients with mild fibrosis (EGALITE)

Ming-Lung Yu[1], Chao-Hung Hung[2], Pin-Nan Cheng[3], Ming-Jong Bair[4], Yi-Hsiang Huang[5], Jia-Horng Kao[6], Shih-Jer Shu[7], Pei-Lun Lee[8], Jyh-Jou Chen[9], Rong-Nan Chien[10], Cheng-Yuan Peng[11], Chun-Yen Lin[12], Tsai-Yuan Hsieh[13], Chia-Yen Dai[14], Jee-Fu Huang[15], Chung-Feng Huang[16], Wan-Long Chuang[17]

[1]Hepatobiliary Division, Department of Internal Medicine and Hepatitis Center, Kaohsiung Medical University Hospital and Hepatitis Research Center, Kaohsiung Medical University, Kaohsiung, Taiwan, [2]Division of Hepatogastroenterology, Department of Internal Medicine, Chiayi Chang Gung Memorial Hospital, Chiayi, Taiwan, [3]Division of Gastroenterology and Hepatology, Department of Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan, [4]Division of Gastroenterology, Department of Internal Medicine, Taitung Mackay Memorial Hospital, Taitung City, Taiwan, [5]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, [6]Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan, [7]Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei, Taiwan, [8]Chi Mei Hospital, Liouying, Tainan, Taiwan, [9]Chi Mei Hospital, Liouying, Tainan, Taiwan, [10]Division of Hepatology, Department of Gastroenterology and Hepatology, Linkou Medical Center, Chang Gung Memorial Hospital, Taiwan, [11]China Medical University Hospital, Taichung, Taiwan, [12]Division of Hepatology, Department of Gastroenterology and Hepatology, Linkou Medical Center, Chang Gung Memorial Hospital, Taiwan, [13]Department of Gastroenterology, Tri-Service General Hospital, Taipei, Taiwan, [14]Hepatobiliary Division, Department of Internal Medicine and Hepatitis Center, Kaohsiung Medical University Hospital and Hepatitis Research Center, Kaohsiung Medical University, Kaohsiung, Taiwan, [15]Hepatobiliary Division, Department of Internal Medicine and Hepatitis Center, Kaohsiung Medical University Hospital and Hepatitis Research Center, Kaohsiung Medical University, Kaohsiung, Taiwan, [16]Hepatobiliary Division, Department of Internal Medicine and Hepatitis Center, Kaohsiung Medical University Hospital and Hepatitis Research Center, Kaohsiung Medical University, Kaohsiung, Taiwan, [17]Hepatobiliary Division, Department of Internal Medicine and Hepatitis Center, Kaohsiung Medical University Hospital and Hepatitis Research Center, Kaohsiung Medical University, Kaohsiung, Taiwan

Background/Aim: Grazoprevir/elbasvir achieved a high sustained virological response (SVR) rate (> 95%) for patients with genotype 1 or 4 (HCV-1/4) infection. The current study aimed to evaluate the efficacy of truncated treatment period of 8-week grazoprevir/elbasvir for naïve, HCV-1b patients with mild fibrosis.
Methods: EGALITE (NCT03186365) was a randomized, open-label, active controlled trial. Eighty-two treatment-naive HCV-1b patients with fibroscan < 9.5 kPa from 11 centers in Taiwan were randomized to receive 8 (n = 41) or 12 (n = 41) weeks of elbasvir/grazoprevir, stratified by baseline viral loads (VL, cutoff: 800,000 IU/ml) and interleukin-28B genotype. The primary end-point was SVR12 (HCV RNA < 12 IU/ml at posttreatment week 12).
Results: Overall, 50 (61%) were female; 46 (56.1%) with VL > 800,000 IU/ml and 22 (26.8%) interleukin-28B rs8099917 non-TT genotype. Both arms had comparable baseline characteristics/clinical features (Table 1). SVR12 was achieved by 87.8% (36/41, 95% confidence intervals [CI]: 81.4%-94.2%) and 100% (41/41, CI: 93.6%-100%) in full-analysis-set population and 90.0% (36/40, CI: 83.5%-96.5%) and 100% (41/41, CI: 93.6%-100%) in per-protocol population (excluding one HCV-6 patient) in 8-week and 12-week arms, respectively (both p = 0.055). In the 8-week arm, high baseline VL (> 1,500,000 IU/mL) was significantly associated with lower SVR12 rate (79% [15/19] vs. 100% [21/21], p = 0.042). Two patients had serious adverse events, degenerative hip replacement (12-week arm) and foot traumatic fracture (8-week arm). Both were study medication-unrelated. None experienced grade 3/4 adverse event and treatment discontinuation.
Conclusions: 8-week regimen with grazoprevir/elbasvir was highly effective and safe in HCV-1b naïve patients with mild fibrosis, especially among those with lower baseline VL.

Table 1. Baseline characteristics and treatment responses of 82 patients

Variables, mean (SD) or n (%)	All patients (N=82)	8-week arm (n=41)	12-week arm (n=41)	P value
Age, year; mean (SD)	56.6±12.0	58.1±12.3	55.1±11.8	0.27
Female; n (%)	50 (61.0%)	24 (58.5%)	26 (63.4%)	0.65
Body mass index, kg/m^2; mean (SD)	24.1±3.4	23.8±3.5	24.5±3.4	0.32
IL-28B, rs8099917 non-TT; n (%)	22 (26.8%)	11 (26.8%)	11 (26.8%)	1
Fibroscan; kPa, mean (SD)	6.0±1.4	6.2±1.5	5.8±1.3	0.27
7-9.5 kPa, n (%)	17 (20.7%)	10 (24.4%)	7 (17.1%)	0.41
HCV RNA (log_{10} IU/mL); mean (SD)	5.9±0.7	6.0±0.6	5.8±0.8	0.18
HCV RNA > 800,000 IU/mL, n (%)	46 (56.1%)	23 (56.1%)	23 (56.1%)	1
HCV RNA > 1,500,000 IU/mL, n (%)	35 (42.7%)	19 (46.3%)	16 (49.0%)	0.50
Undetectable HCV RNA				
Treatment weak 1; n/N (%)	22/82 (26.8%)	8/41 (19.5%)	14/41 (34.1%)	0.21
Treatment weak 2; n/N (%)	61/82 (74.4%)	29/41 (70.7%)	32/41 (78.0%)	0.61
Treatment weak 4; n/N (%)	74/82 (90.2%)	38/41 (92.7%)	36/41 (87.8%)	0.71
End-of-treatment; n/N (%)	82/82 (100.0%)	41/41 (100.0%)	41/41 (100.0%)	-
SVR 4; n/N (%)	82/82 (100.0%)	41/41 (100.0%)	41/41 (100.0%)	-
SVR12, full-analysis-set population, n/N (%)	77/82 (93.9%)	36/41 (87.8%)	41/41 (100.0%)	0.055
SVR12, per-protocol population, n/N (%)*	77/81 (95.1%)	36/40 (90.0%)	41/41 (100.0%)	0.055
Serious Adverse Events, n (%)	2 (2.4%)	1 (2.4%)	1 (2.4%)	-
Discontinuation, n (%)	0 (0)	0 (0)	0 (0)	-

Note: SVR, sustained virological response. *Per-protocol analysis, excluding one patient with HCV genotype 6 mistyped as 1b.

Abstract #213

Evaluation of sofosbuvir-containing regimens in the treatment of chronic liver diseases related to hepatitis C virus in Egyptian patients

Eslam Ahmed Habba[1], Hassan Elsayed Albatea[2], Taher Eldmerdash Attia[3]

[1]Tropical Medicine Department, Faculty of Medicine, Tanta University, Egypt, M.D., [2]Hepatology and Infectious Diseases Department, Faculty of Medicine, Kafr-Elsheikh University, Egypt, M.D., [3]Tropical Medicine Department, Faculty of Medicine, Tanta University, Egypt, M.D

Introduction: Egypt has the highest worldwide prevalence, estimated among the 15–59 years age group, to be 14.7%. Despite aggressive programs toward education, care, and treatment over the last 10 years, Egypt faces the largest burden of HCV infection in the world, predominantly genotype 4.

Aims and Methods: The aim of this study is to evaluate sofosbuvir containing regimens in treatment of chronic liver diseases related to HCV in Egyptian patients.324 patients diagnosed with chronic HCV underwent sofosbuvir-containing regimen in the treatment and followed up during and after the end of the therapy for 3–6 months.

Results: 51.85% were males, 81.48% ≥ 65 ys old, 88.89% naïve vs. 11.11% treatment experienced, 6.17% received IFN + riba + sof with 100% response, 41.98% received sof + riba with 83.87% response, 30.86% sof + dakla with 100.00% response, 3.70% sof + sim with 100.00% response, 17.28% sof. + dakla +riba with 92.31% response. ALT ≥ 40 (i/u) in 58.11%, F4 by fibroscan was elicited in 65.43%, Overall SVR12 response was elicited in 92.11% of patients, fatigue was the commonest side effect (33.33%).

Conclusion: Generic sofosbuvir containing regimens are highly effective in the treatment of HCV Egyptian patients. Predictors of response were age < 65 years, female sex, albmin ≥ 3.662, total bilirubin < 1.370, treatment- naieve and non-cirrhotic patients.

Table R-26: SVR 12 rates by patients' subgroups

		PCR SVR12						Chi-Square	
		SVR12		Non SVR12		Total			
		N	%	N	%	N	%	X^2	P-value
Age groups	<65 Years	232	93.55	16	6.45	248	100.00	3.856	0.050*
	≥65 Years	48	85.71	8	14.29	56	100.00		
Sex	Male	128	86.49	20	13.51	148	100.00	12.522	<0.001*
	Female	152	97.44	4	2.56	156	100.00		
PCR	<800000 PCR	128	94.12	8	5.88	136	100.00	0.409	0.523
	>800000 PCR	92	92.00	8	8.00	100	100.00		
Albumin	Mean ±SD	3.662	0.627	3.174	0.487			3.366	0.001*
Total Bilirubin	Mean ±SD	1.370	0.848	2.140	0.904			-3.483	0.001*
HB	Mean ±SD	12.027	1.731	12.180	1.561			-0.382	0.703
TLC	Mean ±SD	6162.439	3789.041	5618	1323.033			0.638	0.524
Platelets	Mean ±SD	174919.355	71545.189	172000	75139.169			0.175	0.861
IF cirrhotic	Child A	112	90.32	12	9.68	124	100.00	2.550	0.110
	Child B	56	82.35	12	17.65	68	100.00		
TTT	Naive	252	92.65	20	7.35	272	100.00	7.919	0.048*
	Experienced IFN	12	75.00	4	25.00	16	100.00		
	Experienced Sof.	16	100.00	0	0.00	16	100.00		

Abstract #218

Case report: Eosinophilic gastroenteritis complicating perforation in a hepatitis C patient treated with direct-acting antivirals

Ming Xing Huang[1], Ruo Man Ke[2], Chun Na Li[3], Zuo Quan Zhang[4], Zhe Zhu[5], Xiao Mou Peng[6]

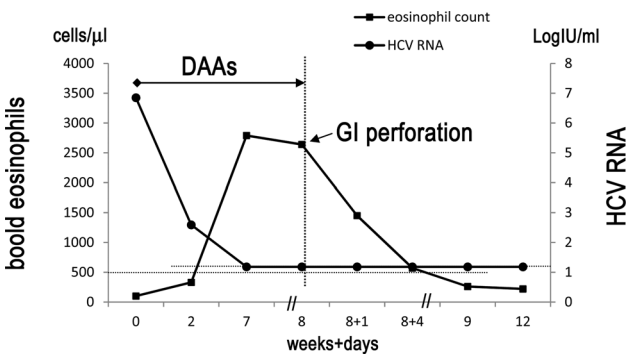
[1]Department of Infectious Diseases, 2 Department of Radiology, and 4 Central Laboratory, The Fifth Affiliated Hospital, Sun Yat-Sen University, [2]The Fifth Affiliated Hospital, Sun Yat-Sen University, [3]The Fifth Affiliated Hospital, Sun Yat-Sen University, [4]The Fifth Affiliated Hospital, Sun Yat-Sen University, [5]The Fifth Affiliated Hospital, Sun Yat-Sen University, [6]The Fifth Affiliated Hospital, Sun Yat-Sen University

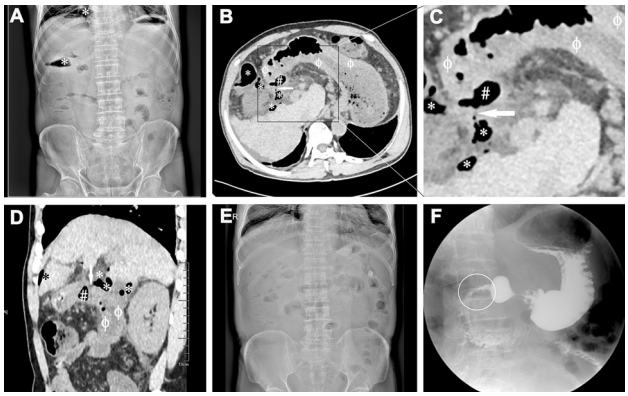
Background: The direct-acting antiviral (DAA) therapy of hepatitis C virus (HCV) infection has demonstrated excellent efficacy and safety profile. Based on large cohort studies, serious adverse events (SAEs) are rare. Here, we reported the first case of a patient with alcoholic liver cirrhosis superinfected by HCV presenting with a SAE of eosinophilic gastroenteritis (EGE) complicating acute perforation during velpatasvir plus sofosbuvir therapy.

Methods: Case description

Result: A 58-year-old Chinese man with history of alcoholic liver cirrhosis (Child–Pugh A) more than 10 years had been diagnosed with HCV infection (serum HCV RNA 6.85 logIU/mL, genotype 6a) (Fig. 1) and was treated with velpatasvir plus sofosbuvir (Velpanat composed of velpatasvir100 mg plus sofosbuvir 400 mg got by himself). On the 8th week during treatment, the man was hospitalized and diagnosed as EGE by abdominal pain, thickened gastric and duodenal walls in CT images with peripheral eosinophilia and no evidence of parasitic or extraintestinal disease. (Fig. 2) With symptomatic and supportive treatments and discontinuation of DAAs, the patient was discharged with normal eosinophils on the 12th day. After discharged, the patient was asymptomatic and the negative serum HCV RNA and normal peripheral eosinophils were monitored at week 12 (Fig. 1).

Conclusion: DAA therapy largely simplifies the treatment of HCV infection. However, this case indicates that some DAAs needs further clinical assessment of their safety, emphasizing the significance to notice peripheral eosinophilia and conduct endoscopy earlier, and to discontinue the therapy in time. Therefore, it reminds us to re-emphasize the significance of comprehensive monitoring.





Abstract #242

Sofosbuvir/Velpatasvir is effective and safe in patients with concomitant proton pump inhibitor use in clinical studies

Rafael Esteban[1], Kosh Agarwal[2], Calleja Luis Jose[3], Francois Jean Dufour[4], Steven L. Flamm[5], Stuart C. Gordon[6], Wei Yi Lu[7], Cathy Lu[8], Luisa Stamm[9], Yun Li Ni[10], Diana Brainard[11], Kris V. Kowdley[12], Curtis Cooper[13], Pineda Antonio Juan[14], Lluis Castells[15], Maria Buti[16], Sabela Lens[17]

[1]Department of Internal Medicine/Liver Unit, Vall D'hebron University Hospital, [2]Institute of Liver Studies, King's College Hospital Nhs Trust, [3]Hospital Universitario Puerta De Hierro, [4]University of Bern, [5]Northwestern University Health System, [6]Henry Ford Health System, Detroit, Mi, [7]Gilead Sciences, Inc, [8]Gilead Sciences, Inc, [9]Gilead Sciences, Inc, [10]Gilead Sciences, Inc., [11]Gilead Sciences Inc., Foster City, California, United States, [12]Swedish Medical Center, [13]The Ottawa Hospital, [14]Hospital Universitario Virgen De Valme, [15]Liver Unit, Internal Medicine Department, Hospital Universitari Vall De Hebrón, [16]Hospital Universitari Vall D'hebron, Barcelona, Spain, [17]University of Barcelona

Background: Prior to the availability of Phase 1 drug interaction data, concomitant PPI use was prohibited in clinical trials of SOF/VEL. Later clinical studies allowed for the use of up to 20 mg omeprazole or equivalent dosing. This analysis evaluated the efficacy and safety of patients who received SOF/VEL and reported concomitant use of a PPI.
Methods: This was a retrospective analysis of efficacy and safety data from 12 Phase 2 and Phase 3 clinical studies in which patients received 12 weeks of SOF/VEL and reported concomitant use of a PPI. Efficacy was assessed by SVR12 and safety was assessed by treatment-emergent AEs.
Results: 87 patients reported concomitant use of a PPI. The mean age was 57 years (26–78), 79% were male and 75% were white; 56% were infected with genotype 3 and 29% with genotype 1; 37% had compensated cirrhosis and 39% were treatment experienced. The most common PPI was omeprazole reported by 68% of patients. The SVR12 rate was 97% (84 of 87 patients). 78% of patients had an AE, 11% had a serious AE. These efficacy and safety are comparable to patients enrolled in the same studies who received SOF/VEL for 12 weeks without concomitant use of a PPI (SVR12 rate 97% [2445 of 2517 patients].
Conclusion: In Phase 2 and Phase 3 clinical studies, SOF/VEL was effective and safe in patients with concomitant PPI use. These data support the use of SOF/VEL according to labeled recommendations co-administrated with PPIs and other acid reducing agents.

Abstract #243

Sofosbuvir/Velpatasvir for 12 weeks is safe and effective in patients undergoing dialysis

Sergio M Borgia[1], Janet Dearden[2], Yoav Lurie[3], Stephen D. Shafran[4], Ashley Brown[5], Wei Yi Lu[6], Cathy Lu[7], Robert Hyland[8], Sophia Lu[9], Svetlana Markova[10], Sobol Dvory Hadas[11], Anu O. Osinusi[12], Eric M. Yoshida[13], Jose Luis Calleja[14], Edward J. Gane[15]

[1]William Osler Health System, [2]Saint Bartholomew's Hospital, [3]Shaare Zedek Medical Center, [4]Department of Medicine, University of Alberta, [5]Imperial College Healthcare Nhs Trust, [6]Gilead Sciences, Inc., [7]Gilead Sciences, Inc., [8]Gilead Sciences, Inc., [9]Gilead Sciences, Inc., [10]Gilead Sciences, Inc., [11]Gilead Sciences, Inc., [12]Gilead Sciences, Inc., [13]Gordon and Leslie Diamond Health Care Centre, [14]Hospital Universitario Puerta De Hierro, [15]Auckland City Hospital

Background: Approved HCV treatments for patients on dialysis are associated with complexities including drug–drug interactions, baseline resistance testing, use of ribavirin, and risk of hepatotoxicity. This study evaluated the safety, efficacy, and pharmacokinetics (PK) of SOF/velpatasvir (VEL) for 12 weeks in patients with HCV infection on dialysis.
Methods: Treatment-naïve or -experienced patients, of any genotype, with or without compensated cirrhosis undergoing hemodialysis or peritoneal dialysis, were enrolled to receive open-label SOF/VEL (400 mg/100 mg daily) once daily for 12 weeks. The primary efficacy endpoint was comparison of SVR12 to a pre-specified historic control rate of 83%. The primary safety endpoint was the proportion of patients who discontinued therapy due to adverse events (AEs).
Results: 59 patients were enrolled at 21 sites in Canada, United Kingdom, Spain, Israel, Australia and New Zealand. The median age was 62 years (range 49–86), 59% were male, 53% white, 32% treatment experienced, 29% had cirrhosis. Most patients had HCV genotype 1 (42%), 2 (11%), or 3 (27%). Most (92%) were on hemodialysis with a mean (range) dialysis duration of 7.3 years (0–40). Treatment was well tolerated; no one discontinued therapy due to AEs. Overall, 56/59 (95%) of patients achieved SVR12. Exposures were consistent with the Phase 1 renal impairment study.
Conclusion: Treatment with SOF/VEL for 12 weeks in patients with and without cirrhosis undergoing dialysis resulted in a 95% SVR12 rate. The regimen was safe and well-tolerated with no treatment related discontinuations or treatment-related SAEs.

Abstract #256

A territory-wide review of common direct-acting antiviral agents (DAAs) for treatment of chronic hepatitis C in public hospitals in Hong Kong

Ronald K. N. Tong[1], Yee Tak Hui[2], Grace Lai Hung Wong[3], Y K Ma[4], M F Yuen[5], Jacky Chan[6], Kin Bon Lai[7], C K Loo[8], Moon Sing Lai[9], C W Chan[10], Joulen Yl Lau[11], Tina TT Fan[12], Aric Josun Hui[13], James YY Fung[14], Vincent WS Wong[15]

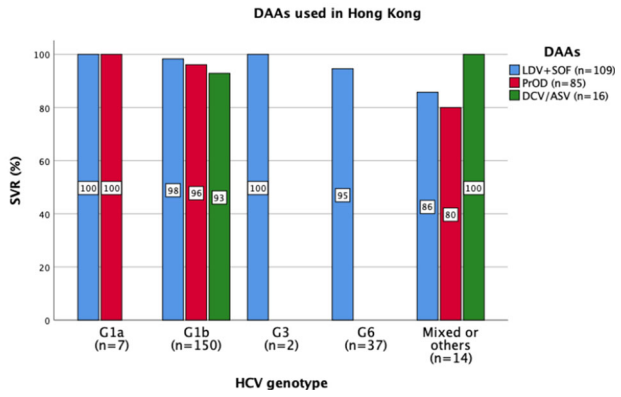
[1]Caritas Medical Center, [2]Queen Elizebeth Hospital, [3]Prince of Wales Hospital, [4]Tuen Mun Hospital, [5]Queen Mary Hospital, [6]Princess Margaret Hospital, [7]United Christian Hospital, [8]Kwong Wah Hospital, [9]North District Hospital, [10]Yan Chai Hospital, [11]Pamela Youde Nethersole Eastern Hospital, [12]Tseung Kwan O Hospital, [13]Alice Ho Miu Ling Nethersole Hospital, [14]Queen Mary Hospital, [15]Prince of Wales Hospital

Background: We report the data on treatment outcome and adverse events in a cohort of patients with chronic hepatitis C virus (HCV) infection treated with direct-acting antivirals (DAAs) in Hong Kong.
Methods: Data were retrieved retrospectively from HK HCV Registry. Inclusion criteria included adult HCV patients, received at least one dose of ledipasvir/sofosbuvir (LDV + SOF), ombitasvir/paritaprevir/ritonavir/dasabuvir (PrOD) or daclatasvir/asunaprevir (DCV/ASV). Sustained virologic response (SVR) was defined as undetectable HCV RNA at 12 weeks or more after stopping DAAs. Patients with no post-treatment SVR data were excluded.
Results: From January 2005 to November 2017, data from a total of 210 patients were analysed. Their median (interquartile range, IRQ) age was 62 (49–75) years, 45.2% were male, 51.9% had compensated cirrhosis and 11.4% had decompensated cirrhosis. The median (IQR) liver stiffness measure of the 148 patients with Fibroscan data was 14.8 (1.2–28.4) kPa. 40% were treatment-experienced. Comorbidities are shown in Table 1.
Genotype distribution were G1b (71.4%), G6 (17.6%), mixed or others (6.7%), G1a (3.3%), G3 (1.0%). The SVR for LDV + SOF, PrOD and DCV/ASV were 96.3% (n = 109), 95.3% (n = 85) and 93.8% (n = 16) respectively (Figure 1). Reported adverse events were fatigue (10.5%), headache (1.4%), nausea (4.3%), diarrhoea (0.5%), insomnia (1%), skin rash (1.5%). Four cases discontinued treatment prematurely (1 LDV + SOF, 3 PrOD; 2 Child–Pugh A, 2 Child–Pugh B) due to hepatic encephalopathy or worsening of liver function, of which one achieved SVR.
Conclusion: Real world data from the three commonest DAAs showed excellent treatment outcome and favourable side effect profiles.

Table 1. Comorbidities of patients receiving DAAs

Diabetes mellitus	16.2%
Hepatocellular carcinoma	8.6%
Chronic hepatitis B	4.8%
Thalassaemia major	3.3%
Chronic renal failure on haemodialysis	1.9%
Chronic renal failure on peritoneal dialysis	0.5%
HIV	1.4 %
Haemophilia	0.5%

Figure 1. SVR rate of different DAAs



Abstract #275

Is sofosbuvir-based regimen safe and effective for hepatitis C infected patients with stage 4–5 chronic kidney disease? A systematic review and meta-analysis

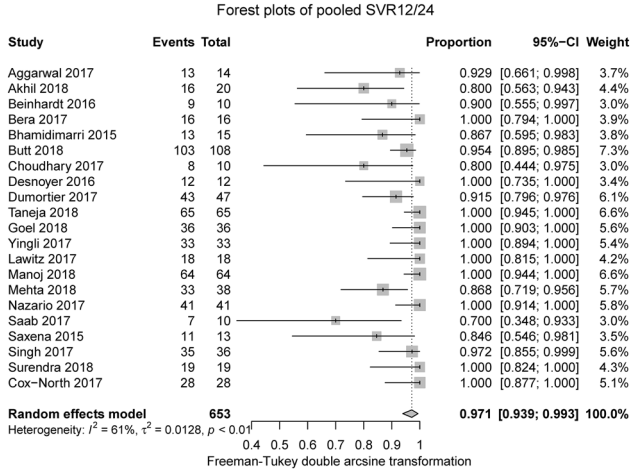
Mingshu Li[1], Jun Chen[2], Zhixiong Fang[3], Yi Li[4], Qian Lin[5]

[1]Xiangya School of Public Health, Central South University & Medical Affairs Department, Gilead Science, [2]Department of Infectious Disease, The Second Xiangya Hospital of Central South University, [3]Department of Infectious Disease, Xiangtan City Central Hospita, [4]Department of Infectious Disease, The Second Xiangya Hospital of Central South University, [5]Xiangya School of Public Health, Central South University

Introduction and objectives: Whether sofosbuvir (SOF) is suitable for HCV infected patients with stage 4 and 5 chronic kidney disease (CKD) is inconclusive. This meta-analysis aims to evaluate the safety and effectiveness of SOF-based regimen for this group of population.
Method: Two reviewers independently searched relevant literature in PubMed, Web of Science, EMBASE and Google Scholar, published up to August 2018. Eligible studies included those applied SOF-based therapy to treat HCV infected patients with stage 4 or 5 CKD. Random effects model was used to estimate pooled sustained virological response (SVR12/24) and serious adverse event (SAE) rate. Subgroup analysis was performed to determine the impact of different dose of sofosbuvir.
PROSPERO registration number: CRD42018107440.
Results: 21 studies with 717 patients (including 421 on dialysis) were extracted out of 496 potential citations. HCV genotypes ranged from GT1 to GT6. SOF-based regimen included: SOF/LDV ± RBV, SOF + DCV ± RBV, SOF + SMV ± RBV, SOF + RBV, and SOF + PR, with varied dose of sofosbuvir: 400 mg daily, 400 mg/48 h, 400 mg three times a week. Pooled SVR12/24 (per protocol) was 97.1% (95% CI 93.9%- 99.3%,), and SAE rate was 4.8% (95% CI 2.1%- 10.3%). There was no significant difference at SVR12/24 (97.1% vs 96.2%, p = 0.72) or SAE rate (8.8% vs 2.9%, p = 0.13) between subgroups applying full and decreased dose of sofosbuvir.
Conclusion: Our study suggests SOF-based regimen might be used safely and effectively in patients living with HCV infection/stage 4–5 CKD, with normal and reduced dose of sofosbuvir. Prospective and well-controlled trials are needed to confirm these findings.

Table. Characteristics of studies and patients

Studies	Geographical origin	No. of patients	No. of dialysis recipients	History of Cirrhosis (%)	mean/median baseline RNA	Genotype	SOF-based regimen	Dose of SOF	SVR12/24 (PP)	NOS score
Aggarwal (2017) [19]	USA	14	14	20% (F3,F4)	8375588.6 IU/ML	GT1-60%, GT2-6.7%, GT3-20%, GT4-13.3%	SOF+SMV, SOF+RBV, SOF/LDV±RBV, SOF+PR, SOF+DCV 12-24W	200mg QD	92.8% 13/14	4
Akhil (2018) [20]	India	22	22	NA	2642495 IU/ML	GT1-63.63%, GT3-27.27%, GT4-9%	SOF+RBV 12W	400 mg QD	80% 16/20	4
Beinhardt (2016) [21]	Austria	10	10	40% (30% decompensation)	6.1±0.8 log IU/ML	GT1a-20% , GT1b-40%, GT3a-20%, GT4-20%	SOF+PR, SOF+SMV, SOF+DCV, SOF+RBV 12-24W	400mg QD	90% 9/10	4
Bera (2017) [22]	India	25	25	20%	6.4±0.57 log IU/ML	GT3-72%, GT1-24%, GT4-4%	SOF+DCV 12-24W	400mg/48h	100% 16/16	4
Bhamidimarri (2015) [23]	USA	15	12	60%	9.7×10^6 IU/ML	GT1a-67%, GT1b-33%	SOF+SMV 12-24W	200mg QD or 400mg/48h	87% 13/15	4
Butt (2108) [24]	USA	137	NA	NA	NA	NA	SOF/LDV±RBV 12-16W	400mg QD	95% 103/108	3
Choudhary (2017) [25]	India	16	16	12.50%	7(5-8) log IU/ML	GT1-69%, GT3-25%, GT-6%	SOF+PR, SOF+DCV±RBV12W	400mg/48h	80% 8/10	4
Desnoyer (2016) [26]	France	12	12	83%	6.59 (6.13-6.86) log IU/ML	GT1-92% GT2-8%	SOF+SMV, SOF+DCV, SOF/LDV, SOF+RBV 12-24W	400mg QD or 400mg TIW	83% 10/12	5
Dumortier (2017) [18]	France	50	35	54%	2603063 IU/ML	GT1-56%, GT2-12%, GT3-10%, GT4-18%, GT5-4%	SOF+RBV, SOF+PR, SOF+DCV±RBV , SOF+SMV ±RBV 12-24W	400mg QD or 400mg/48h or 400mg TIW	91% 43/47	5
Taneja (2018) [27]	India	65	54	32.3% (9% decompensation)	1.65×10^6 (1.2×10^3 - 1.73×10^8) IU/ML	GT1-65%; GT2-1%, GT3-34%	SOF +DCV 12- 24w	200mg QD	100% 65/65	5
Goel (2018) [28]	India	41	31	12%	5.9 (4.12-9.9) log IU/ML	GT3-54%, GT1-42%, GT4-5%	SOF+DCV 12-24W	200mg QD	100% 36/36	4
Yingli (2017) [29]	China	33	33	NA	1.7-7.8 log IU/ML	GT1b-21%, GT2a-73%, GT2a+1b-6%	SOF+DCV	200mg QD	100% 33/33	4
Lawitz (2017) [30]	USA and New Zealand	18	0	11%	NA	GT1a-78%, GT1b-22%	SOF/LDV 12W	400mg QD	100% 18/18	4
Manoj (2018) [31]	India	64	11	NA	NA	NA	SOF+RBV, SOF/LDV, SOF+DCV 12-24W	400mg QD	100% 64/64	5
Mehta (2018) [32]	India	38	38	NA	5.75(5.05-6.36) log IU/ML	GT1a-42%, GT1b-58%	SOF+DCV, SOF/LDV 12W	400mg QD or 400mg/48h	86.8% 33/38	5
Nazario (2017) [33]	USA	41	38	49%	NA	GT1a-66%; GT2-2%, GT3-2%	SOF+SMV, SOF/LDV, SOF+DCV 12-24W	400mg QD	100% 41/41	3
Saab (2017) [34]	USA	12	12	NA	30499500± 29655754 IU/ML	GT1a-42%, GT1b-25%, GT2-17%, GT1-17%	SOF+RBV, SOF/LDV±RBV	400mg QD	70% 7/10	4
Saxena (2015) [35]	USA	18	5	75%	NA	NA	SOF+PR, SOF+RBV, SOF+SMV±RBV	400mg QD	85% 11/13	5
Singh (2017) [36]	India	36	30	27.8% (16.7% decompensation)	9.9×10^5 IU/ML	G1-72%, G3-22%, G4-5%	SOF/LDV, SOF+DCV 12W-24W	400mg QD	97.2% 35/36	4
Surendra (2018) [37]	India	21	21	0	NA (63%>80000 IU/ML)	GT1a-63%, GT1b-37%	SOF/LDV 12W	400mg/48h	100% 19/19	5
Cox-North (2017) [38]	USA	29	NA	44%(14% decompensation)	NA	GT1-72%, GT2-7%, GT3-17% GT6-4%	SOF/LDV±RBV, SOF+DCV±RBV, 8-24W	400mg QD	100% 28/28	4



Abstract #278

Sofosbuvir Plus Ribavirin for the Treatment of Hepatitis C Virus Genotype 2 in Korea: What's the optimal dosage of ribavirin in real-world setting?

Sung Kyu Choi[1], Sung Bum Cho[2], Chung Hwan Jun[3], Jae Hyun Yoon[4]

[1]Division of Gastroenterology & Hepatology, Department of Internal Medicine, Chonnam National University Hospital, [2]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Chonnam National University Hospital, [3]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Chonnam National University Hospital, [4]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Chonnam National University Hospital

Aim: The objective of this study is to examine efficacy and safety of sofosbuvir plus ribavirin for treatment of hepatitis C virus genotype 2 and examine optimal ribavirin dosage. Methods: From May 2016 to March 2017, 199 patients received sofosbuvir plus ribavirin treatment for hepatitis C virus genotype 2 at four centers in Jeollanamdo. After excluding patients lost to follow-up and those with insufficient data, we retrospectively assessed data from 194 patients.

Results: Sustained virological response was gained in 189 patients (intention to treat: 97.4%. per protocol: 99.5%), whose average ribavirin dosage was 937.1 mg/day. The most frequent adverse events were anemia (17.5%) and its incidence increased significantly ($P < 0.001$) with increasing ribavirin dosage (mg/kg, body weight). Ribavirin cessation or dosage reduction occurred in 27 patients (14.2%). The ribavirin dosage reduction rate increased at > 15 mg/kg dosage (Area under the receiver operating curve, 0.652; $P = 0.01$; 95% confidence interval 0.54–0.76). Age $\geq$ 70 years, liver cirrhosis, and female sex were associated with ribavirin dosage reduction on multivariate analysis.

Conclusions: Remarkable outcome was attained in hepatitis C virus genotype 2 patients treated with sofosbuvir plus ribavirin. Age $\geq$ 70 years, liver cirrhosis, and female sex were associated with ribavirin dosage reduction. Thus, sustained virological response can be accomplished with < 1000 mg ribavirin, with an optimal dosage of 15 mg/kg body weight.

Abstract #289

Cryoglobulinemic membranous- glomerulopathy/HCV patient treatment

Hasmik Ghazinyan[1], Hayk Harutyunyan[2]

[1]Nork Infection Clinical Hospital, [2]Astghik Medical Center

Background: 40–74% of patients infected with HCV might develop at least one extrahepatic manifestation (EHM) during the course of the disease. EHM could represent the first signal of HCV infection and many patients show no hepatic symptoms. Renal involvement is the most common severe manifestation of mixed cryoglobulinemia (MC) .

Case presentation: A man in his fifth decade was referred to our clinic with diagnosis chronic viral hepatitis C (CHCV), cryoglobulinemic membranous- glomerulopathy (CMGN).

On admission his urine protein concentration was 1.5 g/g creatinine (reference range 0–0.2 g/g creatinine) and his serum creatinine concentration was 286 mkmol/l (reference range 62–115). A renal biopsy showed membranous-glomerulopathy with positive for cryoglobulinemia. Serum cryoglobulins were found 200 mg/l (reference range 0–60 mg/l). histological diagnosis CMGN after consultation of nephrologist and was treated methipred 60 mg day for 12 weeks With the reduced dose until 8 mg p/o Laboratory findings at the admission in our clinic: Positive HCV-RNA, HBsAg and anti-HBcAg (IgM and IgG) negative, genotype of virus C 1b, stage of fibrosis F2(9.0 kPa) Baseline biochemical parameters: Total bilirubin (TB) 28.4 mkmol/l, AST/ALT 126/154 U/I Creatinine 286 mkmol/l. Ultrasound showed hepatosplenomegaly. Antiviral treatment was started with Sofosbuvir 400 mg/Ledipasvir 60 mg for 3 month with the monitoring renal and virological parameters.

In the end of treatment aviremia was accompanied with the improvement not only liver parameters, but also renal.

Conclusions: • MC and renal disease associated with chronic HCV infection must be treated with IFN-free, ribavirin-free DAA-based anti-HCV combinations. • Clinical remission in HCV-related CMGN correlates with virological response.

Abstract #293

Effectiveness, safety of Paritaprevir/Ombitasvir/r plus Dasabuvir therapy in HCV genotype 1 infection: results from a Chinese real-world cohort

Jing Liang[1], Fengmei Wang[2], Fang Liu[3]

[1]Tianjin Third Central Hospital, [2]Tianjin Third Central Hospital, [3]Tianjin Third Central Hospital

Treatment of chronic hepatitis C (CHC) has entered the interferon free era since approval of the all-oral direct-acting antiviral (DAA) therapy in China. 12 weeks of Paritaprevir/Ombitasvir/r (OBV/PTV/r) plus Dasabuvir (DSV) has been demonstrated to be highly effective and well tolerated in phase III registration trials in Asian. However, real world data of this regimen are lacking in China mainland. We aim to evaluate the efficacy and safety of OBV/PTV/r +DSV in a real-world clinical practice with genotype 1b HCV infection.

Methods: A prospective, single-center cohort study was conducted in Tianjin Third Central hospital of China. All patients with who were newly diagnosed and treated with OBV/PTV/r plus DSV for 12 weeks were included. Sustained virologic response (SVR) rate obtained at 12 weeks posttreatment (SVR12), efficacy and safety were evaluated in patients who received OBV/PTV/r plus DSV.

Results: Totally 102 patients were enrolled, 22 of whom (21.6%) were diagnosed with compensated cirrhosis. The overall rate of end of treatment (EOT) and SVR12 in patients were 99% and 98%. The incidence of common ($\geq$ 10%) adverse events included elevated total bilirubin (19.6%), fatigue (14.7%) and itchy skin (11.8%) 0.3 cases (2.9%) of patients experienced Grade $\geq$ 3 adverse events that were considered to be unrelated to the drug.

Conclusion: In a real-world cohort, treatment with OBV/PTV/r +DSV in Chinese patients with genotype 1 HCV infection appears safe and achieves high SVR12 rates Hyperbilirubinemia is the most frequent on-treatment finding but majority of adverse events were mild.

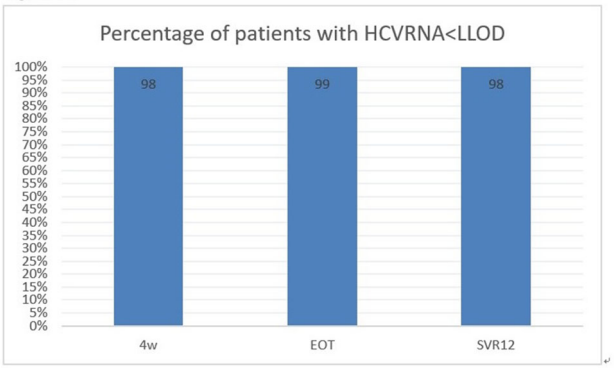
Table 1 Baseline characteristics of patients treated with OBV/PTV/r +DSV

Characteristics	Patients (N=102)
Sex, male, n (%)	54 (52.9)
Age, years, mean (range)	59.4 (26-77)
Cirrhosis, n, (%)	22 (21.6%)
HCV RNA,log_{10}IU/mL,mean, (SD)	6.2(0.8)
ALT,U/L,mean, (SD)	64 (61)
AST,U/L,mean, (SD)	56 (54)
Total bilirubin,μmol/L, mean, (SD)	17(9)
Transient elastography (FibroScan), kPa, mean, (SD)	13.8(6.9)
Creatinine, (mg/dL), mean, (SD)	65(12)
Albumin, g/dL, mean, (SD)	45(5)
HCV antiviral treatment history, Naïve n (%)	90(88.2)

Table 2 Adverse events occurring during treatment patients treated with OBV/PTV/r +DSV

	Patients, n (%) N=102
Adverse event leading to treatment discontinuation	2(1.9)
Any adverse event	37(36.2)
Anemia	2(1.9)
Fatigue	15(14.7)
Elevated total bilirubin	20(19.6)
Itchy skin	12(11.8)
Rash	6(5.9)
Weight loss	9(8.8)
Nausea	5(4.9)
Serious adverse events	3(2.9)
Elevated bilirubin > 5×ULN	1(1.0)
Upper gastrointestinal bleeding	1(1.0)
Infection	1(1.0)
Death	0

Figure 1



Abstract #305

Remarkable liver enzyme normalization and improvement of APRI and Fib-4 score in chronic hepatitis C pateints treated with glecaprevir and pibrentasvir (G/P)

Yang Chen-Ta[1]

[1]Department of Gastroenterology and Hepatology, Changhua Christian Hospital

Introduction: G/P is the first pangenotypic DAA drug in Taiwan. The SVR12 rate of G/P is 97–100% in noncirrhotic or cirrhotic patients. Patients who are difficult to treat (such as GT 3), intolerant to ribavirin, or severe CKD will benefit from G/P.
Objective: To report the effectiveness and adverse events of G/P.
Methods: Total 32 patients had been reimbursed for G/P treatment since 2018/08/23 by health insurance in our hospital (a medical center). The criteria of treatment included chronic hepatitis C with active viremia and fibrosis stage equal to Metavir F3 or F4 (compensated cirrhosis).
Results: Remarkable normalization of liver enzymes (AST 47.1 U/L vs. 30.6 U/L, P value 0.0032; ALT 41.6 U/L vs. 21.5 U/L, P value < 0.0001) and improvement of liver stiffness (APRI 1.04 vs. 0.62, P value 0.0029, and Fib-4 score 3.95 vs. 3.34, P value 0.048) at the 4th week (data available in 24 patients until now) compared to before treatment were observed. Virological response at the forth week is excellent (18 patients with undetected viral load, 5 patients with viral load < 12 IU/mL, 1 patient with viral load 13 IU/mL). Adverse events such as hyperbilirubinemia (14 of 32 patient) and pruritus (9 of 32 patients) were observed. Until now, no patient discontinued G/P due to adverse events.
Conclusion: Our data of G/P revealed remarkable liver enzyme normalization and improvement of liver stiffness with excellent virological response and tolerable adverse events.

Baseline Characteristics (N=32)	Number or mean (± standard deviation)
Age	62.4 ± 9.6
Gender	Male (N=16), female (N=16)
HCV viral load	1,206,630 ± 1,873,969 (6.08 log ± 6.27 log)
Genotype	GT 1b (N=1), GT 2 (N=26), GT 3 (N=4), GT 6 (N=1)
Fibrosis status	F3 (N=11), F4 (N=21)
Treatment (Naïve or experienced)	Naïve (N=27), experienced (N=5)
AST	50.2 ± 32.8
ALT	50.5 ± 41.6
Platelet count	148.5 ± 69.1
Total bilirubin	0.77 ± 0.38
Albumin	3.96 ± 0.46
eGFR	63.09 ± 38.97
CKD stage 3-5	CKD stage 3 (N=3), stage 4 (N=1), stage 5 (N=8)
MELD score	8.2 ± 3.72

Total 24 patients*	Before treatment	Week 4	P value
HCV viral load	1116934 (6.05log)	Undetected (N=18), < 12 IU/mL (N=5), 13 IU/mL (N=1)	<0.001
AST	47.1 ± 30.7	30.6 ± 13.1	0.003
ALT	41.6 ± 26.5	21.5 ± 12.8	<0.001
Platelet count	150.3 ± 77.5	161.3 ± 82.6	0.047
APRI	1.04 ± 0.97	0.61 ± 0.52	0.003
Fib-4	3.95 ± 2.93	3.34 ± 2.26	0.048
Total bilirubin	0.80 ± 0.39	1.18 ± 0.65	<0.001
Direct bilirubin	0.17 ± 0.08	0.27 ± 0.21	0.01
eGFR	59.64 ± 41	55.54 ± 38.22	0.056

*Until now, data at the week 4 are available in 24 of 32 patients. EOT data of all 32 patients will be available in 2019/01 and SVR 12 will be available in 11 patients before APASL 2019.

Abstract #312

The effect of interferon-free direct-acting antivirals therapy on hepatitis C virus infected patients with Cryoglobulinemia

Katsumi Terashita[1], Tomofumi Takagi[2], Takuto Miyagishima[3], Souichirou Matsuda[4], Goki Suda[5], Naoya Sakamoto[6]

[1]JCHO Sapporo Hokushin Hospital & Kushiro Rosai Hospital, [2]JCHO Sapporo Hokushin Hospital, [3]Kushiro Rosai Hospital, [4]Hakodate National Hospital, [5]Hokkaido University Hospital, [6]Hokkaido University Hospital

Background and Aim: Cryoglobulinemia related nephropathy is one of major hepatitis C Virus (HCV) induced extrahepatic manifestations. However, it is not clarified well how direct-acting antiviral (DAA) therapy for HCV infected patients with cryoglobulinemia effects on cryoglobulinemia-related nephropathy. In this prospective single center study, we aimed to evaluated cryoglobulinemia positive rate in the HCV infected patients, and the effect of DAA therapy on cryoglobulinemia induced nephropathy.
Methods: In this study, we evaluated the status of cryoglobulinemia in HCV infected patients between 2014 April and 2018 January. In addition, we evaluated the change in cryoglobulinemia and cryoglobulinemia induced nephropathy in HCV infected patients with cryoglobulinemia before and after DAAs therapy.
Results: A total of 88 HCV infected patients were evaluated with cryoglobulinemia between 2014 April and 2018 January. A total of 51 patients were infected with HCV genotype 1 and 33 patients were infected with genotype 2. Of 88 patients, a total of 30 (34.1%)

patients had Cryoglobulinemia. The prevalence of cryoglobulinemia was significantly higher in female sex and patients with advanced fibrosis. Of 30 patients with cryoglobulinemia, 26 patients were treated with DAAs and were properly evaluated with status of cryoglobulinemia before and after DAAs therapy. Of 26 patients, 18 patients were recovered from cryoglobulinemia after DAAs therapy. In In those patients, serum complete valued were significantly up-regulated ($p = 0.030$), and proteinuria and renal dysfunction were tended to restore.

Conclusions: DAA therapy might be a promising treatment for the HCV-associated cryoglobulinemia.

Abstract #313

Safety and Efficacy of Sofosbuvir/Velpatasvir in genotype 1–6 HCV-infected patients in china: results from a phase 3 clinical trial

Lai Wei[1], Qing Xie[2], Yan Huang[3], Ming Shan Wu[4], Min Xu[5], Hong Tang[6], Jun Cheng[7], Hang Yan Gao[8], Bo Zhuang Mou[9], Guang Xiao Dou[10], Min Yue Nan[11], Qin Ning[12], Min Yi Mao[13], Luisa Stamm[14], Sophia Lu[15], Sobol Dvory Hadas[16], Mei Hong Mo[17], Diana Brainard[18], Feng Yong Yang[19], Qiang Gui Wang[20], Peng Hu[21], Li Lun Zhang[22], Liang Zhi Gao[23], Feng Lin[24], Jia Shang[25], Zhong Guo Gong[26], Jun Li[27], Hua Ming Su[28], Ping Zhong Duan[29], Lin Jin Hou[30], Dong Ji Jia[31]

[1]Peking University Hepatology Institute, Peking University People's Hospital, [2]Ruijin Hospital, [3]Xiangya Hospital Central South University, [4]Shanghai Public Health Center, [5]Guangzhou Eighth Municipal People's Hospital, [6]West China Hospital of Sichuan University, [7]Beijing Ditan Hospital Capital Medical University, [8]1st Hospital of Jilin University, [9]Jinan Infectious Disease Hospital, [10]Shengjing Hospital of China Medical University, [11]The Third Hospital of Hebei Medical University, [12]Tongji Hospital, [13]Shanghai Renji Hospital, [14]Gilead Sciences, Inc., [15]Gilead Sciences, Inc., [16]Gilead Sciences, Inc., [17]Gilead Sciences Inc., Foster City, California, Usa, [18]Gilead Sciences Inc., Foster City, California, Usa, [19]The Second Hospital of Nanjing, [20]Peking University First Hospital, [21]The 2nd Affiliated Hospital of Chongqing Medical University, [22]The 1st Affiliated Hospital of Nanchang University, [23]The 3rd Affiliated Hospital of Sun Yat-Sen University, [24]Hainan General Hospital, [25]Henan Provincial People's Hospital, [26]The Second Xiangya Hospital of Central South University, [27]The First Affiliated Hospital of Nanjing Medical University, [28]Shanghai Public Health Clinical Center, [29]Beijing Youan Hospital, Capital Medical University, [30]Nanfang Hospital, [31]Beijing Friendship Hospital

Background: HCV infection remains a major health threat in China, with a diversity of genotypes (GTs). Treatment with SOF/VEL has resulted in highSVR12 in GT1–6 HCV-infected patients in clinical trials and real-world settings. This study evaluated the efficacy and safety of SOF/VEL for 12 weeks in patients in China.

Methods: Treatment-experienced and treatment-naive patients with GT1–6 HCV infection without cirrhosis or with compensated cirrhosis were enrolled in a single-arm, open-label trial to receive SOF/VEL for 12 weeks. The primary efficacy endpoint was SVR12 and the primary safety endpoint was AEs leading to SOF/VEL discontinuation.

Results: A total of 264 patients were enrolled. 53% were male, 20% had cirrhosis, 18% were treatment-experienced, 31% had GT1b, 23% GT2, 22% GT3 (8% GT3a, 14% GT3b), and 24% GT6. The mean age and BMI were 45 (19–73) years and 24 (16-37) kg/m^2, respectively. The overall SVR12 rate was 96% (93–98%). The SVR12 rate was 100% for patients with GT1b (82/82), GT2 (61/61), and GT6 (62/62). The SVR12 rate was 83% (49/59) for patients with GT3. Among the 9 patients who relapsed, 8 had GT3b HCV infection of whom 7 also had cirrhosis. No patient discontinued treatment due to AEs. 139 patients (53%) experienced treatment-emergent AEs. No serious or severe AEs were assessed by the investigator as related to study drug.

Conclusions: Consistent with earlier studies, treatment with SOF/VEL for 12 weeks was well tolerated and resulted in high overall rates of SVR12. Lower SVR rates were observed among GT3b HCV-infected patients with cirrhosis.

Abstract #314

Sofosbuvir/Velpatasvir for patients with chronic genotype 3 HCV infection with compensated cirrhosis: an integrated analysis of phase 2 and phase 3 clinical trials

Roberts Keith Stuart[1], Maria Buti[2], Graham R. Foster[3], Calleja Luis Jose[4], Ajit Sood[5], Vasily A. Isakov[6], Ola R.[7], J. H. Weiland[8], Wei Yi Lu[9], Cathy Lu[10], Luisa Stamm[11], Yun Li Ni[12], Evguenia Svarovskaia[13], Diana Brainard[14], David L. Wyles[15], Pineda Antonio Juan[16], Alexander Thompson[17], Rafael Esteban[18], Alessandra Mangia[19]

[1]Alfred Hospital, [2]Hospital Universitari Vall D'hebron, Barcelona, Spain, [3]Queen Mary University of London, London, England, [4]Hospital Universitario Puerta De Hierro, [5]Dayanand Medical College and Hospital, [6]Russian Academy of Medical Sciences, [7]Karolinska University Hospital, [8]Karolinska University Hospital, [9]Gilead Sciences, Inc., [10]Gilead Sciences, Inc., [11]Gilead Sciences, Inc., [12]Gilead Sciences, Inc., [13]Gilead Sciences, Inc., Foster City, California, United States, [14]Gilead Sciences Inc., Foster City, California, United States, [15]Denver Health Medical Center, [16]Hospital Universitario Virgen De Valme, [17]St. Vincent's Hospital Melbourne, [18]Vall D'hebron University Hospital, [19]IRCCS-Ospedale Casa Sollievo Della Sofferenza

Background: In the current DAA era, patients with genotype 3 HCV infection and cirrhosis have emerged as a more difficult-to-cure population. SOF/VEL has been assessed in patients with genotype 3 and compensated cirrhosis in multiple Phase 2 and Phase 3 clinical trials.

Methods: This was a retrospective analysis of efficacy data from 337 patients with genotype 3 and compensated cirrhosis treated with SOF/VEL for 12 weeks in one Phase 2 and five Phase 3 trials. The Phase 2 trial was a study which enrolled only patients with genotype 3 and cirrhosis. The Phase 3 trials include dedicated studies of patients with genotype 3 HCV infection, and other studies which enrolled patients of all genotypes. Efficacy was assessed by SVR12 rate.

Results: 337 patients with genotype 3 and compensated cirrhosis treated were enrolled at 147 sites in 11 countries. The mean age was 53 years (21–76), 73% were male, 79% were white, 31% were treatment experienced and 6% had HCV/HIV coinfection. Most patients had cirrhosis determined at screening by fibroscan > 12.5 kPa (76%) or the combination of fibrotest > 0.75 and APRI > 2 (12%). For patients with data available, baseline median fibroscan score was 18 kPa (14, 26) and fibrotest score was 0.79 (0.63, 0.89). The overall SVR12 rate was 94% (316 of 337 patients).

Conclusion: Results in over 330 patients enrolled in Phase 2 and Phase 3 trials demonstrates that SOF/VEL for 12 weeks is highly effective treatment for patients with genotype 3 and compensated cirrhosis.

Abstract #315

Potential Risk of drug–drug interactions associated with direct-acting antiviral regimens in chinese urban patients with chronic Hepatitis C

Lai Wei[1]

[1]Peking University People's Hospital, Peking University Liver Disease Research Institute, Beijing Key Laboratory of Hepatitis C and Liver Disease Immunotherapy

Objectives: To assess the potential risk of drug–drug interaction (DDI) of the direct-acting antiviral (DAA) regimens for chronic hepatitis C (CHC) in Chinese urban patients.
Methods: 2013 to 2016 China Health Insurance Research Association (CHIRA) annual urban claims databases were used to identify patients with CHC and extract their long-term concomitant medications which had indications for chronic diseases or cancers. The maximal degrees of DDI associated with the 8 DAA regimens were identified individually by mapping the identified long-term concomitant medications with available DDI information of DAA agents from the Liverpool HEP Drug Interactions website.
Results: 81.7% of the included 8107 patients had at least one claims record for long-term concomitant medication. Based on the identified long-term concomitant medications, the distributions of maximal DDI associated with the 8 DAA regimens in the study cohort significantly varied in all categories of DDI (contraindication: 2.7–13.1%; dose-additional monitoring required: 7.8–32.7%; no clinically significant interaction expected: 0.2–9.0%; no interaction: 37.1–63.7%; $p < 0.001$). Ombitasvir/paritaprevir/ritonavir/+ dasabuvir was associated with the highest risk of contraindicated DDI (13.1%). Two pan-genotypic DAA regimens [sofosbuvir (SOF) plus ribavirin (SOF + RBV) and SOF/velpatasvir (SOF/VEL)] and one non-pan-genotypic DAA regimen [elbasvir/grazoprevir (EBR/GZR)] were associated with the lowest risk of contraindicated DDI (3.4, 3.4, and 2.7%, respectively).
Conclusions: SOF/VEL and SOF + RBV are likely to be most suitable to Chinese urban patients with CHC because of pan-genotypic nature and low risk for DDI.
Note: abstract was first released at China ID conference in 2018

Abstract #328

Impact of Sofosbuvir-based regimens for chronic Hepatitis C infection: A work productivity model from mainland China

Xiaoguang Ye[1], Xiaoyuan Xu[2], Qing Xie[3], Hong Tang[4], Jianwei Xuan[5]

[1]The 2rd Affiliated Hospital of Guangzhou Medical University, [2]Department of Infectious Diseases, Peking University First Hospital, [3]Shanghai Jiaotong University School of Medicine, [4]West China Hospital of Sichuan, [5]Health Economic Research Institute, School of Pharmacy, Sun Yat-Sen University

Objectives: Untreated Chronic Hepatitis C (CHC) infections are associated with a poor clinical prognosis and impairment in work productivity (WP), which has not been comprehensively evaluated in mainland China. This study models the impact of CHC infection on WP in China and estimates potential WP gains associated with sofosbuvir/velpatasvir (SOF/VEL) treatment.
Methods: An WP economic model was developed, with patients entering the model post-treatment, having achieved sustained virological response at 12 weeks (SVR12), or not. Absenteeism (absence from work) and presenteeism (reduced productivity at work) rates were extracted from ASTRAL trials as measured by the Work Productivity and Activity Index-Specific Health Problem questionnaire (WPAI-SHP); rates were assumed to be unchanged from baseline for patients not achieving SVR12. These rates were converted into hours of lost productivity, multiplied by the average working wage, employment rate, and adult CHC population in mainland China. We assumed universal treatment with SOF/VEL in the model and contrasted the results relative to no treatment.
Results: Total annual work productivity loss due to not treating CHC patients was estimated to be around ¥37.78 billion. Treatment with SOF/VEL would contribute to annual savings of ¥11.37 billion.
Conclusions: Productivity losses due to untreated HCV infection represent a substantial indirect economic burden in China. Treatment with sofosbuvir-based regimens is likely to result in substantial economic savings for society versus no treatment, which should be considered when assessing the value of CHC treatment.
Note: this abstract was first released in ISPOR AP conference in 2018.

Abstract #334

Effect of direct-acting antivirals on liver fibrosis: a single-center experience

Tomoya Takahashi[1], Yuki Haga[2]

[1]National Hospital Organization Chiba Medical Center, [2]National Hospital Organization Chiba Medical Center

Background: We investigated the effect of direct-acting antivirals (DAAs) on hepatic fibrosis in patients with chronic hepatitis C (CHC). Methods: We identified 288 patients with CHC who were administered DAAs between October 2014 and August 2018. We retrospectively followed-up these patients until September 2018 and assessed the degree of hepatic fibrosis using noninvasive serological markers of fibrosis including serum platelet counts, the aspartate aminotransferase to platelet ratio index score, and the fibrosis-4 (FIB-4) index score.
Results: A sustained virologic response 24 weeks post-treatment (SVR-24) was achieved in 212/227 patients (93.4%). We followed-up 14 patients for > 3 years after the end of treatment (EOT). Among these 14 patients, 13 patients received daclatasvir and asunaprevir therapy, and 1 patient received sofosbuvir and ribavirin therapy. Hepatocellular carcinoma occurred in 3 patients, although no mortality was reported. The mean FIB-4 scores at EOT, 1 year after EOT, 2 years after EOT, and 3 years after EOT were 4.54 ± 2.14, 4.09 ± 1.96, 3.43 ± 1.69, and 3.62 ± 2.14, respectively, and these values did not significantly differ from each another across all time points ($p > 0.05$).
Conclusions: DAA treatment was associated with a high probability of achieving SVR24; however, the improvement in liver fibrosis was not expected in the short term. Long-term observation is warranted to gain a better understanding in this context.

Abstract #335

Direct-acting antiviral agents in the treatment of chronic hepatitis C infection in southern Croatia

Boris Lukšic[1], Boris Dželalija[2], Pero Rizvan[3], Mihaela Cikeš[4], Marko Lukšic[5], Marko Sikirica[6], Ljiljana Betica-Radic[7]

[1]Clinical Department of Infectious Diseases, Clinical Hospital Center Split, Split, Croatia & University of Split School of Medicine, Split,

Croatia, [2]Department of Infectious Diseases, General Hospital Zadar, Zadar, Croatia & University of Zadar, Zadar, Croatia, [3]Institute of Public Health of Split-Dalmatia Couty, Split, Croatia, [4]Clinical Department of Infectious Diseases, Clinical Hospital Center Split, Split, Croatia, [5]University of Zagreb School of Medicine, Zagreb, Croatia, [6]University of Rijeka, Faculty of Medicine of Rijeka, Rijeka, Croatia, [7]Department of Infectious Diseases, General Hospital Dubrovnik, Dubrovnik, Croatia

Background and Aims: Croatia is one of the 28 European Union member states with the population of 4,171,000 inhabitants. In southern part of Croatia, in which this research was carried out, there are 860,000 inhabitants. Treatment of HCV with direct-acting antiviral agents (DAA) began in 2014. Methods: In the period between August 2015 and October 2018, 230 HCV infected patients in three hospitals in southern Croatia completed therapy with DAA. Majority of patients, 125/230 (55%) were treatment-experienced (TE). Among them, 72% were relapsers, 23% non-responders, and 2.5% partial responders. Considering genotype distribution, most of the patients were genotype 1 (62%), followed by G3 (33%), G4 (4%) and G2 (1%). In all patients fibrosis was determinated by FibroScan® (range 7.1–70.6 kPa). Majority of patients (80%) had cirrhosis (F4), 8% had fibrosis 3 i 12% had fibrosis 2.
Results: Among 230 patients with chronic HCV infection, 82 (35.65%) were treated with ombitasvir/paritaprevir/ritonavir plus dasabuvir ± ribavirin (RBV); 41 (17.82%) with ledipasvir/sofosbuvir ± RBV; 37 (16%) with sofosbuvir/velpatasvir ± RBV and 37 (16%) with glecaprevir/pibrentasvir; 15 (6.52%) with sofosbuvir + RBV and finally, 18 (7.82%) with elbasvir/grazoprevir ± RBV. SVR 12 weeks after completion of therapy was available for all patients. Only 3 patients did not achieve SVR which gives the SVR rate of 98.69%.
Conclusions: Treatment of chronic HCV with DAAs in southern Croatia is in accordance with other real-life studies. Most patients (88%) had significantly impaired liver function—fibrosis 3 and 4 (F3/F4) and only 12% had fibrosis 2 (F2).

Abstract #341

Retreatment with sofosbuvir, ledipasvir, and add-on ribavirin for patients who failed to respond to HCV NS3/NS5A inhibitor combination therapy

Tomoe Kobayashi[1], Goki Suda[2], Naoya Sakamoto[3]

[1]Tomakomai City Hospital & Department of Gastroenterology, [2]Hokkaido University & Department of Gastroenterology, [3]Hokkaido University & Department of Gastroenterology

Background: The optimal retreatment regimen for patients with hepatitis C virus (HCV) infection who fail to respond to interferon-free, direct-acting antiviral (DAA) therapy is undetermined. In this study, we aimed to evaluate the efficacy and safety of 12-week retreatment with ledipasvir (LDV) and sofosbuvir (SOF) with add-on ribavirin (RBV) for patients who previously failed to respond to HCV-NS5A inhibitors, daclatasvir (DCV), HCV-NS3 inhibitors, or asunaprevir (ASV) therapy.
Methods: This multicenter, prospective study enrolled 15 patients with genotype-1 HCV infection who failed to respond to DCV/ASV combination therapy. They were retreated with SOF, LDV, and RBV for 12 weeks and underwent physical examinations and blood tests at baseline, during treatment, and after therapy. At baseline and relapse, NS3/NS5A and NS5B resistance-associated variants (RAVs) were evaluated.
Results: Of the 15 enrolled patients, 73.3% (11/15), 86.7% (13/15), and 0% (0/15) had RAVs in NS3 D168A/V/T/E, NS5A L31I/M/F/V plus Y93H, and NS5B S282T, respectively. Overall, 86.7% (13/15) of patients achieved a sustained viral response of 12 months (SVR12), and all patients completed therapy. No patients experienced severe adverse events. Two patients who failed to respond to SOF, LDV, and RBV combination therapy were elderly women, had the IL28B non-TT genotype, and NS5A RAVs in L31I/Y93H or NS5A A92 K at baseline.
Conclusions: This study revealed that SOF, LDV, and RBV combination therapy was effective and well-tolerated for patients with genotype-1 HCV infection who failed to respond to DCV and ASV combination therapy. Thus, RBV added to DAA therapy for difficult-to-treat patients might improve treatment outcomes.

Abstract #350

Use of Glecaprevir/Pibrentasvir in patients with chronic hepatitis C virus infection and severe renal impairment

Desmond Yat-Hin Yap[1], Kevin Sh Liu[2], Yu Chun Hsu[3], Grace Lh Wong[4], Ming Chang Tsai[5], Chien Hung Chen[6], Ching Sheng Hsu[7], Yee Tak Hui[8], Michael Kk Li[9], Chen Hua Liu[10], Ching Kong Loo[11], Ming Lung Yu[12], Man Fung Yuen[13]

[1]Division of Nephrology, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, China, [2]Division of Gastroenterology and Hepatology, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, China, [3]Division of Gastroenterology, Department of Internal Medicine, Changhua Christian Hospital, Taiwan, [4]Department of Medicine and Therapeutics, State Key Laboratory of Digestive Disease, Institute of Digestive Disease, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China, [5]Division of Gastroenterology, Department of Internal Medicine, Chung Shan Medical University Hospital, Taiwan, [6]Department of Internal Medicine, National Taiwan University Hospital Yunlin Branch, Douliu City, Yunlin County, Taiwan, [7]Liver Diseases Research Center, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Taipei, Taiwan, [8]Department of Medicine, Queen Elizabeth Hospital, Hong Kong, China, [9]Department of Medicine and Geriatrics, Tuen Mun Hospital, Hong Kong, China, [10]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, [11]Department of Medicine and Geriatrics, Kwong Wah Hospital, Hong Kong, China, [12]Hepatobiliary Division, Department of Internal Medicine and Hepatitis Center, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [13]Division of Gastroenterology and Hepatology, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, China

Introduction: There is limited data on glecaprevir/pibrentasvir (G/P) for the treatment of chronic hepatitis C virus (HCV) infection in Asian patients with severe renal impairment.
Methods: The treatment outcomes of G/P in patients with chronic HCV infection [genotype (GT) 2, 3, 5 and 6], Child's A cirrhosis and eGFR < 30 mL/min/1.73m2 in Hong Kong and Taiwan during 2017–2018 were studied.
Results: 20 patients (GT2 n = 7, GT3 n = 6 and GT6 n = 7) received G/P for 11.2 ± 1.8 weeks. 19 patients were treatment-naive and 1 was treatment-experienced. G/P was initiated in 16 patients while on dialysis [peritoneal dialysis (PD) n = 7; hemodialysis n = 9] and four before dialysis. Mean HCV RNA declined from $6.4 \times 10^6 \pm 1.8 \times 10^7$ IU/mL at baseline to undetectable levels at 4-, 12-, 24- and 48-weeks in patients reaching different post-treatment follow-up time points at the time of writing ($p < 0.001$ for all) (Figure 1A). The rate

of sustained virological response at 12-week (SVR12) was 100%. Patients with deranged ALT showed normalization after 4 weeks which was sustained for 48 weeks (Figure 1B). Patients who were not yet on dialysis showed no renal deterioration after G/P treatment (eGFR were 13.0 ± 5.9 mL/min/1.73 m^2 and 13.8 ± 7.4 mL/min/1.73m2 at baseline and 24 weeks respectively, p = 0.858) (Figure 1C). One PD patient died during treatment due to fungal peritonitis. One patient discontinued G/P at 4 weeks due to unrelated side effects but still achieved SVR12. No other significant adverse event was observed.

Conclusion: G/P treatment was associated with favorable efficacy and tolerability in HCV-infected patients with severe renal impairment.

Abstract #356

12 week Ravidasvir plus ritonavir-boosted Danoprevir and ribavirin achieves 99% SVR12 in treatment-naïve non-cirrhotic HCV GT1 patients: Subanalysis of phase 2/3 clinical trial in China

Lai Wei[1], Xiaoyuan Xu[2], Yujuan Guan[3], Sujun Zheng[4], Jifang Sheng[5], Xingxiang Yang[6], Yuanji Ma[7], Yan Huang[8], Yi Kang[9], Xiaofeng Wen[10], Jun Li[11], Youwen Tan[12], Qing He[13], Qing Xie[14], Maorong Wang[15], Ping An[16], Guozhong Gong[17], Huimin Liu[18], Qin Ning[19], Rui Hua[20], Bo Ning[21], Wen Xie[22], Jiming Zhang[23], Wenxiang Huang[24], Yongfeng Yang[25], Minghua Lin[26], Yingren Zhao[27], Yanhong Yu[28], Jidong Jia[29], Dongliang Yang[30], Liang Chen[31], Yinong Ye[32], Yuemin Nan[33], Zuojiong Gong[34], Quan Zhang[35], Peng Hu[36], Fusheng Wang[37], Yongguo Li[38], Dongliang Li[39], Zhansheng Jia[40], Jinlin Hou[41], Chengwei Chen[42], Jinzi Wu[43]

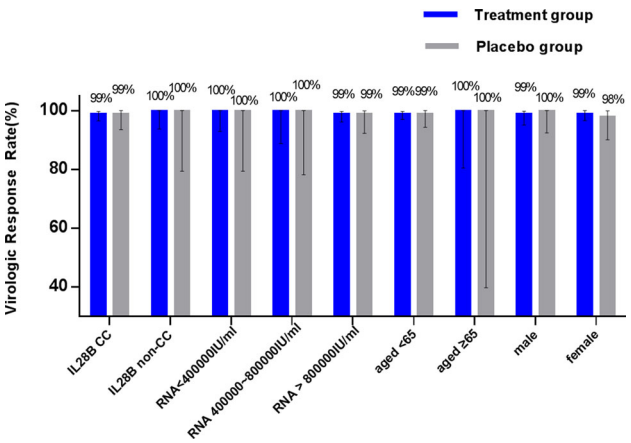
[1]Peking University People's Hospital, [2]Peking University First Hospital, [3]Guangzhou Eighth People's Hospital, [4]Beijing You An Hospital, [5]The First Affiliated Hospital of Medical School of Zhejiang University, [6]Sichuan Provincial People's Hospital, [7]West China Hospital, Sichuan University, [8]Xiangya Hospital, Central South University, [9]Henan People's Hospital, [10]Liuzhou People's Hospital, [11]Jiangsu People's Hospital, [12]Zhenjiang No.3 People's Hospital, [13]The Third People's Hospital of Shenzhen, [14]Ruijin Hospital, Shanghai Jiaotong University School of Medicine, [15]People's Liberation Army Bayi Hospital, [16]Shenyang Sixth People's Hospital, [17]The 2nd Xiangya Hospital of Central South University, [18]Xixi Hospital of Hangzhou, [19]Tongji Medical College of Hust, [20]The First Hospital of Jilin University, [21]Baoji Center Hospital, [22]Beijing Ditan Hospital, [23]Huashan Hospital Affiliated To Fudan University, [24]chongqing Medical University No.1 Affiliated Hospital, [25]The Second Hospital of Nanjing, [26]fujian Fuzhou Municipal Infectious Disease Hospital, [27]No.1 Affiliated Hospital of Xi'an Jiaotong University, [28]The First Affiliated Hospital of Guangxi Medical University, [29]beijing Friendship Hospital, Capital Medical University, [30]Wuhan Union Hospital, [31] Shanghai Public Health Clinical Center, [32]Foshan No.1 People's Hospital, [33]The Third Hospital of Hebei Medical University, [34]Wuhan University Renmin Hospital, [35]The Affiliated Hospital of Guizhou Medical University, [36]The Second Affiliated Hospital of Chongqing Medical University, [37]PLA 302 Hospital, [38]The First Affiliated Hospital of Harbin Medical University, [39]Fuzhou General Hospital of Nanjing Military Command, [40]Tang Du Hospital, Fourth Military Medical University, [41]Nanfang Hospital, Nanfang Medical University, [42]The 85 Branch of The Chinese People's Liberation Army Hospital, [43]ascletis Bioscience Co., Ltd

Objectives: Ravidasvir (RDV) is a new generation pan-genotypic NS5A inhibitor. This phase 2/3 study confirmed the efficacy and safety of RDV and ritonavir-boosted Danoprevir (DNVr) in combination with ribavirin regimen for treatment-naïve HCV genotype 1 (GT1) patients without cirrhosis in a large population in China.

Method: in this multi-center, randomized, double-blind, placebo-controlled phase 2/3 trial (NCT03362814), we enrolled 424 patients. These patients were randomized 3:1 to receive a combination of RDV 200 mg once daily plus DNVr 100 mg/100 mg twice daily and ribavirin 1000/1200 mg/day (body weight < 75/≥ 75 kg) (n = 318) or placebo (n = 106) for 12 weeks, then patients in the placebo group went on to receive 12 weeks' treatment with the above combination. The primary efficacy endpoint was SVR12.

Results: Of the 424 patients (mean age 45yrs) enrolled, 47% were male, 94% were under 65 years old, 82% was IL-28B CC genotype, and 72% had HCV RNA ≥ 800,000 IU/mL at baseline. The overall SVR12 was 99.03%(306/309, 95% CI: 97.19%～99.80%, PPS) and 99.01% (100/101, 95% CI: 94.61–99.97%, PPS) respectively for the treatment group and the placebo group. The Figure depicts the SVR12 of patients in both groups stratified by IL28B genotype, baseline HCV RNA level, age and gender. Given the high SVR12 rate, no difference among patient subgroups was discernible.

Conclusion: For Chinese treatment-naïve non-cirrhotic GT1 HCV adult patients, treatment with RDV and DNVr in combination with ribavirin for 12 weeks resulted in high SVR12, regardless of age, gender, IL28B genotypes or viral load.



Abstract #360

High efficacy and safety of the combination HCV Regimen Elbasvir/Grazoprevir for weeks in treatment-Naive, non-severe fibrosis HCV GT1b-infected Patients: STREAGER study

Armando Abergel[1], Christophe Hezode[2], Tarik Asselah[3], Dominique Larrey[4], Jérome Gournay[5], Véronique Loustaud-Ratti[6], Vincent Di Martino[7], Isabelle Fouchart-Hubert[8], Stanislas Pol[9], François Bailly[10], Didier Samuel[11], Albert Tran[12], Brigitte Chanteranne[1], Marie Dodel[1], Frederic Faure[1], Bruno Pereira[1], Geraldine Lamblin[1], Cecile Campos[1], Leon Muti[1], Maud Reymond[1], Camille Teilhet[1], Benjamin Buchart[1]

[1]Chu Estaing-Clermont Ferrand, [2]Hopital H Mondor, Creteil, [3]Hopital Beaujon, Clichy, [4]Hopital St Eloy, Montpellier, [5]Chu Nantes, [6]Chu Limoges, [7]Chu Besancon, [8]Chu Angers, [9]Hopital Cochin, Paris, [10]Hoiptal Croix Rousse, [11]Hopital Paul Brousse, Villejuif, [12]Hopital L'archet Ii, Nice

Background and Aims: Genotype 1b is the most common HCV genotype globally, accounting for the largest proportion of infections in Europe, Latin America, Russia, Turkey, and East Asia. Reducing treatment duration can improve adherence and reduce drug exposure. Accordingly, we evaluated the efficacy of 8 weeks fixed dose single tablet combination of an NS5A inhibitor elbasvir 50 mg/d (EBR) and protease inhibitor grazoprevir 100 mg/d (GZR) in treatment-naïve patients, with non-severe fibrosis.
Method: Analysis included 112 treatment-naïve (TN), with non-severe fibrosis (Fibroscan® < 9.5 kPa and Fibrotest® < 0.59), HCV GT1b-mono-infected patients were enrolled. This study included 117 patients. Historic labs were used for enrollment. Subsequent genotyping by sequencing during the course of the study identified 5 patients with non-1b genotype. Thus, we will include in the final analysis 112 GT1b patients. The primary end point was the proportion of patients with HCV RNA below the lower limit of quantification (LLOQ) 12 weeks after treatment (SVR12).
Results: Patient characteristics are presented in Table 1. By the end of treatment (EOT), 94.6% (106/112) of patients had HCV RNA < LLOQ. No adverse event grade III or IV related to treatment was observed. Relapse occurred in 3 patients (Table 2). Then, mITT (modified intention-to-treat) SVR12 for patients with genotype 1b (after exclusion of the 5 patients with genotype non 1b) was 109/112 (97.3%). SVR24 results will be available at the APASL meeting.
Conclusion: High SVR12 (109/112, 97.3%) was achieved in a TN non severe fibrosis GT1b-infected patients treated for 8 weeks by the combination of elbasvir/grazoprevir.

Abstract #365

Risk factors and rates of relapses after antiviral treatment (ATV) of 1000 Armenian HCV infected patients with direct acting agents (DAA)

Hasmik Ghazinyan[1], Ruzanna Safaryan[2], Tigranuhi Asatryan[3], Sona Sargsyan[4], Gagik Hakobyan[5]

[1]DEPARTMENT OF HEPATOLOGY, NORK CLINICAL HOSPITAL OF INFECTIOUS DISEASES, [2]YEREVAN STATE MEDICAL UNIVERSITY, [3]DEPARTMENT OF HEPATOLOGY, NORK CLINICAL HOSPITAL OF INFECTIOUS DISEASES, [4]DEPARTMENT OF HEPATOLOGY, NORK CLINICAL HOSPITAL OF INFECTIOUS DISEASES, [5]YEREVAN STATE MEDICAL UNIVERSITY

Aim: There are 71 million people living with CHC infection in the world. DAA for HCV have made revolution in the treatment of the infection. Our study aimed to describe the risk factors and rates of viremia after treatment with DAA of 1000 HCV patients.
Methods: The mean age of 1000 patients was 48 (ranging from 17 to 81) with 65% male dominance. Pre-treatment evaluation included HCV RNA, HBsAg, Anti-HBcAg, Anti-HIV, genotyping of HCV, staging of fibrosis by Fibroscan, biochemical and instrumental investigations. A single regimen was selected for undertaking treatment: Sovaldi and Daclatasvir for naïve patients with all genotypes. Ribavirin was added to the scheme in treatment-experienced and cirrhotic patients. The duration of treatment was 12 weeks with assessment of efficacy including detection of HCV RNA at 4 weeks of treatment and at the end of treatment .
Results: The main genotypes were G1(46%), G3(37.5%) and fibrosis stages were: F0–28%, F1–12%, F2–17%, F3–13%, F4–30%. During the treatment, 14(1.4%) patients were dischareged from treatment due to different reasons. HCV RNA after 4 weaks of treatment (RVR) was positive in 103 (10.3%) patients.
Among 986 patients who complated treatment HCV RNA was positive at EOT in only 38(3.85%) patients. Among wich 30(79%) were infected with HCV genotype 3, 32(94%) with fibrosis 4 and 25(66%) had relapse of HCV infection.
Conclusions: Genotype 3, fibrosis 4 and treatment-experienced patients were the main risk factors of viremia at the end of treatment with DAA.
Abovementioned risk factors are indications for longer duration of ATV treatment.

Abstract #367

Efficacy and safety of ledipasvir/sofosbuvir in 5052 Mongolian patients infected with hepatitis C virus genotype 1: real-life data from multi-center prospective cohort

Baatarkhuu O[1], Naranzul N[2], Enkhtuya D[3], Saruul B[4], Gantuul Ch[5], Gegeebadrakh B[6], Tuvshinbayar N[7], Badamsuren D[8], Ulzmaa G[9], Do Young Kim[10], Amarsanaa J[11]

[1]Department of Infectious Disease, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia & Mongolian Association for The Study of Liver Disease, Ulaanbaatar, Mongolia, [2]Department of Infectious Disease, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [3]Happy Veritas Liver Diagnostic Center, Ulaanbaatar, Mongolia, [4]Department of Hepatology, National Center for Communicable Diseases, Ulaanbaatar, Mongolia, [5]Department of Hepatology, National Center for Communicable Diseases, Ulaanbaatar, Mongolia, [6]Department of Gastroenterology, Second Central Hospital, Ulaanbaatar, Mongolia, [7]Department of Gastroenterology, Second Central Hospital, Ulaanbaatar, Mongolia, [8]Department of Gastroenterology, Third Central Hospital, Ulaanbaatar, Mongolia, [9]department of Gastroenterology, Third Central Hospital, Ulaanbaatar, Mongolia, [10]Department of Internal Medicine, Yonsei University College of Medicine, [11]Mongolian Association for The Study of Liver Disease, Ulaanbaatar, Mongolia

Introduction: According to the approval of the implementation of the National Prevention, Control and Elimination Program between 2016 and 2020 by Mongolian Government, treatment campaign started from January 2016. It can be concluded that as part of preliminary results of the National Program. Up to date, any information and preliminary results of the Program is not available.
Objective: To assess efficacy and safety of LED/SOF in 5052 Mongolian patients infected with genotype 1 HCV, who received brand LED/SOF (Harvoni®) for 12 weeks within the framework of the Program.
Methodology: In this prospective cohort study, treatment-naïve, cirrhotic and non-cirrhotic patients were treated with LED/SOF for 12 weeks; treatment-experienced patients were treated with LED/SOF for 24 weeks. The primary efficacy endpoint was sustained virologic response 12 weeks after treatment (SVR12) and occurrence of adverse events. Serum HCV RNA quantification was performed using a Roche COBAS®TaqMan.
Results: Among total of 5052 patients with HCV-genotype 1 infection, 5016 had successful viral eradication after 12 weeks or 24 weeks of antiviral therapy using LED/SOF, accounting for 99.3% of SVR12. During 12 weeks to 24 weeks antiviral therapy, the most common adverse event was headache 9.4% (473), fatigue 6.2% (312), abdominal discomfort 5.9% (296) and skin rash 2.8% (141).
Conclusion: LED/SOF combination therapy has been shown to be highly effective and well-tolerated in our real-life study with high SVR rates.

Abstract #377

Direct antiviral agent (DAA) treatment of chronic hepatitis C results by APRI and FIB-4 score in Mongolia

Uzmee S[1], Buyankhishig G[2], Munkhbayar D[3], Mandakh E[4], Suvd B[5], Amarsanaa J[6], Tserendejid Ts[7], Amgalan B[8], Ganbyamba T[9], Baatarkhuu O[10]

[1]Health Department, Arkhangai, Mongolia, [2]Health Department, Arkhangai, Mongolia, [3]Health Department, Arkhangai, Mongolia, [4]Health Department, Arkhangai, Mongolia, [5]Mongolian Academy of Medical Professionals, Ulaanbaatar, Mongolia, [6]Mongolian Association for The Study of Liver Disease, Ulaanbaatar, Mongolia, [7]Health Department Arkhangai, Mongolia, [8]Health Department Arkhangai, Mongolia, [9]Health Department Arkhangai, Mongolia, [10]Department of Infectious Disease, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia

Introduction: Viral hepatitis infection is directly associated with the development of liver cancer. According to the WHO report, among patients with liver cancer in Mongolia, 46% have hepatitis C, 34% have hepatitis B and 14% have co-infection with more than one hepatitis virus. Novel DAA targeting hepatitis C virus (HCV) have revolutionized the treatment of chronic hepatitis C infection (CHC).
Objectives: We aimed to determine DAA treatment achievement among 40–65 years old Mongolians.
Methodology: We examined the changes in fibrosis scores FIB-4 and APRI after DAA treatment of CHC. A total of 17,601 (81.1% of target group) underwent screening, of which 3447 (19.5%) were positive for hepatitis C. 3049 of them were tested for HCV RHA. FIB-4 and APRI scores were calculated before and after treatment for each patients. The relevant parametric and nonparametric tests were used.
Results: In total 1778 or 58.3% of individuals who had viral load test had enrolled treatment, 60.7% of them was female, aged between 40 and 65 years old. 98.3% (1748) of individuals who tested by viral load test was undergone to DAA treatment. After DAA treatment 99.4% of them were achieved SVR12. Mean level of FIB-4 and APRI values significantly decreased from 1.48 (SD1.39) [CI 95% 1.26–1.74] and 0.88 (SD 1.68) [CI 95%:0.56–1.32] to 1.05 (SD0.54) [CI 95% 0.92–1.18] ($p = 0.017$) and 0.19 (SD0.17) [CI 95% 0.15–0.23] ($p = 0.001$) respectively.
Conclusion: Patients with SVR after DAA therapy showed significant improvement on fibrosis scores FIB-4 and APRI. Also almost all of treated patients were achieved SVR12 which shows treatment was highly effective.

Abstract #383

The Study of Regional Elimination Mode of HCV in Hainan Island of South China

Tao Wu[1], Jiao Wang[1], Ming Liu[1], Biao Wu[1], Jun Ge[1], Hui Li[1], Furong Xiao[1], Feng Lin[1]

[1]Department of Infectious Diseases Hainan General Hospital

Background: The appearance of DAA drugs provides the drug accessibility conditions for the WHO target of eliminating viral hepatitis C in 2030. In China, the prevention and treatment of HCV is faced with "three low"–low cognitive rate, low diagnostic rate and low treatment rate. The intravenous drug abuse network made rapid transmission of HCV.
Methods: We strive to eliminate regional HCV by solving the problems of low recognition rate and low diagnosis rate with the advantage of multi-party cooperation, so as to improve the cure rate.
Results: From Oct. 2017 to Jan. 2018, this project has selected 709 HCV patients in 12 counties across Hainan province, 12 meetings for physician education, 6 patient education events had been held, which enrolled 709 HCV patients data in HCV BOX that is a new platform for hepatitis C medical, education and research. In Hainan Island of South China, HCV genotypes are mainly type 3 and 6. 48 patients (6.75%) chose DAA drugs to treat. 100% patients have improved their knowledges of HCV by means of the questionnaire. In 96 (13.5%) of these 709 patients said that they have changed their treatment willings according to the experts' recommendations in the study.
Conclusion: The multi-party cooperation model can screen out chronic HCV infections and improve the cognitive rate of patients in a short time, thus promoting some conditional patients to get treatment.

Abstract #391

Failure of Direct-Acting Antivirals to achieve sustained virologic response of chronic hepatitis C treatment: a real-world experience

Tsang-En Wang[1], Ching-Chung Lin[2], Chih-Jen Chen[3], Ching-Wei Chang[4], Shu-Jung Tsai[5], Shee-Chan Lin[6]

[1]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan & Department of Medicine, Mackay Medical College, New Taipei City, Taiwan, [2]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan & Department of Medicine, Mackay Medical College, New Taipei City, Taiwan, [3]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan, [4]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan, [5]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan, [6]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan

Introduction: Eradicating chronic HCV infection become possible in this interferon (IFN)-free Direct-Acting Antivirals (DAAs) era. Real successful HCV therapy is resulted in viral clearance and sustained virologic response (SVR). However, the failure of DAAs to clear HCV-RNA may occur in some patients.
Aim: We shared DAAs failure experience and analyzed the possible related factors in a real-life practice.
Methods: 2017 Jan to 2018 Mar, 332 patients were enrolled follow-up 6 months after initiate treatment. They met the criteria for advanced liver disease: cirrhosis or F3-F4 fibrosis. They took one of DAAs regimens depending on benefit package of National Health Insurance. The clinic and laboratory data were recorded at the start, 4 weeks, end of treatment and 12 weeks later.
Results: The majority of HCV genotype was GT1a (18), GT1b (213) and GT2 (89). Most of the GT1 patients took 3D or Harvoni. All GT2 patients received sofosbuvir plus ribavirin. 3.4% patients (11) did not achieved SVR12; GT1b (1/213, 1%) and GT2 (10/89, 11%). Their mean age was 65-year-old, 5 male and 6 female. HCV-RNA was undetected at end of treatment except one in GT2 of DAA failure patients. In GT2 group, five patients (5/10, 50%) had PEG-Interferon failure history and 4 patients (4/40, 40%) had DM.
Discussions: Taiwan Ministry of Health and Welfare approved the budget and priority strategy for HCV treatment since 2017. In our experience, sofosbuvir-ribavirin had a high failure rate for GT2, especially in patients who were treatment-experienced and with DM.

Abstract #410

Effectiveness and safety of direct acting antiviral therapies in treatment experienced chronic hepatitis C patients

Bengu Gireniz Tatar[1], Melda Ulusoy Turken[2], Nadide Ergün Çolak[3], Sukran Kose Kose[4]

[1]Tepecik Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, [2]Tepecik Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, [3]Tepecik Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, [4]Tepecik Training and Research Hospital, Infectious Diseases and Clinical Microbiology

Background: Recently development of direct-acting antiviral agents (DAAs) has dramatically changed the chronic hepatitis C (CHC) treatment, and interferon-free regimes have become poor choise for treatment in clinical practice. Today the new DAAs offers shorter, well-tolerated, highly efficacious curative therapies. Rates of SVR approach 95–100%.
The aim of this study was to evaluate the effectiveness and safety of DAA in treatment experienced CHC in real clinical practice.
Methods: Fifty-three treatment experienced CHC patients were taken in the study. At baseline patients were tested for Anti HCV, HCVRNA, genotype, hemogram and biochemical test. At each visit (2., 4., 8., 12. weeks) HCV RNA, ALT, AST, hemoglobin levels were measured.
Results: Of the 53 treatment-experienced patients the mean age was 55.8 year (30–86) and 58.5% of them male. Mean body mass index was 24.6 ± 6.4. Genotypes of patients were given in table 1. Previous and current DAA treatments were presented in table 2.
At baseline HCVRNA was 984434 ± 53191 IU/mL. At week 2, week 4, treatment end and 12 weeks after treatment end (SVR12); 84.9, 100, 100 and 100% had HCV viral load < 15 IU/mL, respectively.

Hyperbilirubinemia and elevations in aminotransferase levels were not observed. Hemoglobin, and platelet counts were not significantly different from baseline values. During therapy 9.4% patients had side effects and the most common were fatigue, headache, arthralgia, pruritus, loss of appetite and stomach pain.
Conclusion: In this study, treatment with DAA resulted in high rates of SVR in treatment experienced CHC patients with few side effects.

Abstract #452

Sofosbuvir + Velpatasvir + Voxilaprevir in DAA failure patients with cirrhosis. Final results of the French compassionate use program

Christophe Hezode[1], Dominique Guyader[2], Eric N Guyen-Khac[3], Dominique Larrey[4], Regine Truchi[5], Vincent Di Martino[6], Yvon Calmus[7], Valerie Canva[8]

[1]Hopital Henri Mondor, [2]CHU Rennes, [3]CHU Amiens, [4]CHU Montpellier, [5]CHU Nice, [6]CHU Besançon, [7]Hopital La Pitie Salpetriere, [8]CHU Lille

Background: SOF/VEL/VOX is approved for 12 weeks based on the phase 3 POLARIS studies for HCV patients who failed with DAA-containing regimens. We report the efficacy and safety of SOF/VEL/VOX ± RBV in DAA failure patients with cirrhosis included in the French compassionate use program.
Methods: 46 patients (33 males; mean age 58.7 years) treated with SOF/VEL/VOX with RBV for 8 (n = 1) or 12 weeks (n = 9) or SOF/VEL/VOX for 12 weeks without RBV (n = 36). Patients infected with HCV genotype 1 (1a n = 10; 1b n = 3; 1e n = 2), 2 (n = 4), 3 (3a n = 17; 3b n = 1), 4 (n = 8), 5 (n = 1) and 41 had cirrhosis (Median FibroScan 16 kPa, [13.5–24.9]). Previous treatment was SOF/LDV (n = 16), SOF/DCV (n = 23), 2D/3D (n = 5), GZR/EBR (n = 2). Baseline resistance testing was performed in 39 (85%) patients.
Results: All patients (n = 44) who achieved EOT had undetectable HCV RNA. Among these 44 patients, SVR4 and SVR12 were observed in 43 (97.7%) and 42 (95.5%) patients, respectively. Two patients relapsed. At baseline, Y93H was observed in one genotype 3a patient and, both NS3 and NS5A RASs were identified in one genotype 1a patient. Resistance testing at the time of the relapse is pending. 3 serious adverse events were reported in 2 patients. One liver decompensation, and 2 cases of HCC.
Conclusion: In a real-world cohort, the combination SOF/VEL/VOX ± RBV for 12 weeks is effective in patients with cirrhosis who failed with DAA combination containing 1st generation NS5A inhibitor and/or protease inhibitor. This strategy is safe in patients with compensated cirrhosis.

Abstract #469

Serum Alpha-fetoprotein levels and response to direct antiviral therapy in patients with chronic Hepatitis C: real-world results from 1716 patients in Egypt

Sherief M Abd-Elsalam[1], Mohamed A Alboraie[2], Mohamed Z El Kassas[3], Rehab. Badawi[4]

[1]Tropical Medicine Department-Egypt, [2]Internal Medicine Department-Alazhar University, [3]Tropical Medicine Department-Helwan University, [4]Tropical Medicine Department-Tanta University

Background and Aims: Alpha-fetoprotein (AFP) is an A1-globulin secreted by embryonic liver cells and a small number of other cells in the embryonic digestive system. Elevated AFP was associated with chronic HCV. Direct antiretroviral agents (DAAs), sofosbuvir-based therapies, have opened a new era in the treatment of chronic HCV infection, allowing the treatment of the majority of chronic HCV with a significantly greater elimination rate and limited side effects than previous treatments. The aim of the study was to investigate the potential use of baseline and in serial serum AFP levels as a predictor for response to DAAs in Patients with Chronic Hepatitis C.
Methods: This multicenter observational study was carried out on 1716 chronic hepatitis C virus- infected patients who received direct anti-viral drugs for 12 weeks. The primary end point was sustained virological response at 12 weeks after the end of treatment determined by quantitative PCR for HCV RNA. Serum AFP was quantitatively assessed at baseline then after 12 week after stoppage of treatment (SVR12).
Results: SVR12 rate was 97.8%. Elevated serum AFP was significantly higher in non –SVR group P value (< 0.001). A significant correlation was found between AFP and thrombocytopenia, elevated liver enzymes (ALT and AST), elevated serum bilirubin, hypoalbuminia, elevated blood glucose level, and elevated white blood cells and prolonged INR. There was a marked significant decrease of AFP after treatment in comparison to pretreatment values.
Conclusions: Serum AFP levels was a predictor for response in patients with chronic HCV with the administration of direct antiviral drugs.

Abstract #474

Predictors for Eltrombopag response in patients with Hepatitis C virus associated thrombocytopenia

Sherief M. Abd-elsalam[1], Tamer A. Elbedewy[2]

[1]Tropical Medicine Department, [2]Internal Medicine Department-Tanta University

Background/Aims: Thrombocytopenia is a common hematological abnormality observed in hepatitis C virus (HCV) patients. The use of eltrombopag has been approved for HCV-associated thrombocytopenia. This is the first study aiming to determine the predictive factors of response to eltrombopag therapy in patients with HCV-associated thrombocytopenia.
Methods: This prospective study was carried out on 130 patients with chronic HCV associated thrombocytopenia (< 50,000 x109/L) that preclude with the initiation of HCV therapy. Eltrombopag was initiated at a dose of 25 mg once daily; the dose was adjusted in 25 mg increments every 2 weeks to achieve the target platelet count. The primary endpoint was to achieve stable target platelet count (50,000–100,000 x109/L) required to initiate anti-viral therapy.
Results: Treatment response was achieved in 111 (85.38%) patients. Based on this prospective study, megakaryocyte hypoplasia or aplasia, and splenectomy were independent risk factors for eltrombopag non-response in chronic HCV associated thrombocytopenic patients.
Conclusion: Eltrombopag is safe and effective for patients with HCV- associated thrombocytopenia. Bone marrow examination should be considered before initiating the treatment with eltrombopag in chronic HCV associated thrombocytopenic patients especially in patients with splenectomy.

Abstract #488

Twelve-week treatment for non-cirrhotic HCV genotype 1b patient with ravidasvir plus ritonavir-boosted danoprevir and ribavirin in mainland China

Lanlan Xiao[1], Xiaowei Xu[1], Xiaoxin Wu[1], Lan-Juan Li[1]

[1]The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310003, China

Background and Aim: Chronic hepatitis C is an important public health problem in Asia. The phase 2/3 study (NCT03362814) investigated the efficacy and safety of ravidasvir (RDV) plus ritonavir-boosted danoprevir (DNVr) and ribavirin (RBV) regimens for treatment-naïve non-cirrhotic hepatitis C virus (HCV) genotype 1b patients in mainland China.
Method: Sixteen treatment-naïve HCV genotype 1b patients without cirrhosis were enrolled and randomized 13:3 to study treatment (RDV plus DNVr and RBV) and placebo treatment (4 mimic drugs) for 12-wk. In placebo group, 3 patients received study treatment after receiving 12-wk placebos. The primary endpoint was sustained virological response at post-treatment week 12 (SVR12).
Result: During the study, no treatment related serious adverse events or deaths was reported. All (3/3) patients in placebo group remained high HCV-RNA level after receiving 12-wk placebo. All (16/16) patients had rapid virological response (RVR) with lower limit of quantitation (< 25 IU/mL, LLOQ) at week 2 and achieved SVR12 after receiving study treatment. Only one patient experienced the virus relapse at SVR24.
Conclusion: 12-week RDV and DNVr plus RBV treatment demonstrated strong antiviral activity and was tolerated in treatment-naïve non-cirrhotic HCV genotype 1b patients from mainland China.

Abstract #506

Retreatment with glecaprevir and pibrentasvir for genotype 1 or 2 HCV-infected hemodialysis patients who previously failed to DAAs

Goki Suda[1], Naoya Sakamoto[2]

[1]Hokkaido University, [2]Hokkaido University

Clinical trials and real-world data have proven that hepatitis C virus (HCV) in most infected patients can be eradicated by direct-acting antivirals (DAAs). However, proper retreatment regimen for hemodialysis patients with HCV infection, who have previously failed to respond to DAAs, has not been clarified. We report for the first time the successful retreatment with glecaprevir and pibrentasvir for three hemodialysis patients with genotype 1 or 2 HCV infection, who previously failed to respond to treatment with HCV-NA5A inhibitor, daclatasvir and HCV protease inhibitor, and asunaprevir combination therapy.

The first hemodialysis patient was a 57-year-old female with genotype 2b HCV infection. Because HCV serotype examination indicated that it was serotype 1, the patient was treated with daclatasvir and asunaprevir. However, HCV-RNA was detectable 3 months after treatment initiation; thus, this therapy was terminated. The second hemodialysis patient was a 69-year-old female with genotype 1b HCV infection, who had previously failed to respond to daclatasvir and asunaprevir. The third hemodialysis patient was a 68-year-old female with genotype 1b HCV infection who at 66 years of age had failed to respond to daclatasvir and asunaprevir. These three patients were retreated with 12 weeks glecaprevir and pibrentasvir. All three patients completed the therapy without severe adverse events during the treatment, and achieved sustained virological response at 12 weeks after treatment completion. These results indicate that combination therapy with glecaprevir and pibrentasvir is a suitable retreatment regimen for hemodialysis patients who have previously failed to respond to DAAs.

Abstract #510

Adverse effects of ombitasvir/paritaprevir/ritonavir ± dasabuvir ± ribavirin therapy in patients with hepatitis C virus genotype 1/4 infection: Real-life experience in Turkey

Bilgehan Aygen[1], Nese Demirtürk[2], Orhan Yildiz[3], Mustafa Kemal Çelen[4], Ilhami Çelik[5], Ayse Batirel[6], Sener Barut[7], Onur Ural[8], Resit Mistik[9], Funda Simsek[10], Ali Asan[11], The Study Group for Viral Hepatitis[12]

[1]Department of Infectious Diseases and Clinical Microbiology, Medical School of Erciyes University, Kayseri, Turkey, [2]Department of Infectious Diseases and Clinical Microbiology, Afyon Kocatepe University Medical Faculty, Afyonkarahisar, Turkey, [3]Department of Infectious Diseases and Clinical Microbiology, Medical School of Erciyes University, Kayseri, Turkey, [4]Department of Infectious Diseases and Clinical Microbiology, Dicle University Medical Faculty, Diyarbakir, Turkey, [5]Department of Infectious Diseases and Clinical Microbiology, Saglik Bilimleri University Kayseri Training and Research Hospital, Kayseri, Turkey, [6]Department of Infectious Diseases and Clinical Microbiology, Saglik Bilimleri University Kartal Dr. Lütfü Kirdar Training and Research Hospital, Istanbul, Turkey, [7]Department of Infectious Diseases and Clinical Microbiology, Gaziosmanpasa University Medical Faculty, Tokat, Turkey, [8]Department of Infectious Diseases and Clinical Microbiology, Selçuk University Medical Faculty, Konya, Turkey,

[9]Department of Infectious Diseases and Clinical Microbiology, Uludag University Medical Faculty, Bursa, Turkey, [10]Department of Infectious Diseases and Clinical Microbiology, Okmeydani Training and Research Hospital, Istanbul, Turkey, [11]Department of Infectious Diseases and Clinical Microbiology, Saglik Bilimleri University Yüksek Ihtisas Training and Research Hospital, Bursa, Turkey, [12]istanbul

Introduction: Ombitasvir/paritaprevir/ritonavir (OMV/PTV/r) ± dasabuvir (DSV) ± ribavirin (RBV) combination improved the efficacy, safety, and tolerability of the treatment of chronic hepatitis C virus (HCV) infection.
Objective: The aim of the study is to evaluate the safety of the OMV/PTV/r ± DSV ± RBV therapy in a large population of genotype 1/4 patients with chronic HCV infection in Turkey.
Methods: Data from HCV genotype 1 and 4 patients treated with OMV/PTV/r ± DSV ± RBV (n = 862) in 34 centers across Turkey between April 1, 2017 and August 31, 2018 were recorded in a large national database. Study patients were treatment-naïve or interferon plus RBV-experienced with or without companse cirrhosis. Patient follow-up ranged from 24 to 36 weeks depending on-treatment duration. Safety endpoints were clinical and laboratory adverse events (AEs) recorded.
Results: The mean age of the patients was 55.63 years and 49.9% were male. The majority had HCV genotype 1 infection (93.6%), and 66.2% were treatment-naïve. Non-cirrhosis was present at baseline in 789 patients (91.5%). There were at least one AE in 515 patients (59.7%). Treatment was discontinued in 6 patients due to clinical AEs (arrhythmia, vomiting) or laboratory abnormalities (jaundice, hepatotoxicity). The most common AEs were asthenia (10.4%), skin pruritus (5.7%), headache (5.3%) and fatigue (5.1%).
Conclusions: The OBV/PTV/r ± DSV ± RBV combination was demonstrated a very good safety profile in our cohort. AEs were mostly mild and did not require medical intervention. The incidence of laboratory abnormalities was uncommon.

Abstract #512

Sustained viral response following treatment with direct acting antiviral regimens is durable in more than 6600 patients: results of the Gilead SVR registry study

Christian Schwabe[1], Eric J Lawitz[2], Stanislas Pol[3], Stephen David Shafran[4], Naoto Fujiyama[5], Chenyu Wang[6], Robert H Hyland[7], Frances Chen[8], Hadas Dvory-Sobol[9], Anu O Osinusi[10], Diana M Brainard[11], Christophe Moreno[12], Alessio Aghemo[13], Simone I Strasser[14], Stefan Zeuzem[15]

[1]Auckland Clinical Studies Ltd, [2]Texas Liver Institute, University of Texas, [3]Hôpital Cochin and Université Paris Descartes, [4]University of Alberta, [5]Gilead Sciences, [6]Gilead Sciences, [7]Gilead Sciences, [8]Gilead Sciences, [9]Gilead Sciences, [10]Gilead Sciences, [11]Gilead Sciences, [12]Cub Hôpital Erasme, Université Libre De Bruxelles, [13]Humanitas University and Research Hospital and Humanitas University, [14]Royal Prince Alfred Hospital, [15]Klinikum Der Johann Wolfgang Goethe-Universität

Background: Direct-acting antiviral (DAA) therapy for HCV has provided the potential for large numbers of patients to achieve a sustained virologic response (SVR) raising the potential for elimination. While SVR rates are high in clinical studies and real world settings, it is important to demonstrate the durability of response.
Methods: Patients were eligible for enrollment within 3 months of achieving SVR in this study. Patients were followed with visits every 24 weeks for up to 144 weeks. At each visit, clinical assessment, HCV RNA measurements, and liver function tests were performed. For patients with virologic failure, sequencing and comparison with the pre-treatment baseline including phylogenetic analysis was performed differentiating relapse and reinfection.
Results: 6607 patients (1724 [26%] SOF + RBV ± PEG, 2204 [33%] LDV/SOF ± RBV, 1422 [22%] SOF/VEL ± RBV, 597 [9%] SOF/VEL/Voxilaprevir, and 660 [10%] other regimens) were enrolled. Overall 99.3% of patients maintained SVR. Thirty patients experienced virologic failure of whom 8 (0.1%) had experienced relapse after completing their treatment study and 22 (0.3%) had reinfection. 232 patients experienced liver disease events, including HCC. No patients with F0-F1 disease developed HCC; the exposure adjusted incident rates for HCC in patients with F2, F3, or F4 disease were 0.06, 0.25, and 0.58% respectively.
Conclusion: In this heterogeneous population SVR12 is confirmed as the optimal time to determine SVR as late relapses beyond this time point are rare. In patients who achieve SVR liver related complications are infrequent. Together, these findings emphasize the value of achieving SVR, regardless of fibrosis score at the time of treatment.

Abstract #535

Patients with non-alcoholic Steatohepatitis and cirrhosis experience severe impairment of physical functioning aspects of health-related quality of life

Zobair Younossi[1], Maria Stepanova[2], Eric J. Lawitz[3], K. Rajender Reddy[4], Ira M. Jacobson[5], C. Stephen Djedjos[6], Anuj Gaggar[7], Robert P. Myers[8], Issah Younossi[9], Fatema Nader[10], Andrei Racila[11]

[1]Center for Liver Diseases, Department of Medicine, Inova Fairfax Hospital & Betty and Guy Beatty Center for Integrated Research, Inova Health System, [2]Center for Outcomes Research in Liver Disease, [3]Texas Liver Institute, University of Texas Health San Antonio, [4]University of Pennsylvania, [5]NYU Medical Center, [6]Gilead Sciences, [7]Gilead Sciences, [8]Gilead Sciences, [9]Center for Outcomes Research in Liver Disease, [10]Center for Outcomes Research in Liver Disease, [11]Center for Outcomes Research in Liver Disease

Background: Chronic hepatitis C (CHC) and non-alcoholic steatohepatitis (NASH) are both associated with impairment of health-related quality of life (HRQL). The most profound impairment is usually seen in patients with cirrhosis.
Aim: To compare HRQL scores in patients with cirrhosis due to CHC to NASH.
Methods: Patients with CHC and NASH and compensated cirrhosis completed SF-36, CLDQ, and Work Productivity and Activity questionnaires while off-treatment.
Results: We included 1460 patients with NASH or CHC and cirrhosis: 57.4 ± 8.2 years, 44% male, 40% history of psychiatric disorders, 50% employed (all $p > 0.05$ between NASH and CHC). Cirrhotic patients with NASH had higher BMI (mean 33.8 vs. 28.2) and more type 2 diabetes (77% vs. 18%) ($p < 0.01$). Patients with NASH had lower HRQL in Physical Functioning, Bodily Pain, General Health domains, and Physical Summary of SF-36 (by 3.6–4.4 points on a 0–100 scale, all $p < 0.01$). Despite this, patients with CHC had lower Mental Health score of SF-36 (mean 69.5 vs. 73.0) and Emotional score of CLDQ (mean 4.9 vs. 5.3 on a 1–7 scale), and higher Activity Impairment score of WPAI (0.27 vs. 0.19) (all $p < 0.002$). In multivariate regression analysis, after adjustment for demographic and clinical parameters, having NASH was independently associated with lower physical HRQL scores (beta − 3.6 to − 4.3 for SF-36 domains) and higher mental health-related scores (beta +3.8 for Mental Health of SF-36, +0.33 for Emotional of CLDQ) (all $p < 0.01$).

Conclusions: Patients with NASH and cirrhosis have more impairment of their physical health-related scores than demographically similar patients with hepatitis C.

Abstract #548

Ledipasvir/Sofosbuvir for 12 weeks is safe and effective in HCV-infected asian patients with difference stages of liver fibrosis: In tegrated analysis of four clinical studies

Chun-Jen Liu[1], Masashi Mizokami[2], Lai Wei[3], Seung Woon Paik[4], Qing Xie[5], Chen-Yu Wang[6], Joe Llewellyn[7], Anu Osinusi[8], Gerald Crans[9], Wan-Long Chuang[10], Nobuyuki Enomoto[11]

[1]National Taiwan University Hospital, [2]Genome Medical Sciences Project & National Center for Global Health and Medicine, [3]Beijing Key Laboratory for Hepatitis C and Immunotherapy for Liver Disease & Peking University People's Hospital & Peking University Hepatology Institute, [4]Samsung Medical Center & Sungkyunkwan University School of Medicine, [5]Ruijin Hospital & Shanghai Jiaotong University, [6]Gilead Sciences, [7]Gilead Sciences, [8]Gilead Sciences, [9]Gilead Sciences, [10]Kaohsiuang Medical University Hospital, [11]University of Yamanashi

Ledipasvir (LDV)/sofosbuvir (SOF) fixed-dose combination is approved as a 12-week regimen for patients with HCV genotype 1, 2, 4–6 infection in several Asian countries. This integrated analysis describes the efficacy and safety of LDV/SOF treatment in HCV-infected Genotype (GT) 1 and 2 Asian patients across the spectrum of fibrosis stages.

This is a retrospective analysis from 797 Asian patients with GT 1 or 2 HCV infection treated with LDV/SOF for 12 weeks in 4 phase 2 and phase 3 studies. Fibrosis stages were defined by liver biopsy, transient elastography, or Fibrotest. Efficacy was assessed by sustained virologic response 12 weeks after treatment (SVR12). Safety data was analyzed.

797 Asian subjects were treated with LDV/SOF for 12 weeks. 56% were female, 70% had IL28B CC genotype, 45% had prior treatment failure and 78% were infected with genotype 1. Overall 70% were F0-F2, 13% were F3, and 17% were F4. The overall SVR rate was 99% (789/797), and was 99% (551/554), 97% (103/106), and 99% (133/135) in subjects with F0–F2, F3, and F4 fibrosis respectively. Among previously treated subjects, the SVR rate was 99% (228/229), 95% (55/58), 99% (72/73) in F0–F2, F3, and F4 subjects respectively. The treatment was well tolerated with 2% (9/797, 6 in F0–F2 and 3 in F4 subjects) severe adverse events and 0.4% (3 in F0–F2 subjects) discontinuations due to adverse event.

12 weeks of LDV/SOF treatment is highly efficacious and well tolerated in Asian patients with GT1 and GT2 HCV infection regardless of fibrosis stages.

Abstract #552

Improving access to hepatitis C treatment for prisoners through innovation and collaboration in a tertiary hospital in Western Australia

Saroj Nazareth[1], Nadine Leembruggen[1], Guizhi Li[1], Marilyn Sebastian[1], Gurkiran Flora[1], Kim Hill[1], Rhoda Tuma[1], Wendy Cheng[1], Adam Doyle[1]

[1]Royal Perth Hospital

Introduction: Treating prisoners is crucial to the elimination hepatitis C (HCV). A high incidence of HCV is contrasted by low treatment uptake in prisons. In December 2017, the Video Call Model was established to improve access to therapy.
Objectives: This study describes the prison population treated via Video Call with comparison to clinic-based treatment.
Methodology: Prisoners participating in at least one Video Call during the first 12 months of the program were included and compared to the previous 10 years of clinic-based treatment of prisoners.
Results: 183 prisoners attended a Video Call. Average age 37 years, 78.7% male, 50.3% genotype 3, 91.0% treatment naïve, 9.7% (17/176) cirrhotic, with no hepatic decompensation. 14.8% hepatitis B core antibody positive. HIV was not detected.
174 (95.1%) commenced therapy. Five patients were awaiting fibrosis assessment, two cleared spontaneously, one refused treatment and one was awaiting medication availability. Sofosbuvir/velpatasvir was most commonly prescribed (n = 93).

Of the 51 patients at 6 months post-treatment, 42 patients completed follow-up and 90.5% (38/42) achieved a sustained virological response. 17.6% (9/51) did not attend follow-up testing.

During the preceding 10 years, 88 prisoners initiated HCV therapy. Significantly more females were seen by Video Call (21.3%) than in clinic (11.4%) ($p < 0.05$). No significant difference in age, genotype, treatment experience or fibrosis stage was identified.
Conclusion: Video Call proved to be an effective model, significantly improving access, with a 19-fold increase in HCV treatment initiation in prisons. Further evaluation of treatment adherence, sustained virological response rates and reinfection rates would be beneficial.

Abstract #571

Efficacy of Glecaprevir/Pibrentasvir in patients with hepatitis C virus genotype 1 or 2 and past direct-acting antiviral treatment failure

Atsushi Suetsugu[1], Takafumi Naiki[2], Syogo Shimizu[3], Junichi Sugihara[4], Eiichi Tomita[5], Masahito Shimizu[6]

[1]Department of Gastroenterology, Gifu University Graduate School of Medicine, Gifu, Japan, [2]Department of Gastroenterology and Hepatology, Gifu Municipal Hospital, Gifu, Japan, [3]Department of Gastroenterology, Gifu Prefectural General Medical Center, Gifu, Japan, [4]Department of Gastroenterology, Gifu Prefectural General Medical Center, Gifu, Japan, [5]Department of Gastroenterology and Hepatology, Gifu Municipal Hospital, Gifu, Japan, [6]Department of Gastroenterology, Gifu University Graduate School of Medicine, Gifu, Japan

Background: Interferon-free, direct-acting antiviral (DAA)-based combination therapies for hepatitis C virus (HCV) infection can now be cured in > 95% of patients. Glecaprevir (300 mg)/pibrentasvir(120 mg) (G/P) is a pangenotypic, once-daily, ribavirin-free DAA treatment for HCV infection. An efficacy analysis of 8- and 12-week G/P therapy in patients with HCV genotype 1 or 2 was performed.
Methods: Patients aged 31–86 years (n = 158) infected with HCV genotype 1or 2 among whom 16 had undergone curative treatment for hepatocellular carcinoma (HCC) started the treatment. Oral G/P was administered once daily for 8- weeks to 96 non-cirrhotic DAA-naïve patients with HCV genotype 1 or 2, and for 12 weeks to 34 cirrhotic and 13 DAA-failure. Prior regimens included: DCV/ASV (n = 7), SOF/LDV (n = 2), EBV/GZR (n = 1), SOF + RBV (n = 3). Transient efficacy was defined as a sustained virological response at end-of-treatment (EOT) and post-treatment week 12 (SVR12).

Results: In baseline lab data, mean RNA was 6.11 ± 0.93 log10 IU/mL, mean ALT was 47.2 ± 64.7 U/L, mean total bilirubin was 0.81 ± 0.44 mg/dL, mean albumiin was 4.08 ± 0.47 g/dL, and mean platelet was 17.1 ± 7.7 103/uL. SVR12 rates were 100% based on per-protocol analysis, respectively. SVR12 was achieved by 96/96 (100%) non-cirrhotic patients in the 8-week G/P (GT1: 58.2%, GT2: 41.8%). All 34 (100%) patients with compensated cirrhosis achieved SVR12.
Conclusion: G/P for 8 and 12 weeks had a marked anti-HCV effect. The G/P therapy seems to be an effective treatment option for patients in whom prior therapy failed irrespective of prior DAA regimen.

Abstract #579

Efficacy and safety of HCV treatment with direct antiviral agents (DAA's)/ribavirin in patients with advanced liver disease and ulcerative colitis (stable disease, under treatment)

Dimitrios Dimitroulopoulos[1], Stylianos Karatapanis[2], Vasilios Sevastianos[3], Ioannis Elefsiniotis[4], Ioannis Elefsiniotis[5], Dimitrios Kypreos[6], Dimitrios Katsinelos[7], Eleni Mihalopoulou[8], Xenofon Tsamakidis[9], Klisthenis Tsamakidis[10]

[1]Gastroenterology Dpt, Agios Savvas Hospital, [2]1st Internal Medicine Dpt, General Hospital of Rhodes, [3]Internal Medicine Dpt, Evangelismos Hospital, [4]Internal Medicine Dpt, Agioi Anargyri Hospital, [5]Internal Medicine Dpt, Agioi Anargyri Hospital, [6]Gastroenterology Dpt, Agios Savvas Hospital, [7]Gastroenterology Dpt, Agios Savvas Hospital, [8]Gastroenterology Dpt, Agios Savvas Hospital, [9]Gastroenterology Dpt, Agios Savvas Hospital, [10]Gastroenterology Dpt, Agios Savvas Hospital

The efficacy the safety of DAA's against HCV in patients with advanced liver disease and ulcerative colitis (UC) under treatment, with stable disease, is unclear.

for this reason we reviewed all our patients who underwent treatment with DAA's/ribavirin during the last 2 years.
Materials/methods: Were included 482 HCV patients, (cirrhosis/advanced fibrosis) treated with DAA's/ribavirine for 12 weeks. 8(1.65%-5 males, 3 females) suffered simultaneously from UC and were treated for this disease with 5-ASAs (3), thiopurines/corticosteroids (2) and anti-TNF agents (3). The stage of fibrosis in this population was F2-F3 and the genotypic distribution was G1a 3(2 M, 1F), G1b(2 M) 2, G3 2(1 M, 1F) and G4 (1F). The pre-treatment viral load was 0.54–0.92 × 106 IU/ml and the aminotransferase levels were: ALT 248–99 U/l, AST 179–98 U/l, γGT 54–203 U/l. HCV-RNA was measured at weeks 4, 12, 24. General blood count, ESR, liver biochemistry, CRP were monitored monthly, and measurements of AFP, stool calprotectin and upper abdominal ultrasound were performed every 3 months. Dasabur/Ombitasvir/Paritaprevir/Ritornavir for G1, Sofosbuvir/Velpatasvir or Sofosbuvir/Daclatasvir for G3, and Elbasvir/Grazoprevir for G4 were administered.
Results: Although, HCV-RNA was undetectable at week 4 in all patients, aminotransferase and γGT were abnormal during the first 12 weeks in 2 (M, one treated with 5-ASAs and one with anti-TNF). 12 weeks after the end of treatment all patients achieved undetectable HCV-RNA. No side effects or exacerbation of UC were observed. Calprotectin was within normal limits during the study period.
Conclusion: DAA's/ribavirin is a safe and effective treatment for patients with HCV and UC under treatment.

Abstract #604

Long-term health outcomes of pan-genotypic direct acting antiviral (DAA) treatment of chronic Hepatitis C (CHC) in China

Wu Jiuhong[1], Wu Bin[2], Xu Xiaoyuan[3], Ye Xiaoguang[4], Zhang Wenhong[5]

[1]Department of Pharmacy, 306 Hospital, [2]Medical Decision and Economic Group, Department of Pharmacy, Ren Ji Hospital, South Campus, School of Medicine, Shanghai Jiaotong University, [3]Department of Infectious Diseases, Peking University First Hospital, [4]Second Affiliated Hospital of Guangzhou Medical University, [5]Huashan Hospital, Fudan University

Objectives: This study evaluated the long-term health outcomes of treating CHC patients with DAA regimens in China.
Methods: A Markov model simulated liver-related outcomes for a cohort of 10,000 CHC treatment-naive (TN; 36.4%) and treatment-experienced (TE; 63.6%) patients with an average age of 46 over a lifetime horizon. The model assumed 61.6% of patients were GT1b; 24.2%, GT2; 8.1%, GT3; and, 6.1% GT6. Compensated cirrhosis (CC) patients accounted for 15.2% of GT1-2/6 and 21.3% for GT3. For those receiving peg-interferon and ribavirin (PR), it was assumed from literature that 43% were PR-ineligible or intolerant. Model inputs were extrapolated from clinical trials, published literature, or expert opinion (Chinese-specific where possible).
Results: Across all genotypes, sofosbuvir/velpatasvir (SOF/VEL) led to the highest sustained virologic rate (SVR) (99.2%) as compared to glecaprevir/pibrentasvir (GLE/PIB) (98.3%) and PR (39.0%). Furthermore, SOF/VEL led to the largest reductions in advanced liver disease events relative to PR across the patient population (Table 1), including cases of decompensated cirrhosis (− 96%/− 95%; SOF/VEL, GLE/PIB vs. PR respectively), hepatocellular carcinoma (− 91%/− 90%; SOF/VEL, GLE/PIB vs. PR respectively), liver transplant (− 96%/− 95%; SOF/VEL, GLE/PIB vs. PR respectively) and liver-related death (− 93%/− 92%; SOF/VEL, GLE/PIB vs. PR respectively). Relative increase in quality-adjusted life years was also highest for SOF/VEL (+17.3% vs. PR; Table 1) compared to GLE/PIB (+17.2% vs. PR; Table 1).
Conclusions: SOF/VEL provides the highest SVR rates compared to all other DAAs, leading to better modelled long-term health benefits across the overall CHC population.

Abstract #611

Efficacy of Generic Velpatasvir + Sofosbuvir in treatment of Genotype 3 infected Hepatitis C patients: a Real life experience from Pakistan

Tayyab Saeed Akhter[1], Mohammad Umar[2], Samar Saleem[3], Hamama-Tul Bushra Khaar[4], Gul Nisar[5], Seemab Abid[6]

[1]Center for Liver and Digestive Diseases(Cld), Department of Medicine, Holyfamily Hospital, Rawalpindi, [2]Center for Liver and Digestive Diseases(Cld), Department of Medicine, Holyfamily Hospital, Rawalpindi, [3]Center for Liver and Digestive Diseases(Cld), Department of Medicine, Holyfamily Hospital, Rawalpindi, [4]Center for Liver and Digestive Diseases(Cld), Department of Medicine, Holyfamily Hospital, Rawalpindi, [5]Center for Liver and Digestive Diseases(Cld), Department of Medicine, Holyfamily Hospital, Rawalpindi, Pakistan, [6]Benazir Bhutto Hospital, Rawalpindi

Introduction: Genotype 3 is the most prevalent genotype in Pakistan. Velptasvir and Sofosbuvir is currently the best possible available

treatment in Pakistan and the generics are quite affordable but there is no real life local data regarding their efficacy.
Materials and Methods: This open-label, non-randomized, uncontrolled study is carried out at Center for Liver and Digestive Diseases, Pakistan from February 2018 through November 2018. The patients are offered single pill containing Sofosbuvir 400 mg and Velpatasvir 100 mg once daily for a period of 12 weeks. Follow-up PCRs were performed at end of treatment and 12 weeks post treatment.
Results: A total of 80 patients are enrolled in the study with a mean age of 46.53 + 11.389 including 34 males and 46 females. 47.5% (38/80) are cirrhotics, 82.5% (66/80) are treatment naïve whereas 17.5% (14/80) are treatment experienced. End of treatment response (ETR) is 95% (76/80). 4 patients, who are unable to achieve ETR, extended the treatment for 3 more months along with Ribavirin. 2 of these patients have completed the extended course and have achieved ETR. 14 patients have a follow-up PCR at 12 weeks post treatment and 3 patients have relapsed making a sustained viral response at 12 weeks(SVR12) of 78.5%.
Conclusion: Velpatasvir and Sofosbuvir with an ETR of 95% seem to be a promising combination for genotype 3. Although limited follow-up but SVR12 of only 78.5% raises concerns on the possibility of high underline DAA resistance. More real life data can guide for modification in treatment recommendations.

Abstract #637

No impact of RASs on the efficacy of SOF/VEL + RBV for 24 weeks in DAA-experienced Japanese patients

Namiki Izumi[1], Kazuaki Chayama[2], Hiroshi Yatsuhashi[3], Gregory Camus[4], Hongmei Mo[5], Hadas Dvory-Sobol[6], Silvia Chang[7], Deyuan Jiang[8], Anuj Gaggar[9], Satoshi Mochida[10], Masashi Mizokami[11]

[1]Japanese Red Cross Musashino Hospital, Tokyo, Japan;, [2]Hiroshima University Hospital, Hiroshima, Japan, [3]Nagasaki Medical Center, Nagasaki, Japan, [4]Gilead Sciences, Inc, Foster City, Ca, [5]Gilead Sciences, Inc, Foster City, Ca, [6]Gilead Sciences, Inc, Foster City, Ca, [7]Gilead Sciences, Inc, Foster City, Ca, [8]Gilead Sciences, Inc, Foster City, Ca, [9]Gilead Sciences, Inc, Foster City, Ca, [10]Saitama Medical University Hospital, Saitama, Japan, [11]National Center for Global Health and Medicine, Chiba, Japan

Introduction: In a phase 3 study of HCV-infected Japanese patients who previously failed direct-acting antivirals (DAAs), treatment with sofosbuvir/velpatasvir (SOF/VEL) plus ribavirin (RBV) for 24 weeks resulted in 97% (58/60) SVR12 rates.
Objectives: To evaluate the effect of baseline resistance-associated substitutions (RASs) on treatment outcome and the emergence of RASs in patients who experienced virologic failure following treatment with SOF/VEL + RBV for 24 weeks.
Methodology: NS5A and NS5B deep sequencing was performed at baseline for all patients and at the time of virologic failure for relapse patients.
Results: Overall, 93% (56/60) of patients had baseline NS5A RASs; 96% (54/56) of patients with baseline RASs and 4/4 patients without baseline RASs achieved SVR12 following 24 week treatment with SOF/VEL + RBV. No new NS5A or NS5B NI RASs emerged in the 2 patients who relapsed. In genotype 1b, NS5A-Y93 RASs were present in 83% (39/47) of patients, as a single substitution in 1/47 patient (threefold change in EC50 to VEL), and in combination with other NS5A RASs in 38/47 patients (7- to 510-fold change in EC50 to VEL). All patients with NS5A-Y93 RASs achieved SVR12. The NS5A-P32 deletion, which confers high-level resistance to NS5A inhibitors, was detected at baseline in 5 daclatasvir-experienced patients with genotype 1b, of whom 2/2 treated for 12 weeks and 2/3 treated for 24 week achieved SVR12.
Conclusion: High prevalence of NS5A RASs in Japanese DAA-experienced patients had no impact on the virologic response to SOF/VEL + RBV for 24 weeks. Viral relapse was not associated with emergence of viral resistance.

Abstract #642

Sofosbuvir/velpatasvir (S/V) vs elbasvir/grazoprevir (E/G): is the non-pan-genotypic HCV treatment regimen dead?

Brian Conway[1], David Truong[2], Tianna Magel[3], Astou Thiam[4], Letitia Chu[5], Rossitta Yung[6], Julie Holeksa[7]

[1]Vancouver Infectious Diseases Centre, [2]Vancouver Infectious Diseases Centre, [3]Vancouver Infectious Diseases Centre, [4]Vancouver Infectious Diseases Centre, [5]Vancouver Infectious Diseases Centre, [6]Vancouver Infectious Diseases Centre, [7]Vancouver Infectious Diseases Centre

Background: With the use of direct acting antiviral(DAA) therapy, cure of hepatitis C virus(HCV) infection can be achieved in > 90% cases. For 12-week single tablet regimens, sofosbuvir/velpatasvir(S/V) is effective against all genotypes(GT), while elbasvir/grazoprevir(E/G) is effective against GT-1a, 1b, 4 and can be administered for 8 weeks in GT-1b patients with mild fibrosis.
Objective: The aim of this analysis was to compare the efficacy of S/V and E/G administered to patients at a multidisciplinary clinic which serves people who use drugs(PWUD).
Methods: A retrospective analysis was performed on HCV-infected patients(GT-1a, 1b, 3, 4 treated with E/G or S/V) initiating treatment at our center between 06/15 and 04/18. Multidisciplinary care was provided to address medical, psychological, social and addiction-related needs. The primary outcome was SVR12 achievement.
Results: 97 patients were identified: mean age 53 years, 75% males, 92% active PWUD, 48 GT1a(33E/G, 15S/V), 4 GT1b(3E/G, 1S/V), 43 GT3(7E/G with sofosbuvir, 36S/V), 2 GT4(2E/G). SVR12 was achieved in 84% ITT/100% mITT and 87% ITT/96% mITT with E/G and with S/V respectively. 2 GT3 relapsed after end of treatment. No discontinuations due to side-effects occurred. 11(7E/G, 4S/V) were lost to follow up(LTFU), all occurring in active PWUD, 8 after week-8 of treatment.
Conclusion: E/G and S/V appear equally safe and effective when used appropriately. In this population, the main reason for not achieving SVR12 was LTFU. Shorter course regimens of 8-week may represent an advantage. This strategy may be applicable in Asia, where GT1b is dominant and a significant proportion of individuals may be eligible to receive 8-week of E/G.

Abstract #664

Clinical outcomes of Hepatitis C in the era of direct acting antivirals in Cebu City, Philippines: a single-center cross sectional study

Kevin Clifford Busa Duenas[1], Jenny Lim Limquiaco[2], Virna Gonzales Amor[3]

[1]Chong Hua Hospital, [2]Research Coordinator, Department of Internal Medicine, Section of Gastroenterology & Medical Staff Department of Internal Medicine, Section of Gastroenterology, Chong Hua Hospital, [3]Medical Staff Department of Internal Medicine, Section of Gastroenterology, Chong Hua Hospital

Introduction: Treatment with pegInterferon with ribavirin has been considered the standard of care for Hepatitis C Virus (HCV) infection but with high relapse rates and non-responders. This led to the direct-acting antivirals (DAAs) development with a goal of obtaining sustained virologic response (SVR). Philippines has an increasing number of HCV infection, but to date, no local data exists regarding treatment outcomes with DAA's.
Objective: To determine the outcome of HCV infected patients treated with DAA's in the local setting.
Methodology: This is a retrospective, cross-sectional single center study. Data from 2015 to 2018 were gathered using data base from private clinics. Patient's demographic data and HCV RNA levels at baseline, 4 and 12 weeks of treatment were recorded.
Results: A total of 111 patients were included with a mean age of 45.9 years with male preponderance (73%), acquired through IV drug use (80%). Majority are genotype 1 (91.9%), 26% had Child–Pugh A cirrhosis. Most were treatment naïve (96.6%). Associated diseases included 8 (7.2%) hepatocellular carcinoma, 4 (3.9%) Chronic Kidney Disease, 1 (0.9%) esophageal adenocarcinoma, and 1 (0.9%) Non-Hodgkin Lymphoma. 99% of patients had undetectable HCV RNA at end of treatment. One female Childs B cirrhotic patient with prior pegIFN + Ribavirin treatment relapsed. She completed 12 weeks of Ledipasvir + Sofosbuvir with undetectable HCV RNA at 4 weeks. However, patient relapsed at 12 weeks of therapy and subsequently treated with Sofosbuvir + Daclatasvir for 24 weeks.
Conclusion: DAA treatment for HCV infection is highly effective with low relapse rates in Cebu City, Philippines.

Abstract #688

Direct antiviral agent (DAA) treatment of chronic hepatitis C results by APRI and FIB-4 score in Mongolia

Amgalan B[1], Ganbyamba T[2], Tserendejid Ts[3], Uzmee S[4], Buyankhishig G[5], Munkhbayar D[6], Mandakh E[7], Suvd B[8], Amarsanaa J[9], Baatarkhuu O[10]

[1]Health Department, Arkhangai, Mongolia, Health Department, Arkhangai, Mongolia, [3]Health Department, Arkhangai, Mongolia, [4]Health Department, Arkhangai, Mongolia, [5]Health Department, Arkhangai, Mongolia, [6]Health Department, Arkhangai, Mongolia, [7]Health Department, Arkhangai, Mongolia, [8]Mongolian Academy of Medical Professionals, Ulaanbaatar, Mongolia, [9]Mongolian Association for The Study of Liver Disease, Ulaanbaatar, Mongolia, [10]Department of Infectious Disease, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia

Introduction: Viral hepatitis infection is directly associated with the development of liver cancer. According to the WHO report, among patients with liver cancer in Mongolia, 46% have hepatitis C, 34% have hepatitis B and 14% have co-infection with more than one hepatitis virus. Novel DAA targeting hepatitis C virus (HCV) have revolutionized the treatment of chronic hepatitis C infection (CHC).
Objectives: We aimed to determine DAA treatment achievement among 40–65 years old Mongolians.
Methodology: We examined the changes in fibrosis scores FIB-4 and APRI after DAA treatment of CHC. A total of 17,601 (81.1% of target group) underwent screening, of which 3447 (19.5%) were positive for hepatitis C. 3049 of them were tested for HCV RHA. FIB-4 and APRI scores were calculated before and after treatment for each patients. The relevant parametric and nonparametric tests were used.
Results: In total 1778 or 58.3% of individuals who had viral load test had enrolled treatment, 60.7% of them was female, aged between 40 and 65 years old. 98.3% (1748) of individuals who tested by viral load test was undergone to DAA treatment. After DAA treatment 99.4% of them were achieved SVR12. Mean level of FIB-4 and APRI values significantly decreased from 1.48 (SD1.39) [CI 95% 1.26–1.74] and 0.88 (SD 1.68) [CI 95%: 0.56–1.32] to 1.05 (SD0.54) [CI 95%:0.92–1.18] ($p = 0.017$) and 0.19 (SD0.17) [CI 95%:0.15–0.23] ($p = 0.001$) respectively.
Conclusion: Patients with SVR after DAA therapy showed significant improvement on fibrosis scores FIB-4 and APRI. Also almost all of treated patients were achieved SVR12 which shows treatment was highly effective.

Abstract #693

Efficacy and safety of Glecaprevir/Pibrentasvir for Japanese Hepatitis C virus infected patients in real world: KTK49 liver study group

Makoto Nakamuta[1], Koichi Takaguchi[2], Haruki Uojima[3], Hiroki Ikeda[4], Hidenori Toyoda[5], Takashi Kumada[6], Norio Itokawa[7], Tadashi Ikegami[8], Chikara Ogawa[9], Toru Asano[10], Yasuhito Tanaka[11], Noritomo Shimada[12], Shigeru Mikami[13], Shinya Fukunishi[14], Hiroshi Abe[15], Akihito Tsubota[16], Taeang Arai[17], Takuya Genda[18], Atsushi Hiraoka[19], Akito Nozaki[20], Yoshio Aizawa[21], Masanori Atsukawa[22]

[1]National Hospital Organization Kyushu Medical Center, [2]Kagawa Prefectural Central Hospital, [3]Kitasato University School of Medicine, [4]St. Marianna University School of Medicine, [5]Ogaki Municipal Hospital, [6]Ogaki Municipal Hospital, [7]Nippon Medical School of Chiba Hokusoh Hospital, [8]Tokyo Medical University Ibaraki Medical Center, [9]Takamatsu Red Cross Hospital, [10]Tokyo Metropolitan Bokutoh Hospital, [11]Nagoya City University Graduate School of Medical Sciences, [12]Otakanomori Hospital, [13]Kikkoman General Hospital, [14]Osaka Medical College, [15]Shinmatsudo General Hospital, [16]Jikei University School of Medicine, [17]Nippon Medical School of Musashi Kosugi Hospital, [18]Juntendo University Shizuoka Hospital, [19]Ehime Prefectural Central Hospital, [20]Yokohma City University Medical Center, [21]Joban Hospital, [22]Nippon Medical School

Objectives: Glecaprevir (NS3/4A inhibitor) and pibrentasvir (NS5A inhibitor) are approved as direct acting antivirals (DAA) for Hepatitis C Virus (HCV) genotype (GT) 1–6 infected patients. High sustained virologic response (SVR) rate and tolerability of glecaprevir/pibrentasvir (G/P) was demonstrated for GT1–3 infected patients with or without compensated cirrhosis. Here we report on real world efficacy and safety of G/P in Japan.
Methods: Data from consecutively treated patients by G/P were collected between Nov 2017 and June 2018 from 16 sites in Japan, retrospectively. Efficacy and safety were assessed.
Results: 1003 patients have been enrolled. Of these, male 533 (53.1%); median age 67; HCV GT 1a 8 (0.8%); GT 1b 426 (42.5%); GT2a 279 (27.8%); GT 2b 160 (16.0%); HCV GT3 13 (1.3%); others/unknown 117 (11.6%) compensated cirrhosis 277 (27.6%); CKD stage 4 28 (2.8%); CKD stage 5 114 (11.4%); prior DAA experienced 174 (17.3%). Overall SVR12 rate was 99.4% (643/647) by ITT analysis. All cirrhotic patients achieved SVR12 (108/180). The patients with CKD stage 4 or 5 achieved SVR12 of 99.1%. Regarding prior DAA failures, all patients except one (99.1%) achieved SVR12. 245 adverse events (AE) were reported, but most of which were mild to moderate. The most common AE was pruritus (11.7%).
Conclusions: G/P therapy demonstrated high SVR12 and tolerability for HCV GT1–3 infected Japanese patients in real world including cirrhotic patients, those with severe renal failure, and prior NS3/4A

inhibitor and NS5A inhibitor treatment failures. We will present updated data at the congress.

Abstract #697

Dose modification is a good strategy to avoid drug discontinuation due to adverse event developed in the combination therapy with glecaprevir and pibrentasvir

Ken Sato[1], Yuichi Yamazaki[2], Takeshi Kobayashi[3], Hiroki Tojima[4], Norio Horiguchi[5], Satoru Kakizaki[6], Toshio Uraoka[7]

[1]Department of Gastroenterology and Hepatology, Gunma Graduate School of Medicine, [2]Department of Gastroenterology and Hepatology, Gunma Graduate School of Medicine, [3]Department of Gastroenterology and Hepatology, Gunma Graduate School of Medicine, [4]Department of Gastroenterology and Hepatology, Gunma Graduate School of Medicine, [5]Department of Gastroenterology and Hepatology, Gunma Graduate School of Medicine, [6]Department of Gastroenterology and Hepatology, Gunma Graduate School of Medicine, [7]Department of Gastroenterology and Hepatology, Gunma Graduate School of Medicine

Direct-acting antivirals (DAAs) are 1st choice of the therapy in patients with chronic hepatitis C regardless of genotypes in Japan. The combination therapy with glecaprevir and pibrentasvir (GLE/PIB) is one of DAA-based therapies and has proven to be very effective and well-tolerated. However, hyperbilirubinemia as an adverse event (AE) was reported in 2.4% of the subjects in the domestic Phase III clinical trial. 72-year-old woman with liver cirrhosis started to receive the combination therapy with GLE/PIB. Serum bilirubin level increased at week 1 of the therapy complaining with itching. Serum bilirubin level reached to a maximum of 4.0 mg/dL at week 4 of therapy. GLE/PIB is co-formulated and essentially taken three tablets once a day. Then, we decreased to one tablet once a day. The serum bilirubin level gradually decreased and returned to the baseline level. After dose reduction of GLE/PIB, itching was ameliorated. Nalfurafine also contributed to reduce itching. However, serum alanine aminotransferase and aspartic aminotransferase started to increase at week 6 of the therapy. We administered ursodeoxycholic acid and these transaminase levels returned to the normal levels without drug discontinuation. The patient achieved sustained virological response at week 4 of treatment (SVR4). She had chronic kidney disease and this may be one of the reasons of developed hyperbilirubinemia and/or increased transaminase levels. Dose modification was a tip to ensure established treatment duration in patients developed AEs in the combination therapy with GLE/PIB. Hopefully, we will present SVR12 as a marker of viral eradication in the meeting.

Abstract #701

Management of Hepatitis C infection in Mandalay, Myanmar

Thandar Tun[1]

[1]Mandalay General Hospital

Introduction: In Myanmar, the prevalence of hepatitis C infection (HCV) infection is 2%. HCV infected patients have been treated with various direct acting antiviral (DAA) regimens according to availability and affordability.
Objective: To evaluate the outcome of HCV treatment according to DAA regimens and genotypes.
Methodology: From Oct 2015 to April 2018, 796 HCV infected patients were treated with available DAA regimens such as 12 weeks of Sofosbuvir plus Ledipasvir (SOF/LDV), Sofosbuvir plus Daclatasvir (SOF/DCV) and Sofosbuvir plus Velpatasvir (SOF/VEL). Ribavirin (RBV) 800 mg was added in patients with fibrosis score F4. 734 patients were studied for sustained virological response (SVR) at 12 weeks after treatment.
Results: Mean age in this study was 52 ± 11.9 years. Female gender constituted about 60%.
Genotype 3 was the commonest (35%) followed by genotype 6(31%) and genotype 1(14%)0.18% of patients had not been done for genotype. Majority of patients was treated by (SOF/DCV ± RBV) (44%) and (SOF/LDV ± RBV) (42%).

Overall SVR rate was 98% in this study.

15 patients failed to achieve SVR. 8 patients were genotype 3 and 5 patients were genotype 6.

9 relapse patients were retreated by (SOF/VEL) and obtained SVR. However, hepatocellular carcinoma had been changed in 2 patients.
Conclusion: This study showed that available DAA regimens achieved overall 98% SVR. Although (SOF/VEL) gave 100% SVR, (SOF/DCV) combination regimen still remained highly effective. Genotype 3 and 6 are not only the commonest genotypes but also the most difficult ones to treat.

Abstract #741

Real life Myanmar experience with Sofosbuvir plus Ribavirin and Sofosbuvir, Daclatasvir plus Ribavirin in the treatment of Chronic Hepatitis C virus Genotype 3 Cirrhotic patients

SI Thu Sein Win[1], Aung Hlaing BWA[2], Soe Thiha Maung[3], Moe Pwint Oo[4], Khin Aye Wint Han[5], Su Su Htar[6], Khin Maung Win[7]

[1]Yangon Gi and Liver Center, [2]Yangon Gi and Liver Center, [3]Yangon Gi and Liver Center, [4]Yangon Gi and Liver Center, [5]Yangon Gi and Liver Center, [6]Yangon Gi and Liver Center, [7]Honorary Professor, University of Medicine (1) & Yangon Gi and Liver Center

Introduction: Myanmar has a large burden of chronic HCV infection with an estimated 2.65% of general adult population and genotype 3 (GT3) accounts for 41%. Sofosbuvir (SOF) plus Ribavirin (RBV) or Sofosbuvir, Daclatasvir (DCV) plus RBV was initiated in HCV GT3 patients with cirrhosis.
Objectives: The analysis evaluated the treatment outcome and safety of SOF + RBV and SOF + DCV + RBV in chronic HCV GT3 patients with cirrhosis as a real-life setting in Myanmar.
Methodology: Retrospective analysis was conducted at Yangon GI and Liver Center in Yangon, Myanmar between January 2016 and December 2017 as an investigator-initiated study. The primary end point was a sustained virologic response (HCV RNA level of < 25 IU/mL) at week 12 after the end of therapy (SVR12). Data was analyzed using SPSS version 22.0.
Results: A total of 225 GT3 cirrhotic patients was randomized and treated for 24 weeks, 35%(male), 68%(BMI(Body Mass Index) < 25), 87%(treatment naïve) and genotype subgroup were 72%(GT3b), 21%(GT3a) and 7%(GT3 not available). Child Turcotte Pugh Score (CTP) A (88%) and B (12%).
Overall SVR12 was achieved in 216/225 patients (96%). SOF + RBV 24-week therapy achieved 97.4% (114/117) of SVR12 and 94.4% (102/108) in SOF + DCV + RBV 24-week therapy(p = 0.5).

Poorer SVR12 was found in high BMI (≥ 25) in both therapy, 96%(SOF/RBV24) and 87%(SOF/DCV/RBV24) (p = 0.008).

No patients discontinued the treatment regimen due to adverse events.

Conclusion: Real life study revealed SOF + RBV 24-week therapy was as high effectiveness as SOF + DCV + RBV 24-week therapy with comparatively lower adverse events in cirrhosis, treatment naïve or experienced chronic HCV GT 3 patients in Myanmar.

Abstract #742

Narlaprevir/ritonavir and daclatasvir combination in treatment-naïve patients with chronic hepatitis C genotype 1b infection

Vladimir P Chulanov[1], Denis A Gusev[2], Edward Z Burnevich[3], Olga O Znoyko[4], Elena A Klimova[5], Svetlana N Kizlo[6], Sergey N Batskikh[7], Nina A Mamonova[8], Elena P Tarkhova[9], Emiliya N Krasavina[10], Mikhail Yu Samsonov[11]

[1]Central Research Institute of Epidemiology & I.M. Sechenov First Moscow State Medical University, [2]Centre for The Prevention and Control of Aids and Infectious Diseases, [3]I.M. Sechenov First Moscow State Medical University & City Clinical Hospital #24 of Moscow Healthcare Department, [4]A.I. Evdokimov Moscow State University of Medicine and Dentistry, [5]A.I. Evdokimov Moscow State University of Medicine and Dentistry, [6]Centre for The Prevention and Control of Aids and Infectious Diseases, [7]Central Research Institute of Epidemiology, [8]Central Research Institute of Epidemiology, [9]JSC R-Pharm, [10]JSC R-Pharm, [11]JSC R-Pharm

Narlaprevir is a potent inhibitor of hepatitis C virus NS3 protease used with ritonavir. Interferon-free combination of narlaprevir/ritonavir with NS5A or NS5B inhibitors is a promising approach of chronic hepatitis C (CHC) treatment.

We investigated efficacy and safety of narlaprevir/ritonavir plus NS5A inhibitor–daclatasvir combination in treatment-naïve non cirrhotic patients with CHC genotype 1b infection.

This was phase II, open-label study. Patients with NS5A- Y93C/H/N/C and/or L31F/M/V/1 resistance-associated substitutions (RASs) were excluded from study at screening. Narlaprevir 200 mg with ritonavir 100 mg plus daclatasvir 60 mg were administered once daily for 12 weeks. Primary efficacy endpoint was proportion of patients with sustained virologic response at posttreatment week 12 (SVR12).

In total, 120 patients with CHC were screened and 105 patients were enrolled. 14% of patients (19 individuals) with NS5A variants at amino acid positions 31 or 93, detected at screening, were excluded. SVR12 was achieved approximately in 90% (94/105) of patients. 1 virologic breakthrough and 10 post-treatment viral relapses occurred. In most cases treatment failure was associated with selection of NS5A RASs at positions 93 and/or 31. NS3 RASs were detected in 6/11 patients at baseline.

Frequency of AEs was low. Two serious AEs were considered not related to study treatment. Other AEs were mild or moderate in severity. AEs reported $> 4\%$ of patients were neutropenia (5.7%), headache (4.8%). No discontinuations occurred.

Narlaprevir/ritonavir plus daclatasvir was effective and well tolerated in CHC genotype 1b patients.

NS3 baseline resistance polymorphisms at positions 54, 56 and 132 affected SVR12 rates.

Abstract #782 Sofosbuvir/Daclatasvir regimen in Chronic Hepatitis C patients. Real world experience from tertiary care centre, Myanmar

Thet Nwe Oo[1], Win Naing[2]

[1]Yangon Specialty Hoapital, [2]Yangon Specialty Hospital

Introduction: In Myanmar, the overall prevalence of chronic hepatitis C infection is 2.7% and the most common genotypes are 3 (47%), 1(31%) and 6 (21%). National Hepatitis C programme was developed in 2017 and implemented at selected centres. All the patients were treated with Sofosbuvir/Daclatasvir, 12 weeks for non-cirrhosis and 24 weeks for cirrhotic patients.

Methods: This is a retrospective analysis of a prospectively maintained database according to National programme in Yangon Specialty Hospital. During one year period, 345 treatment eligible patients were treated and monitored on follow up visits to record any adverse events. Treatment response was assessed by Sustained Viral Response (SVR) at 12 weeks after completion of treatment.

Results: The cohort consisted of 345 patients, out of which 163 patients had compensated cirrhosis. Eleven patients lost to follow while four patients died during variable treatment course.

Overall SVR was 92.7%. Non-cirrhotic patients got SVR of 91.5% while cirrhotic ones 94.1%.

Retrospective analysis of the patients who did not achieve SVR was done based upon the factors that increase the risk of HCV Disease progression. None of the patients had to stop treatment because of serious side effects.

Conclusion: Sofosbuvir/Daclatasvir regimen achieved good SVR (92.7%) with few mild side effects. It can still be used as one of the treatment options for chronic Hepatitis C patients in Myanmar, although in an advent of new more DAAs, provided that fibrosis stage needs to be assessed to determine treatment duration.

Abstract #796

Real life study: comparison of sustained virological response 12 achievement between genotype 3 and 1 chronic Hepatitis C patients using Sofosbuvir-Daclatasvir

Evie Rosa W Napitupulu[1], Irsan Hasan[2], Juferdy Kurniawan[3], Pringgodigdo Nugroho[4]

[1]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo Hospital, [2]Hepatobilier Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo Hospital, [3]Hepatobilier Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo Hospital, [4]Nephrology Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo Hospital

Introduction: Chronic hepatitis C is a global health problem with high morbidity and mortality in the condition of cirrhosis and hepatocellular carcinoma. Sofosbuvir-daclatasvir is pangenotypic therapy that expected to overcome this disease. However, the achievement of sustained virological response 12 (SVR 12) was varied and lower in genotype 3 compared to genotype 1. In Indonesia, there is no data about achievement SVR 12 in both genotypes using sofosbuvir-daclatasvir.

Objectives: The aim of this study was to find out the achievement of SVR 12 in chronic hepatitis C patients genotype 3 compared to genotype 1 who received sofosbuvir-daclatasvir therapy.

Methodology: This study is a retrospective cohort of hepatitis C chronic genotype 3 and 1 patients. Samples were divided into two groups according to its genotype and achievement of SVR 12 data was compared between groups using Chi square test analysis. Liver cirrhosis was considered as possible confounding of achievement SVR 12 were analyzed using Chi square test and logistic regression test.

Results: There are 209 patients participated in this study consisting of 45 genotype 3 and 164 genotype 1. There was 84.4% and 98.8% SVR

12 in patients respectively. Genotype 3 patients had lower SVR 12 achievement compared to genotype 1 patients with adjusted OR = 0.065 (95% CI 0.013–0.330) and absolute risk reduction (ARR) 14.4. Hepatic cirrhosis did not affect SVR 12 (p = 1.00). Five from nine patients who failed have co-infection with HIV.
Conclusion: Chronic hepatitis C patients using sofosbuvir-daclatasvir therapy had lower SVR 12 achievement in genotype 3 than genotype 1.

Abstract #827

Effectiveness of Sofosbuvir and Declatasvir in the treatment of hepatitis C: an experience from tertiary care hospital

Anoshia Fahad[1], Nazish Butt[2]

[1]Jinnah Post Graduate Medical Centre, [2]Jinnah Post Graduate Medical Centre & Agha Khan Hospital

Background: Hepatitis C infection and its related complications is a major public health problem affecting about 170 million people worldwide. Now, direct acting antivirals are available for treatment of hepatitis C which provide high SVR rates, interferon free treatment, reduced side effects and shorter duration of therapy.
Aim: To assess the effectiveness of Sofosbuvir and Declatasvir with or without Ribavirin in patients with chronic hepatitis C and cirrhosis either treatment naïve or experienced.
Methods: This was a prospective, cross sectional study, conducted from July 2017 to October 2018 at Jinnah Postgraduate Medical Centre, Karachi. All patients above 12 years of age whose HCV RNA PCR was detected were included in the study. Sofosbuvir and Declatasvir for 12 or 24 weeks was given to each patient. Ribavirin was given to treatment experienced and cirrhotic patients. Primary end point was End of Treatment Response (EoTR) and secondary end point was Sustained Virological Response (SVR) at post treatment week 12 or 24.
Results: Total 185 consecutive patients with mean age of 40.9 ± 14.2 were enrolled. Males were 69 (37.3%) and females were 116 (62.7%). Chronic Hepatitis C patients were 147 (79.5%) while cirrhotics were 38 (20.6%). Treatment naïve patients were 163 (88.1%) and 22 (11.9%) patients were experienced. SVR was checked in 167 out of 185 patients which was achieved in 157 (94%).
Conclusion: The results suggest that use of Sofosbuvir and Declatasvir achieved very high SVR rates in naïve or experienced patients including those with cirrhosis.

Abstract #828

Genotype 3 still the bad boy in Hepatitis C Virus infection—a real world scenario from a tertiary care hospital in South India

Simna Lubina[1], Krishnadas Devadas[2], Bincy B K[3], Atul Hareendran[4], Tharun Tom Oommen[5]

[1]Department of Medical Gastroenterology & Government Medical College, Trivandrum & Kerala University of Health and Applied Sciences, [2]Department of Medical Gastroenterology & Government Medical College, Trivandrum & Kerala University of Health and Applied Sciences, [3]Department of Medical Gastroenterology & Government Medical College, Trivandrum & Kerala University of Health and Applied Sciences, [4]Department of Medical Gastroenterology & Government Medical College, Trivandrum & Kerala University of Health and Applied Sciences, [5]Government Medical College, Trivandrum & Department of Medical Gastroenterology & Kerala University of Health and Applied Sciences

Introduction: Hepatitis C virus (HCV) infection is one of the major cause of liver disease worldwide amounting to 1.6% of population. Directly Acting Antivirals(DAAs) have markedly improved the cure rates in HCV marked by Sustainable Virological Response at 12 weeks after treatment completion(SVR12).
Objectives: The primary objective is to study the efficacy of DAAs in HCV patients. The secondary objective is to study the factors influencing treatment failure in various genotypes.
Methodology: This was a three year, single-centre, observational study performed at a tertiary hospital in South India from April 2015-April 2018.
Results: Of the 203 patients treated with DAAs, 123 patients(60.5%)belonged to genotype 3.40 patients(19.7%) each in genotype 1 and 4.112 patients were cirrhotics(55.1%). The overall SVR was 91.6% (87.8–95.4 CI). Among 40 patients with genotype 1, SVR 12 was 100% (n = 40/40) and among 123 patients with genotype 3, SVR 12 was 87.8. %(n = 108/123). 95% patients from genotype 4 (n = 38/40) attained SVR12. The presence of cirrhosis did not influence treatment failure statistically ($p > 0.5$). A subgroup analysis of 17 treatment failure cases showed that genotype 3 contributed 88.2%(15/17). Of these 15 cases, 11 were cirrhotics(73.3%). 9 and 6 cases received daclatasvir and velpatasvir based regimes respectively.
Conclusion: The increase in treatment failure cases in genotype 3, especially cirrhotics, raises a concern being the commonest genotype in India. The modification of current recommendations for the treatment of genotype 3 in resource limited setting where mutation analysis for resistance is unavailable needs to be considered.

Abstract #836

Interferon-free sofosbuvir-based direct-acting antiviral (DAA) regimens for hepatitis C virus (HCV)-associated glomerular diseases: a case series report

Ni Cai He[1], Yu Li [2], Fu Wei[3], Wen Jun Wang[4], Ning Gao[5], Juan Juan Shi[6], Fan Pu Ji[7]

[1]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China, [2]Department of Infectious Diseases, Shaanxi Provincial People's Hospital, Xi'an, China, [3]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China & Department of Intensive Care Unit, Xi'an No.4 Hospital, Xi'an, China, [4]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China, [5]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China, [6]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China, [7]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China & Shaanxi Provincial Clinical Research Center for Hepatic & Splenic Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University & National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University

Background/Aims: HCV infection is associated with a large spectrum of glomerular diseases. The most frequently observed is the cryoglobulinemic glomerulonephritis, followed by membranoproliferative glomerulonephritis, focal segmental glomerulosclerosis, mesangioproliferative glomerulonephritis, membranous nephropathy, fibrillary glomerulonephritis and IgA nephropathy. Remission of renal diseases has been associated with viral clearance, but few studies have reported the effectiveness of DAA drugs in these patients.

Methods: We performed a retrospective study of the effectiveness and tolerance of an interferon-free sofosbuvir-based regimens in patients with HCV-associated glomerular diseases. Clinical and laboratory features were recorded at baseline, every 4 weeks until the end of treatment (EoT), and 12/24 weeks afterwards.
Results: Four consecutive patients with active HCV-associated glomerular diseases (age range, 27–81y; 3 male; one cirrhosis; 3 genotype 1b and 1 genotype 2a) were recruited from our hospitals from 06/2016 to 03/2018. They received sofosbuvir + ribavirin (n = 2) or ledipasvir/sofosbuvir (n = 2) for 12 or 24 weeks. All 4 patients achieved SVR12. Compared with baseline, alanine transaminases were significantly decreased at EoT and SVR12. A significant reduction of 24-h urine protein and a parallel increase of serum albumin levels were also detected (Fig. 1). Serum urea nitrogen and creatinine improved or remained unchanged (Fig. 1). Urinary erythrocyte negativity or improvement in 2 and 2 patients, respectively. Mild adverse events was recorded in one patient.
Conclusions: Interferon-free sofosbuvir-based regimens were effective and well tolerable in patients with HCV-associated glomerular diseases. A much longer follow-up is desirable to achieve useful information in terms of persistent viral clearance and clinical improvement in renal diseases.

Abstract #843

Risk of hepatocellular carcinoma in HCV patients treated with direct-acting antiviral agents

Kyoko Fukuhara[1], Shunhei Yamashina[1], Kei Ishizuka[1], Masahiro Tada[1], Akira Uchiyama[1], Kazuyoshi Kon[1], Shuichiro Shiina[1], Kenichi Ikejima[1]

[1]Juntendo University

Background: The recent development of direct-acting antivirals (DAAs) for HCV has radically improved the cure rate to above 90%; however, it is still controversial whether antiviral therapeutics efficiently prevent hepatocellular carcinoma (HCC) during long-term follow up period. We analyzed the data to identify the factors associated with the risk of HCC.
Methods: Data were collected from 1143 patients received DAAs for HCV infection in our institution and affiliate hospitals since September 2014. Pre-treatment FIB-4 indices in all patients were calculated.
Results: 96.1% of patients were achieved a sustained virologic response (SVR). There were 110 HCC occurrence after DAAs treatment (HCC group). 77.2% of HCC group have the treatment history of liver cancer, in contrast to non-HCC group (11.2%). HCC group (72.1 ± 0.8 y.o) was significantly older than non-HCC group (66.1 ± 0.4 y.o). Significant increases in serum AFP, ALT, total bilirubin levels and FIB-4 index before DAAs treatment were observed in HCC group more than non-HCC group. Platelet count and albumin in HCC group was lower than non-HCC group significantly. Multivariate analysis of the HCC occurrence/recurrence identified the treatment history of liver cancer and FIB-4 indices as an independent predictive factor.
Conclusion: It is obvious that the treatment history of liver cancer and high FIB-4 indices are important for the risk of HCC. Therefore, it is recommended that long-term surveillance for HCC should be continued particularly in patients with a history.

Abstract #847

Successful treatment of chronic hepatitis C with combination of ombitasvir/paritaprevir/ritonavir and dasabuvir in a patient who failed previous daclatasvir and asunaprevir treatment: A case report

Soo Hyung Ryu[1], Jong Hyun Choi[2], Bo Kyung Lee[3], Tae Young Park[4], Jeong Seop Moon[5]

[1]Division of Gastroenterology, Department of Internal Medicine, Seoul Paik Hospital, Inje University College of Medicine, Seoul, Korea, [2]Division of Gastroenterology, Department of Internal Medicine, Seoul Paik Hospital, Inje University College of Medicine, Seoul, Korea, [3]Division of Gastroenterology, Department of Internal Medicine, Seoul Paik Hospital, Inje University College of Medicine, Seoul, Korea, [4]Division of Gastroenterology, Department of Internal Medicine, Seoul Paik Hospital, Inje University College of Medicine, Seoul, Korea, [5]Division of Gastroenterology, Department of Internal Medicine, Seoul Paik Hospital, Inje University College of Medicine, Seoul, Korea

Introduction: We report a rare case that acquired sustained viral response (SVR) with combination of ombitasvir/paritaprevir/ritonavir and dasabuvir for 4 months in a patient who failed previous DAA treatment with daclatasvir and asunaprevir.
Case: A − 53 year-old woman came to the hospital for elevated liver enzyme. Blood tests showed a white blood cell count of 2820/mm^3, hemoglobin level of 10.9 g/dL, platelet count of 70,000/ul, aspartate aminotransferase of 210 IU/L, alanine aminotransferase of 174 IU/L, total protein of 7.5 g/dL, total albumin of 3.8 g/dL, prothrombin time of 75%, and total bilirubin of 0.9 mg/dL. The abdominal ultrasonography revealed Child–Pugh Class A cirrhosis without ascites. She had positive anti-HCV, HCV RNA level of 597,000 IU/ml, and genotype 1b. She had failed previous pegylated interferon and subsequent DAAs with daclatasvir and asunaprevir for 6 months due to appearance of mutations in NS5A region of HCV genome. We treated her with ombitasvir/paritaprevir/ritonavir and dasabuvir. After 1 month of therapy, the level of HCV RNA decreased rapidly to 20 IU/ml, the levels of aspartate aminotransferase and alanine aminotransferase were normalized. At 2 months after treatment, HCV RAN was not detected. At 1 month, 3 months, and 6 months after a total of 4 months treatment, HCV RNA was not detected and liver enzymes was still normalized, therefore, she acquired sustained viral response (SVR).
Conclusion: A combination of ombitasvir/paritaprevir/ritonavir and dasabuvir for 4 months might be a successful treatment option in a patient who failed previous DAA treatment with daclatasvir and asunaprevir.

Abstract #858

The impact of direct- acting antivirals therapy on the serum alpha-fetoprotein levels of chronic hepatitis C patients

Kader Arslan[1], Sami Kinikli[2], Necla Tulek[3], Serife Altun Demircan[4], Gunay Ertem[5], Fatma Sebnem Erdinc[6]

[1]Ankara Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, [2]Ankara Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, [3]Ankara Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, [4]Ankara Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, [5]Ankara Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology,

[6]Ankara Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology

Introduction: Serum concentration of alpha-fetoprotein (AFP) is often elevated in patients with hepatocellular carcinoma (HCC) and a high AFP level has been identified as a risk factor for development of HCC in chronic hepatitis C (CHC) patients.
Objectives: The aim of this study was to investigate the impact of direct-acting antivirals (DAAs) therapy on the AFP level of CHC patients.
Methodology: 63 patients received DAAs for CHC treatment were enrolled the study. Age, gender, treatment regimen, genotype and AFP were recorded. Treatment duration was 12 weeks for ombitasvir-paritaprevir-ritonavir and dasabuvir (PrOD), 24 weeks for ledipasvir/sofosbuvir (LDV-SOF), and 24 weeks for sofosbuvir + ribavirin (SOF + RBV). The changes of AFP values of the patients were evaluated according to the DAAs and histopathological fibrosis scores.
Results: 33 male (35%), 30 female (47%), with the mean age of 52.6 ± 16.5 years (range 18–81 years) were included. 38 of the patients (60.3%) received PrOD, 21 (33.3%) received LDV-SOF, 4 (6.3%) received SOF + RBV. The predominant genotype was genotype 1b (93.6%), followed by genotype 3 (6.4%). Sustained viral response-12 was achieved in all patients but serum AFP levels could be measured in 43 patients three months after therapy. Changes in AFP values are presented in Table1.
Conclusion: DAAs therapy with PrOD significantly reduced AFP levels in patients with low stages of fibrosis. LDV-SOF combination therapy only reduced AFP levels at the end of therapy but the fibrosis stage of the patients were higher. Long-term follow up the patients might give better results about the impact of DAAs on AFP levels.

Abstract #898

Combination of daclatasvir and sofosbuvir for hepatitis C virus infection in the setting of no genotype testing: real-world data

Irsan Hasan[1], Evie Rosa W Napitupulu[2], Imelda Loho[3], Rino A Gani[4], Andri Sanityoso[4], Juferdy Kurniawan[4], Rinaldi Lesmana[4], Chyntia Jasirwan[4]

[1]Hepatobilier Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo Hospital, [2]Department of Internal Medicine, Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo Hospital, [3]Departement of Gastroenterology and Hepatology, Dharmais Hospital, Indonesian National Cancer Center, [4]Hepatobilier Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo Hospital

Introduction: In order to achieve HCV eradication, the Indonesian government with the support of Clinton Health Access Initiative conducted a national hepatitis C program which offered free access to direct-acting antiviral (DAA) therapy, i.e. daclatasvir and sofosbuvir with or without ribavirin, for patients with chronic hepatitis C virus (HCV) infection. This program is currently available in 26 hospitals appointed by the government, across seven provinces. Due to socioeconomic issue, genotype testing is not a prerequisite before starting treatment.
Objectives: This study aimed to determine sustained virologic response at 12 weeks post-treatment (SVR-12) for chronic hepatitis C patients treated with daclatasvir- sofosbuvir combination with or without ribavirin, in the setting of unavailable genotype testing.
Methodology: Data from national health information system was retrieved. Patients documented to have started hepatitis C treatment with DAA between June 2017 and December 2018, were included.
Results: A total of 2923 subjects initiating DAA therapy were recorded. Outcome data were available for 641 patients, of whom 622 (97.0%) achieved an SVR-12. Of the 19 patients who failed to achieve SVR-12, baseline data could be obtained in only three patients. All of these three patients were treatment-naïve, non-cirrhotic, had baseline viral load ≥ 400,000 IU/mL, and had HIV co-infection.
Conclusion: In the setting of low socioeconomic status, where genotype testing is not available, combination of daclatasvir and sofosbuvir with or without ribavirin, appears to be a very good treatment option.

Abstract #917

Use of ledipasvir/sofosbuvir in a test-and-treat model of care for hepatitis C virus micro-elimination in Arkhangai Province, Mongolia

Byambasuren Amgalan[1], Altangerel Enkhjargal[2], Delgerkhangai Munkhbayar[3], Sarjita Naik[4], Boon-Leong Neo[5], Dennis Israelski[6], Buyanjargal Azjargal[7], Eondonperenlei Baatarbileg[8], Riimaadai Gandiimaa[9]

[1]AIMAG General Hospital, [2]Mongolian Academy of Medical Professionals, [3]AIMAG General Hospital, [4]Gilead Sciences, [5]Gilead Sciences, [6]Gilead Sciences, [7]AIMAG Health Department, [8]Parliament of Mongolia, [9]AIMAG Health Department

Introduction: To achieve elimination of Hepatitis C virus (HCV) globally by 2030, the World Health Organization has set an 80% target treatment goal of people living with chronic HCV. Introduction of highly efficacious direct-acting antivirals provides an unprecedented opportunity to globally eliminate HCV. More countries now have access to these life-saving medicines. Mongolia is one such country which is highly endemic with HCV.
Objective: The aim of this study was to describe the real world effectiveness of Ledipasvir/Sofosbuvir (LDV/SOF) in a cohort of patients aged 40 to 65 years enrolled in a test-and-treat program in rural Mongolia.
Methodology: From December 2016 to February 2017, a government sponsored birth cohort screening campaign was conducted. Subjects in the target population were recruited from primary care clinics. Patients were screened with HCV rapid diagnostic tests with reflex confirmatory antibody assays and viral loads by PCR. All PCR positive patients were offered LDV/SOF. Baseline characteristics and clinical outcomes are described below.
Results: Of the 1778 patients who qualified for treatment, 1748 (98%) initiated treatment and were included in this analysis. Baseline characteristics were as follows: age > 50 years (45%), male (40%), and noncirrhotic (84%). The overall sustained virologic response (SVR) at week 12 was 94% in patients who completed treatment.
Conclusions: Once daily LDV/SOF is a safe and well-tolerated option for patients as part of a test-and-treat model of care for HCV micro-elimination. This program shows health equity is possible in resource limited settings in remote regions of lower and middle income countries.

Abstract #921

Sofosbuvir, Velpratasvir, Veloxpravir Efficacy in 12 week treatment in triple infected (Chronic Hepatitis C, Chronic Hepatitis B and HIV} Geno 3 naive population: SOLVVE-C

Patrick Basu[1], Nimy John[2], Mark Aloysius[3], Robert Brown Jr.[4]

[1]Weill Cornell Medicine, [2]St. Vincent Hospital, [3]James J. Peters Va Medical Center, [4]Weill Cornell Medicine

Objectives: Chronic Hepatitis C treatment is no longer challenging in the era of DAAs with an SVR of up to 97%. Triple infection treatment with HCV, HIV and Hepatitis B has not been explored in real life situations. HCV Genotype 3 is still the most challenging clinical state in Hepatitis C treatment. Regardless of concomitant triple infection, shorter duration of therapy revealed favorable outcome with the highest retention, fewer side events, and cost containment. This study evaluates the efficacy and safety of Sofosbuvir, Velpratasvir, and Veloxpravir in the treatment of triple infection with HBV, HIV, and HCV (Genotype 3).
Methods: Twenty-two (n = 22) HCV treatment-naive patients with Triple Infection (HIV HBV HCV Genotype-3) were recruited for the study.
Patients with HIV were on Atripla for over 3 years with HIV with Undetectable Viral load and HBV Viral load Undetectable. HCV-infected patients had a Median Viral load of 3 million IU and Genotype 3 prior to treatment.
Demographics:
Table 1
Results:
Table 2

One patient dropped out of study due to severe bilateral Pneumonia.

One patient stopped therapy due to Rectal Bleed after three weeks of treatment.

One patient stopped therapy due to Virological Failure with RAS y93.

One patient developed Herpes Zoster in the 10th week of treatment.

Intention to Treat (ITT): 18/21.
Conclusion: The study demonstrates the efficacy of DAAs in 12-week treatment with an SVR of 87% in a triple infected cohort, with significant efficacy, tolerability, and safety. A larger trial is needed to validate the results.

Abstract #951

Efficacy and safety of glecaprevir/pibrentasvir in elderly patients with hepatitis C virus genotype 1b or 2a/2b and past antiviral treatment failure

Kenichi Kitada[1], Makoto Kuboki[2], Norikuni Shibata[3], Kenji Ohmoto[4], Akinobu Kato[5]

[1]Morioka Municipal Hospital, [2]Morioka University, [3]Kurashiki Medical Center, [4]Kurashiki Medical Center, [5]Morioka Municipal Hospital

Introduction: Glecaprevir and pibrentasvir (G/P) are direct-acting antiviral agents with pangenotypic activity and a high barrier to resistance.
Objectives and Method: We evaluated the efficacy and safety of treatment with 300 mg of glecaprevir plus 120 mg of pibrentasvir in elderly (age > 65) compensated liver cirrhosis who had hepatitis C virus (HCV) genotype 1b with past direct-acting antiviral treatment failure or chronic HCV genotype 2a/2b with past peginterferon plus ribavirin treatment failure. We analyzed the consecutive data from the elderly patients who were treated with G/P.
Result: Fourteen patients were collected from Dec.2017 to Mar.2018. Mean age is 72.1 y/o (65 to 86 y/o, M/F; 4/10). Seven patients (M/F; 3/4) with compensated liver cirrhosis HCV genotype 1b were received 12 weeks of G/P. Seven patients (M/F; 1/6) with chronic hepatitis HCV genotype 2a/2b were received 8 weeks of G/P. The rate of sustained virologic response at 24 weeks after the end of treatment (SVR24) among genotype 1–infected patients was 100% (7/7). Genotype 2a/2b–infected patients who were treated for 8 weeks had a rate of SVR24 of 100% (7/7). There were no patients who have experienced treatment-related serious adverse events and treatment withdrawal.
Conclusions: Treatment with G/P for 12 weeks achieved complete sustained virologic response among all elderly compensated liver cirrhosis patients with HCV genotype 1b. Genotype 2a/2b–infected elderly patients for 8 weeks also achieved complete sustained virologic response.

Abstract #960

Role of shear wave elastography (SWE) in assessment of hepatic fibrosis regression after direct-acting antiviral drugs (DAAs)

Mohamed Kohla[1], Mohamed Rady[2], Ahmed El-Fayoum[3], Mervat Abd Elkareem[4], Mahmoud Elsakhawy[5]

[1]National Liver Institute, Menoufia University & National Liver Institute, Menoufia University, [2]National Liver Institute, Menoufia University & National Liver Institute, Menoufia University, [3]National Liver Institute, Menoufia University & National Liver Institute, Menoufia University, [4]National Liver Institute, Menoufia University, [5]National Liver Institute, Menoufia University & National Liver Institute, Menoufia University

Background: Shear wave elastography (SWE) is one of the non-invasive markers of hepatic fibrosis which is ultrasound-based.
DAAs therapy was associated with regression of hepatic fibrosis assessed by transient elastography, however data on the utility of SWE is still lacking.
Aim of the work: Assessment of liver fibrosis by SWE before and after treatment with DAAs.
Methods: We enrolled 161 patients with chronic HCV infection who received DAAs. Patients' demographics, laboratory and imaging characteristics were evaluated at baseline and the end of treatment (12 weeks).
Liver stiffness measurements by SWE were performed before and after treatment.
Results: ALT levels were significantly lower at the end of treatment (18 ± 4.3 IU/L) compared to those at base line (46.23 ± 30.92 IU/L), P value < 0.001, as well as AST levels (19.7 ± 4.9 IU/L at the EOT compared to 45.8 ± 30.3 IU/L at baseline), P-value < 0.001.
Liver stiffness measurements showed marked improvement at the end of treatment (week 12), from a baseline value of 7.43 ± 4 KPas down to an end of treatment value of 6.25 ± 3.6 KPas, which was statistically significant (P-value < 0.001).

Advanced fibrosis (F3&F4) was detected in 35 out of 161 patients at baseline (21%) compared to 20 out of 161 patients (12%) at the end of treatment.
Conclusion: These results showed early improvement of liver stiffness scores after administration of DAAs. SWE is an easy and reliable method for assessment of fibrosis regression after DAAs.

Abstract #965

Changing of skeletal muscle index after direct acting antivirals treatment in chronic hepatitis C infected patients with advanced fibrosis

Chanin Chareesil[1], Phunchai Charatcharoenwitthaya[2], Supot Nimanong[3], Siwaporn Chainuvati[4], Tawesak Tanwandee[5], Watcharasak Chotiyaputta[6]

[1]Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, [2]Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, [3]Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, [4]Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, [5]Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, [6]Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: Sarcopenia has emerged as an independent predictor of poor clinical outcomes in cirrhotic patients especially the overall survival. The aim of this study was to compare SMI between chronic hepatitis C (CHC) patients with advanced fibrosis who achieved SVR after DAAs therapy with those without treatment.
Methods: Patients were divided into 2 groups; group A were patients who achieved SVR after DAAs treatment whereas patient who didn't receive DAAs treatment was classified as group B. Clinical data's including liver biochemistry, CT or MRI scan were prospectively collected at baseline and at 12 months after enrollment. SMI was assessed using the sum of cross-sectional area of skeletal muscle mass in lumbar (L3) region divided by height squared (cm2/m2).
Result: A total of 59 patients met the inclusion criteria. The proportion of the patients who were diagnosed with HCC before enrollment in Group A (25.8%) was significantly higher than those in group B (3.6%), p = 0.027. The Mean of SMI in group A and group B were 43.54 ± 5.69 cm2/m2 and 42.53 ± 10.32 cm2/m2 (p = 0.649) respectively. There were no significant percentage differences of 1st and 2nd SMI between group A and group B (1.66 ± 6.47 and 1.73 ± 6.92 cm2/m2/year respectively, p = 0.969). In group A, sarcopenia was diagnosed in 58.1% of patients before treatment and did not significantly decrease after treatment (51.6%).
Conclusion: This study demonstrated that DAAs treatment was not associated with the improvement of SMI or the decrease in proportion of sarcopenia in CHC patients with advanced fibrosis.

Abstract #979

Sustain virology response of Sofosbuvir and ribavirin for compensated liver cirrhosis with genotype 2 hepatitis C infected patient

Hsu Po Ke[1], Su Wei Wen[2]

[1]Division of Hepatology, Department of Internal Medicine Changhua Christian Hospital, Changhua, [2]Division of Hepatology, Department of Internal Medicine Changhua Christian Hospital, Changhua

Introduction: Sofosbuvir(SOF) and weight-based ribavirin(RBV) are considered standard treatments for genotype 2(GT) hepatitis C virus(HCV). In real world experience, sustain virology response at 12 weeks(SVR12) is still lower than the antiviral drugs against other genotypes.
Objectives: Analysis of the rate of sustained virology response of SOF/RBV in patients infected with compensated liver cirrhosis GT 2 HCV.
Methodology: In 101 treatment naïve compensated GT2 HCV infected patient were treated with SOF/RBV. Median age is 67(46–92). Four patients were loss follow up and one had stopped due to acute myocardial infraction and severe anemia. 94 had Child–Pugh score A and 2 B. SVR12 with completed treatment showed 97.91%.
Result: SVR12 with completed treatment showed 97.91% in compensated liver cirrhosis GT2 HCV infected patients.
Conclusion: In real world report in Changhua County, Taiwan, treatment naïve compensated liver cirrhosis GT2 HCV infected patient treated with SOF/RBV had higher SVR12 rate(97.91%). Adverse event is sometimes anemia and may induce severe cardiovascular event.

Abstract #980 Impact of adding Daclatasvir in Sofosbuvir based therapy in genotype 3 of hepatitis C: Real World experience in Pakistan

Shahid Sarwar[1]

[1]Doctors Hospital Lahore & Services Institute of Medical Sciences

Objective: To determine effect of Daclatasvir addition to chronic hepatitis C treatment by comparing sustained viral response of Sofosbuvir/Daclatasvir (SOF/DCV) with or without ribavirin and Sofosbuvir + ribavirin (SOF/RBV) combination in patients of genotype 3.
Methodology: Patients of chronic hepatitis C, genotype 3 presenting at DHMC Hepatology Clinic from October 2014 till March 2018 were treated with 6 months therapy of SOF/RBV and once Daclatasvir was available for treatment, with SOF/DCV with or without ribavirin for 3–6 months. Negative HCV RNA by PCR, 12 weeks post-treatment (SVR12) was the primary end-point of study for per-protocol analysis.
Results: Mean age of 440 enrolled patients was 51.04(± 11.9) and male to female ratio was 0.97/1(217/223). Liver cirrhosis was present in 260(59.1%) patients, 89(20.2%) of these had decompensated disease. Treatment experienced patients were 124(28.2%). We included 398 (90.4%) patients with completed follow-up in final analysis, remaining either dropped out, failed to complete therapy or died during follow-up. SVR12 was achieved in 366 (91.9%), significantly lower (P value 0.001) in cirrhosis patient 89.9% (205/228), even lower SVR12 (P value 0.006) was seen in decompensated cirrhosis 87.01% (67/77). SVR12 was also inferior (p value 0.005) in treatment experienced patients 85.8% (97/113) than treatment-naïve patient's SVR of 94.3% (269/285). Among 285 patients treated with SOF/RBV, SVR12 was achieved in 264 (92.6%), not different from SVR12 of SOF/DCV ± RBV, 90.2% (102/113) (p value 0.57).
Conclusion: In patients of chronic hepatitis C genotype 3, SOF/RBV and SOF/DCV ± RBV have similar sustained viral response. Patients with liver cirrhosis and prior treatment experience have suboptimal response.

Abstract #999

5-Year Evaluation of drug utilization, costs and outcomes of chronic hepatitis c treatment in malaysia: picture of pre-compulsory licensing era

Mohamad Fadli Abd Rahman[1], Muhammad Radzi Abu Hassan[2], Chan Huan Keat[3], Haniza Omar[4], Rosaida Md Said[5], Chan Lai Yue[6], Nik Razima Wan Ibrahim[7], Nur Aliza Mutalib[8]

[1]Medical Department, Sultanah Bahiyah Hospital, Alor Setar, Malaysia, [2]Medical Department, Sultanah Bahiyah Hospital, Alor Setar, Malaysia, [3]Clinical Research Center, Sultanah Bahiyah Hospital, Alor Setar, Malaysia, [4]Hepatology Department, Selayang Hospital, [5]Medical Department, Ampang Hospital, [6]Pharmacy Practice and Development Division, Petaling Jaya, [7]Medical Department, Ampang Hospital, [8]Hepatology Department, Selayang Hospital

Introduction: While Malaysia began using generic sofosbuvir through compulsory licensing in early 2018, this study aimed to evaluate the drug utilization, costs and outcomes of chronic hepatitis C (CHC) treatment in the preceding 5 years.
Methods: The 5-year data (2013–2017) on drug utilization and acquisition costs of all the 52 public hospitals providing CHC treatment in Malaysia was collected. All non-trial patients from 4 selected hospitals, who completed 12- or 24-week treatment with direct-acting antiviral (DAA), were also further studied to determine the overall treatment cost (drugs, facilities, personnel, laboratory tests and imaging procedures) and sustained virologic response at 12 weeks following the treatment (SVR12).
Results: Over the 5-year period, drug treatment was only given to 1764 CHC patients, 82.8% of whom were non-trial patients. Nevertheless, the total drug expenditure reached 36,036,370.4MYR (9,009,092.6USD). Approximately 80% of the drug expenditure was contributed by the first 3 years, in which interferon-based therapy was still the cornerstone of CHC treatment. As complimentary DAAs had been provided by the Drugs for Neglected Disease (DNDi) Trial to 40.5% of the patients in 2016 and 2017, a relatively low drug expenditure was reported. Despite the high overall treatment cost of DAAs (170,315.7MYR or 42,578.9USD per patient), all the 47 non-trial patients studied were found to achieve SVR12.
Conclusion: While DAAs revolutionized the CHC treatment, the consequent financial burden is of concern, particularly after the completion of the DNDi Trial. Compulsory licensing is a timely strategy, but the confirmation of its impact is warranted.

Abstract #1033

Vitamin D and viroloic response on pegylated interferon alpha 2 and ribavirin therapy in patients with chronic hepatitis C, genotype-1

Elena I Kukhareva[1], Olga I Tarasova[2], Pavel P Ogurtsov[3]

[1]Peoples' Friendship University of Russia (Rudn University), [2]Peoples' Friendship University of Russia (Rudn University), [3]Peoples' Friendship University of Russia (Rudn University)

Aim: To study the effect of vitamin D (25-Oh) deficiency correction on the outcomes of antiviral therapy (AVT) with Pegylated interferon alpha 2(peg-IFN–2) and Ribavirin(RBV) in patients with chronic hepatitis C, genotype − 1.
Materials: The 90 treatment-naive HCV-1 patients, with an initial deficiency of vitamin D. 55 patients (study group) was appointed AVT peg-IFN–2/RBV in combination with a water-soluble vitamin D- vitamin D3 (cholecalciferol) at a dose of 2000 mg/day, 35 patients (control group) assigned to only peg-IFN-α-2/RBV.
Results: There was an inverse correlation between reduced vitamin D level, HOMA-insulin resistance(HOMA-IR), body mass index(BMI), viral load ($p < 0.05$). The level of vitamin D with relative degree is affected by BMI, $\beta = -0.433$, $p < 0.001$ and HOMA-IR, $\beta = -0.252$($p = 0.013$). The addition of vitamin D–vitamin D3 (cholecalciferol) in the dosage of 2000 IU/day to the AVT increased the SVR from 42.9% to 74.5%($p = 0.002$). The probability of sustained virologic response (SVR) in patients with HCV-1 who were taking vitamin D in combination of peg-IFN-α-2/RBV increases by 3.9 times($p = 0.003$). In patients with a BMI over 25 kg/m2 and patients with HOMA-IR > 2.0 SVR odds ratio was 7.0($p = 0.01$) and 3.3($p = 0.03$) in the study group, respectively. On vitamin D therapy there was a statistically significant decrease in HOMA-IR, $p < 0.001$ and adverse events of AVT($p < 0.05$).
Conclusions: The addition of vitamin D–vitamin D3 as a third component of the interferon based AVT increases the efficiency of AVT from 40.0% to 74.5% ($p = 0.002$). On vitamin D therapy there was a statistically significant decrease in HOMA-IR ($p < 0.001$) and adverse events of AVT($p < 0.05$).

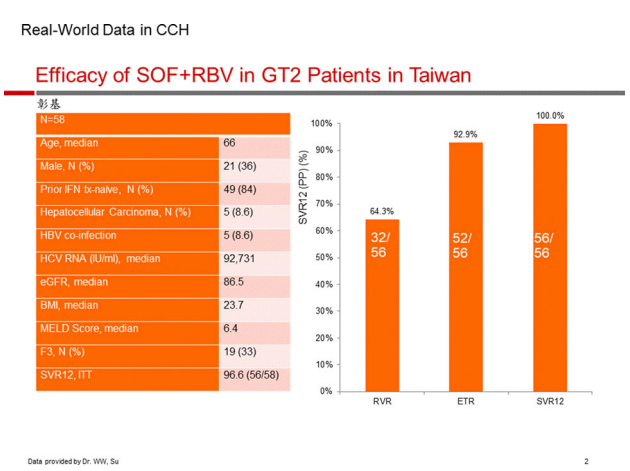
Abstract #1068

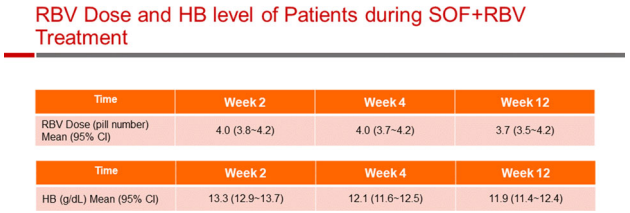
Sustain virology response of Sofosbuvir and ribavirin for compensated liver cirrhosis with genotype 2 hepatitis C infected patient: a real world experience

Hsu Po Ke[1], Su Wei Wen[2]

[1]Division of Hepatology, Department of Internal Medicine, [2]Division of Hepatology, Department of Internal Medicine

Introduction: Sofosbuvir(SOF) and weight-based ribavirin(RBV) are considered standard treatments for genotype 2(GT) hepatitis C virus(HCV). In real world experience, sustain virology response at 12 weeks(SVR12) in Asian population had showed in relative low. We had analysis of our hospital of SVR12.
Objectives: Analysis of the rate of sustained virology response of SOF/RBV in patients infected with compensated liver cirrhosis GT 2 HCV.
Methodology: In 58 compensated GT2 HCV infected patient were treated with SOF/RBV from January 1, 2018 to September 11th, 2018. Median age is 56. One patient was loss follow up and one had stopped due to acute myocardial infraction with severe anemia(hemoglobin : 6.8 g/dl). MELD score median: 6.4. SVR12 with completed treatment showed 100%.
Result: SVR12 with completed treatment showed 100% in compensated liver cirrhosis GT2 HCV infected patients.
Conclusion: In real world report in Changhua County, Taiwan, treatment compensated liver cirrhosis GT2 HCV infected patient treated with SOF/RBV had higher SVR12 rate(100%). Adverse event is sometimes anemia and may induce severe cardiovascular event.





Abstract #1073

The efficacy and safety of sofosbuvir and ribavirin treatment for genotype 2 chronic hepatitis C patients: a single center study

Ik Sung Choi[1], Sang Goon Shim[2], Dong Kyu Lee[3], Byung Soo Kwan[4]

[1]Department of Internal Medicine, Samsung Changwon Hospital, Sungkyunwan University School of Medicine, [2]Department of Internal Medicine, Samsung Changwon Hospital, Sungkyunkwan University School of Medicine, [3]Department of Internal Medicine, Samsung Changwon Hospital, Sungkyunwan University School of Medicine, [4]Department of Internal Medicine, Samsung Changwon Hospital, Sungkyunwan University School of Medicine

Aim: The combination of sofosbuvir and ribavirin is more effective than the peg-IFN based treatment in patients with chronic hepatitis C genotype 2 (CHC GT2). The aim of this study was to evaluate the treatment efficacy and safety of sofosbuvir and ribavirin treatment for CHC GT2 patients in a single center.
Methods: The primary endpoint was sustained virologic response at 12 weeks (SVR12). The secondary endpoint was the occurrence of side effects during treatment.
Results: SVR12 was confirmed in 105 of 106 patients (99.1%). One patient with treatment failure was combined liver cirrhosis and hepatocellular carcinoma, HCV RNA titer was not detected at 4 weeks and 8 weeks after initiation of treatment, but HCV RNA detected at 12 weeks. Twenty-five patients were combined liver cirrhosis (CTP-A; n = 24, C; n = 1), SVR12 was confirmed in 24 patients (96.0%). The mean HCR RNA titer was 2,456,240 IU/ml. The Hemoglobin level decrease occurred in 21 patients during treatment (2.59 mg/dL, Mean) and ribavirin dose reduction was required. (365.22 mg, Mean).
Conclusions: This study was performed on a small group of patients compared with other studies, but showed that treatment with sofosbuvir and ribavirin was highly effective in patients with CHC GT2. In aspect of safety, there was no serious side effects about treatment although hemoglobin decrease.

Abstract #1079

Effect of direct acting antiviral treatment on quality of life of chronic hepatitis C patients

Raefa Refaat Alam[1], Gamal Shiha[2], Abdel-Hady El-Gilany[3]

[1]Nursing, Faculty of Nursing, Mansoura University, Egypt, [2]Professor of Internal Medicine Faculty of Medicine, Mansoura University, Egyptphd in Gerontology, [3]Professor of Public Health, Faculty of Medicine, Mansoura University, Egypt

Background: Hepatitis C virus constitutes an epidemic in Egypt having the highest prevalence in the world of 14.7%, making it the most challenging public health problem facing the country with genotype 4 is the dominant. The study objective is to compare the QoL score immediately and three months after direct acting antiviral treatment with score before treatment in chronic hepatitis C in patients with and without SVR.
Methods: This is a pre-post study carried out in the Egyptian Liver Hospital, Sherbin City, Dakahlia Governorate, Egypt. Data was collected from 38 patients before treatment and QoL scale. They received SOF and ribavirin for 12 and 24 weeks. They were retested by PCR for sustained virological response (SVR) three months after completed treatment. The Arabic version of the Short Form-36 (SF-36) scale was used to measure the QoL.
Results: A significant improvement was observed in the total QoL score in late post compared to pre and early post-treatment (medians were 740 vs. 657.1 and 473.3; respectively) in patients with SVR. This significant improvement was observed in scores of all domains. There is a non-significant improvement in the total QoL score in late post compared to pre and early post-treatment (medians were 399 vs. 597 and 749; respectively) in non-responders. However, a significant improvement was observed in scores of physical functioning and general health domains only.
Conclusions: In addition to its efficacy and safety SOF improves QoL of HCV patients with SVR.

Table 1: Socio-demographic features of studied patients.

	N(%)
Age: mean ±SD	49.7±12.2
Median (min-max)	52.5(20-70)
Sex: Male	26(68.4)
Female	12(31.6)
Education:	
Less than secondary	12(31.6)
Secondary & above	26(68.4)
Currently working	21(55.3)

Table 2: Comparison of total QoL and its domains in the pre, immediate post and late post-treatment in patients with SVR.

	Pre (31) Median (min-max)	Immediate post (31) Median (min-max)	Late post (31) Median (min-max)	Friedman test
Physical function	50(0-50)^{A,B}	80(5-100)^{A,C}	90(5-100)^{B,C}	χ^2=54.5,P≤0.001
Role limitation/ physical	0(0-100)^{A,B}	100(0-100)^{A,C}	100(0-100)^{B,C}	χ^2=20.3,P≤0.001
/Role limitation/ emotional	0(0-100)^{A,B}	100(0-100)^{A}	100(0-100)^{B}	χ^2=29.9,P≤0.001
Energy/fatigue	55(20-95)^{A,B}	85(20-95)^{A,C}	85(20-95)^{B,C}	χ^2=48.2,P≤0.001
Emotional wellbeing	56(16-80)^{A,B}	72(4-84)^{A,C}	80(4-92)^{B,C}	χ^2=47.2,P≤0.001
Social functioning	100(37.5-100)	100(12.5-100)	100(12.5-100)	χ^2=7.1,P=0.03
Bodily pain	100(25-100)	100(45-100)	100(45-100)	χ^2=8.8,P=0.02
General health	80(55-90)^{A,B}	85(60-100)^{A,C}	95(65-100)^{B,C}	χ^2=57.8,P≤0.001
Total QoL	485 (340-713)^{A,B}	669 (291.5-761)^{A,C}	740 (287-769)^{B,C}	χ^2=49.7,P≤0.001

A, B & C significant differences between the corresponding group by Wilcoxon sign test post-hoc multiple comparisons.

Abstract #1080

Towards HCV elimination; feasibility of complete linkage to care by testing and treatment on the same day of screening: a pilot study

Gamal Shiha[1]

[1]Faculty of Medicine, Mansoura University, Egypt & Egyptian Liver Research Institute and Hospital

Introduction: We developed a community-based-model for prevention, diagnosis and treatment of hepatitis C. It has been implemented in 73-villages across 7-governates in Egypt. The availability of an FDA/WHO pre-qualified GeneXpert for measurement of HCV Viral load in 105 min presents an opportunity to offer "test, evaluate and treat" on the same-day.
Aim: Our objective was to establish the feasibility of a same-day-model through point-of-care HCV-viral-load confirmation using GeneXpert, and on-site Fibroscan and clinical evaluation in one village in northern Egypt.
Methods: This pilot study was conducted at a village in northern Egypt. Portable laboratory instruments were transferred from the Egyptian liver research institute and hospital to the village. A team of 3-physicians, 2-radiologists, 2-fibroscan operators, 1-pharmacist, 4-lab specialists, 7-nurses and 2-data entry personnel were mobilised for the pilot in the village. Screening was done using HCV antibody RDT.
Results: Staff arrived at 8:30am, and screening commenced at 9:00am. Results of the first 100RDTs were available by 10:00am, (16 HCV antibody positive). PCR results were available by 12:00 pm, (11 cases were positive HCV RNA). Results of other lab tests, abdominal ultrasound and Fibroscan were obtained by 12:00 pm. Treatment was offered to the first 11 patients by 12:30 pm. By the end of the day (6:00 pm), 475 individuals were screened by RDT, 56 had their HCV-PCR done, 43 were positive for HCV-RNA by PCR, and 40 patients received their treatment.
Conclusion: We report the feasibility of implementation of screening, testing, clinical evaluation and treatment on the same-day with almost complete linkage to care.

Abstract #1084

Real world efficacy of antiviral therapy in chronic hepatitis C in New Zealand: REACH-C

Ed Gane[1]

[1]Liver Transplant Unit, Auckland City Hospital, Auckland, New Zealand

Introduction: In 2016, New Zealand initiated public funding of Direct Acting Antiviral (DAA) VIEKIRA PAK for all chronic genotype 1 Hepatitis C (HCV) patients. Unconventional community prescribing methods including prisons, drug/alcohol centres and sexual health were utilised in addition to hospitals. REACH-C database includes all HCV patients treated nationally thus far.
Objectives: To review patterns of VIEKIRA PAK prescription, uptake and outcomes and inform the Pharmaceutical Management Agency (PHARMAC) and government about future models of care, including pan-genotypic treatment, to aim for national HCV elimination.
Methodology: PHARMAC provided national prescription data. Patient demographics and outcomes (determined by sustained virological response 12 weeks post-treatment—SVR12) requested from all prescribers. Data collated and reviewed at Auckland City Hospital in accordance with Ethics Committee and local Research Review Committee approval.
Results: Data has been collected for 1487 patients. Demographic data demonstrated most prevalent genotype = 1a (82%), male (65%, with median age 55–59 years), cirrhotic (19%)., treatment experienced (23%). SVR12 data available for 1244 patients demonstrating overall 95.9% cure (1193/1244). High cure rates were attained for all patient populations, including those treated in hospital (96%), treated in the community (96%), cirrhotic (94%), non-cirrhotic (96%), treatment experienced (94%), treatment naïve (96%), genotype 1a (96%) and 1b (96%). Treatment failures were recorded in 51/1244, of whom 23 stopped due to side effects, 4 terminated for other reasons, 2 were non-complaint, 12 had unknown compliance, 10 were considered compliant. Overall virologic failure from resistance is estimated to be 2%—complete resistance testing will be presented.
Conclusion: High cure rates achieved with VIEKIRA PAK supports treatment in the community in addition to hospitals.

Abstract #1089

Reversal of liver cirrhosis after treatment of HCV in 428 mongolian patients

Batbayar Purev[1], Zolzaya Sumiyajav[2], Nasanbayar Tumurbaatar[2], Budmaa Dashlkhundev[2], Namuuntsetseg Gankhuyag[2], Ankhbayar Bat-Ochir [1], Erdenebayar Gonchig[3], Badamgerel Chinzorigt [1], Baatarkhuu Oidov[3], Bold Manaljav[2], Amarsanaa Jazag[3]

Happy Veritas Hospital[1]; Etugen University[2]; Mongolian Association for the Study of Liver (MASLD)[3]

Background: HCV Ab prevalence in Mongolia is one of highest in the world (15.6%) among apparently healthy population. Chronic hepatitis C is one of major causes of liver cirrhosis and HCC related death in the country.

Dual, all-oral treatment of HCV started in Mongolia since 2016. Evidence is small regarding liver cirrhosis reversal after cure of HCV. We selected cirrhotic patients to assess their fibrosis scoring before and after the treatment.
Method: Prospective analysis 428 cirrhotic patients who had 3 months of all oral treatment with 90 mg/Ledipasvir, 400 mg/Sofosbuvir were assessed for liver stiffness before and after the HCV treatment by transient elastography at Happy Veritas Hospital.
Transient elastography was performed using equipments Fibrotouch (HISKY) and Fibroscan (Echosens). There was no difference in results between the 2 equipment. First fibrosis measurement was performed right before the start of treatment, while the second measurement was done 6–12 months after the start of treatment.
Results: All patients 100% (n = 428) had decreased in liver stiffness score. 31% (n = 135) of patients were descended from stage 4 to stage 3 of liver fibrosis. 5.1% (n = 22) of patients have descended from stage 4 to stage 2 of liver fibrosis. 3.9% (n = 17) of patients were descended from stage 4 to stage 1 of liver fibrosis. 1.1% (n = 5) of patients were descended from stage 4 to stage 0 of liver fibrosis. 58.34% (n = 179) of patients remained at stage 4.
Mean ALT and AST level was 102 IU/L, 73.6 IU/L and 29.4 IU/L, 29.8 IU/L respectively before and after the treatment. Baseline biochemical markers as total bilirubin, ALP, PLT, Albumin, GGT, AFP were assessed as well.
Conclusion: Though fibrosis score improvements are definite (100%) after successful HCV treatment, the speed of improvement varies greatly among patients. Some cirrhotic patients (n = 5; 1.1%) managed to reach total recovery within 1 year after start of treatment. Long term (3–10 years) follow up of cirrhotic patients is mandatory even after successful eradication of HCV.

Other Viral Hepatitis

D01 - Viral hepatitis A/D/E and other viral hepatitis

Abstract #359

The prevalence and management of hepatitis delta in Azerbaijan A multi-center, retrospective study

Gulnara Aghayeva[1], Sevda Aghayeva[2], Yusif Alkhazov[3], Mahira Gadirova[4]

[1]Ege Hospital, [2]"Baku Medical Plaza" Private Hospital, [3]"Euromed" Private Medical Centre, [4]Spero Hospital

Background and aims: Hepatitis delta is the most severe form of viral hepatitis in humans. This study is aimed to investigate the prevalence of delta virus among the patients with hepatitis B as well as management of it.
Methods: We collected data for 2169 patients with chronic hepatitis B admitted to clinics between January 2008 and June 2018 from four largest private hospitals in Baku, Azerbaijan. Abbot Laboratory and Cobas Tagman equipment were used for evaluation of viral load of both hepatitis B and D.
Results: Hepatitis Delta co-infection was detected in 258 out of 2169 chronic hepatitis B patients (11.9%). The mean age was 38.6 + 0.7 years (age range 18–71 years). Patients were predominantly males – 159 (61.3%). At the first admission, 42% of the patients presented with advanced liver disease (compensated cirrhosis), 27% with 1 or more episode of hepatic decompensation and 2.3% with hepatocellular carcinoma (HCC).
During the median follow-up of 6.8 years (average time 1.8–9.7 years), 51 patients with hepatitis D (19.8%) were treated with Pegylated interferons and 4 patients (0.15%) with Lonafarnib. 4 patients (0.15%) had liver transplantation.
Conclusions: Dual HBV/HDV infection is one of the most rapidly progressive cause of advanced liver disease that can end up with dangerous complications such as cirrhosis and HCC. The prevalence on HDV infection is 11.9% in Azerbaijan. For detailed evaluation of the disease burden, nationwide screening program is required.

Abstract #434

Clinical difference between symptomatic acute sporadic hepatitis A and E

Wajana Thaweerat[1], Tawesak Tanwandee[2], Sirajuk Khongviwatsathien[3], Chulaluk Komoltri[4]

[1]Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [2]Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [3]Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [4]Research Group and Research Network Division, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Introduction: Hepatitis A virus (HAV) and hepatitis E virus (HEV) are endemic in Thailand and presented as sporadic cases where most people are not immunized. Regarding HEV, only genotype 3 is found which is different from nearby countries where genotype 1 is more usual.
Objectives: The aims were to investigate clinical pattern of acute sporadic HAV and HEV and identify contrast in clinical presentation and outcome between both viruses.
Methodology: All HAV and HEV patients at Siriraj Hospital from January 2007 to August 2018 were retrospectively reviewed. HAV and HEV infection was diagnosed if HAV IgM and HEV IgM was positive, respectively. Patient demographic, laboratory data and clinical outcome were retrieved.
Results: 102 acute HAV cases and 52 acute HEV cases were diagnosed. Baseline characteristics is shown in Table 1. Majority of patients did not have risk exposure to both viruses. However, 13 cases of HEV (25%) were found in post-organ transplantation or immunosuppressed patients and 3 cases of HAV were found in MSM HIV infection. HAV had more severe presentation with high fever and higher ALT comparing with HEV. Nevertheless, diarrhea was more common in HEV. There were 2 HAV cases (0.02%) and 5 HEV cases (9.6%) died.
Conclusion: Sporadic acute hepatitis A and E were found without specific risk factors. For hepatitis in post-organ transplantation and immunosuppressed patients, HEV should be suspected. Acute hepatitis with high grade fever as prodromal symptom and extremely high ALT is suspicious of HAV. Mortality rate is higher for acute hepatitis E.

Abstract #484

Acute cholestatic hepatitis induced by Epstein–Barr virus infection in an adult

Kyoung Min Sohn[1]

[1]Gastroenterology, Hansol Hospital

Acute cholestatic hepatitis without features of infectious mononucleosis is a rare presentation of primary Epstein–Barr virus(EBV) infection, with only several cases previously reported in the medical

literature. A 24 years old young man with a febrile illness was noted to have a cholestatic picture of deranged liver function tests. Over the following week a progressive obstructive jaundice developed, with no evidence of choledocholithiasis on ultrasound. Specific immunoglobulin M antibodies against EBV were detected in his serum and the diagnosis of EBV associated hepatitis was confirmed by polymerase chain reaction testing. Supportive treatment was implemented and his liver function had normalized 3 months after presentation. EBV is associated with a wide variety of clinical manifestations and can present as cholestatic hepatitis with or without features of infectious mononucleosis. While the diagnosis is often suggested by serological testing, EBV polymerase chain reaction is a new non-invasive laboratory study that can help identify infection in cases where the clinical presentation is atypical. Early investigation for EBV in febrile patients with deranged liver function tests and no demonstrable biliary obstruction on imaging can expedite both diagnosis and treatment, thereby avoiding costly or invasive procedures such as liver biopsy.

Abstract #515

AMPK activation in response to hepatitis E virus infection inhibited viral infection by attenuating autophagy and promoting innate immunity

Yijin Wang[1], Jingmin Zhao[2]

[1]The 5th Medical Center, Chinese Pla General Hospital, [2]The 5th Medical Center, Chinese Pla General Hospital

Introduction: Hepatitis E virus (HEV) infection generally leads to asymptomatic or acute disease. However, the mechanism of host-cell defence against HEV is unclear. AMP-activated protein kinase (AMPK) activation is crucial for cell homeostasis.
Objectives: We thus investigated the role of AMPK in HEV infection.
Methodology: Huh-7 and HepG2 cells inoculated with infectious HEV viral particle or transfected with HEV genome RNA were used to model HEV infection.
Results: HEV infection can trigger AMPK activation by phosphorylation of AMPK at threonine 172. Meanwhile, HEV also induced autophagy. Inhibition of HEV induced AMPK phosphorylation with specific AMPK inhibitor dose-dependently enhanced HEV replication. Conversely, treatment with pharmacological AMPK activator strongly inhibited HEV replication. These results suggested that AMPK activation is a potent strategy of host cells for HEV clearance. Interestingly, we found AMPK activation upon HEV infection can promote mTOR to supress HEV induced autophagy. Our previous study showed that rapamycin, an activator of autophagy by inhibiting mTOR, has a potent pro-HEV effect. Together, these results suggested that HEV induced AMPK activation can protect HEV infected cells from autophagy and inhibit HEV infection. In addition, we found interference of AMPK activation significantly abrogated a subset of HEV induced interferon-stimulated genes (ISGs), which are considered the ultimate antiviral effectors, suggesting that HEV induced AMPK activation also contributes to stimulation of innate immunity, thereby facilitating cell-defence against HEV.
Conclusion: AMPK activation in response to HEV infection is critical in host cells for rapid viral clearance by coordinating autophagic process and establishing persistent antiviral immunity.

Abstract #575

Hepatitis E virus infection induces mitochondrial fusion to facilitate viral replication through induction of autophagy

Yijin Wang[1], Yiyun Jiang[2], Jingmin Zhao[3], Qiuwei Pan[4]

[1]The 5th Medical Center, Chinese Pla General Hospital, [2]The 5th Medical Center, Chinese Pla General Hospital, [3]The 5th Medical Center, Chinese Pla General Hospital, [4]erasmus University Medical Center

Introduction: Mitochondrial morphological dynamics play important roles in various pathogenesis.
Objectives: To understand mitochondrial morphological alteration in response to hepatitis E virus (HEV) infection and its implication.
Methodology: Huh7 cells inoculated with infectious HEV viral particle or transfected with HEV genome RNA were used to model HEV infection.
Results: Both ultrastructural analysis and immunofluorescent observation of HEV-infected Huh7 cells displayed elongated mitochondria, in contrast to dispersive and fragmented mitochondria in uninfected cells (Fig. 1A-B). Mitochondrial fusion is modulated by proteins Optic atrophy 1 (OPA1) and Mitofusion 1 (Mfn1). Consistently, western blot analysis demonstrated an increase of both OPA1 and Mfn1 and a decrease of Fis1 and Drp1 (regulators of mitochondrial fission) in HEV infected cells (Fig. 2A). Importantly, silencing of OPA1 or Mfn1, with a concomitant persistent fragmentation of mitochondria, resulted in a significant suppression of HEV replication, suggesting that HEV-induced mitochondrial fusion facilitates viral infection (Fig. 1C). Mechanistically, we found HEV infection can stimulate autophagy by inhibiting mTOR (Fig. 2B-C). While interference of mitochondrial fusion potently abrogated HEV induced autophagy by rescuing mTOR (Fig. 2B). Our previous study demonstrated that pharmacological or genetic activation of mTOR can facilitate HEV replication. Taken together, these results suggested that induction of autophagy could contribute to mitochondrial fusion mediated pro-HEV activity.
Conclusion: HEV infection induces mitochondrial fusion to facilitate HEV infection by induction of autophagy through suppressing mTOR. Mitochondrial dynamics represents a viable option for prevention and treatment for hepatitis E.

Abstract #713

Guillain–Barre syndrome following acute hepatitis A infection: a case report

Precious Diamond Chua Chua[1], Caroline Copeng Lim[2], Arlinking Ong Go[3], Mary Mildred Delgado Delos Santos[4]

[1]Metropolitan Medical Center, [2]Metropolitan Medical Center, [3]Metropolitan Medical Center, [4]Metropolitan Medical Center

Introduction: Guillain–Barre Syndrome (GBS) is an acute inflammatory polyradiculopathy. It is a rapidly ascending motor weakness accompanied by areflexia with or without sensory deficit, often triggered by a respiratory or gastrointestinal infection. Despite being rare, there are a number of cases of hepatotrophic virus induced GBS. Objective: It is to increase the awareness of the possible association of acute hepatitis A infection with GBS.
Methodology: The subject of this case is a 58-year-old Chinese male who had acute onset of jaundice, tea colored urine and acholic stool. This was followed by paresthesias of the palms and soles and proximal bilateral upper extremities which progressed to lower extremity weakness. The patient was diagnosed with acute hepatitis A and GBS,

which was then treated with intravenous immunoglobulin. However, bulbar symptoms rapidly progressed requiring tracheostomy and gastrostomy. He gradually recovered and after 2 months, only had minimal neurologic symptoms.
Conclusion: GBS is a neurological emergency that require a high index of suspicion to diagnose. It is important to be aware of the association of acute hepatitis A and GBS so that diagnosis and treatment are not delayed.
Keywords: Guillain–Barre Syndrome, Hepatitis A, Acute Inflammatory Polyradiculopathy

Abstract #839

HAV IgG seroprevalence among HBV patients in South Korea

Daejin Kim[1]

[1]Daegu Fatima Hospital

Introduction: Coinfection of hepatitis A can aggravate liver damage in HBV liver disease patient. HAV IgG seroprevalence is lower in young generation.
Method: We checked HAV IgG in 38 patients who have HBV from 2015 to 2017. Seroprevalence was analyzed retrospectively.
Result: Seropositivity of IgG is 63%(24/38). (1)According to age, 10–19 years 25%(1/4), 20–29 years 25%(2/8), 30–39 years 70%(7/10), 40–49 years 87%(14/16). Seropositivity of IgG is increasing as age becomes higher($p < 0.05$). (2)Seropositivity of patients below 30 years old is 25%(3/12) and above 30 years old is 80%(21/26). Seropositivity is high in patient above 30 years old ($p < 0.05$).
Conclusion: Seropositivity of HAV IgG was not high in HBV young generation. HAV vaccination can be reasonable for HBV patient under 30 years old without HAV IgG test in South Korea.

Abstract #841

Etiology and clinical features of acute viral hepatitis at the biggest tertiary care centre in Karachi

Anoshia Fahad[1], Nazish Butt[2]

[1]Jinnah Post Graduate Medical Centre, [2]Jinnah Post Graduate Medical Centre & Agha Khan Hospital

Background: Acute viral hepatitis is a major cause of morbidity and mortality in Pakistan. Most cases of acute hepatitis are caused by Hepatitis A and E viruses which are transmitted by the oro-fecal route. Local data regarding the etiology and risk factors for developing acute viral hepatitis is not available. Moreover, the etiology and patterns of acute viral hepatitis has changed dynamically worldwide over the recent years.
Aims: To evaluate the etiology, risk factors, clinical features and prognosis of acute viral hepatitis.
Methods: This was a prospective, cross sectional study, conducted over a period of 22 months (from January 2017 to October 2018). Demographic and clinical data including, full blood count, liver function tests, clotting profile and viral serology were recorded on designed proforma.
Results: Total 120 consecutive patients were enrolled in the study. Mean age of patients was 30.3 ± 11.5. Males were 68 (56.7%) and females were 52 (43.3%). The most common etiology was anti HEV in 83 patients (69.2%), followed by anti HAV in 23 patients (19.2%), anti HBcIgM and anti HCV in 10 patients (8.3%) respectively. Most common symptom was jaundice (99.2%), followed by anorexia (79.2%) and fatigue (70%). Most common risk factor was unboiled water (93.3%), followed by poor sanitation (74.2%) and barber shaving (25%). Overall prognosis is good with complete recovery in 85.8% cases.
Conclusions: The most common etiology of acute viral hepatitis in our setup was hepatitis E and A virus, attributable to unhygienic conditions.
Key words: Acute Viral Hepatitis, Hepatitis A, Hepatitis E.

Abstract #865

Epstein-Barr Virus (EBV) hepatitis masquerade as EBV-associated lymphoproliferative disease – A case report

Wei Lun Liou[1], Chee Leong Cheng[2], Ling Cao[3], Yu Jun Wong[4]

[1]Department of Gastroenterology and Hepatology, Changi General Hospital, [2]Department of Pathology, Singapore General Hospital, [3]Department of Haematology, Singapore General Hospital, [4]Department of Gastroenterology and Hepatology, Changi General Hospital

Epstein–Barr virus associated lymphoproliferative disorder (EBV-LPD) is a potential complication of chronic active EBV infection. Distinguishing EBV-LPD from acute EBV hepatitis is crucial because EBV-LPD can be life-threatening.

A 22-year-old female without significant past medical history presented with one week history of fever, myalgia and night sweat. She developed maculopapular rashes following a dose of Cefadroxil from primary physician. Physical examinations revealed presence of hepatomegaly, generalised lymphadenopathy, and maculopapular rashes. Initial laboratory investigations showed elevated bilirubin (32 μmol/L) and mixed pattern of deranged liver enzymes (ALP 302U/L, ALT 310U/L, AST 315U/L). Atypical lymphocytosis and monocytosis were seen on full blood count. EBV Virus capsid immunoglobulin-M and immunoglobulin-G antibody were positive. Human immunodeficiency virus and tuberculosis screening were negative. Computer tomography of abdomen and pelvis showed hepatosplenomegaly with cervical, axilla, intra-abdominal and inguinal lymphadenopathy. EBV-LPD was a concern because of worsening hyperbilirubinemia (bilirubin 69.5 μmol/L) with elevated beta-2-microglubilin and lactate dehydrogenase. To exclude LPD, the inguinal lymph node was biopsied. Histology revealed predominance of EBV positive cells being B-lymphocytes with relative preservation of nodal architecture, in keeping with infectious mononucleosis. Patient received supportive treatment and had spontaneous virological and clinical improvement.

EBV hepatitis can mimic LPD with fever, deranged liver function test, hepatosplenomegaly and generalized lymphadenopathy. While such florid presentation is uncommon, the chronicity of symptom could be helpful to distinguish EBV hepatitis from EBV-LPD, potentially avoiding unnecessary invasive investigations in these patients.

Abstract #982

Epstein-Barr virus infection-associated smooth-muscle tumor of the liver in a patient with aids, a case report

Marlon John Tejada Joson[1]

[1]Makati Medical Center

We report a case of smooth-muscle tumors of the liver in patients with acquired Immunodeficiency virus who initially presented as Hepatocellular Carcinoma based on imaging. A 36 y.o. male, known case of

HIV (on treatment) with CD4 count of 421 mm3 came in as a referral due to an incidental finding of a liver mass from an abdominal ultrasound. Abdominal computed tomography (CT scan) and other tests showed a mass in the liver consistent with hepatocellular carcinoma.

A CT scan guided liver biopsy with 30 needle passes done revealed spindle cell proliferation with smooth muscle differentiation. Immunohistochemical stains showed that the tumor was positive for SMA and focally positive for EBER, while negative for CD117, CD34 and desmin.

Immunochemical staining found the presence of smooth muscle actin and Epstein-Barr virus, supporting the diagnosis of Epstein-Barr virus associated with Smooth Muscle Tumor. Cancer markers showed negative results.

The number of reported cases of smooth muscle tumor (SMT) arising in patients with AIDS has been increasing since the mid-1990s. Based on articles, coinfection with Epstein-Barr Virus (EBV) appears to be a necessary cofactor for the development of these tumors. Human immunodeficiency virus–SMT, which accounts for the majority of the reported cases so far, is most frequently encountered in the central nervous system, gastrointestinal tract and liver, skin, and larynx/lungs/pharynx.

Therapeutic strategies target the tumor location as well as the etiology of immunosuppression. However, given the rarity and uncertain behavior of these tumors, no fixed approach has been described to treat these tumors.

Abstract #983

Molecular characterization of genotypic profile of hepatitis D virus in Libya

Abdel-Naser Elzouki[1], Saleh Muftah Bashir[2], Omer Elahmer[3]

[1]National Center for Diseases Control, [2]National Center for Diseases Control, [3]National Center for Diseases Control

Introduction: Hepatitis D virus (HDV) is a hepatotropic virus that is dependent on the hepatitis B virus (HBV) and supplies the viral envelope containing the surface antigen of hepatitis B. An estimated 15–20 million people are co-infected with HBV and HDV worldwide; with areas of high endemicity in the Middle East, and the Mediterranean region. Viral genetic diversity is related to the geographical origin of the isolates, and there are at least eight genotypes that are referred to as HDV-1 through HDV-8. Data on molecular characterization of HDV in Libya are lacking.
Objective: This study aims to assess the HDV genotypic of patients infected with HDV in Libya.
Methodology: HDV was genotyped by nested PCR–RFLP and sequencing from serum samples of 10 patients with HDV infection whom found to be positive in a cohort of 400 patients with hepatitis B infection. The genotypes were correlated with the clinical characteristics presented by patients with HBV/HDV infection.
Results: All HDV strains belonged to genotype 1, with a wide distribution within the HDV-1 group. They all share the African amino acid marker, a serine at position 202 of the large hepatitis D virus protein.
Conclusion: HDV genotype-1 is the only genotype found, with a high diversity within this group. Further studies are needed in order to better characterize and manage the HBV/HDV-infected patients according to the genetic variability of the viral strains.

Abstract #1061

Development and validation of a novel score system for liver failure in patients with hepatitis E virus infection

Jian Wu[1], Yan Ping Xu[2], Jiong Yu[3], Jun Liu[4], Hong Cui Cao[5]

[1]State Key Laboratory for The Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University; Collaborative Innovation Center for The Diagnosis and Treatment of Infectious Diseases, 79 Qingchun Rd., & Department of Laboratory Medicine, The First People's Hospital of Yancheng City, Yancheng 224005, Jiangsu, China; [2]State Key Laboratory for The Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University; Collaborative Innovation Center for The Diagnosis and Treatment of Infectious Diseases, 79 Qingchun Rd, [3]State Key Laboratory for The Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University; Collaborative Innovation Center for The Diagnosis and Treatment of Infectious Diseases, 79 Qingchun Rd.,, [4]Department of Laboratory Medicine, The Fifth People's Hospital of Wuxi, Affiliated To Jiangnan University, Wuxi214005, Jiangsu, China;, [5]State Key Laboratory for The Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University; Collaborative Innovation Center for The Diagnosis and Treatment of Infectious Diseases, 79 Qingchun Rd.

Background and Aims: Non-invasive assessment methods for liver failure in patients with hepatitis E virus (HEV) infection are urgently needed. The present study aimed to develop a novel diagnostic model for HEV-related liver failure patients (HEV-LF).
Methods: A cross-sectional set of 351 HEV-LF patients were identified and enrolled from 509 patients with liver failure. Guidelines for diagnosis and treatment of liver failure in China (GDTLF) were adopted as the reference diagnosis and staging of HEV-LF patients.
Results: The level of cholinesterase (CHE) decreased gradually with GDTLF score. While, the level of urea nitrogen (UREA) increased gradually with GDTLF score (both $P < 0.001$). HEV-LFS, a novel diagnosis model that incorporates data on CHE, UREA, platelets, international normalized ratio was developed using the deriving set. For the diagnosis of HEV-LF stage F1 to F3, the HEV-LFS model had significantly higher AUROC than did the CLIF-C-ACLFs and iMELD (both $P < 0$ 0.01), among which HEV-LFS model has the best sensitivity and specificity. The differences in HEV-LFS model were significant between GDTLF F1 to F3 ($P < 0.001$), while as CLIF-C-ACLFs and iMELD, the differences were not significant. Encouragingly, HEV-LFS model also performed better than CLIF-C-ACLFs and iMELD for previously treated and treatment-naive HEV patients. In addition, the HEV-LFS model was correlated with prothrombin time, albumin and total bilirubin. These results were validated by a validation set.
Conclusion: Both CHE and UREA may be indicators for HEV-LF patients. The HEV-LFS model is an efficient and accessible model for diagnosis HEV-LF.

Abstract #1074

Acute viral hepatitis in patients with diabetes mellitus and acute viral hepatitis: delayed recovery & increased hepatic decompensation

Harun Or Rashid[1], Abdul Alim[2], Md. Khalilur Rahman[3], Mahbubur Rahman Khan[4], Humaira Rashid[5], Tasnova Rashid[6], Mamun Al Mahtab[7]

[1]Hepatology Department Rajshahi Medical College, Rajshahi, [2]Department of Gastroenterology, Rajshahi Medical College, Rajshahi, Bangladesh, [3]Department of Medicine, Rajshahi Medical College, Rajshahi, Bangladesh, [4]Department of Medicine, Rajshahi Medical College, Rajshahi, Bangladesh, [5]Brac University, Dhaka, Bangladesh, [6]Department of Medicine, Medical College for Women & Hospital, Uttara-Dhaka, Bangladesh, [7]Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Background: Diabetes mellitus and acute viral hepatitis common in Bangladesh. AVH self-limiting disease, DM has long-term influence on different Organs. The study presented to assess if DM has any role on AVH.
Methods: This cross sectional study accomplished in Rajshahi Medical College Hospital, May 2010 to July 2013. Total 300 patients with AVH enrolled in this study into two groups; Group-A; patients of AVH with DM (N = 140) and Group-B; patients with AVH without DM (N = 160).
Result: The cause of AVH was hepatitis E virus in 100 of 140 patients (71%) in Group A, HEV was etiological factor in 112 of 160 patients (70%) of Group-B. The clinical course showed marked variation between two groups. Jaundice persisted for more than 6 months in 68 of 140 (49%). In Group B 149 of 160 Patients (93.12%) became jaundice free within 30 days, 11 of 160 patients (6.88%) jaundice persisted for 1 to 3 months. 42 patients (30%) of Group-A showed esophageal varices; Endoscopic assessment did not reveal any abnormality in Group-B.Mild to severe hepatic fibrosis seen in 26 of 140 patients (18.55%), not detected in Group-B. Important fact is that 4 patients (2.45%) of Group-A died of liver failure, there was no mortality in Group-B.
Conclusion: AVH is self-limiting condition. The study presented here reveals that presence of DM in AVH patients alters the clinical course. In conclusion, all patients with DM & AVH should be carefully followed up with possibility of development of severe liver disease and mortality.

Alcoholic Liver Disease

E01 - Experimental

Abstract #682

Faecalibacterium prausnitzii modulates gut microbiota and prevents ethanol-induced liver injury

Xianwan Jiang[1], Yating Li[2], Lanjuan Li[3]

[1]State Key Laboratory for Diagnosis and Treatment of Infectious Disease, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, [2]State Key Laboratory for Diagnosis and Treatment of Infectious Disease, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, [3]State Key Laboratory for Diagnosis and Treatment of Infectious Disease, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou

Background: Intestinal microbiota dysbiosis and intestinal inflammation contribute to the pathogenesis of alcoholic liver disease (ALD). Several studies have found that the abundance of an anti-inflammatory bacterium Faecalibacterium prausnitzii was obviously reduced in patients with ALD. The aim of the study was to evaluate the protective effect of F. prausnitzii administration on ethanol-induced liver injury.
Methods: Chronic and binge feeding model was used to study the protective effect of F. prausnitzii on alcoholic liver disease. Twenty-eight femal C57BL/6 mice were treated with F. prausnitzii or PBS by intragastric infusion once a day for ten days. Mice were fed a Lieber-DeCarli diet containing 5% ethanol or maltose for 10 days, and gavaged with either ethanol (5 g/kg body weight) or isocaloric maltose dextran at day 11 and euthanized 9 h later. Blood and tissue samples of liver and intestine were collected. Caecal stool was collected for 16S rRNA sequencing and gut microbiota analysis.
Result: F. prausnitzii administration resulted in alleviating hepatic injury, steatosis and neutrophil infiltration with significantly decreased the ALT levels and significantly decreased the expression of proinflammatory cytokines (TNF-α, IL-1β, IL-5, IL-6, MCP-1). F. prausnitzii restored gut microbiota and intestinal barrier function, with significantly increased the expression of tight junction proteins and decreased the endotoxin levels. The intestinal microbiome composition of F. prausnitzii group was significantly different from ethanol-fed group but with similar microbiota composition compared to pair-fed group.
Conclusion: Our findings suggest that F. prausnitzii administration restores the microbiota balance and protects against ethanol-induced liver injury.

Abstract #784

Hyperoxidized albumin promotes platelet activation induces oxidative stress and systemic inflammation in severe alcoholic hepatitis

Adil Rafiq Bhat[1], Sukanta Das[1], Gaurav Yadav[1], Sudrishti Chaudhary[1], Mojahidul Islam[1], Ashish Kumar Vyas[1], Renu Goel[1], Meenu Bajpai[1], Rakhi Maiwall[1], Jaswinder Singh Maras[1], Shiv Kumar Sarin[1]

[1]Institute of Liver and Biliary Sciences

Introduction: Hyperoxidized albumin promotes inflammation in severe alcoholic hepatitis (SAH). However its contribution in platelet activation, alteration of platelet phenotype and linked functions is yet not known. Objective: We investigated the platelet proteome and the ability of oxidized albumin to induce platelet activation in SAH patients.
Method: Fifty SAH patients, 20 alcoholic cirrhosis (AC) and 20 healthy controls (HC) were studied. Quantitative platelet proteomics done in the derivative cohort was confirmed in the validation cohort (n = 40). Causality of platelet activation/dysfunction was determined by in vitro treatment of healthy platelets with patient plasma, purified albumin from the study groups or ex vivo modified albumin (human mercaptalbumin-HMA, human nonmercaptalbumin-HNA1 and HNA2) in the presence or absence of CD36 (receptor for oxidised albumin) blockade.
Results: Upregulated proteins (n = 202) were linked to platelet activation, complement regulation and lipid transportation whereas downregulated proteins (n = 321) related to platelet hemostasis and coagulation (fold change ± 1.5, $p < 0.01$). Validation studies confirmed increase in platelet-activation markers (PAC-1, P-selectin), intracellular-Ca2 + and aggregation in SAH patients ($p < 0.05$). Gene expression linked to platelet activation ($r2 > 0.3$) and granular

secretions ($r2 > -0.3$, $p < 0.05$) correlated with the disease severity. In-vitro stimulation of healthy platelets showed enhanced activation under patient plasma or purified albumin treatment. Blocking of CD36 blunted this effect ($p < 0.05$). Ex-vivo modified albumin (mainly HNA2-1 mg/mL) showed markedly high activation/aggregation and intracellular ROS production in healthy platelets ($p < 0.05$), which significantly got reduced under CD36 neutralization.

Conclusion: Hyperoxidized albumin triggers platelet activation potentially through CD-36 receptor; promotes inflammation, oxidative-stress and may contribute to thrombotic events in SAH patients.

E02 - Clinical

Abstract #134

Significance of serum interleukin-6 for mortality prognosis in patients with acute alcoholic hepatitis

Pavel Petrovich Ogurtsov[1], Nataliya Vladimirovna Mazurchik[2], Anastasiya Sergeevna Zhuravleva[3], Olga Ivanovna Tarasova[4]

[1]Peoples Friendship University of Russia (Rudn University), [2]Peoples Friendship University of Russia (Rudn University), [3]Peoples Friendship University of Russia (Rudn University), [4]Peoples Friendship University of Russia (Rudn University)

Acute alcoholic hepatitis (AAH) is sever variant of alcoholic liver disease, often occurs fulminant and may be the cause of death of many patients—28-day mortality in severe AAH is more than 60%.

In addition to the direct cytotoxic effect, alcohol causes a cascade reaction of synthesis in the liver of a large number of biologically active substances—cytokines, one of which is interleukin-6 (IL-6). Even if the regime of absolute abstinence is observed, the immune inflammatory reaction continues, which leads to fibrosis, progression to cirrhosis of the liver, accompanied by a violation of its synthetic function with the development of lethal complications. According to numerous studies, the role of determination of interleukin-6 (IL-6) in the serum of patients with AAH seems to be unclear.

Methods: Our study included 98 patients with AAH. The level of IL-6 was studied by solid-phase non-competitive enzyme immunoassay ("sandwich method"), test system of the company eBioscience (Austria) before the therapy. The average values of IL-6 from 15 healthy volunteers (IL-6 = 0 PG/ml) were taken as " control". Patients with non-alcoholic and mixed etiology of liver damage, infectious diseases, with severe cardiac diseases, diabetes, obesity, with suspicion of cancer were excluded.

Results: The level of IL-6 was 15.67 ± 1.90 (median 11.2) PG/ml in survivors, which was significantly lower than the level of IL-6 in patients who died during hospitalization 42.26 ± 12.60 (median 27.10) PG/ml, $p = 0.004$.

Conclusion: High baseline serum IL-6 levels is a predictor of in-hospital mortality in patients with AAH.

Abstract #153

Biochemical and histological features of patients with alcoholic liver disease

Le Thi Thu Hien[1]

[1]Thai Nguyen University of Medicine and Pharmacy & Thai Nguyen University of Medicine and Pharmacy & Thai Nguyen University of Medicine and Pharmacy

Background: Alcohol-attributable burden on global health is increasing, and the relationship between population alcohol consumption and liver-related deaths is strong. Longstanding scientific and clinical work has led to a relatively thorough, if not complete, understanding of the effects of alcohol consumption on the liver. Some biochemical indications in blood and histological features of alcoholic liver disease (ALD) are used to assist clinicians in diagnosing and determining severity of disease in patients with ALD.

Aims: This study intends to describe in detail biochemical and histological features of patients with ALD.

Subjects and Methods: Liver biopsy was required for the diagnosis of histologic ALD. A total of 95 patients with ALD were included in the study. Evaluate the stage of liver fibrosis according to Metavir classification (F0, F1, F2, F3, F4). Clinical and laboratory parameters were recorded.

Results: Age group 45–59 accounts for the highest proportion (50.5%). Patients with decreasing serum albumin (51.6%), increasing glucose (56.8%), increasing AST < 400 U/L, ALT increasing < 200 U/L (66.3%), GGT increasing (97.9%). Fatty liver (69.5%), moderate fatty liver (42.1%), fatty liver at zone 1(95.8%). F2 stage liver fibrosis accounted for 26.3%, F3 accounted for 25.3% and F1 accounted for 21.1%. Severe liver fibrosis (F2-F3) accounts for 51.6%. Degeneration foam (84.2%), mitochondria giant (62.1%), Mallory (64.2%) are common histopathological features.

Conclusions: The patients had salient points on histological features of ALD such as foamy degeneration, megamitochondria, Mallory body, fatty liver, fibrosis liver. Tissue histology not only yields diagnostic information but also important information about prognosis.

Abstract #234

Relationship between antioxidants and alcoholic liver disease

Le Thi Hoang Yen[1], Le Thi Thu Hien[2]

[1]Thai Nguyen Natinal Hospital, [2]Thai Nguyen University of Medicine and Pharmacy & Thai Nguyen University of Medicine and Pharmacy

Background: Alcoholic liver disease (ALD) is associated with a spectrum of liver injury ranging from steatosis and steatohepatitis to fibrosis and cirrhosis. Many studies have shown that ethanol consumption may result in increased oxidative stress with increased free radicals, one of the key factors in the various aspects of pathophysiology of ALD.

Aims: To investigate the antioxidative status of patients with alcoholic liver disease.

Methods: This study was conducted in Thai Nguyen Nation Hospital and 103 Military Hospital, located in northeast Vietnam (from January 2015 to June 2017). Liver biopsy was required for the diagnosis of histologic ALD. Total antioxidant status (TAS), superoxide dismutase (SOD), glutathione peroxidase (GPx) were measured in 83 cases of ALD and 35 healthy volunteers which was regarded as the control group. Using ELISA kit supplied by Wkea Med Supplies Corp, China. Evaluate the stage of liver fibrosis according to Metavir classification (F0, F1, F2, F3, F4).

Results: There was a statistically significant decrease in the plasma SOD, GPx, TAS in patients with alcoholic liver disease as compared to controls. Levels of serum SOD is associated with liver fibrosis stage ($p < 0.05$). Levels of serum TAS is associated with Chigh-Pugh score ($p < 0.05$).

Conclusions: The results of our study suggests that there was higher oxygen free radical production, supporting the hypothesis that there is increased oxidative stress in patients with ALD. These antioxidants are able to use in clinical medicine as biomarkers on prognosis ALD.

Abstract #240

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Le Thi Hoang Yen[1], Le Thi Thu Hien[2]

[1]Thai Nguyen Natinal Hospital, [2]Thai Nguyen University Medicine and Pharmacy

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Conclusions: The results of our study suggests that there was higher oxygen free radical production, supporting the hypothesis that there is increased oxidative stress in patients with ALD. These antioxidants are able to use in clinical medicine as biomarkers on prognosis ALD.

Abstract #455

The impact of previous acute decompensation on long-term prognosis according to the severity of alcoholic hepatitis in cirrhotic patients

Eileen L. Yoon[1], Tae Yeob Kim[2], Do Seon Song[3], Jin Mo Yang[4], Hee Yeon Kim[5], Chang Wook Kim[6], Young Kul Jung[7], Hyung Joon Yim[8], Soung Won Jeong[9], Sang Gyune Kim[10], Jae Young Jang[11], Moon Young Kim[12], Dong Hyun Sinn[13], Ki Tae Suk[14], Dong Joon Kim[15]

[1]Inje University College of Medicine, [2]Leeheart Medical Clinic, [3]The Catholic University of Korea, [4]The Catholic University of Korea, [5]The Catholic University of Korea, [6]The Catholic University of Korea, [7]Korea University, [8]Korea University, [9]Soonchunhyang University, [10]Soonchunhyang University, [11]Soonchunhyang University, [12]Wonju College of Medicine, Yonsei University, [13]Samsung Medical Center, [14]Hallym University College of Medicine, [15]Hallym University College of Medicine

Background/Aims: To investigate long-term mortality according to severity of alcoholic hepatitis and the presence of previous acute decompensation (AD) in alcoholic cirrhotic patients with acute deterioration.
Methods: A total of 894 alcoholic cirrhotic patients (male 747, mean age 53.1 years) with acute deterioration were prospectively followed-up. Enrolled patients were divided into 3 groups according to the presence and severity of AH; group1, alcoholic cirrhosis without AH; group2, alcoholic cirrhosis with non-SAH; group3, alcoholic cirrhosis with SAH. AD was defined as: acute development of overt ascites, hepatic encephalopathy, gastrointestinal bleeding, and infection.
Results: During follow-up duration (14.3 ± 10.7 months), long-term mortality were higher in patients with group 3 than those in group 1 and 2, but there was no significant difference between group 1 and 2 (group 1, 160/596; group 2, 27/141; group 3, 76/157, $P < 0.001$). Also, in 671 patients who survived for more than 3 months following acute deterioration (long-term survivors), long-term survival curve between groups showed a similar pattern ($P = 0.004$). Interestingly, in group 1, the presence of previous AD negatively affected long-term survival in total and long-term survivors ($P < 0.001$ and $P = 0.004$, respectively). However, in group 3, previous AD negatively affected long-term survival in long-term survivors ($P = 0.009$), but not in total patients (figure 1). Especially in long-term survivors of group 3, previous AD showed hazard ratio of 2.47 (95% confidence interval, 1.16–5.28, $P = 0.019$).
Conclusions: In patients with acute deterioration except for AH and SAH patients overcoming acute deterioration, the presence of previous AD had a great impact on long-term prognosis.

Abstract #543

Prevalence and associated factors of fatty liver disease: a large-scale cross-sectional study

Rebecca Jen-Ling Hsieh[1], Claire Huang[2], Yu-Ju Lin[3], Yu-Han Huang[4], Chi Chan[5], Mei-Hsuan Lee[6]

[1]Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan, [2]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan & Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan, [3]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan & Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan, [4]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan & Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan, [5]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan & Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan, [6]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan & Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan

Introduction and Objectives: Fatty liver is an increasing health issue. The study aimed to investigate the prevalence and the associated factors of fatty liver among adults.
Methodology: A cross-sectional study included 102,938 adults ($\geq$ 30 years old) who participated in a health examination between 2008 and 2013, with the exclusion of HBV-infected individuals. Demographic data, life styles, and previous history of diseases were collected via a structured questionnaire. Anthropometric measurements and biochemical testing were examined for the participants. Fatty livers were defined using the fatty liver index (FLI), a simple algorithm incorporating waist circumference, body mass index, triglyceride and gamma-glutamyl transferase levels. The definition of fatty liver was FLI $\geq$ 35 for males and $\geq$ 20 for females. Multiple logistic regressions were performed to estimate the odds ratios (ORs) and 95% confidence intervals (95% CIs) for associated factors and fatty liver.
Results: The prevalence rate of the total population is 30.36%. Old age, cigarette smoking, alcohol consumption, history of CVD, hypertension were significantly associated with fatty liver ($p < 0.05$). Elevated serum ALT ($\geqq$45 vs. $<$ 45 IU/L) and AST ($\geqq$35 vs. $<$ 35 IU/L) levels were positively associated with fatty liver, with the adjusted OR of 5.69 (5.32–6.10) and 1.84 (1.69–2.01), respectively. Individuals with fasting glucose $\geqq$126 mg/dL had 2.9 (2.66–3.16)

times likelihood to have fatty liver. The adjusted OR was 2.02 and 4.62 for cholesterol level 125–200 and ≧200 mg/dL, respectively, by using < 125 as a reference group.
Conclusions: Individuals with fatty liver associated factors have to be educated for life-style modifications.

Abstract #798

Systemic inflammatory response predicts multiorgan failure and mortality in severe alcoholic hepatitis

Neeraj V[1], Krishnadas Devadas[1], Sandesh K[1], Jose Mathew[1], Manoj Yadav[1], Atul Hareendran[1], Jijo Varghese[1]

[1]Department of Medical Gastroenterology, Government Medical College, Thiruvananthapuram

Background and Aims: Severe alcoholic hepatitis(SAH) (DF ≥ 32) has a 30d mortality of 30–40%. We cannot predict which of these patients are going for multiorgan failure(MOF) or 30d mortality. Since most of them have upregulated cytokine levels, we hypothesize that presence of SIRS could predict MOF and mortality in these patients.
Aims: 1. Estimate predictive accuracy of Day1 SIRS in determining MOF in patients with SAH.
2. Estimate predictive accuracy of Day1 SIRS in determining the 30 day mortality in patients with SAH.
Method: Prospective study.
Exclusion criteria: Patients with HCC, sepsis, hepatitis

Day 1 SIRS score taken and followed up for 1 m to look for MOF and mortality. Sensitivity, specificity of SIRS, graded severity of SIRS with 30d mortality and MOF was calculated.
Results: Total of 133 patients with SAH were included. 94 had D1 SIRS, 50 had 30d mortality, 54 patients had MOF. All MOF and 30d mortality had D1 SIRS.
D1 scores of SIRS(3 and 4) were found to predict the development of MOF and 30d mortality a higher specificity of 92% and 87% respectively.
Conclusions: 1. D1 SIRS can be used to predict development of multiorgan failure and 30d mortality in patients with SAH with high sensitivity and lower specificity.
2. However, higher D1 scores of SIRS were found to have higher sensitivity and specificity in predicting the development of MOF and 30d mortality.

D1 SIRS can be used as a screening tool to stratify patients with SAH and facilitate early referral reducing adverse outcomes.

Abstract #1049

DLQI and Impact of comorbidity among chronic alcoholic liver diseases in developing countries

Shambhu D Joshi[1]

[1]Far Western Community Hospital

Methods: The retrospective data study with CALD 91 patients: 51 men(82.4%) and 40 wo- men(17.6%), aged 75 to 93 yrs(mean age 80 yrs). The Dermatology Life Quality Index (DLQI), WHO ICD-10 codes, Hospital Anxiety A), Depression(D) Scale(HADS) was taken for validation. Cases were evaluated with clinical, Lab wherever needed.
Results: Skin disorders like Fungal diseases(n = 6), benign skin tumors and xerosis (seborrhoeic keratosis, papilloma) in 90% of cases; rosacea (n = 2); herpes zoster(n = 7); eczema(n = 22); seborrheic dermatitis(n = 24); recurrent chronic urticaria(n = 9), allergic contact dermatitis(ACD) (n = 7), dyshidrotic eczema on the hands(n = 14). Systemic disorders as cardiovascular disorders (n = 11), Endocrine disorders(n = 10) urogenital(n = 20): GI(n = 27), neurological disorders(n = 15) pulmonary disorders (n = 3), rheumatoid arthritis (n = 3), others (n = 2). In this study for HADS, the anxiety level(A) was from 2 to 16 points (mean = 6.94). Depression level (D) from 2 to 20 points (mean = 7.35). Cardiovascular disorders A:D = 11.2:9 Endocrine disordersA:D = 10:6.2, urogenital disorders A:D = 7.2:9.2, GI disorders A:D = 7.3:5:3, neurological disorders A:D = 11:6.3, pulmonary disorders A:D = 5.6:2.3, rheumatoid arthritis A:D = 7.3:5.2, Skin disorders A:D = 6.3:7.1. Stigma and discrimination about the social security and marriage of their off springs.
Conclusions: In this study, Both having subclinical levels of anxiety and depression. Patients are more anxious with Skin disorders, pulmonary and rheumatic disorders than depression in neurological, urogenital and GI disorders. Marriage, fear of rejection by neighbor, and the need to hide the fact from others were some of the more stigmatizing aspects. Many caregivers reported feelings of depression and sorrow. The relevance of stigma in the cultural context is increasing due to illiteracy, poverty, superstition and lack of awareness.

Autoimmune and Cholestatic Disease

F01 - Autoimmune hepatitis

Abstract #192

NUDT15 polymorphisms confer increased susceptibility to thiopurine-induced leukopenian in patients with autoimmune hepatitis and related cirrhosis

Xiaoli Fan[1], Dandan Yin[2], Ruoting Men[3], Heng Xu[4], Li Yang[5]

[1]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, Chengdu, China, [2]Department of Laboratory Medicine, National Key Laboratory of Biotherapy/ Collaborative Innovation Center of Biotherapy and Precision Medicine Key Laboratory of Sichuan Province, West China Hospital, Sichuan University, Chengdu, Sichuan, China, [3]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, Chengdu, China, [4]Department of Laboratory Medicine, National Key Laboratory of Biotherapy/Collaborative Innovation Center of Biotherapy and Precision Medicine Key Laboratory of Sichuan Province, West China Hospital, Sichuan University, Chengdu, Sichuan, China, [5]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, Chengdu, China

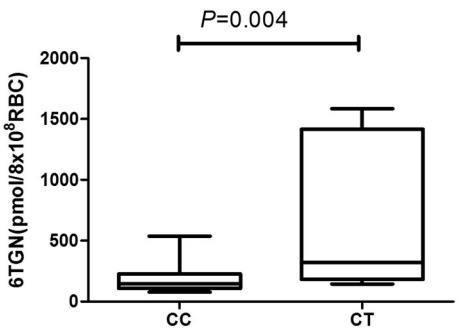
Background: The aim of this study was to investigate the influence of NUDT15 R139C and thiopurine S-methyltransferase (TPMT) on azathioprine (AZA) induced leukopenia in in patients with autoimmune hepatitis and related cirrhosis.
Methods: A total of 149 Chinese AIH patients with a history of azathioprine treatment were retrospectively evaluated. The clinical and epidemiological characteristics of the patients were obtained from an electronic database and reviewed. NUDT15 (rs116855232) and TPMT*3C (rs1142345) SNPs were genotyped using a real-time PCR method.
Results: 12 patients developed leukopenia, and this adverse drug reaction was significantly associated with the T risk allele in NUDT15 (P < 0.00001, odds ratio = 20.41; 95% confidence interval (7.84,

53.13)), with the sensitivity and specificity of 91.67% and 89.05%, respectively. The median maintenance dosages for patients with the rs116855232 CC and CT genotypes were 1.23 (0.95, 1.53) mg kg^{-1} day^{-1} and 0.96 (0.83, 1.19) mg kg^{-1} day^{-1}, respectively (P = 0.028). In contrast, no significant association was observed for TPMT*3C genotypes. Notably, subgroup analysis of the 13 patients with leukopenia before therapy (12/13 of these patients were NUDT15 wild-type homozygotes), these white blood cell counts did not show further reduction after azathioprine treatment and maintenance dosage was 1.13 (0.94, 1.60) mg kg^{-1} day^{-1}.

Conclusion: NUDT15 polymorphisms are significantly associated with thiopurine-induced leukopenia in Chinese patients with AIH and related cirrhosis, and adjusting the azathioprine dosage should be considered in patients according to the NUDT15 R139C genotypes.

Table1.

Clinical Features	With leukopenia(N=12)	Without leukopenia(N=137)	*P*
Age, y	49.0(46.0, 63.5)	52.0(44.0, 58.5)	0.997
Female	10(83.3%)	119(86.9%)	>0.999
TBil, umol/L	29.8(19.4, 55.0)	29.6(14.5, 52.2)	0.807
ALT, IU/L	142.0(42.5, 181.3)	101.0(48.0, 189.5)	0.976
AST, IU/L	137.0(48.3, 208.0)	98.0(44.0, 180.0)	0.577
ALB, g/L	39.3(33.5, 40.9)	39.6(35.1, 42.8)	0.463
GLB, g/L	42.0(34.6, 47.2)	37.0(31.9, 42.6)	0.083
ALP, IU/L	139.0(93.5, 230.5)	154.9(98.5, 267.5)	0.867
GGT, IU/L	124.5(37.0, 231.8)	137.0(66.0, 301.5)	0.330
IGG, IU/L	24.0(17.1, 29.6)	18.3(15.3, 25.3)	0.244
IGM, IU/L	2.5(1.8, 3.6)	2.3(1.5, 3.7)	0.861
Decompensated cirrhosis (n, %)	5(41.6%)	29(21.2%)	0.157
Splenomegaly (n, %)	6(50.0%)	44(32.1%)	0.348
WBC at diagnosis, $x10^9$/L	5.1(4.0, 5.9)	5.0(3.9, 6.4)	0.947
AIH/AIH-PBC	6/6	73/64	0.827
rs116855232 CC/CT/TT	1/9/2	122/15/0	<0.001
rs1142345 TT/TC/CC	11/1/0	134/2/1	0.283



Abstract #393

Macrophages contribute to the pathogenesis of autoimmune hepatitis through modulating the activation of NF-κB signaling pathway

Ting Ting Wang[1], Ruo Ting Men[2], Xiao Li Fan[3], Ting Hong Ye[4], Li Yang[5]

[1]Division of Gastroenterology & Hepatology, West China Hospital, Sichuan University, Chengdu, China, [2]Division of Gastroenterology & Hepatology, West China Hospital, Sichuan University, Chengdu, China, [3]Division of Gastroenterology & Hepatology, West China Hospital, Sichuan University, Chengdu, China, [4]Laboratory of Liver Surgery, West China Hospital, Sichuan University, Chengdu, China, [5]Division of Gastroenterology & Hepatology, West China Hospital, Sichuan University, Chengdu, China

Backgrounds: Autoimmune hepatitis (AIH) is an orphan disease characterized by an autoimmune attack against hepatocytes with incompletely understood pathogenesis. Macrophages are among the first immune cells responding to liver injury and the key regulators of the inflammatory responses. However, their role in AIH remains unclear.

Objectives: The aim of this study was to test the hypothesis that macrophages contribute to the pathogenesis of AIH.

Methodology: Liver tissues and peripheral blood from AIH patients and ConA-induced mouse models of AIH were collected to evaluate the percentage of macrophages by immunohistology, flow cytometry. RAW264.7 macrophages and murine bone marrow-derived macrophages (BMDMs) were used to study the regulation of NF-κB signaling on inflammatory responses of macrophages in AIH.

Results: Compared to normal controls, the percentage of macrophages in the peripheral blood of AIH patients(CD163 + CD206 +) and the AIH mouse models(CD11b + F4/80high) both significantly increased. Furthermore, the accumulation of CD68 + macrophages were more pronounced in the liver of AIH patients and mouse models than normal controls. Stimulation of Raw 264.7 macrophages and BMDMs with ConA upregulated the percentage of CD11b + F4/80 + CD206 + macrophages. Moreover, NF-κB signaling was activated by ConA in RAW264.7 macrophages and BMDMs, which was manifested as the protein levels of P-P65 increased and IKBα decreased. Notably, BAY11-7082, the specific inhibitor of the NF-κB signaling pathway, and Methylprednisolone, the effective therapeutic drugs for AIH, predominantly weakened the inflammatory reaction caused by the increase and activation of macrophages.

Conclusion: Taken together, our data indicate that macrophages may contribute to AIH pathogenesis through NF-κB pathways.

Abstract #490

Long-term clinical outcomes in patients with autoimmune hepatitis according to treatment response in Asian country

Kang Mo Kim[1], Jonggi Choi[1], Gwang Hyun Choi[1], Danbi Lee[1], Ju Hyun Shim[1], Young-Suk Lim[1], Han Chu Lee[1], Young-Hwa Chung[1], Yung-Sang Lee[1]

[1]Department of Gastroenterology, Asan Medical Center & University of Ulsan College of Medicine

Introduction: Long-term prognosis of autoimmune hepatitis (AIH) patients who achieved complete biochemical remission (CBR) in comparison with the patients who achieved only biochemical remission (BR) is uncertain.

Methodology: A total of 291 patients (89.7% female) diagnosed with AIH were retrospectively evaluated by reviewing electronic medical records in a single Asian center. According to International Autoimmune Hepatitis Group revised criteria, 200 (68.7%) and 91 (31.3%) patients met criteria for definite and probable AIH, respectively. BR was defined as normal serum alanine aminotransferase (ALT) levels after starting treatment, while CBR was defined as normal serum ALT and immunoglobulin G (IgG) levels. Liver-related outcomes included liver-related death, liver transplantation, and development of hepatocellular carcinoma.
Results: With immunosuppressive treatment, 168 (57.7%) patients achieved CBR, 87 (29.9%) achieved only BR, and 36 (12.4%) did not achieve remission within 1 year after starting treatment. During a median follow-up period of 6.6 years (range: 0.6–21.2 years), the annual incidence of liver-related mortality was lower in patients with CBR (0.25/100 person-years [PY]) than in patients with BR (0.72/100 PY), although this difference was not statistically significant. Twenty-seven liver-related adverse outcomes occurred. The annual incidence of liver-related adverse outcomes was significantly higher in patients with BR than with CBR (2.06/100 PY vs 0.58/100 PY, P = 0.003).
Conclusions: Patients who achieved CBR had a lower risk of liver-related adverse outcomes than the patients who only achieved BR, suggesting that CBR is a more reliable surrogate marker to reflect long-term clinical outcomes in AIH patients.

Abstract #534

Case of two lupus patients with autoimmune hepatitis

Carlos Paolo Dimatatac Francisco[1], Katrina Joy Camarillo Chua[2], Juan Javier Tayengco Lichauco[3]

[1]Department of Medicine-St. Luke's Medical Center, Quezon City, Philippines, [2]Section of Rheumatology-St. Luke's Medical Center, Quezon City, Philippines, [3]Section of Rheumatology-St. Luke's Medical Center, Quezon City, Philippines

Background: Abnormalities in liver function tests was observed in as many as 60% of patients with SLE.1 Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease associated with circulating autoantibodies and hypergammaglobulinemia. The co-occurrence of AIH and SLE is considered to be rare. They have shown overlapping features such as female preponderance, polyarthralgia, hypergammaglobulinemia, and positive anti-nuclear antibodies, anti-SMA, and anti-ribonucleoprotein.5 Liver biopsy is necessary to differentiate between the two since complications and therapy are different.
Case Description: An 18-year-old female with SLE, presented suddenly with jaundice associated with pruritus, tea-colored urine, right upper quadrant pain, and flu-like symptoms. Liver function test showed mixed hepatocellular-cholestatic injury. A 35-year-old female, presenting with hair loss, polyarthritis, and pancytopenia newly diagnosed with SLE. Further work-up showed elevated liver transaminases.
Management: Lupus hepatitis versus AIH was considered in both cases. Anti-smooth muscle antibody (anti-SMA), anti-liver kidney microsome 1 (anti-LKM 1), anti-mitochondrial antibody (AMA), and serum IgG were requested. Both presented with elevated serum IgG. Percutaneous liver biopsy showed severe interface hepatitis and bridging fibrosis. Hepatocyte rosettes and lymphocytic infiltration were also noted in both cases.
Conclusion: Serological tests for AIH are helpful; however, liver biopsy is necessary to establish a definite diagnosis with interface hepatitis as the hallmark of AIH. The Revised Original Scoring System for the diagnosis of AIH can be used as an objective measure for establishing a diagnosis. Successful treatment involves targeting both diseases with glucocorticoids, hydroxychloroquine, and azathioprine. Untreated AIH carries a poor prognosis; prompting identification and adequate treatment necessary.

Abstract #544

Autoimmune hepatitis mimicking drug-induced liver injury: a case report and review of the literature

Dong Bo Wu[1], Wei Jiang[2], En Qiang Chen[3], Hong Tang[4], Tao You Zhou[5]

[1]Center of Infectious Diseases, West China Hospital, Sichuan University, [2]Center of Infectious Diseases, West China Hospital, Sichuan University, [3]Center of Infectious Diseases, West China Hospital, Sichuan University, [4]Center of Infectious Diseases, West China Hospital, Sichuan University, [5]Center of Infectious Diseases, West China Hospital, Sichuan University

Autoimmune hepatitis (AIH) is an unresolved progressive liver disease with an unknown etiology that leads to the loss of tolerance to hepatocyte-specific autoantigens, and it is characterized by immune dysfunction and autoimmune attack in genetically susceptible individuals, which ultimately results in chronic persistent inflammation of the liver surface parenchyma. However, AIH is often misdiagnosed as drug-induced liver injury (DILI) in the clinical setting. A 50-year-old woman was admitted to our hospital thrice for repeated abnormal liver function test results. However, after multiple etiological examinations and expectant treatments, the diagnosis remained unclear, and her liver function was repeatedly abnormal. After three admissions and many follow-ups, based on her liver histological characteristics, she was eventually diagnosed with AIH. When a patient has unexplained abnormal liver function, while evaluating the clinical data and previous medical history, clinicians should consider the possibility of AIH and actively perform liver biopsy.

Abstract #634

The worldwide incidence and prevalence of autoimmune hepatitis: a systematic review and meta-analysis

Tingting Lv[1], Na Zeng[2], Jingqi Zhang[3], Jidong Jia[4]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China, [2]Clinical Epidemiology and Ebm Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, 100050, [3]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China., [4]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China

Objective: The incidence and prevalence rate of autoimmune hepatitis (AIH) have been sparse, with results that do not always agree. So our aim was to investigate the current epidemiology characteristics of AIH worldwide, helping to establish confidential epidemiological data.
Methods: Published articles about the epidemiology of AIH (up to April 2nd, 2018) in PubMed, EMBASE, and Cochrane Library have been systematically searched. A limited hand search of the references was also done. Two investigators independently screened these literatures according to the criteria and evaluated them for study quality. Inverse-variance random-effects method in Stata14.0 software has been used to summarize incidence and prevalence. Potential factors, such as sex, age, publication year, geographical distribution and study design, which may affect the heterogeneity, were furtherly discussed by meta regression and subgroup analysis.

Findings: 18 studies were eventually retrieved and the pooled worldwide incidence and prevalence of AIH was 1.42 (95% CI: 0.93–1.91) and 16.17 (95% CI: 11.19–21.24) per 100,000 persons. Among them, the pooled annual incidence for Asia, Europe and America were 1.31 (95% CI: 0.42–2.20), 1.38 (95% CI: 1.08–1.67) and 1.53 (95% CI: − 1.07 to 4.13) per 100,000 persons respectively. And the prevalence in Asia was low with 7.8 (95% CI: 4.63–10.96), compared with that in Europe with 19.3 (95% CI: 15.92–22.68) and in America with 22.80 (95% CI: − 13.48 to 59.07) per 100,000 persons.
Conclusion: AIH is more common than previously thought and the prevalence rate of AIH was lower in Asia–Pacific area. More nationwide epidemiology investigations of AIH are still necessary for confirm conclusion.

Abstract #635

Post-operative jaundice as an unusual presentation of autoimmune hepatitis overlap syndrome: a case report

Enrik John Torres Aguila[1], Juliet Lingat Gopez-Cervantes[2]

[1]St. Luke's Medical Center Global City, [2]St. Luke's Medical Center Global City

Introduction: Jaundice following an abdominal surgery has an incidence of less than 1% but may increase among critically ill patients. 25–75% of patients have abnormal postoperative liver function tests, and 47% of cirrhotic patients develop jaundice after general anesthesia. It is usually evident within the first week and is of multifactorial cause.
Methodology: This is a case of a 52-year-old, male, Filipino who was initially managed as gallbladder hydrops presenting with abdominal pain. Work-ups revealed elevated transaminases and bilirubins. He had an endoscopic ultrasound which was unremarkable. He underwent laparoscopic cholecystectomy and was discharged stable. 5 days post-operatively, he noted deepening jaundice. An ERCP done showed unremarkable results ruling out retained stone and leaks. Work-up for autoimmune hepatitis (AIH) showed elevated serum IgG level and positive anti-SMA at 1:40. Liver biopsy revealed interface hepatitis with a Knodell 14 and Metavir activity A3. Using the International Autoimmune Hepatitis Group Scoring System, patient had a score of 7 which is definitive of the diagnosis of autoimmune hepatitis. Overlap syndrome with PBC was considered due to the positive AMA result.
Results: Patient was started on Prednisone and Ursodeoxycholic acid and on follow-up, there was noted significant improvement in his bilirubin levels within a 6-week treatment from a baseline of 24.61.
Conclusion: When in a diagnostic dilemma, the pattern of liver chemistry tests would lead to the proper subsequent diagnostic and treatment approach. High clinical suspicion and early detection of AIH is key, as early and effective treatment is associated with better patient outcomes.

Abstract #662

Serum cholesterol levels is associated with response to ursodeoxycholic acid in primary biliary cholangitis

Zhichao Hu[1], Ping Ni[2], Xiaoli Fan[3], Ruoting Men[4]

[1]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, [2]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, [3]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, [4]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University

Introduction: Patients with primary biliary cholangitis (PBC) often present hypercholesterolemia. Increasing evidence suggests another role of serum cholesterol levels in various autoimmune and liver diseases.
Objective: To investigate the clinical relevance of serum cholesterol levels in PBC, especially their association with the therapeutic effects of ursodeoxycholic acid (UDCA).
Methodology: Consecutive PBC patients were retrospectively reviewed. serum cholesterol levels were determined initiation of UDCA treatment. Response to UDCA was evaluated by Paris-II. Logistic regressions were performed to identify the treatment response-associated parameters.
Results: Among 272 patients, the mean serum cholesterol level concentration was 5.04 ± 2.5 mmol/L.100 patients failed to achieve complete response according to Paris-II criteria after 1 year of UDCA therapy. The baseline serum cholesterol level was significantly lower in nonresponders($P = 0.005$). hypercholesterolemia at baseline was associated with an increased risk of incomplete response independent of advanced stages (OR = 3.85, 95% CI = 1.01–14.08, $p = 0.045$) .
Conclusions: Serum cholesterol level is associated with biochemical features in PBC. Pre-treatment cholesterol status is independently related to subsequent response to UDCA. Our results suggest that serum cholesterol level may have important clinical significance in PBC.

Abstract #837

Serological, clinical and histologic features of autoimmune liver disease "A case series"

Anoshia Fahad[1], Nazish Butt[2]

[1]Jinnah Post Graduate Medical Centre, [2]Jinnah Post Graduate Medical Centre & Agha Khan Hospital

Background: Autoimmune liver disease (ALD) is a rare spectrum comprising of autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC). The incidence of the ALD is around 1–2 per 100,000 population/year and the prevalence is estimated to range from 50–200 cases per million in western Europe and North America. Till today, the etiology is unknown and there is wide heterogeneity in clinical, laboratory and histological presentations.
Aim: To evaluate the epidemiological, serological and histological features in patients presenting with autoimmune liver disease.
Methods: It was a cross-sectional case series of 15 patients which were enrolled in study from January 2017 to June 2018 presenting at Jinnah Postgraduate Medical Center, Karachi. Demographic and clinical data including liver function tests, autoimmune serology and liver histology were recorded on designed proforma.
Results: Mean age was 26.4 ± 9 years. Females were 11 (73.3%) and males were 4 (26.7%). Type I AIH was present in 12 (80%), Type II AIH in 2 (13.3%) and AIH/PBC overlap in 1 (6.7%) patient respectively. ANA was positive in 53.3%, ASMA in 26.7%, anti LKM-1 in 13.3% and AMA in 6.7% patients. Steroid and azathioprine was given in 12 patients while 3 patients did not receive any treatment. Remission was achieved in 10 (66.7%) patients.
Conclusion: ALD can occur at any age, in both sexes with favorable results on immunosuppression. Liver biopsy should be performed in all cases not only for diagnosis but also for accessing disease severity.
Keywords: Autoimmune Hepatitis, Interface Hepatitis, Antimitochondrial Antibodies.

Abstract #840

A case of autoimmune hepatitis with multiple extrahepatic manifestations

Nyein Mon Yu[1], May Kyi Kyaw[2], Win Naing[3]

[1]Department of Hepatology, University of Medicine (I), Yangon, Myanmar, [2]Department of Hepatology, 500-Bedded Yangon Specialty Hospital, Yangon, Myanmar, [3]Department of Hepatology, University of Medicine (I), Yangon, Myanmar

Introduction: Autoimmune hepatitis (AIH) patients can present with a variety of extrahepatic manifestations. It is an important part of managing autoimmune hepatitis to look for these manifestations.
Case Description: A 29-year old thin, frail lady presented with deep jaundice, low grade fever and joint pains for 1-month duration. Initial investigations revealed high serum bilirubin (461umol/L), mildly raised liver enzymes and low serum potassium (1.8 mmol/L). Viral serology was all negative. Ultrasound (abdomen) showed hepatitis. On autoimmune liver screening, there were strongly positive anti-nuclear antibodies, positive antibodies to Ku, SS-A, SS-B, Ro-52 and histones and negative anti-mitochondrial antibodies. As the patient developed supraventricular tachycardia during admission and diffuse goiter was also noted, thyroid function test was done and found out to have hyperthyroidism. She was diagnosed as probable AIH according to revised original autoimmune hepatitis scoring system and steroid therapy was initiated. Her bilirubin level improved gradually and began to normalize after one month.
During the course of the illness, proximal weakness of both upper and lower limbs developed. Even after correcting hypokalaemia and giving anti-thyroid medications, the weakness did not improve. Neuropathy was excluded by normal nerve conduction studies and EMG showed irritable myopathy. Left biceps muscle biopsy revealed marked endomysial inflammatory cells infiltration around non-necrotic muscle fibers, compatible with polymyositis. She was treated again with IV methylprednisolone pulse therapy, followed by oral prednisolone and azathioprine. Her weakness gradually improved.
Conclusion: This is a case of autoimmune hepatitis with acute severe presentation and concurrent autoimmune diseases, successfully managed with steroid therapy.

F02 - PBC/PSC and other cholestatic diseases

Abstract #82

Primary biliary cholangitis patients with features of autoimmune hepatitis warrant special attention

Maoyao Wen[1,2], Ruoting Men[1], Xiaoli Fan[1], Ping Ni[1], Zhichao Hu[1], Yi Shen[1], Li Yang[1]

[1]Division of Gastroenterology and Hepatology, West China Hospital, [2]Department of Day Surgery Center, West China Hospital

Aim: This study was to elucidate the clinical characteristics of primary biliary cholangitis (PBC) patients with features of autoimmune hepatitis (AIH).
Methods: A total of 275 PBC patients were divided into two groups. Patients were divided into two groups: the PBC-only group and PBC with AIH features group. All patients were treated with UDCA for more than one year.
Results: Overall, 99 patients did not respond to UDCA, and 81 were females. The median age of the non-response group was 55.14 years old. Patients who did not achieve response had higher IgG, AST, alkaline phosphatase (ALP), glutamyl transpeptidase (GGT) and total bilirubin (TB) levels ($P < 0.05$). The UDCA-responsive ratios of patients in different serum immunoglobulin G (IgG) levels were 74.3% (normal IgG level), 57.7% (1.0xULN < IgG ≤ 1.3xULN) and 55.2% (1.3xULN < IgG < 2.0xULN) ($X2 = 9$ and $P = 0.011$). In addition, response ratios of the different serum aminotransferase levels were 87.2% (normal ALT/AST level), 64.8% (0 < ALT/AST ≤ 3.0xULN) and 46.7% (3.0xULN < ALT/AST < 5.0xULN) ($X2 = 16.96$ and $P = 0.000$). Patients in the PBC with AIH features group had a significantly lower response ratio than patients in the PBC-only group. Among the 72 patients who underwent liver biopsy, twenty-one were non-responsive to UDCA, and 12 of 21 patients (57.2%) had mild interface hepatitis on histology and PBC with AIH features.
Conclusion: Patients with PBC with AIH features had poorer responses to UDCA and should receive more attention.

Abstract #224

Case report: a case of successful treatment of autoimmune hepatitis–primary biliary cholangitis overlap syndrome

Li Juan Ouyang[1], Luo Wen Tao[2], Gan Chong Jie[3], Ming Xing Huang[4], Xia Jin Yu[5]

[1]The Fifth Affiliated Hospital of Sun Yat-Sen University, [2]The Fifth Affiliated Hospital, Sun Yat-Sen University, [3]The Fifth Affiliated Hospital, Sun Yat-Sen University, [4]The Fifth Affiliated Hospital, Sun Yat-Sen University, [5]The Fifth Affiliated Hospital, Sun Yat-Sen University

Background: Autoimmune Hepatitis-Primary Biliary Cholangitis (AIH-PBC) overlap syndrome is usually difficult to cure and very severe Herein, we present a successfully case of AIH-PBC overlap syndrome .
Methods Case Description:
Result: A 55-year-old woman developed Intermittent abdominal distension, fever, chilly, icterus about six years, admitted in our hospital on 14 May 2018. The laboratory tests results showed that the ALT 250U/L, total bilirubin was 38.7umol/L, the glutamic-oxalacetic transaminase was163.00U/L, glutamic-pyruvic transaminase was416.00U/L, Antinuclear antibody (+), Antimitochondrial antibody M2 (AMA-M2) (+), AMA-3E (+), r-glutamyl transpeptidase (r-GT)546.00U/L, Alkaline phosphatase(ALP)369.00 UL, ImmunoglobulinA2.310 g/L, ImmunoglobulinM3.13 g/L, Immunoglobulin G14.33 g/L, Magnetic resonance cholangiopancreatography of epigastrium and ultrasonic examination was normal. And AIH-PBC could be diagnosed. we gave the prescription of prednisone (30 mg per day), azathioprine (30 mg per day) and Ursodeoxycholic acid capsules (250 mg per day) combined treatment to the patient for 12 days. The liver function showed that ALT was 43 U/L, the total bilirubin was 21umol/L, glutamic-pyruvic transaminase was 74 UL/L , glutamic-oxalacetic transaminase was 20U/L, r-glutamyl transpeptidase was 295.00U/L, Alkaline phosphatase was 190.00 UL.
Conlusion: Although AIH-PBC overlap syndrome is rare, But it still needs more attention. combination of drugs in treatment is good therapy for such patients, Therefore, AIH-PBC overlap syndrome shoud be diagnosis and cured early to prevent progression to cirrhosis and liver cancer.

Abstract #235

Non-steroidal farnesoid X receptor (FXR) agonist GS-9674 improves liver biochemistry and decreases serum bile acids in patients with primary sclerosing cholangitis (PSC)

Michael Trauner[1], Aliya Gulamhusein[2], Bilal Hameed[3], Stephen Caldwell[4], Mitchell L Shiffman[5], Charles Landis[6], Bertus Eksteen[7], Kosh Agarwal[8], Andrew Muir[9], Simon Rushbrook[10], Chuhan Chung[11], Alain Chan[12], Christopher Bowlus[13], Kris Kowdley[14]

[1]Meidcal University of Vienna, [2]University of Toronto, [3]University of California, San Francisco, School of Medicine, [4]University of Virginia, [5]Bon Secours Liver Institute, [6]University of Washington School of Medicine, [7]Aspen Woods Clinic, [8]King's College, [9]Duke University School of Medicine, [10]Norfolk and Norwich University Hospital, [11]Gilead Sciences, Inc., [12]Gilead Sciences, Inc., [13]University of California Davis, [14]Swedish Organ Transplant and Liver Center

Introduction/Objectives: The safety and efficacy of non-steroidal FXR agonist GS-9674 in a Phase 2 trial of patients with PSC is described.
Methodology: 52 non-cirrhotic subjects with large-duct PSC were randomized 2:2:1 to receive GS-9674 100 mg (n = 22), GS-9674 30 mg (n = 20), or placebo (n = 10) orally QD for 12 weeks (W12) and stratified by stable ursodeoxycholic acid (UDCA) use. Subjects had baseline (BL) alkaline phosphatase (ALP) $> 1.67 \times$ ULN and total bilirubin ≤ 2 mg/dL. Safety, tolerability, pharmacodynamic effects of GS-9674 (C4 and bile acids), liver biochemistry, and serum fibrosis markers were evaluated.
Results: Median age was 43 years, 58% male, 60% with intra- and extra-hepatic duct involvement, 60% with IBD, 46% on UDCA. Median BL ALP and bilirubin were 348 U/L and 0.7 mg/dL, respectively. At W12, reductions in liver biochemistry were observed between GS-9674 and placebo-treated subjects. GS-9674 100 mg significantly reduced ALP (− 21%), GGT (− 30%), ALT (− 49%), AST (− 42%), and TIMP-1 (− 8.2%). GS-9674 100 mg ALP reductions were similar between UDCA-treated and untreated patients (− 19% vs. − 21%). BL ALP response predictors included lower ELF score and PIII-NP. At W12, ALP responders had greater reductions in ALT, AST, GGT, TIMP-1, CRP, and total bile acids compared with non-responders. GS-9674 reduced C4 compared with placebo; reductions in bile acids were greatest with 100 mg. GS-9674 was well-tolerated. Grade 2/3 pruritus was lower with GS-9674 100 mg (13.6%) and 30 mg (20%) compared with placebo (40%).
Conclusion: GS-9674 improves liver biochemistry and markers of cholestasis without aggravating pruritus in PSC patients.

Abstract #322

Evaluation of a novel multi-analyte assay for the detection of autoantibodies in the diagnosis of primary biliary cholangitis

Mary Ann Aure[1], Danilo Villalta[2], Andrea Seaman[3], Marychel Tiongson[4], Charles Warren[5], Chelsea Bentow[6], Nicola Bizzaro[7], Maria Grazia Alessio[8], Brunetta Porcelli[9], Gary L Norman[10], Michael Mahler[11]

[1]Research and Development, Inova Diagnostics, [2]Allergologia E Immunologia Clinica, Ao S. Maria Degli Angeli, [3]Research and Development, Inova Diagnostics, [4]Research and Development, Inova Diagnostics, [5]Research and Development, Inova Diagnostics, [6]Research and Development, Inova Diagnostics, [7]Laboratorio Di Patologia Clinica, Ospedale San Antonio, [8]Dipartimento Di Patologia Clinica, Laboratorio Analisi, Ao Papa Giovanni Xxiii, [9]Università Di Siena, Policlinico Le Scotte Siena, [10]Research and Development, Inova Diagnostics, [11]Research and Development, Inova Diagnostics

Introduction: Primary biliary cholangitis (PBC) is characterized by the presence of anti-mitochondrial antibodies (AMA). While > 85% of patients have AMA, at least 10–15% of patients with clinically-proven PBC are seronegative for AMA. Besides the classical AMA, other autoantibodies including those directed against hexokinase 1 (HK-1) and Kelch-like 12 peptide (KL-p) can be used as an aid in the diagnosis of PBC.
Objective: This study aimed to analyze the clinical performance of a new fully automated particle-based multi-analyte test (PMAT) system for the detection of autoantibodies to classic and novel PBC antigens using clinically characterized PBC patient samples and controls.
Methodology: A total of 399 patient samples from the SIPMeL multi-center cohort (Italy) were analyzed. Of these, 215 were PBC patients (enriched for AMA negativity), 73 were autoimmune hepatitis (AIH), 66 were from various other liver conditions and controls, and 45 had an unconfirmed diagnosis. Of the 215 PBC patients, 89 were considered AMA-negative by routine laboratory testing at each site. Samples were tested for antibodies to MIT3, HK-1, sp100, gp210, and KL-p using PMAT (research use only, Inova Diagnostics, USA).
Results: The sensitivity and specificity for all PBC autoantibodies and combinations thereof are outlined in the table below. Using a combination of MIT3, gp210, sp100, HK-1 and KL-p, 65.2% (58/89) of the AMA-negative PBC patients were detected with a specificity of 93.5% (Table 1).
Conclusion: Our data show excellent clinical performance of the new fully automated PMAT system for the detection of antibodies in the diagnosis of PBC.

Performance Characteristic	MIT3	gp210	sp100	HK-1	KLHL12
Sensitivity in PBC (AMA+ and AMA -) (95% CI)	68.8% (62.4-74.7%)	14.9% (10.7-20.3%)	29.8% (24.1-36.2%)	42.8% (36.4-49.5%)	19.5% (14.8-25.3%)
Sensitivity in PBC (AMA+ only) (95% CI)	91.8% (86.2-96.6%)	11.6% (7.4-17.9%)	27.4% (20.8-35.1%)	52.7% (44.7-60.7%)	22.6% (16.6-30.0%)
Sensitivity in PBC (AMA- only) (95% CI)	37.1% (27.8-47.5%)	19.1% (12.3-28.5%)	29.2% (20.8-39.4%)	31.5% (22.8-41.7%)	13.5% (7.9-22.1%)
p value AMA+ vs. AMA-	$p<0.0001$	$p=0.0648$	$p=0.4300$	$p<0.0001$	$p=0.2688$
Specificity (95% CI)	93.5% (88.2-96.6%)	99.3% (96.0-99.0%)	74.8% (67.0-81.3%)	87.1% (80.5-91.6%)	98.6% (94.9-99.6%)
Likelihood ratio + (95% CI) All PBC	10.6 (5.8-20.1)	20.6 (3.8-119.2)	1.2 (0.84-1.7)	3.3 (2.1-5.3)	13.5 (3.7-50.5)
Likelihood ratio - (95% CI) All PBC	0.33 (0.27-0.41)	0.86 (0.80-0.90)	0.94 (0.83-1.1)	0.66 (0.57-0.75)	0.82 (0.76-0.87)
Odds ratio (95% CI) All PBC	31.9 (15.5-65.7)	24.1 (4.1-141.3)	1.3 (0.78-2.0)	5.0 (2.9-8.8)	16.6 (4.4-63.4)

Abstract #353

Alteration of liver-infiltrated and peripheral blood double-negative T-cells in primary biliary cholangitis

Shu Xiang Li [1], Ting Ting Lv[2], Chun Pan Zhang[3], Tian Qi Wang[4], Dan Tian[5], Guang Yong Sun [6], Yan Wang[7], Xin Yan Zhao [8], Wei Jia Duan[9], Min Li [10], Dong Zhang[11], Ji Dong Jia[12]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [2]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [3]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [4]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [5]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [6]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [7]Liver Research Center, Beijing Friendship Hospital, Capital Medical

University, Beijing, China, [8]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [9]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [10]Clinical Epidemiology and Ebm Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [11]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [12]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China

Introduction: Primary biliary cholangitis (PBC) is an idiopathic autoimmune chronic liver disease. Excessively inflammatory responses, and defects of immunoregulatory system, both play critical role in the pathogenesis of PBC. Double-negative (DN) T-cell is a unique regulatory T-cell, which is essential for maintaining immune system homeostasis. However, the role of DN T-cells in the pathogenesis of PBC is still unknown.
Objectives: The aim of our study was to identify the role of DN T cells in the pathogenesis of PBC.
Methodology: In the current study, we investigated the number and function of DN T-cells in peripheral blood and liver biopsy specimens of patients with PBC. Results: Our results showed that the number and frequency of DN T-cells significantly decreased in peripheral blood and liver tissue of patients with PBC. Furthermore, the frequency of DN T-cells in PBC was negatively correlated with disease severity. In vitro assays showed that perforin expression and the suppressive capability of DN T-cells on the proliferation of CD4 + and CD8 + T-cells were impaired in PBC. Finally, lithocholic acid, the most hydrophobic acid, could downregulate the proliferation and perforin expression of DN T-cells.
Conclusion: Our results suggest that decreased quantity and function of DN T-cells in PBC may result in the loss of immune regulation on effector CD4 + and cytotoxic CD8 + T-cells, and thereby may break the immune tolerance and promote the pathogenesis of PBC.

Abstract #398

Detection of classical and novel liver autoantibodies in PBC patients and biochemically normal AMA-positive individuals

Luis E.C. Andrade[1], Mary Ann Aure[2], Chelsea Bentow[3], Michael Mahler[4]

[1]Rheumatology Division, Escola Paulista De Medicina, Universidade Federal De São Paulo & Research and Development Division, Fleury Medicine and Laboratories, [2]Research and Development, Inova Diagnostics, [3]Research and Development, Inova Diagnostics, [4]research and Development, Inova Diagnostics

Introduction: The serologic signature of primary biliary cholangitis (PBC) includes the presence of anti-mitochondrial antibodies (AMA) which is found to precede the development of biochemical liver abnormalities and clinical onset of disease by years. Since PBC is a slowly evolving condition, biochemically normal AMA-positive (BN/AMA +) individuals have been frequently observed which may represent opportunities for early intervention and potential prevention of PBC. Besides AMA, anti-sp100, anti-gp210, antibodies to two novel proteins Hexokinase 1 (HK-1) and Kelch-like 12 peptide (KL-p) have been described in PBC.
Objective: This study aimed to evaluate the prevalence of classical and novel liver autoantibodies in a cohort of clinically diagnosed PBC patients and BN/AMA + .
Methodology: The study included 297 sequential samples from PBC patients (n = 32) and asymptomatic BN/AMA + (n = 58). All samples were tested blinded for antibodies to MIT3, sp100, gp210, HK-1, and KL-p using a novel fully automated particle-based multi-analyte test system (PMAT, research use only, Inova Diagnostics, USA).
Results: Anti-MIT3, anti-HK-1 and anti-sp100 antibodies were detected in 93.8, 37.5, and 6.3% of the PBC baseline samples, respectively. Of the BN/AMA + baseline samples, 77.6% tested positive for anti-MIT3, 17.2% for anti-HK-1, and 10.3% for anti-sp100 antibodies. Double positivity (combinations of anti-MIT3, anti-sp100 and anti-HK-1) show significant differences between PBC and BN/AMA + . When comparing autoantibody titer levels at baseline, non-significant differences were found between the PBC and BN/AMA + except for anti-MIT3 and KL-p (Table 1).
Conclusion: Our data show potential utility of established and novel autoimmune liver disease-associated autoantibodies in the prediction of clinical onset of PBC.

Table 1. Frequency of autoantibodies and combinations thereof in PBC patients (n=32) and BN/AMA+ individuals (n=58) measured at baseline. *Area under the curve (AUC) and Odds Ratios (OR) with 95% confidence intervals (CI) considering PBC as true positive state

Analyte	PBC N (%)	BN/AMA+ N (%)	AUC*	OR* (95% CI)	PBC vs. BN/AMA+ Autoantibody prevalence *p*-value	PBC vs. BN/AMA+ Autoantibody titer level *p*-value
MIT3	30 (93.8)	45 (77.6)	0.697	4.3 (1.0-18.4)	0.0489	0.0021
HK-1	12 (37.5)	10 (17.2)	0.555	2.9 (1.1-7.7)	0.0323	0.3921
sp100	2 (6.3)	6 (10.3)	0.558	0.6 (0.1-2.8)	0.5135	0.3616
gp210	0 (0.0)	0 (0.0)	0.554	n/a	n/a	0.3926
KL-p	0 (0.0)	0 (0.0)	0.635	n/a	n/a	0.0346
MIT3 + HK-1	11 (34.4)	8 (13.8)	n/a	3.3 (1.2-9.2)	0.0220	n/a
MIT3 + sp100	2 (6.3)	6 (10.3)	n/a	0.6 (0.1-2.7)	0.5135	n/a
HK-1 + sp100	0 (0.0)	3 (5.2)	n/a	n/a	n/a	n/a
Any positive	31 (96.9)	47 (81.0)	n/a	7.3 (1.1-45.7)	0.0343	n/a
Any double positive	13 (40.6)	11 (19.0)	n/a	2.9 (1.1-7.6)	0.0261	n/a
Any triple positive	0 (0.0)	3 (5.2)	n/a	n/a	n/a	n/a

Abstract #400

Reactivity profile of different human monoclonal antibodies to anti-glycoprotein-210 and anti-liver kidney microsome type 1

Mary Ann Aure[1], Chelsea Bentow[2], Richard Fowler[3], Michael Mahler[4]

[1]Research and Development, Inova Diagnostics, [2]Research and Development, Inova Diagnostics, [3]Research and Development, Inova Diagnostics, [4]Research and Development, Inova Diagnostics

Background: Autoimmune liver disease (ALD) consists of autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC), which are all diagnosed based on clinical, serologic, and liver pathology findings. Anti-nuclear envelope-glycoprotein-210 (gp210) antibodies are specifically detected in 20–30% of PBC patients while anti-liver kidney microsome type 1 (LKM-1) antibodies are key for the diagnosis of type 2 AIH. Monoclonal antibodies are important tools to study ALD and to aid in the standardization of antibody assays. Here we report the development and reactivity profile of human recombinant monoclonal antibodies (hr-mAbs) to gp210 and LKM-1 derived from phage display technology.
Methods: Human recombinant monoclonal antibodies (n = 3 per analyte) were developed by phage display technology using the full-length recombinant protein of LKM-1 and a peptide for gp210 as the antigens for the bio-panning procedure. Serial dilutions starting at 50 μg/mL were carried out until 3 ng/mL to assess analytical sensitivity. The antibodies were tested alongside native human sera by a novel particle-based multi-analyte technology (PMAT, research use

only), as well as QUANTA Lite gp210 and LKM-1 ELISAs (all methods Inova Diagnostics, San Diego, USA).
Results: All hr-mAbs reacted with the gp210 and LKM-1 on PMAT and ELISA, demonstrating a dose dependent linear dilution response similar to their native human sera counterpart. For PMAT, analytical sensitivity was defined as 10 ng/mL for LKM-1 and as 1.5 ug/mL for gp210.
Conclusion: The hr-mAbs to gp210 and LKM-1 display reactivity similar to human sera and represent useful tools for the standardization of antibody assays in ALD.

Abstract #440

Interleukin-17 producing Nature killer T phenotypes promote primary biliary cholangitis-related fibrosis

Hongyu Jia[1], Jianing Chen[2], Hongyan Diao[3]

[1]Zhejiang University, The First Affiliated Hospital, [2]Zhejiang University, The First Affiliated Hospital, [3]Zhejiang University, The First Affiliated Hospital

Primary biliary cholangitis (PBC) characterized as interlobular bile duct injury resulted from loss of the tolerance to self-antigens. Previous studies showed Treg defect in quantity and inhibition on co-stimulation in the progression of PBC. Also accumulated iNKT cells and higher Th1/Th17 signaling response were both reported to occur in the established mouse models. However, the precise initiator that led to and exacerbated PBC in the PBC patients is still needed further investigation. In the present study, we analyzed the lymphocytes distributions and Th17 cytokines production. We found that CD3 + CD56 + NKT cells and iNKT cells showed higher frequencies in the patients with PBC when compared with the HCs. And these two NKT subpopulations-derived IL-17A levels significantly higher than the HCs, which were also positively correlated with the disease severity. Furthermore, IL-17A production from CD3 + CD56 + NKT cells and iNKT cells were both increased after the stimulation by the autoantibodies from the PBC patients. And the elevated IL-17A levels promoted the PBC-related fibrosis, thus presenting that the alternation of frequencies and functions of NKT cells phenotypes in the deterioration of the duct damage related fibrosis.

Abstract #620

A 6 years old girl suffering from granulomatous hepatitis due to common variable immunodeficiency: case report

Jhumur Ghosh[1], Prof. Mamun Al Mahtab [2], Md. Noor E Alam[3]

[1]M H Samorita Hospital and Medical College, [2]Bangabandhu Sheikh Mujib Medical University, [3]Bangabandhu Sheikh Mujib Medical University

Granulomatous hepatitis is an important cause of fever of unknown origin in up to 13% of patients. Granulomatous disease due to common variable immunodeficiency (CVID) might affect about 10–22% of patients. CVID is the second most common cause of primary immunodeficiency after IgA deficiency. Here we reported a 6 years old girl presented with recurrent episodes of fever since her 6 months of age and diagnosed as a case of CVID on the basis of low IgG, IgM, also with low levels of IgG1 and IgG2. Flow cytometric immunophenotyping for B cells showed reduced memory B cells and switch memory B cells. She had evidence of granulomatous hepatitis in view of deranged liver function tests with very high Alkaline Phosphatase and suggestive liver biopsy report. She was treated with IVIg, Prednisolone, Ursodeoxycholic acid and antibiotic. Report of our case points to the possible occurrence of granulomatous hepatitis due to common variable immunodeficiency.

Abstract #691

Effects of fenofibrate on outcome in primary biliary cholangitis with suboptimal ursodeoxycholic acid response

Guanya Guo[1], Lu Wang[2], Xinmin Zhou[3], Ying Han[4]

[1]The Department of Digestive Disease, Xijing Hospital, The Military Medical University of Air Force, [2]The Department of Digestive Disease, Xijing Hospital, The Military Medical University of Air Force, [3]The Department of Digestive Disease, Xijing Hospital, The Military Medical University of Air Force, [4]The Department of Digestive Disease, Xijing Hospital, The Military Medical University of Air Force

Background: Fibrates appear to improve biochemistry in patients with primary biliary cholangitis (PBC). But there are no consistent data on the course and outcome.
Aims: To evaluate the effect and the safety of fenofibrate in PBC with incomplete ursodesoxycholic acid (UDCA) response.
Methods: Consecutive PBC patients with incomplete UDCA response were retrospectively reviewed. Changes in clinical features and biochemistries after therapy were assessed. The 5-, 10-, and 15-year GLOBE Risk Scores were compared to predict long-term effects.
Results: A total of 107 patients with incomplete UDCA response were included (UDCA + FF group n = 42, UDCA group n = 65) in this study. The significant decrease in serum alkaline phosphatase (ALP) were seen in the FF group even at the third month ($p = 0.001$). After one year of therapy, 52.4% (22/42) vs. 27.6% (18/65) met the Barcelona criteria for biochemical response in the FF and UDCA groups, respectively ($p = 0.010$). What's more, the 5-, 10-, and 15-year GLOBE Risk Scores were significantly higher in the FF group (median 0.65 vs. 0.49, $p = 0.007$; 0.31 vs. 0.15, $p = 0.007$ and 0.12 vs. 0.03 $p = 0.006$, respectively) than those in the UDCA group. The serum triglycerides levels decreased more conspicuously in the FF group ($p = 0.018$). However, the urea nitrogen and creatinine were not significantly different between the two groups.
Conclusions: FF therapy improves improvement in ALP, and the 5-, 10-, and 15-year GLOBE Risk Scores in PBC. Further studies are still required to assess the validity of ALP as an appropriate response criteria for fibrate therapy.

Abstract #814

Maternal bile acid levels predict maternal and neonatal outcomes in Intrahepatic Cholestasis of Pregnancy; a retrospective cohort study

Madhumita Premkumar[1], Aakash Roy[1], Saurabh Mishra[1], Aswath Venkitaraman[1], Surender Singh[1], Sunil Taneja[1], Ajay Duseja[1], Nipun Verma[1], Radha K Dhiman[1]

[1]Assistant Professor, Department of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh, India-160012

Introduction: Intrahepatic Cholestasis of Pregnancy (ICP) is the commonest pregnancy-related liver disorder characterized by pruritus without rash and increased serum bile acids (BA) > 10 mmol/L.

Objectives: We reviewed the management and outcomes of patients with ICP referred to the Hepatology Clinic at the Post Graduate Institute of Medical Education and Research, Chandigarh. (Figure 1)
Methods: All pregnancies associated with ICP (defined as pruritus with serum bile acids) were prospectively included between July 2017 and November 2018 with analysis of demographics, maternal/perinatal outcomes co-morbidities and treatment response.
Results: Four hundred and forty-three pregnant women were screened and 375(mean age 29 years; 45.8% primigravida) of these patients met diagnostic criteria for ICP. Within the cohort, the incidences of pregnancy induced hypertension (PIH; 10.3%; OR4.8, 95% CI 2.6–9.7, P = 0.043), gestational diabetes (12.5%; OR 2.6, 95% CI 2.3–4.1, P = 0.029), and spontaneous preterm labour (15.1%; OR 1.8, 95% CI 1.3–2.9, P = 0.034) were higher than in the general pregnant population. Response to UDCA (median daily dose 900 mg; 600–1800 mg) was seen in 79% patients. Patients with severe ICP (serum BA > 40 mmol/L) presented earlier (26vs.32 weeks, P = 0.036), required induction (12%; OR2.1 95% CI 1.8–4.3, p = 0.045) with increased foetal distress than those with mild ICP. (Table 1). There were 8 stillbirths.
Conclusion: This large cohort study confirms safe maternal outcomes associated with mild ICP but with persistent risk for stillbirths and need for induction in severe ICP. A high proportion of pregnancies were also affected by gestational diabetes (26.4%), PIH (52.9%), and pre-term labour (12.5%) when BA level was ≥ 40 mmol/L.

Abstract #923

A rare case of small duct primary sclerosing cholangitis

Charisse Que Ignacio[1], Lovell B. Gatchalian[2]

[1]Section of Gastroenterology, Department of Internal Medicine, East Avenue Medical Center; Quezon City, Philippines, [2]Section of Gastroenterology, Department of Internal Medicine, East Avenue Medical Center; Quezon City, Philippines

Significance: Small duct primary sclerosing cholangitis (SDPSC) is considered a rare variant of classic Primary Sclerosing Cholangitis. It is diagnosed based on clinical, biochemical, and histologic features consistent with primary sclerosing cholangitis but with normal cholangiogram findings. We report a case of small bile duct primary sclerosing cholangitis in a patient who presented with jaundice and normal MRCP findings.
Clinical Presentation: A 22-year-old Filipino male with no known comorbidities sought consult due to a 2-week history of jaundice with elevated transaminases, bilirubin and alkaline phosphatase. The physical examination findings were unremarkable except for jaundice. Hepatitis markers were all within normal levels. Anti-nuclear antibody and anti-mitochondrial antibody were requested to rule out autoimmune hepatitis and primary biliary cirrhosis, respectively. Both results were negative.
Management: Magnetic resonance cholangiopancreatography (MRCP) was normal with no evidence of dilated intra- and extrahepatic bile ducts. Liver biopsy showed intrahepatic cholestasis with fibrosis. Diagnosis of SDPSC was made and ursodeoxycholic acid was started at 20 mg/kg/day which showed significant decrease in jaundice and improvement in liver biochemistries after 2 months of treatment. Screening colonoscopy was done to rule out concomittant inflammatory bowel disease which revealed negative results.
Recommendation: Small duct primary sclerosing cholangitis appears to have a more favorable prognosis than classic PSC in terms of survival and development of cholangiocarcinoma. However, further studies with long-term follow up are recommended to determine disease progression.

Inflammation and Fibrosis

G01 - Liver injury and inflammation

Abstract #245

IL-21 ameliorates diethylnitrosamine (DEN)-induced liver injury by inhibiting intrahepatic inflammatory responses

Chunhua Wen[1], Xinchun Zheng[2], Yang Zhou[1], Xuan Yi[1], Libo Tang[1], Yongyin Li[1], Jinlin Hou[1]

[1]Department of Infectious Diseases and Hepatology Unit, Nanfang Hospital, Southern Medical University, Guangzhou, China, [2]Department of Infectious Diseases, The Fifth Affiliated Hospital of Sun Yat-Sen University, Zhuhai, China

Background: Previous publication has shown that IL-21 is associated with liver inflammation. However, the role of IL-21 in liver injury is not very clear. Herein, we aim to investigate the role of IL-21 signaling in diethylnitrosamine (DEN)-induced liver injury.
Methods: IL-21 receptor knock out (IL-21R-KO) mice and C57BL/6 wide type (WT) mice were used to establish DEN-induced liver injury mice model. Mice were intraperitoneally injected with recombination murine IL-21 (rmIL-21) or PBS every 2 weeks for 6 times (Fig. 1). The changing profile of body weight, survival rate, ALT level, and liver histology were examined. Intrahepatic and spleen lymphocytes were separated for flow cytometry analysis.
Results: In DEN-induced WT mice, administration of rmIL-21 resulted in significantly decreased level of serum ALT (Fig. 2A) and reduced distribution of infiltrating intrahepatic lymphocytes in the liver (Fig. 2B) when compared with that treated with PBS. Moreover, the body weight and survival rate were also significantly decreased in WT mice with rmIL-21 injection(Fig. 2C), while no significant difference regarding liver index was observed between the two groups. Interestingly, all the IL-21R-KO mice were dead when they were treated with DEN for no more than 24 weeks. Furthermore, the frequencies of IL-17A-secreting CD4 + T cells, IFN-gamma-producing CD8 + T, NK, and NKT cells were significantly decreased in WT mice with rmIL-21 injection (Fig. 3). However, the percentages of CD4, CD8, and NK cells in the liver were comparable between the two groups.
Conclusions: IL-21 may ameliorate DEN-mediated liver injury by inhibiting the inflammatory responses in the liver.

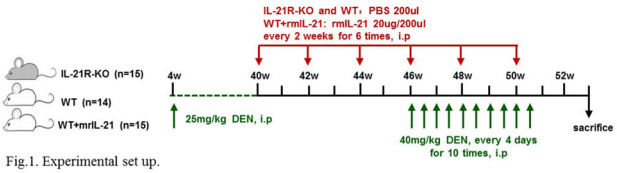


Fig.1. Experimental set up.

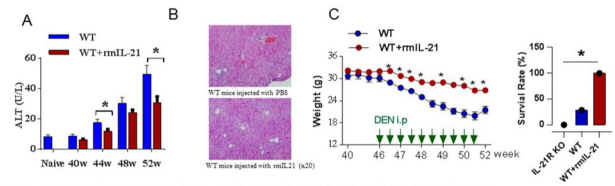


Fig.2. IL-21 can increase the tolerance of DEN injury and reduce liver damage in mice.

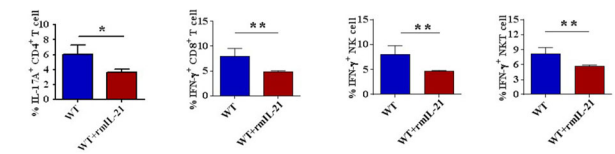


Fig.3. IL-21 affects hepatic lymphocyte cytokine secretion in DEN-induced liver injury mice.

Abstract #560

Hepatic sinusoidal obstruction syndrome: a rare complication of Paroxysmal Nocturnal Hemoglobinuria

Xiaohe Li[1], Rui Huang[2], Guangde Zhou[3], Lai Wei[4]

[1]Peking University Hepatology Institute, Beijing Key Laboratory of Hepatitis C and Immunotherapy for Liver Diseases, Peking University People's Hospital, [2]Peking University Hepatology Institute, Beijing Key Laboratory of Hepatitis C and Immunotherapy for Liver Diseases, Peking University People's Hospital, [3]Department of Pathology and Hepatology, 302 Military Hospital of China, [4]Peking University Hepatology Institute, Beijing Key Laboratory of Hepatitis C and Immunotherapy for Liver Diseases, Peking University People's Hospital

Subjects: We reported hepatic sinusoidal obstruction syndrome (SOS) as a rare complication of aplastic anemia/paroxysmal nocturnal hemoglobinuria (AA/PNH) syndrome.
Case presentation: 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 and 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 40 mg/day for 3 days then transitioned to oral prednisolone 50 mg/day, with the stabilization of hemoglobin, the dose of corticoid decreased quickly.
Literature Review: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired disorder of hematopoietic stem cell that manifests with uncontrolled complement–mediated intravascular hemolysis, bone marrow failure and thrombophilia. Budd-Chiari syndrome (BCS) is the most common complication of PNH. However, thrombosis occurs in central lobular vein and cause sinusoidal obstruction syndrome (SOS) were not reported.

Abstract #588

OX40 Expression in neutrophils promotes hepatic ischemia–reperfusion injury

Hua Jin[1], Hufeng Xu[2], Chenyang Sun[3], Chunpan Zhang[4], Guangyong Sun[5], Yanmeng Li [6], Xinyan Zhao [7], Tianqi Wang [8], Yaning Wang [9], Dan Tian [10], Kai Liu [11], Yue Tian[12], Wen Shi[13], Dong Zhang [14]

[1]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China, [2]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China, [3]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China, [4]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China, [5]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China, [6]National Clinical Research Center for Digestive Diseases, Beijing, China, [7]National Clinical Research Center for Digestive Diseases, Beijing, China, [8]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China, [9]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China, [10]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China, [11]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China, [12]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China, [13]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China, [14]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China

Introduction: Hepatic ischemia and reperfusion injury (HIRI) is a major cause of postoperative complications following liver transplantation and hepatic surgery. Neutrophils play critical roles during the initial phase of liver injury after reperfusion. However, the regulation of neutrophil activation, infiltration, and pro-inflammatory cytokine secretion has not been fully elucidated.
Objectives: To investigate the role and mechanism of OX40 in neutrophils in HIRI.
Methodology: The expression and function of OX40 in neutrophils were studied in a mouse model of partial warm HIRI.
Results: In this study, we revealed that OX40 was expressed by neutrophils, its expression in neutrophils was time-dependently upregulated following HIRI, and the OX40 knockout markedly alleviated liver injury. Decreased liver damage and reduced neutrophilic infiltration were also observed following the adoptive transfer of OX40-deficient neutrophils to B6.Rag2/Il2rγ double knockout mice. Moreover, consistently, the in vitro experiments using bone marrow-derived neutrophils showed that OX40 not only prolonged cell

survival but also promoted pro-inflammatory cytokine and ROS production and even neutrophil chemotaxis. Further investigation demonstrated that the knockout of OX40 in neutrophils inhibited NF-κB signaling via the TRAF1/2/4 and IKKα/IKKβ/IκBα pathways.
Conclusion: We demonstrate that OX40 is expressed in neutrophils in a HIRI model. OX40 is involved in both adaptive immunity and innate immune responses. Our study provides a novel potential therapeutic target for the prevention of HIRI during liver transplantation or hepatic surgery.

Abstract #597

Causes of acute liver dysfunction, clinical course, biochemical features and outcome in a rural Sri Lankan population—a single center study

Hasitha Srimal Wijewantha[1], Ayanka Devindi Ariyasena[2], Chathurika Mihirani Kulathunga[3], Tharange Pradeep Gunasekara[4], Bandusiri Hospital Rathnayake[5]

[1]Department of Gastroenterology and Hepatology & Provincial General Hospital-Badulla, Sri Lanka, [2]Department of Gastroenterology and Hepatology & Provincial General Hospital-Badulla, Sri Lanka, [3]Department of Gastroenterology and Hepatology & Provincial General Hospital-Badulla, Sri Lanka, [4]Department of Internal Medicine & Provincial General Hospital, Badulla, Sri Lanka, [5]Department of Internal Medicine & Provincial General Hospital-Badulla, Sri Lanka

Introduction: Causes of acute liver dysfunction (ALD) vary from region to region, no reported data from Sri Lanka. Data on liver dysfunction not fulfilling the criteria of acute liver failure are sparse.
Objectives: To describe causes, clinical and biochemical features and outcome of ALD in a cohort of rural Sri Lankan patients.
Methodology: Study was conducted in the gastroenterology unit of a tertiary care general hospital in Uva province of Sri Lanka from 15th January to 15th June 2018. All consenting patients with transaminases > 10 times or total bilirubin > 5 times the upper limit of normal were included. Diagnoses were made using clinical history, biochemistry, blood picture, serological tests and histopathology data. Data collected from hospital patient records.
Results: 56 patients were included—Table 1.
10/56 patients (Ischemic hepatitis 4; Viral Hepatitis 4; DILI 2) had INR > 1.5

4/36 (11%) patients had Hepatitis A. None had hepatitis B or C. 1/36 (3%) patient had cytomegalovirus infection. One patient had dengue infection. One patient with viral hepatitis died due to acute liver failure. Two patients with ischemic hepatitis died; one had severe sepsis and the other cardiac failure.
Conclusion: Commonest cause of ALD in this population is viral hepatitis. Hepatitis A is a common cause for viral hepatitis. Patients with ischemic hepatitis and Dengue infection had AST > ALT with minimal elevation of bilirubin, patients with cholangitis had marked elevations of ALP and GGT. Clinical features and basic liver biochemistry can give valuable clues regarding etiology of ALD.

Abstract #670

TFF3 ameliorates liver injury of nonalcoholic steatohepatitis

Yifan Zhang[1], Yang Liu[2], Yiping Li[3], Haiyan Song[4]

[1]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, [2]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, [3]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, [4]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine

Background and objective: Trefoil fator 3(TFF3), well-known protective peptide for gastrointestinal mucosa, was found decreased in fat liver of obese mice. This study aims to investigate the effect of TFF3 on liver injury in nonalcoholic steatohepatitis (NASH).
Methods: Serum of NAFLD patients and healthy adults were measured for transaminases and TFF3 level. HepG2 and Huh7 cells with TFF3 endogenous overexpression(LV-TFF3) were constructed. Recombinant human TFF3(rhTFF3) protein was implicated on HepG2, Huh7 and AML12 cells to test effect of exogenous TFF3. Lipid accumulation and injury of cells were induced by palmitic acid(PA) for 24 h. Cell apoptosis and inflammatory factors, cell proliferation and migration were detected. AKT activation were measured to explore regulated signaling.
Results: The level of serum TFF3 in NASH patients was significantly lower than that in healthy people, and that in NAFLD patients. Negative correlation exists between serum TFF3 and ALT. This suggests a beneficial effect of TFF3 in NASH. The in vitro experiments demonstrated LV-TFF3 cells versus scramble had higher cell viability, less ratio of apoptosis, and reduced inflammatory factors. In addition, cell proliferation and migration were increased. In consistence, HepG2, Huh7 and AML12 cells treated with rhTFF3 displayed accelerated proliferation and migration, decreased apoptosis and inflammatory factors. More activated AKT was observed in cells treated with rhTFF3.
Conclusions: TFF3 play a role in ameliorating liver injury induced by lipid. Down-regulated TFF3 expression during NASH development may be related with liver injury. TFF3 is a potential therapeutic medicine or as the regulated target for liver injury in NASH.

Abstract #823

Runt-related transcription factor (RUNX1) regulates angiogenesis and inflammation in the pathogenesis of non-alcoholic steatohepatitis

Savneet Kaur[1], Preety Rawal[2], Hamda Siddiqui[3], Sumati Rohilla[4], Sukriti Sukriti[5], Dinesh Tripathi[6], Shvetank Sharma[7], Anupama Kumari[8], Chaggan Bihari[9], Shiv K Sarin[10], Thomas Weiss[11]

[1]ILBS, [2]Gautam Buddha University, [3]ILBS, [4]Gautam Buddha University, [5]ILBS, [6]ILBS, [7]ILBS, [8]ILBS, [9]ILBS, [10]ILBS, [11]University of Regensburg

Aim: The study investigated role of Runt-related transcription factor 1 (RUNX1), a regulator of developmental angiogenesis, in pathogenesis of non-alcoholic steatohepatitis (NASH).
Methods: Microarray, RT-PCRs and transcription factor analysis of angiogenesis-associated differentially expressed genes in liver tissues of healthy controls (n = 33), patients with steatosis (n = 46) and NASH (n = 43), indicated increased expression of RUNX1 in NASH. Gene expression of RUNX1 was correlated with histopathological attributes of patients. Protein expression of RUNX1 in liver and circulating cells was studied by immunohistochemistry and flow cytometry. In vitro studies using RUNX1 siRNA were performed in palmitate-treated hepatoma cells, endothelial (ECs) and hepatic stellate (HSC) cell lines. RUNX1 expression was studied in high-fat diet (HFD) and methionine-choline-deficient diet (MCD) mice models.
Results: Gene and protein expression of RUNX1 significantly correlated with inflammation in NASH patients. Its expression was

conspicuous in liver non-parenchymal and inflammatory cells of liver and blood. In vitro, VEGF and TGF-β induced expression of RUNX1 in ECs and HSCs. Expression of angiogenic genes including CCL2, PI3KCA, PRKCE, eNOS and VEGFR1 exhibited substantial decrease in ECs under RUNX1-knockdown conditions, which also displayed reduced angiogenic ability. HSCs incubated with TGF-β showed increased gene expression of RUNX1 and after RUNX1-knockdown, illustrated decreased expression of CCL2, VEGFR1, PI3KCA, VIM1, COL1A1 and αSMA. Increased expression of RUNX1 was also observed in MCD mice with higher inflammation as compared to HFD mice.
Conclusion: The study reports that increased expression of RUNX1 in liver and blood cells may be a vital mediator of angiogenesis and possibly fibrogenesis in NASH.

Abstract #838

Study of serum ferritin to predict early mortality in patients with decompensated cirrhosis of liver

Mohammad Shawkat Hossain[1], Nooruddin Ahmad[2], Mamun Al Mahtab[3], Salimur Rahman[4], Ayub Al Mamun[5], Md Fazal Karim[6], Sheikh Mohammad Noor-E-Alam[7]

[1]Department of Hepatology, Sir Salimullah Medical College and Mitford Hospital, [2]Department of Hepatology, Bangabondhu Sheikh Mujib Medical University, [3]Department of Hepatology, Bangabondhu Sheikh Mujib Medical University, [4]Department of Hepatology, Bangabondhu Sheikh Mujib Medical University, [5]Department of Hepatology, Bangabondhu Sheikh Mujib Medical University, [6]Department of Hepatology, Sir Salimullah Medical College and Mitford Hospital, [7]Department of Hepatology, Bangabondhu Sheikh Mujib Medical University

Introduction: Serum ferritin is a known marker of hepatic necro-inflammation and has been studied to predict mortality in patients with decompensated cirrhosis of liver. **Objectives:** To evaluate serum ferritin level for prediction of early mortality in patients with decompensated cirrhosis of liver.
Methodology: This cross sectional observational study was carried out in the Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka from April 2017 to October 2017. Blood samples were collected to measure serum ferritin level. Patients were longitudinally followed up of mortality for a period of 30 days. Statistical analysis was done by dividing the patients into two groups (Group A and Group B) according to serum ferritin level > 500 μg/L which was considered, elevated for the study outcome.
Result: Out of total 79 patients majority of patients were in Child–pugh C. Mean MELD score found 19.0 ± 5.7 in group A and 24.4 ± 6.8 in group B. 1(1.9%) patient died in group A and 16(64.0%) in group B. Several factors found significantly associated with mortality in univariate analysis including serum ferritin, serum sodium, ALT, prothrombin time and MELD score. In multivariate analysis, only serum ferritin (OR 0.11, 95% CI 0.01–0.99%, $p = 0.001$) found significantly associated with mortality within 30 days. ROC curve was constructed using serum ferritin level, which gave a cut-off value 612 μg/L, with 94.1% sensitivity and 91.9% specificity.
Conclusion: Raised serum ferritin level is an independent predictor of early mortality in patients with decompensated cirrhosis of liver.

Abstract #894

Myoglobinuria, a Rare but Major Complication of RFA: A Case Report

Marianne Linley Loo SY[1], Juliet Lingat Gopez-Cervantes[2]

[1]Institute of Digestive and Liver Diseases, St. Luke's Medical Center-Global City, [2]Institute of Digestive and Liver Diseases, St. Luke's Medical Center-Global City.

Introduction: Radiofrequency ablation (RFA) is an alternative management for selected liver masses. It is an ablative technique that uses a needle electrode to deliver a high-frequency alternating current into the peripheral tissue surrounding the electrode, resulting to thermal injury. The reported incidence of complications is low, and procedure-related mortality is rare.
Objective: To present a case of acute kidney injury secondary to myoglobinuria following RFA of metastatic liver lesions.
Case Presentation: A 43-year-old Filipino female, with multiple metastatic liver masses at segment II, III, VIII, and VII measuring 7.6 cm x 5.4 cm, 3.3 cm x 2.8 cm, 1.7 cm x 1.3 cm, 1.3 cm x 0.8 cm, and 0.5 cm x 0.5 cm, respectively, underwent laparoscopic guided RFA. Multiple overlapping ablation of the masses were done with total ablating time of 146 min. Post-RFA showed hyperechoic masses with shadowing echogenicities. Doppler studies showed no bleeding at the needle tracts or punctured sites. After the procedure, the patient had acute kidney injury prompting hemodialysis. Work up revealed myoglobinuria.
Discussion: Myoglobinuria may develop after RFA of hepatic tumors. It might be secondary to the hemolysis related to the thermal injury of the liver tissues. Devastating complications such as acute kidney injury prompting hemodialysis may occur as presented in this case.
Conclusion: Myoglobinuria after liver RFA is a rare complication that may potentially result to significant morbidity and prolonged hospital stay. Patients with large tumor volumes requiring longer ablation times may be at risk. Close monitoring is recommended.

Abstract #901

Deranged VEGFR3-positive gut lymphatic vessels correlate with intestinal and systemic inflammation in liver cirrhosis

Savneet Kaur[1], Dinesh Tripathi[2], Sumati Rohilla[3], Anupama Kumari[4], Preety Rawal[5], V Rajan[6], Archana Rastogi[7], Sm Shasthry[8], Shiv Sarin[9]

[1]ILBS, [2]ILBS, [3]Gautam Buddha University, [4]ILBS, [5]Gautam Buddha University, [6]ILBS, [7]ILBS, [8]ILBS, [9]ILBS

Introduction and Aim: Given the significance of lymphatic system in tissue inflammation, here, we characterized gut lymphatic vascular system in liver cirrhosis.
Methods: Duodenal (D2) biopsies were collected from patients with liver cirrhosis (n = 12) and non-cirrhotic controls (n = 7). Intestinal/gut lymphatic vessels were identified by VEGFR3 immunohistochemistry (IHC). Systemic levels of inflammatory cytokine, TNF-alpha levels were measured by ELISA. Real Time-PCR analysis for intestinal inflammation and lymphatic marker genes including TNF-α, iNOS, LYVE1 and VEGFR3 was done. VEGFR3 IHCs was also done in the mesenteric and duodenal tissues in animal models of thioacetamide (TAA)-induced liver cirrhosis.
Results: Expression of lymphatic endothelial marker gene, VEGFR3 was higher in patients with cirrhosis as compared to that in controls ($P < 0.05$). Histologically, a marked dilation of VEGFR3-positive

lymphatic vessels was observed in mucosal and submucosal regions in cirrhotic biopsies in comparison to control biopsies (23.47 + 6.6 versus 9.7 + 3 μm, $P < 0.05$). Increased number of dilated VEGFR3 lymphatic vessels showed significant positive correlation with systemic levels of TNF-α ($r = 0.89$, $p = 0.01$) in cirrhotics. Further, dilated VEGFR3-positive lymphatic channels in biopsies positively correlated with expression of inflammatory genes, iNOS and TNF-α genes ($P < 0.05$, each). Models of TAA-induced cirrhosis also demonstrated presence of increased number of dilated VEGFR3-positive lymphatic vessels in mesentery and duodenal regions in comparison to that in controls ($P < 0.01$).

Conclusion: Liver cirrhosis leads to a disorder of the VEGFR3-positive gut lymphatic channels that may be a cause and/or effect of intestinal and systemic inflammation.

Abstract #962

Salvia Miltiorrhiza inhibits the activation of proinflammatory macrophage via regulating the expression of immune checkpoint PD-L1 in liver fibrosis

Yuan Peng[1], Yuanyuan Ma[2], Yanyan Tao[3], Chenghai Liu[4]

[1]Institute of Liver Diseases, Shuguang Hospital Affiliated To Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China, [2]Institute of Liver Diseases, Shuguang Hospital Affiliated To Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China, [3]Institute of Liver Diseases, Shuguang Hospital Affiliated To Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China, [4]Institute of Liver Diseases, Shuguang Hospital Affiliated To Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China & Shanghai Key Laboratory of Clinical Chinese Medicine, Shanghai 201203, China & Key Laboratory of Liver and Kidney Diseases (Shanghai University of Traditional Chinese Medicine) , Ministry of Education, Shanghai 201203, China

Background: Blocking interaction of the immune checkpoint receptor programmed death 1 (PD-1) with its ligand programmed death 1 (PD-1) is closely associated with good clinical outcomes in a broad variety of liver injuries. High expression of PD-L1 on proinflammatory macrophage contributes to liver fibrosis. Salvia miltiorrhiza (SM), a Chinese herbal medicine, is effective in treating liver fibrosis. But the immunological mechanism remains unclearly. Here, we tested the hypothesis that the anti-fibrotic effect of SM was associated with inhibiting the activation of hepatic proinflammatory macrophage via modulating the expression of immune checkpoint PD-L1.

Methods: Liver fibrosis was induced with carbon tetrachloride (CCl4) or 0.1% diethyl 1,4-dihydro-2,4,6-trimethyl-3,5-pyridinedicarboxylate (DDC) diet in C57BL/6 mice in vivo. The in vitro experiments were carried out in LPS-treated RAW264.7 cells. Effects of SM on proinflammatory macrophages were investigated in vivo and in vitro.

Results: We found SM attenuated liver fibrosis in both CCl4 and DDC-diet models. Expression of PD-L1 in liver tissue was alleviated after SM treatment in vivo. Levels of TNF-α and IL-6 in supernatant secreted by LPS-induced proinflammatory macrophages were down-regulated after incubation with SM in vitro. Moreover, high expression of PD-L1 on proinflammatory macrophage were also significantly decreased by SM administration. Besides, more early apoptotic proinflammatory macrophages stained with annexin V were investigated after SM treatment.

Conclusion: SM could inhibit the activation of proinflammatory macrophage via regulating the expression of immune checkpoint PD-L1 in liver fibrosis in vivo and in vitro.

Abstract #1066

Ginko biloba is hazardous to liver in low and high doses

Ali Ghweil[1], Soha A Soliman[2], Maha Abdelbaki[3]

[1]Tropical Medicine and Gastroenterology Department South Valley University, [2]Histology Department Veterinary Medicine South Valley University, [3]Anatomy Department South Valley University

Ginkgo biloba leaves contain a complex mixture of chemical constituents, which can vary depending on the strain of ginkgo, conditions of growth, time of harvest, etc. (Smith and Luo, 2004). However, the terpene trilactones represent a group of chemicals that are unique to the ginkgo (Hasler, 2000). The main chemical agent in Ginkgo biloba leave include terpene trilactones, flavonol glycosides, biflavones, proanthocyanidins, alkylphenols, phenolic acids, and polyprenols (van Beek and Montoro, 2009). Experimental designThe rats were divided into three equal groups (10 rats each) and treated once a day, as follows: (1) Group 1 (control group; n = 10): received distilled water (1 ml/rat) orally by dailygavage for 4 weeks.(2) Group 2 (low dose group; n = 10): received EGb at a dose of 100 mg/kg; orallyby daily gavage for 4 weeks. This dose is equivalent to the human therapeuticdose.(3) Group 3 (high dose; n = 10): received a dose of EGb 200 mg/kg; orally by dailygavage for 4 weekResult in low doses show mild degenerative disease in high doses show severe degenerative and fibrotic changes

Conclusion Gingko biloba is hazardous to liver in small and high doses.

Abstract #1075

Assessment of severity of acute liver injury and its outcome in patients with dengue fever in Lahore and Rawalpindi

Talal Khurshid Bhatti[1], Talal Khurshid Bhatti[2]

[1]PIMS, [2]PIMS

Introduction: To evaluate the impact of Dengue Virus infections on liver by measuring aminotransferase levels of the patients suffering from DF during epidemic in Lahore in 2011 and in Rawalpindi in 2015.

Materials and methods: It is a multi-centered retrospective analysis of 1700 patients (1000 from LGH Lahore and 700 from HFH, Rawalpindi in 2011 & 2015 respectively. Data was analyzed in SPSS 19 with 16 variables on which relevant details were noted.

Degree of Liver Damage: The degree to which the liver was affected was evaluated in these patients and classified into four groups according to AST and ALT levels (The laboratory reference values of AST & ALT for males and females were 28 & 26 IU and 30 & 29 IU/L, respectively) at the time of presentation.

- Group A: Patients with normal AST and ALT levels.
- Group B: Patients with one of the aminotransferases increased but not > UNL × 3.
- Group C: Patients with transaminitis of 3–10 × reference values.
- Group D: Patients with transaminitis > 10 × reference values.

Results: The patients were classified into classical DF, DHF and DSS (77.6, 20.6 and 1.8% respectively. The degree of rise in aminotransferases indicating liver injury observed in LGH, Lahore was 34.9% (Grade A), 48.5% (Grade B), 14.8% (Grade C) and 1.8% (Grade D). However, in BBH, Rawalpindi, it was observed as 43.8% (Grade A), 49.3% (Grade B), 6.6% (Grade C) and 0.3% (Grade D).

G02 - Basic and clinical fibrosis research

Abstract #103

The combination of Hepatic elastography and Doppler ultrasound can predict the risk of upper gastrointestinal bleeding (UGIB) in patients with cirrhosis

Andreas Kapatais[1], Theofani Karaoulani[2], Solon Solomou[3], Evaggelia Ouranou[4], Panagiotis Labropoulos[5], Antonia Koudouri[6], Filippos Filippou[7], Margarita Theodorou[8], Eirini Peteinelli[9], Maria Kyriazopoulou[10]

[1]General Hospital of West Attica-General Hospital of Pireaus-Nikaia & General Hospital of West Attica-General Hospital of Pireaus-Nikaia & General Hospital of West Attica-General Hospital of Pireaus-Nikaia, [2]Biopathologist & Department of Transfussion & General Hospital of West Attica-General Hospital of Pireaus-Nikaia, [3]Head-Doctor & General Hospital of West Attica-General Hospital of Pireaus-Nikaia & General Hospital of West Attica-General Hospital of Pireaus-Nikaia, [4]Pathologist & General Hospital of West Attica-General Hospital of Pireaus-Nikaia & General Hospital of West Attica-General Hospital of Pireaus-Nikaia, [5]Pathologist & General Hospital of West Attica-General Hospital of Pireaus-Nikaia & General Hospital of West Attica-General Hospital of Pireaus-Nikaia, [6]Biologist & General Hospital of West Attica-General Hospital of Pireaus-Nikaia & General Hospital of West Attica-General Hospital of Pireaus-Nikaia, [7]Cardiologist & General Hospital of West Attica-General Hospital of Pireaus-Nikaia & General Hospital of West Attica-General Hospital of Pireaus-Nikaia, [8]Biochemistrist & General Hospital of West Attica-General Hospital of Pireaus-Nikaia & General Hospital of West Attica-General Hospital of Pireaus-Nikaia, [9]Head-Biopathologist & General Hospital of West Attica-General Hospital of Pireaus-Nikaia & General Hospital of West Attica-General Hospital of Pireaus-Nikaia, [10]Head-Biopathologist & General Hospital of West Attica-General Hospital of Pireaus-Nikaia & General Hospital of West Attica-General Hospital of Pireaus-Nikaia

Introduction: The role of ultrasound elastography was studied in assessing the severity of esophageal varices and the risk of upper gastrointestinal bleeding (UGIB) and none of the methods was satisfactory enough to be recommended in every day-clinical practice.
Objectives: Evaluating a method in assessing the risk of UGIB in patients with cirrhosis that combines the results from elastography with those from Doppler evaluation of the portal circulation.
Methodology: 72 patients were diagnosed with Child–pugh A or B cirrhosis based on clinical and laboratory criteria. From all patients were noted the hemodynamic parameter of the portal and liver blood flow, elastography values (it excluded the patients with ascites and Child–pugh C stage). Patients were followed on an average of 16 months (12–24) and monitored of episodes of UGIB. The etiology of cirrhosis in all patients was 31 CHB, 20 CHC, 4 CHB + D, 5 NASH, 6 ASH, others 6.
Results: The correlation between the results of liver elastography and portal vein velocity allowed diving the cirrhotic patients in three groups: low risk group(28 patients, liver stiffness < 20kpa and portal vein velocity > 15 mm/sec) in which UGIB occurred at only 2 patients(annual average frequency of UGIB 6%); the high risk group (12 patients, liver stiffness > 30kpa and portal vein velocity < 12 mm/sec)6 patients(annual average frequency of UGIB 33.2%); and intermediate risk group (32 patients that do not fit in the above groups) 8.
Conclusion: The combination of elastography and values obtained of Doppler ultrasound can select high-risk patients to be referred for endoscopic examination and prophylactic treatment for UGIB.

Abstract #132

PSOAS muscle thickness as measure for sarcopenia and prognosis in liver cirrhosis

Randall Isaac Felitro Tan[1], Ira Inductivo Yu[2]

[1]Department of Internal Medicine, National Kidney and Transplant Institute, [2]National Kidney and Transplant Institute & Philippine Heart Center

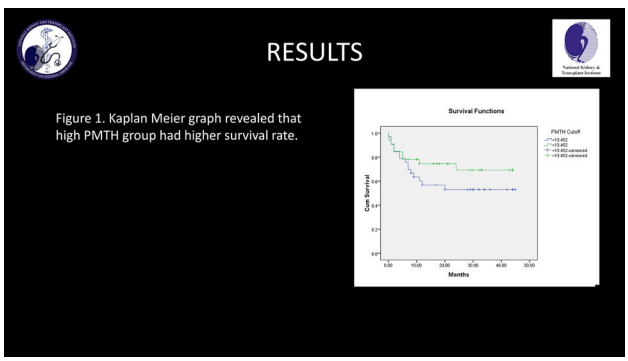
Sarcopenia—marker of malnutrition, is an independent prognostic factor for mortality in liver cirrhosis.

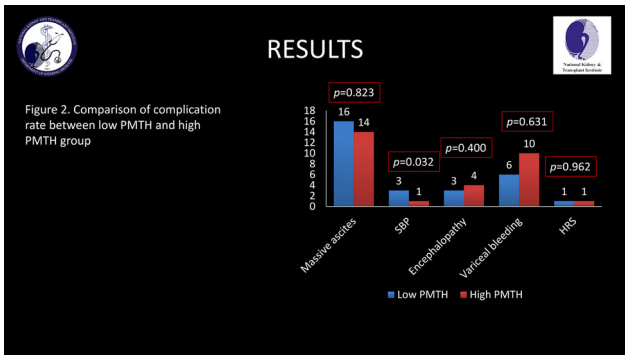
We aimed to evaluate psoas muscle thickness divided by height (PMTH) as measure for sarcopenia and determine its correlation with clinical outcomes.

Sixty-five liver cirrhosis patients were reviewed in this retrospective cohort study. PMTH were measured and correlated with clinical parameters. The diagnostic performance for predicting long-term mortality of PMTH, Child–Pugh, MELD and MELD-Na score was determined by calculating the area under the receiver-operating curve (AUROC) and cut-off values were derived. Event rate of specific complications were analyzed using the cut-off. Kaplan–Meier with log rank test was used to compare survival rates in the low PMTH vs high PMTH group. Cox regression analysis was used to determine the variables predictive of mortality.

A weak negative correlation was noted between liver-related complications and PMTH. The diagnostic performance of PMTH in predicting 6-month mortality was not significant ($p = 0.517$). The best cut-off value of PMTH to predict 6-month mortality was derived at 13.45 mm/m. Low PMTH was significantly predictive of occurrence of SBP with $p = 0.032$. The performance of PMTH in 6-month mortality was not significant ($p = 0.517$). Kaplan–Meier graph revealed that high PMTH group had higher survival rate. The univariate Cox-regression analysis demonstrated that age and lower serum Na were significantly associated with mortality ($p = 0.005$ and $p = 0.045$).

Low psoas muscle thickness is predictive of SBP occurrence. PMTH can be a supplemental prognostic marker on top of the available scoring systems in liver cirrhosis.





Abstract #163

Comparison of nutritional screening tools—NRS-2002 and RFH-NPT to predict malnutrition risk in patients with liver cirrhosis

Yuchao Wu[1], Yang Yuan[2], Zhao Yingren[3]

[1]Xi'an Jiaotong University First Affiliated Hospital, [2]Xi'an Jiaotong University First Affiliated Hospital, [3]Xi'an Jiaotong University First Affiliated Hospital

The aim of study was to compare two screening tools for malnutritional risk and prognosis of patients with liver cirrhosis. The study randomly evaluated 213 adult liver cirrhosis patients treated between October 2015 and May 2016. The patients were selected to utilize Nutritional Risk Screening 2002 (NRS-2002) and Royal Free Hospital- Nutritional Prioritizing Tool (RFH-NPT) to assess the risk of malnutrition and followed up for survial analysis. The prevalence of patients at higher nutritional risk was 53.05% with NRS-2002 and 62.91% with RFH-NPT in all patients, which had significantly difference (P = 0.001). Besides, more cirrhosis patients in Child C were preticted high malnutrition risk by RFH-NPT (88.46%) vs NRS-2002 (67.95%) (P < 0.001); no significant difference were found in Child A and B. More patients in MELD score < 10 and 10 ~ 20 were availuable to RFH-NPT (56.49%, 80.95%) vs NRS-2002 (46.75%, 61.90%) (P = 0.004, P = 0.21), no difference were evaluated in score > 20. In addition, poor survial prognostic analysis was calculated in high malnutrition risk assessed by RFH-NPT (Log Rank χ^2 = 5.79, P = 0.016), compared to NRS-2002 (Log Rank χ^2 = 0.192, P = 0.661). Therefore, the better screening tool was observed in RFH-NPT for liver cirrhosis patients. Further multicenter studies will enhance our understanding of current tools for malnutrition detection of chronic liver disease patients in cirrhosis.

Table 1 Baseline characteristics between low-risk and high-risk groups among the 213 patients assessed by NRS-2002(a) and RFH-NPT(b)

a.

index	NRS-2002		t	P
	Low Risk	High Risk		
BMI(kg/m2)	24.97±2.97	21.80±3.49	7.07	<0.01
MAC(cm)	28.37±3.09	25.38±3.51	6.57	<0.01
TSF(mm)	25.98±11.96	16.44±9.19	6.56	<0.01
Total Protein(65-85g/L)	65.91±8.41	64.89±9.96	0.804	0.422
Albumin(40-55g/L)	34.96±7.11	33.28±5.68	1.91	0.057
Prealbumin(150-380mg/L)	127.49±67.95	93.93±61.61	3.125	0.002
Total bilirubin(3.4-17.1umol/L)	35.12±49.90	81.40±125.24	-3.46	0.001
Na(137-147mmol/L)	140.77±4.54	137.50±13.05	2.38	0.018
Cr(57-111umol/L)	61.78±31.28	68.62±68.19	-0.91	0.358
BUN(3.1-8.8mmol/L)	5.24±2.10	5.86±4.74	-1.21	0.228
Ferroprotein (30-400ng/mL)	289.71±333.83	448.79±537.44	-1.34	0.186
INR(0.94-1.30)	1.33±0.26	1.66±1.39	-2.32	0.021
PT(11-14s)	16.27±2.52	17.75±5.97	-2.301	0.022
PTA(84%-128%)	63.30±17.00	56.75±20.95	2.24	0.027
Total lymphocyte count(1.1-3.2×10^9/L)	1.15±0.83	1.02±0.64	1.27	0.205
Blood ammonia(9-47umol/L)	53.76±26.69	60.02±33.70	-0.947	0.346
Child-Pugh score	7.71±2.24	9.26±2.24	-5.04	<0.01
MELD score	6.45±5.81	10.22±8.92	-3.60	<0.01

b.

index	RFH-NPT		t	P
	Low Risk	High Risk		
BMI(kg/m2)	24.71±3.26	22.45±3.56	4.62	<0.01
MAC(cm)	28.63±3.25	25.69±11.59	6.16	<0.01
TSF(mm)	26.26±11.58	17.77±10.40	5.49	<0.01
Total Protein(65-85g/L)	67.02±7.97	64.40±9.84	2.00	0.046
Albumin(40-55g/L)	37.04±5.88	32.32±6.11	5.53	<0.01
Prealbumin(150-380mg/L)	139.81±64.47	88.45±60.00	2.99	<0.01
Total bilirubin(3.4-17.1umol/L)	38.73±69.33	72.03±112.62	-2.375	0.018
Na(137-147mmol/L)	139.97±14.71	138.48±5.95	1.04	0.30
Cr(57-111umol/L)	60.84±31.62	68.10±63.69	-0.947	0.345
BUN(3.1-8.8mmol/L)	4.94±1.90	5.94±4.46	-1.90	0.058
Ferroprotein (30-400 ng/mL)	261.14±282.19	439.89±526.03	-1.43	0.16
INR(0.94-1.30)	1.29±0.27	1.63±1.28	-2.43	0.020
PT(11-14s)	15.83±2.52	17.77±5.52	-2.95	0.004
PTA(84%-128%)	67.07±17.62	55.09±18.97	4.17	<0.01
Total lymphocyte count(1.1-3.2 ×10^9/L)	1.26±0.89	0.9778±0.61	2.76	0.006
Blood ammonia(9-47umol/L)	53.58±29.30	58.93±31.76	-0.71	0.480
Child-Pugh score	6.96±1.77	9.46±2.18	-8.64	<0.01
MELD score	5.92±5.93	9.94±8.43	-3.72	<0.01

Table 2 Comparison of prevalence of manultrition using different screening tools

NRS-2002	RFH-NPT		Total	P
	Low risk	High risk		
Low risk	71	29	100	
High risk	8	105	113	0.001
Total	79	134	213	

Table 3 Relationship between nutrition risk screening tools among different Child Pugh grade.

Child	RFH-NPT	NRS-2002		Total	P
		Low risk	High risk		
A	Low risk	41	2	43	1
	High risk	2	10	12	
	Total	43	12	55	
B	Low risk	23	4	27	0.267
	High risk	9	44	53	
	Total	32	48	80	
C	Low risk	7	2	9	<0.001
	High risk	18	51	69	
	Total	25	53	78	

Table 4 Relationship between nutrition risk screening tools among different MELD score.

MELD	RFH-NPT	NRS-2002		Total	P
		Low risk	High risk		
≤10	Low risk	62	5	67	0.004
	High risk	20	67	87	
	Total	82	72	154	
10 ~ 20	Low risk	7	1	8	0.021
	High risk	9	25	34	
	Total	16	26	42	
20 ~ 30	Low risk	2	2	4	0.50
	High risk	0	8	8	
	Total	2	10	12	
> 30	Low risk	0	0	0	-
	High risk	0	5	5	
	Total	0	5	5	

Figure 1

Kaplan–Meier curves of survival analysis for the patients stratified as low risk and high risk using the NRS-2002 scale.

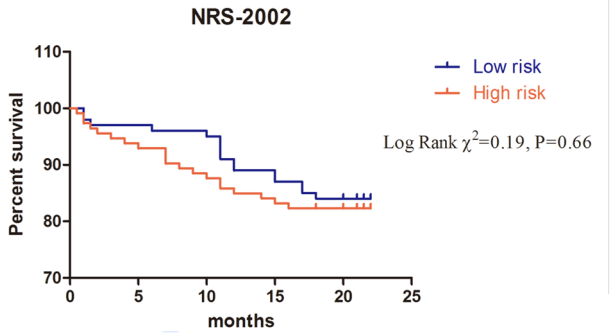
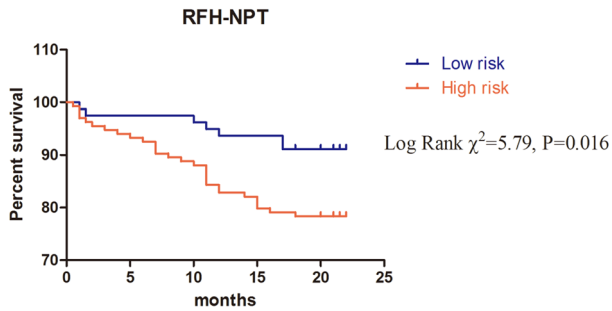


Figure 2

Kaplan–Meier curves of survival analysis for the patients stratified as low risk and high risk using the RFH-NPT scale.



Abstract #345

Fgl2 regulates liver fibrosis progression and reversal by promoting profibrotic infiltrating macrophages maintenance

Ran Tao[1], Wei Yuan[1], Fang Xiao[1], Meiqi Liu[1], Hongwu Wang[1], Di Wu[1], Jiaquan Huang [1], Xiaoping Luo[1], Xiaoyang Wan[1], Qin Ning[1]

[1]Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology

Introduction: Fibrinogen-like protein 2 (Fgl2) is known as a crucial inflammatory regulator. However, its contribution in the pathogenesis of liver fibrosis remains unclear.
Objectives: We aimed to investigate the molecular mechanism underlying the involvement of Fgl2 in macrophages function in the pathogenesis of liver fibrosis.
Methods: Twenty patients with HBV-induced fibrosis were recruited. FGL2 levels were determined via enzyme-linked immunosorbent assay and reverse transcription-polymerase chain reaction. Genetic ablation of the Fgl2 gene in rodent models were used to evaluate the phenotype of monocyte/macrophages in the liver by using flow cytometry. Administration of muramyl dipeptide (MDP) was used to alleviated fibrosis in fgl2-/- mice. Blood circulating monocytes were further analyzed. We sought investigation on macrophage-dependent regulation of hepatic stellate cells (HSCs) by using primary HSCs and HMs coculture system in vitro. The expression of fibrogenic factors in HSCs were evaluated.
Results: We identified increased Fgl2 expression was associated with high grade of liver fibrosis in chronic Hepatitis B patients and experimental models. Genetic ablation of the Fgl2 alleviated fibrosis progression and promoted reversal during the resolution, which was linked to a restorative phenotype of macrophage in Fgl2-/- mice. Moreover, administration of MDP alleviated fibrosis in fgl2 deficient mice, which was associated with coordinated an increased Ly6Clow phenotype. Fgl2 depletion in macrophages significantly dampened the activation of primary HSCs in vitro in response to macrophage-dependent stimulation.
Conclusion: Fgl2 regulates liver fibrosis by maintaining profibrotic phenotype in resident and infiltrating macrophages, thereby providing novel insights into therapeutic strategy for fibrosis treatment.

Abstract #446

Combination treatment with epigallocatechin gallate and silibinin restored antioxidant defense mechanisms and prevented N-nitrosodimethylamine induced hepatic fibrosis in rats

Joseph George[1], Takahiro Minato[1], Yasuhiro Matsue[1], Yuki Hirakawa[1], Mikihiro Tsutsumi[1], Mutsumi Tsuchishima[1]

[1]Department of Hepatology, Kanazawa Medical University, Uchinada, Ishikawa 920-0293, Japan

Introduction: Hepatic fibrosis is the result of exuberant wound healing response to a persistent stimulus. Epigallocatechin-3-gallate (EGCG) and silibinin are powerful antioxidants present in green tea and milk thistle, respectively. Oxidative stress and reactive oxygen species (ROS) play significant role in the pathogenesis of hepatic fibrosis.
Objectives: Evaluate the combination effect of EGCG and silibinin to prevent experimentally induced liver injury and fibrosis in rats.
Methodology: N-nitrosodimethylamine (NDMA) was used to induce liver injury and fibrosis. A group of animals received 0.2 mg EGCG/100 g body weight orally 2 h prior to NDMA administration. Another

group received silibinin 2 mg/100 g body weight and the next group received both EGCG and silibinin in combination. Alanine transaminase (ALT), aspartate transaminase (AST), osteopontin, collagen type IV, TGF-β1, and hyaluronic acid (HA) were measured in serum. Glutathione, glutathione peroxidase, and malondialdehyde were determined in the liver. Collagen type I, α-smooth muscle actin (α-SMA), 4-hydroxy-2-nonenal (4-HNE), and osteopontin were stained on liver sections.

Results: Serum ALT, AST, osteopontin, collagen type IV, TGF-β1, and HA were significantly decreased after EGCG and silibinin treatment. While glutathione and glutathione peroxidase significantly increased in the liver tissue, malondialdehyde levels markedly decreased indicating improved antioxidant status. Furthermore, staining depicted remarkable decrease in collagen type I, α-SMA, 4-HNE, and osteopontin after EGCG and silibinin treatment with a synergistic effect after the combination therapy.

Conclusion: The data indicates both EGCG and silibinin are effective to protect liver from oxidative stress and ROS induced liver injury and subsequent hepatic fibrogenesis.

Abstract #587

The Role of CX43 in Human Menstrual Blood-Derived Stem Cell's suppression in activating hepatic stellate cell

Sainan Zhang[1], Ya Yang[2], Fen Zhang[3], Lanjuan Li[4]

[1]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases & The First Affiliated Hospital & Zhejiang University School of Medicine, [2]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases & The First Affiliated Hospital, School of Medicine, & Zhejiang University, [3]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases & The First Affiliated Hospital, School of Medicine, & Zhejiang University, [4]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases & The First Affiliated Hospital, School of Medicine, & Zhejiang University

Introduction: Liver fibrosis is a reversible wound healing response to acute or chronic hepatocellular injury from various etiologies. Activation of hepatic stellate cell plays a pivotal role in the development of liver fibrosis. Human menstrual blood-derived stem cells (MenSCs), also known as menstrual blood-derived mesenchymal stem cells, are reported to protect liver from injury. Connexin43(CX43) is a ubiquitous gap junction protein expressed in a wide variety of tissues and organs that regulates celluar functions such as cell growth, differentiation, migration, metabolism and so on.

Objectives: The aims of the study were to verify the hypothesis that CX43 participates in activation of hepatic stellate cell. The protective effect of MenSCs against liver fibrosis was regulated by CX43 expression.

Methodology: In this study, we investigated differential expression in LX2 (an immortalized hepatic stellate cell line) that were cocultured with MenSCs. Gap26, an inhibitor of CX43, was added to clarify the communication between LX2 and MenSCs. CX43 Cell proliferation was tested by CCK8. Protein secretion in culture supernates were tested by ELISA and protein expression of cell were tested by western blotting.

Results: MenSCs suppressed proliferation of LX-2 cells and the secretion of α-SMA and TGF-β1. Expression of CX43 in LX2 increased when cocultured with MenSCs. Inhibition of CX43 suppressed the protective effect of MenSCs against liver fibrosis. MAPK signal pathway maybe the possible function method.

Conclusion: MenSCs suppressed the activation of hepatic stellate cell. Gap junction communication based on CX43 maybe the possible approach that MenSCs protected liver against fibrosis.

Abstract #792

Non-heavy drinking and worsening of non-invasive fibrosis markers in nonalcoholic fatty liver disease: A cohort study

Yong Kyun Cho[1], Yoosoo Chang[2], Yejin Kim[3], Eunju Sung[4], Jiin Ahn[5], Hyun-Suk Jung[6], Kyung Eun Yun[7], Seungho Ryu[8]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea, [2]Center for Cohort Studies, Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea & Department of Occupational and Environmental Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea & Department of Clinical Research Design & Evaluation, Saihst, Sungkyunkwan University, Seoul, South Korea, [3]Center for Cohort Studies, Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea, [4]Center for Cohort Studies, Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea, [5]Center for Cohort Studies, Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea, [6]Center for Cohort Studies, Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea, [7]Center for Cohort Studies, Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea, [8]Center for Cohort Studies, Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea & Department of Occupational and Environmental Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea & Department of Clinical Research Design & Evaluation, Saihst, Sungkyunkwan University, Seoul, South Korea

The effect of modest alcohol consumption on fibrosis progression in the general population with NAFLD remains unclear. We examined the association of non-heavy alcohol consumption with worsening of non-invasive fibrosis indices in a large-scale, low-risk population with non-alcoholic fatty liver disease (NAFLD). A cohort study was performed in 58,927 Korean adults with NAFLD and low fibrosis scores who were followed for a median of 8.3 years. Non-, light, and moderate drinkers were defined as 0 g/day, 1–9.9 g/day, and 10–29.9 g/day (10–19.9 g/day for women), respectively. Progression from low to intermediate or high probability of advanced fibrosis was assessed using non-invasive indices including NAFLD fibrosis score (NFS) and FIB-4. Parametric proportional hazards model was used to estimate the multivariate-adjusted hazard ratios and 95% confidence intervals. During 347,925.4 person-years of follow-up, 5630 subjects with low FIB-4 progressed to intermediate or high FIB-4. The multivariable-adjusted HRs (95% CI) for worsening of FIB-4 comparing light-drinkers and moderate-drinkers with non-drinkers were 1.06 (0.98–1.16) and 1.29 (1.18–1.40), respectively. Similarly, using NFS, corresponding HRs (95% CI) comparing light-drinkers and moderate-drinkers with non-drinkers were 1.09 (1.02–1.16) and 1.31 (1.23–1.40), respectively. Furthermore, the association of moderate drinkers with worsening of either FIB-4 or NFS remained significant after introducing alcohol use and confounders treated as time-varying covariates.

Conclusion: In this large-scale cohort of young and middle aged individuals with NAFLD, non-heavy alcohol consumption, especially moderate alcohol consumption, was significantly and independently associated with worsening of noninvasive markers of fibrosis, indicating that even moderate alcohol consumption might be harmful.

Abstract #844

Orphan nuclear receptor NR4A1 impedes Hepatic stellate cell activation

Dinesh Mani Tripathi[1], Savneet Kaur [2], Abhishak Gupta [3], Juan Carlos Garcia-Pagan[4], Shiv Kumar Sarin[5]

[1]Institute of Liver and Biliary Sciences, New Delhi, India, [2]Institute of Liver and Biliary Sciences, New Delhi, India, [3]Institute of Liver and Biliary Sciences, New Delhi, India, [4]Barcelona Hepatic Hemodyanimic Lab, Hospital Clínic, Idibaps, Ciberehd, Barcelona, Spain, [5]Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Hepatic stellate cell (HSC) activation promotes fibrosis. Orphan nuclear receptors and their role in fibrosis remain unexplored.
Objectives: We evaluated the role of orphan nuclear receptor NR4A1 in HSC activation and liver fibrosis.
Methodology: NR4A1 expression was assessed in healthy and cirrhotic liver tissues from human subjects with different aetiologies and in healthy and cirrhotics rats [thioacetamide (TAA) and carbon tetrachloride (CCl4)]. HSC were isolated from healthy rats, activated in vitro up to 3 passages (p0, p2, p3) and treated with the NR4A1 agonist, cytosporane B (CsnB; 10 μg/ml) or vehicle (Veh; DMSO). HSC activation markers and NR4A1 expression, total NR4A1 and phosphorylated/inactivated (pNR4A1) protein expression was evaluated.
Results: In cirrhotic livers, NR4A1 protein expression was significantly increased as compared to healthy, both in humans (+200 to 350%) and rats (TAA: + 20%; CCl4: + 49%) with an increase in expression of inactivated (phosphorylated) NR4A1 (pNR4A1, TAA: + 11%; CCl4: + 57%). In vitro data demonstrated significant induction of NR4A1 during HSC activation. NR4A1 mRNA expression was significantly increased from p0 to p2 (> eightfold) and further up-regulated in p3 (> 30 fold) in comparison to p0 HSC. Increased NR4A1 positively correlated with HSC activation markers (αSMA, Col1a1 and PDGFBR). Pharmacological activation of NR4A1 by CsnB caused down-regulation of HSC activation markers αSMA (− 93%, − 97%), PDGFRβ (− 84%, − 86%) and Col1a1 (− 49%, − 75%) in comparison to vehicle-treated cells.
Conclusion: Our study demonstrates for the first time NR4A1 as a novel modulator of HSC phenotype. Inactive form of this transcription factor is highly expressed in cirrhotic livers, thereby proposing modulation of NR4A1 activity as a promising avenue to treat chronic liver diseases.

Abstract #850

Circulatory endothelial progenitor cells (CEPCs) from cirrhotics enhances liver fibrosis and angiogenesis in bile duct ligated cirrhotic rats

Dinesh Mani Tripathi[1], Mohsin Hassan[2], Savneet Kaur[3], Shiv Kumar Sarin[4]

[1]Institute of Liver and Biliary Sciences, New Delhi, India, [2]Institute of Liver and Biliary Sciences, New Delhi, India, [3]Institute of Liver and Biliary Sciences, New Delhi, India, [4]Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Cirrhotic patient-derived endothelial progenitor cells (EPCs) secrete higher proangiogenic factors in comparison to the control-derived endothelial progenitor cells and lead to greater enhancement of angiogenesis via interaction with resident liver endothelial cells.
Objectives: The effect of cirrhotic and control EPCs on hepatic angiogenesis and fibrosis in vivo was evaluated.
Methodology: Cirrhotic animal models were prepared (n = 10) and circulating EPCs isolated from cirrhotic and healthy human blood were cultured ex vivo and transplanted in control and patient EPC-treated group of BDL rats (n = 5). The untreated group of rats received only saline (n = 5). Rats were sacrificed one week after the transplantation of cells. Biochemical parameters were analysed and fibrosis was evaluated by histopathology of the liver tissues, alpha-SMA expression was evaluated by western blotting and immunohistochemistry and angiogenesis was studied by evaluating the expression of CD31 by immunohistochemistry in the treated and untreated animals.
Results: In comparison to the healthy-EPC-treated and saline-treated rats, cirrhotic-EPC-treated rats had higher ALT (204 IU/L) and bilurubin (3.4 mg/dl) ($p < 0.05$ vs both) while lower hepatic glucose (20 mg/dl) and microalbumin (30 mg/dl) low ($p = 0.05$ vs both). An increase in fibrosis (from grade 2 to 4) was observed in cirrhotic-EPC-treated rats as compared to healthy EPC-treated and saline-treated rats. Immunohistochemical data showed an enhancement of both fibrosis and angiogenesis markers, alpha-SMA and CD31 in cirrhotic EPC-treated rats as compared to healthy EPC-treated and untreated rats ($P < 0.05$).
Conclusion: The study suggests that cirrhotic patient-derived circulating EPCs lead to a significant increase in liver fibrosis by enhancing intrahepatic angiogenesis.

Abstract #964

Correlation of Factors associated with minimal and advanced fibrosis among HbeAg negative chronic hepatitis B patients using fibroscan and controlled attenuation parameter

Orlando II Villanueva Pariñas[1], Marilyn Talingdan TE[1], Diana Alcantara Payawal[1]

[1]Fatima University Medical Centre

Objective: This study aims to identify factors associated with mild and advanced hepatic fibrosis using Transient Elastography (FibroScan) and Controlled Attenuation Parameter (CAP) among HBeAg negative Chronic Hepatitis B (CHB) patients.
Methods: All patients with HBeAg negative CHB who underwent FibroScan were enrolled in this study. Presence of hepatic steatosis and fibrosis using FibroScan were assessed and correlated with demographic factors, transaminases, HBV DNA and imaging studies.
Results: A total of 56 patients were enrolled in the study to evaluate the association of liver stiffness measurement using FibroScan® with laboratory and imaging studies among HBeAg negative CHB patients. Patients with mild fibrosis (F0-F1) were grouped into Group I and those with higher fibrosis (F2-F4) were grouped into Group II. Results of the study showed the following: (1) age, gender and BMI are not associated with liver stiffness among two groups; (2) there is no difference in the rate of advanced fibrosis between normal and elevated transaminases; (3) there is no significant difference between two groups in relation to the ultrasound findings and quantification of steatosis using CAP and (4) level of HBV DNA is associated with progression of hepatic fibrosis.

Conclusion: The results of this study demonstrated that the use of transaminases and liver imaging studies does not accurately assess the extent of hepatic injury while detectable levels of HBV DNA is associated with fibrosis among HBeAg negative CHB patients. It is therefore recommended that these subset of CHB patients should undergo FibroScan to monitor progression of fibrosis.

Abstract #966

Fuzheng Huayu Recipe combined with entecavir ameliorates liver fibrosis in HBV transgenic mice by regulating hepatic natural killer cells function

Xin Sun[1], Da-Bing Ping[1], Yuan Peng[1], Cheng-Hai Liu[1,2]

[1]Institute of Liver Diseases, Shuguang Hospital, Affiliated To Shanghai Uversity of Tcm, Shanghai, China, [2]Shanghai Key Laboratory of Traditional Chinese Clinical Medicine, Shanghai, China

Background: Natural killer (NK) cells are known for their ability to kill activated HSCs, which has been confirmed both in patients and animal models. HBV infection can weaken the innate immune response and decrease the activity of NK cells in liver. Enhancing the function of hepatic NK cells may be a new way to fight liver fibrosis after HBV infection.
Methods: HBV transgenic C57BL/6 male mice were adopted to prepare HBV fibrosis model by intraperitoneal injection of 10% CCl4. ETV + FZHY, ETV alone were administered to mice by intragastric gavage, respectively. The virological markers, liver function markers, liver pathology was considered the main efficacy evaluation index. And flow cytometry was used to detect the proportion of NK cells and the expression of its activated receptor NKG2D in liver.
Results: FZHY + ETV can significantly inhibit HBV replication, effectively prevent the development of liver fibrosis, and up-regulate the proportion of hepatic NK cells and its activated receptor NKG2D.
Conclusions: The effect of ETV + FZHY against fibrosis in HBV transgenic mice may be related to regulating hepatic NK cells function.

Abstract #1003

Blocking mild liver fibrosis in chronic hepatitis B patients treated with traditional chinese medicine: a multicenter, double-blind, placebo randomized controlled trial

Xiaoling Chi[1], Huanming Xiao[1], Junmin Jiang[1], Guangjun Tian[1], Gaoshu Cai[1], Yubao Xie[1], Meijie Shi[1], Qin Li[2], Dewen Mao[3], Jingdong Xue[4], Hongzhi Yang[5], Wei Lu[6], Hui Guo[7], Chunliang Lei[8], Liang Chen[9], Huabao Liu[10], Jing Wang[11], Yueqiu Gao[12], Zehuai Wen[1], Yafeng Wang[13], Jiezhen Chen[1], Shuduo Wu[1], Huijun Chen[1], Bo Tan[1], Pengtao Zhao[1], Yingxian Li[1], Chaozhen Zhang[27], Hongcai Liang[1], Chanyuan Xu[1]

[1]Guangdong Provincial Hospital of Chinese Medicine, [2]Fuzhou Infectious Diseases Hospital, [3]First Affiliated Hospital of Guangxi University of Chinese Medicine, [4]Shanxi Provincial Hospital of Chinese Medicine, [5]Third Affiliated Hospital of Sun Yet-Sen University, [6]Tianjin Infectious Diseases Hospital, [7]First Affiliated Hospital of Tianjin of Chinese Medicine, [8]Guangzhou No 8 People's Hospital, [9]Shanghai Public Health Clinical Center, [10]Chongqing Hospital of Chinese Medicine, [11]Affiliated Hospital of Chinese Medicine of Luzhou Medical Colledge, [12]Shuguang Hospital Affiliated of Shanghai University of Traditional Chinese Medicine, [13]World Federation of Chinese Medicine Societies

Background: Although previous studies have concluded that Traditional Chinese Medicine (TCM) can block liver fibrosis in Chronic Hepatitis B (CHB) patients, there are limited data on patients with mild liver fibrosis. The aim of this study is to evaluate the efficacy of TCM tablets of the compound biejiaruangan (RGT) and anluohuaxian pills (ALHXP) on CHB patients with mild fibrosis ($G < 2$, $S \leq 2$).
Methods: This double-blind, placebo randomized controlled trial was designed to treat 540 CHB patients with mild fibrosis in 12 hospitals. The treatment group and placebo group were randomly divided into two groups at a ratio of 2:1. The treatment group was treated with ALHXP or RGT based on syndrome differentiation. The placebo group was treated with placebo. The primary end point is the histological change after 48-week treatment.
Results: A total of 540 patients were enrolled and 270 of them had two liver biopsies. As a result, the fibrosis improvement rate was 37.4% (70/187) in treatment group, which is significantly higher than that in placebo group (19.3%, P = 0.003). Moreover, the fibrosis progression rate in treatment group was 16.0% (30/187), which was significantly lower than that in placebo group (32.5%, P = 0.002). More interestingly, the fibrosis progression rate in placebo group with abnormal baseline ALT was significantly higher than that in ALT normal group (44.4% vs 18.4%, P = 0.012). For safety evaluation, no serious side effects were found in this study.
Conclusion: ALHXP and RGT are both effective and safe in treatment of CHB patients with mild fibrosis.

Abstract #1020

Assessment of bone mineral density in cirrhotic patients at cardinal santos medical center

Kenji Madriaga Sato[1]

[1]Cardinal Santos Medical Center

Introduction: Bone disease is an important and common complication of cirrhosis because of its negative effect on quality of life. Since the liver produces various molecules that can act as growth factors or hormones it has been further postulated that a decrease in liver function will result in osteoporosis.
Objectives: The present study aimed at estimating the prevalence and factors influencing the osteoporosis in patients with liver cirrhosis and its association to severity of liver dysfunction.
Methodology: This is a retrospective cross-sectional study on 153 cirrhotic patients. Review of medical records and database records of patients was done. Bone Mineral Density (BMD) was correlated with DEXA scans. Chi square test was used to assess the statistical significance of the association.
Results: The mean age was 65 years. Subjects most commonly belonged to Child's Pugh class (CTP) B (54%), followed by Child's A (31%) with Child's C with only 14%. The most common etiology was NAFLD at 39%. As the CTP scoring increase from A to C the numbers of patients were increased from normal to osteopenia (p Value = 0.000). Statistical significance was found between Low

BMD with Model for end-stage liver disease (MELD) (p value = 0.001) and duration of diseases (p value = 0.015). Serum markers such as elevated Bilirubins, AST, AST is associated with low BMD (p Value = 0.001).

Conclusion: Liver disease is associated with bone loss that is due to decreased bone formation or increased bone resorption. This is associated with increased fracture risk.

G03 - Imaging and non-invasive assessment of fibrosis

Abstract #178

Serum exosomal miR-92a as a novel noninvasive biomarker for hepatic fibrosis in chronic hepatitis B patients

Qianqian Wang[1], Chenlu Huang[2], Yuxian Huang[3]

[1]Department of Hepatology, Shanghai Public Health Clinical Center, Fudan University, Shanghai, China, [2]Department of Hepatology, Shanghai Public Health Clinical Center, Fudan University, Shanghai, China & Department of Infectious Diseases, Huashan Hospital, Fudan University, Shanghai, China, [3]Department of Hepatology, Shanghai Public Health Clinical Center, Fudan University, Shanghai, China & Department of Infectious Diseases, Huashan Hospital, Fudan University, Shanghai, China

Introduction: Emerging evidence shows that miRNAs are involved in hepatic fibrosis progression and can serve as biomarkers for liver fibrosis in chronic hepatitis B patients (CHB).

Objectives: We investigated the role of serum exosomal miRNAs as potential biomarkers for discriminating no or mild fibrosis (S0–1) from significant fibrosis (S2–4) in CHB patients.

Methodology: Next generation sequencing was performed in 9 CHB patients for serum exosomal miRNAs and 72 miRNAs were differentially expressed between patients with no or mild versus significant liver fibrosis. Eventually, serum exosomal miR-92a was identified as a candidate biomarker for hepatic fibrosis. We analyzed the expression levels of serum exosomal miR-92a and serum miR-92a by qRT-PCR in 106 patients and 82 patients, respectively.

Results: Serum exosomal miRNA-92a was significantly higher in patients with significant fibrosis (S2–4) than no or mild fibrosis (S0–1) ($p < 0.0001$) and the expression levels of exosomal miR-92a were positively correlated with hepatic fibrosis progression($r = 0.76$, $p < 0.0001$). Exosomal miR-92a was also the best independent predictor for significant fibrosis (OR = 1.492, p = 0.002). The AUROC of exosomal miR-92a was 0.87 with the sensitivity of 77.78% and specificity of 88.37% at cut-off value of 1.195. Intriguingly, further analysis showed that exosomal miR-92a were most closely related to the TGF-β signaling pathway. However, there were no significant difference in the levels of serum miR-92a between significant fibrosis and no or mild fibrosis.

Conclusions: Serum exosomal miR-92a may be used as a novel noninvasive biomarker for significant hepatic fibrosis and exerts obvious advantages over APRI and FIB-4 in Chinese CHB patients.

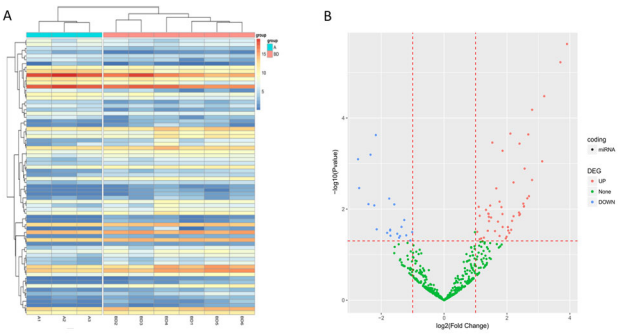


Fig. 2. Serum exosomal microRNA expression profiling using Illumina HiSeq sequencing in 9 CHB patients.

Figure Legends

Fig. 2. Serum exosomal microRNA expression profiling using Illumina HiSeq sequencing in 9 CHB patients. (A) The hierarchical clustering based on the normalized signal intensities of 72 microRNAs which were differentially expressed (51 up-regulated and 21 down-regulated) in moderate-to-severe fibrosis (S2-4) compared with no or mild fibrosis (S0-1). 3 patients with no or mild fibrosis (S0-1) are represented in group A; 6 patients with moderate-to-severe fibrosis (S2-4) are represent in group BD. Fold changes (FC) >2or<-2and P-values<0.05 are considered significant. Up-regulated microRNAs are represented in red, and down-regulated ones are in blue. (B) Volcano plot of differentially expressed 72 microRNAs in serum exosomes between no-or-mild fibrosis (S0-1) and significant fibrosis (S2-4). The red circle indicates a fold change with values greater than 2, and blue circles indicate a fold change with values lower than -2. The green circle indicates there is no statistically difference between two groups.

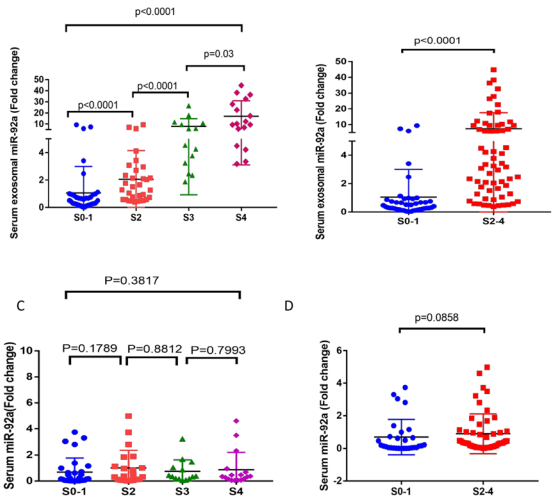


Fig. 3. Serum exosomal microRNA-92a expression levels in 106 patients (A,B)and serum microRNA-92a expression levels in 82 patients (C,D) grouped by staging of fibrosis.

Figure Legends ：

Fig. 3. Serum exosomal microRNA-92a expression levels in 106 patients (A,B) and serum microRNA-92a expression levels in 82 patients (C,D) grouped by staging of fibrosis. (A) Distribution of serum exosomal miRNA-92a levels in patients at different fibrosis stages from S0 progression to S4 are showed in scatter diagram. (S0-1, n=43; S2, n=32; S3, n=14; S4, n=17). In scatter dot plots, the horizontal bars over the dots represent the median values, and the upper and lower lines of the horizontal bars represent the interquartile range of the median. (B) The expression levels of serum exosomal miR-92a in patients grouped by staging of fibrosis between S0-1 (n=43) and S2-4 (n=63). (C) Distribution of serum microRNA-92a in patients at different fibrosis stages from S0 progression to S4 are showed in scatter diagram. (S0-1, n=30; S2, n=21; S3, n=14; S4, n=17). (D) The expression levels of serum microRNA-92a in patients grouped by staging of fibrosis between S0-1 (n=30) and S2-4 (n=52).

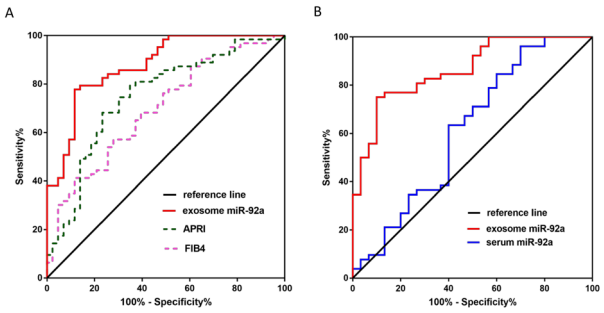


Fig. 4. Discrimination of significant hepatic fibrosis by serum exosomal miR-92a.

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Fig 4. Discrimination of significant hepatic fibrosis by serum exosomal miR-92a. (A) ROC curve analyses were carried out and AUC for exosomal miR-92a was 0.87, APRI was 0.75 and FIB4 was 0.7 in 106 patients. (B) AUC for serum exosomal miR-92a-3p was 0.87, serum miR-92a-3p was 0.61 in 82 patients. APRI, aspartate aminotransferase-to-platelet ratio index; FIB-4, the fibrosis-4 score.

Table 1. Logistic regression analysis to discriminate significant fibrosis in CHB patients.

	Univariate analysis		Multivariate analysis	
	OR (95%CI)	P value	OR (95%CI)	P value
Serum exosomal miR-92a	1.65 (1.246-2.186)	<0.0001	1.492 (1.154-1.93)	0.002
Gender, male/female	0.603 (0.269-1.355)	0.221		
Age, years	0.992 (0.958-1.028)	0.678		
HBeAg, +/-	0.999 (0.999-1.000)	0.034	0.999 (0.999-1.000)	0.064
HBV DNA, log10copies/ml	1.026 (0.85-1.238)	0.798		
Platelet count, ×10^9/L	0.995 (0.988-1.003)	0.22		
ALT, IU/L	1.003 (0.999-1.006)	0.153		
AST, IU/L	1.007 (0.999-1.015)	0.08		
ALP, IU/L	1.003 (0.988-1.019)	0.666		
GGT, IU/L	1.009 (0.999-1.02)	0.091		
Total bilirubin, μmol/L	1.044 (0.994-1.096)	0.086		
Albumin, g/L	0.88 (0.776-0.997)	0.045	0.836 (0.708-0.987)	0.035
Globulin, g/L	1.135 (1.037-1.242)	0.006	1.15 (1.014-1.305)	0.03

CHB, chronic hepatitis B; HBV, hepatitis B virus; HBeAg, hepatitis B e antigen; ALT, alanine transaminase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, γ-glutamyl transpeptidase

Table 2.Diagnostic performances of serum exosomal miR-92a and other noninvasive models for significant hepatic fibrosis in the entire cohort of 106 patients.

	AUROC	95%CI	P value	Cut-off value	Sensitivity%	Specificity%
Serum exosomal miR-92a	0.87	0.89-0.97	P<0.0001	1.195	77.78	88.37
APRI	0.75	0.65-0.85	P<0.0001	0.513	68.25	76.74
FIB-4	0.7	0.60-0.80	P=0.0006	1.114	65.08	62.79

APRI, aspartate aminotransferase-to-platelet ratio index; FIB-4, the fibrosis-4 score

Table 3. Diagnostic performances of serum exosomal miR-92a and serum miR-92a for significant hepatic fibrosis in 82 patients

	AUROC	95%CI	P value	Cut-off value	Sensitivity%	Specificity%
Serum exosomal miR-92a	0.87	0.93-0.99	P<0.0001	1.195	75	90
Serum miR-92a	0.61	0.48-0.75	P=0.08	0.245	63.46	60

Abstract #294

Role of liver and spleen stiffness measured by magnetic resonance elastography for the non-invasive diagnosis of liver fibrosis

Han Wang[1], Wenping Luo[1], Yu Wang[1], Hong Ma[4]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China

Background and Aims: Magnetic resonance elastography (MRE) is a method based on magnetic resonance technique to calculate elasticity of tissue. The purpose was to assess the diagnostic accuracy of liver stiffness and spleen stiffness measured by MRE (LS-M, SS-M) for assessing liver fibrosis. To compare the diagnostic accuracy of LS-M and liver stiffness measured by Acoustic Radiation Force Impulse (ARFI) (LS-A), SS-M and spleen stiffness measured by ARFI(SS-A) for assessing liver fibrosis, respectively.

Methods: In this study, we enrolled 84 subjects who underwent liver biopsy and MRE in Beijing Friendship Hospital, Capital Medical University. Area under the receiver operating characteristic (AUC) analysis was performed to assess the accuracy of LS-M and SS-M in diagnosing fibrosis. The influencing factors with LS-M and SS-M were explored using multivariate analysis.

Results: 1. Cut-off values of LS-M for diagnosing $F \geq 2$, $F \geq 3$ and $F = 4$ were 3.47 kPa, 4.05 kPa and 5.41 kPa, respectively. AUC were 0.946, 0.934 and 0.925. 2. Cut-off values of SS-M for diagnosing $F \geq 2$, $F \geq 3$ and $F = 4$ were 7.19 kPa, 7.19 kPa and 7.40 kPa, respectively. AUC were 0.719, 0.884 and 0.897, respectively. 2. There were significantly greater diagnostic accuracy for diagnosing $F \geq 2$ and $F \geq 3$ in LS-M than that in LS-A($p < 0.05$), no significantly difference for diagnosing $F = 4$. 3. There were significantly greater diagnostic accuracy for diagnosing $F \geq 2$, $F \geq 3$ and $F = 4$ in SS-M than that in SS-A($p < 0.05$). 4. SS-M was correlated with platelet (PLT). LS-M was correlated with grade of inflammation, PLT and Albumin.

Conclusions: MRE can be effective method for assessment of liver fibrosis.

Table 1. Clinical Characteristics of Subjects

Variables	Patients (n=84)
Demographic	
Age, years	49(40,53)
Sex （Male/female）	29/55
BMI(kg/m^2)	23.8(22.2,26.9)
Etiology	
Viral hepatitis/PBC/NASH/AIH/Others	4/15/34/21/10
Biochemical profile	
ALT, IU/L	76(43.5,143)
AST, IU/L	57.2(34,100.8)
ALP, IU/L	129(88,171)
GGT, IU/L	76.5(39,171)
TBIL, μmol/L	14.78(11.33,24.18)
WBC, *10^9/L	4.74(3.8,6.1)
PLT, *10^9/L	192(132,254)
ALB, g/L	39.7(35.1,42.9)
PTA, %	89.5(81.4,100.7)
Fibrosis stage	
F0/F1/F2/F3/F4	12/17/17/24/14
Inflammation grade	
G0/G1/G2/G3/G4	18/21/20/11/14

Table 2. Diagnostic Performances of MRE and ARFI for fibrosis

Fibrosis Stage	Cut-off	AUROC	Sensitivity	Specificity
F≥2				
LS-M, kPa	3.47	0.946	0.96	0.83
LS-A, m/s	1.54	0.678	0.71	0.65
SS-M, kPa	7.19	0.719	0.69	0.96
SS-A, m/s	2.13	0.700	0.50	0.88
F≥3				
LS-M, kPa	4.05	0.934	0.87	0.83
LS-A, m/s	1.64	0.789	0.96	0.68
SS-M, kPa	7.19	0.884	0.87	0.88
SS-A, m/s	2.17	0.679	0.45	0.96
F=4				
LS-M, kPa	5.41	0.925	0.93	0.81
LS-A, m/s	1.91	0.828	0.69	0.99
SS-M, kPa	7.4	0.897	0.93	0.72
SS-A, m/s	2.23	0.642	0.39	0.99

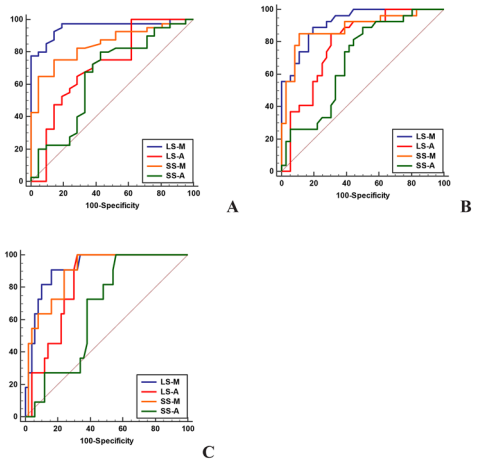


Figure 1. ROC curves for ARFI and TE for the diagnosis of F≥2(A), F≥3(B) and F=4(C)

Table3. Diagnostic test characteristics of MRE and ARFI for the diagnosis of fibrosis

p-value	LS-M vs. LS-A	SS-M vs. SS-A
F≥2	0.002	0.023
F≥3	0.025	0.005
F=4	0.072	0.001

Table 4. The influencing factors of LS-M and SS-M in Multivariate analysis

Variables	beta	p
LS-M		
PLT	-0.008	0.007
ALB	-0.104	0.028
G	0.712	0.003
SS-M		
PLT	-0.009	0.01

Abstract #295

Assessment of liver fibrosis with FibroTouch in patients with chronic liver disease

Wenping Luo[1], Han Wang[1], Hong Ma[1], Yu Wang[1]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China

Introduction: FibroTouch(FT) is a noninvasive device based on two-dimensional transient elastography to quantify liver fibrosis, developed in China.

Objectives: To research the diagnostic efficacy of FT for liver fibrosis.

Methodology: Patients who took percutaneous liver biopsy in Beijing Friendship hospital from 03/2014 to 05/2018 were enrolled. We collected clinical data and evaluated fibrosis with liver biopsy as the gold standard. The diagnostic accuracy were assessed by area under the receiver operating characteristic curves(AUROCs). The correlating factors were explored by multivariate analysis.

Results: 286 patients were enrolled, including viral hepatitis(n = 63), non-alcoholic fatty liver disease(n = 68), primary biliary cirrhosis(n = 58), autoimmune hepatitis(n = 33) and other liver diseases(n = 64).

1. FT, FS and ARFI were correlated with liver fibrosis stages, and the correlation coefficient were 0.671, 0.728 and 0.573, respectively ($P < 0.05$).

2. By AUROC, the optimal cutoff values of FT, FS and ARFI were 9.6 kPa (AUROC:0.855), 8.1 kPa (AUROC:0.875) and 1.59 m/s (AUROC:0.801) for ≥ F2, 12.8 kPa(AUROC:0.869), 9.1 kPa(AUROC:0.875) and 1.65 m/s (AUROC:0.800) for ≥ F3, and 18.3 kPa (AUROC:0.902), 17.1 kPa (AUROC:0.913), and 1.88 m/s (AUROC:0.825) for = F4.

3. By pairwise comparison of AUROC, FibroTouch has similar diagnostic efficacy for liver fibrosis compared with FibroScan while predicting each stages of liver fibrosis. FibroTouch was superior to ARFI for a diagnosis of ≥ F3 and similar to ARFI when predicting ≥ F2 and = F4.

4. In multivariate analysis, FT were correlated with histological activity grade, platelet, direct bilirubin, alkaline phosphatase and prothrombin activity.

Conclusions: FibroTouch has similar diagnostic efficacy for liver fibrosis with FibroScan, while was superior to ARFI for a diagnosis of advanced fibrosis.

Table 1. Baseline characteristics of the patients enrolled in the study.

Characteristics	Patients
Age (years)	45 ± 14
Gender(male)	108 (37.7%)
BMI (kg/m^2)	23.4 (20.8,25.6)
Etiology	
Viral hepatitis	63 (22.0%)
NAFLD	68 (23.8%)
PBC	58 (20.3%)
AIH	33 (11.5%)
Others	64 (22.4%)
PLT (*10^9/L)	181 (118,234)
WBC(*10^9/L)	4.8 (3.8,6.0)
ALT (U/L)	50 (28,106)
AST (U/L)	47 (29,85)
ALP (U/L)	109 (83,173)
GGT (U/L)	72 (36,183)
TBIL (μmol/L)	15.24 (10.20,22.80)
DBIL (μmol/L)	3.50 (2.02,6.27)
ALB(g/L)	39.2 ± 5.4
PTA(%)	94.0 ± 18.9
PA(mg/L)	175.0 (127.5,214.4)
Fibrosis stage	
F0	48 (16.8%)
F1	94 (32.9%)
F2	58 (20.3%)
F3	49 (17.1%)
F4	37 (12.9%)
Inflammatory stage	
G0	55 (19.2%)
G1	76 (26.5%)
G2	99 (34.6%)
G3	22 (7.7%)
G4	27 (9.4%)
FibroTouch(kPa)	10.0 (6.2,16.6)
FibroScan(kPa)	8.9 (6.0,15.6)
ARFI(m/s)	1.56 (1.23,2.08)

Quantitative variables were expressed as mean±standard deviation (SD) for normal distribution, and median (P25, P75) for skewed distribution.Qualitative variables were expressed as number (percent).

Abbreviations: BMI, body mass index;NAFLD,non alcoholic fatty liver disease; PBC, primary biliary cirrhosis;AIH,autoimmune hepatitis;PLT, platelet;WBC,white blood cell;ALT, alanine aminotransferase;AST,aspartate aminotransferase;ALP,alkaline phosphatase;GGT, gamma-glutamyl transpeptidase;TBIL,total bilrubin;DBIL,direct bilrubin;ALB,albumin;PA,prealbumin;PTA, prothrombin activity;ARFI,acoustic radiation force impulse.

Table 2 .Diagnostic Performances of FT,FS and ARFI for liver fibrosis.

Fibrosis stages		Cut-off	AUC (95%CI)	Se(%)	Sp(%)	*FT vs FS (P)*	*FT vs ARFI (P)*	*FS vs ARFI (P)*
F≥2						0.2089	0.0612	0.0084
	FT	9.6	0.855 (0.806-0.896)	79.43	73.94			
	FS	8.1	0.875 (0.828-0.913)	84.21	76.12			
	ARFI	1.59	0.801 (0.747-0.849)	71.43	76.30			
F≥3						0.7417	0.0314	0.0106
	FT	12.8	0.869 (0.821-0.908)	75.90	83.00			
	FS	9.1	0.875 (0.828-0.913)	87.34	70.21			
	ARFI	1.65	0.800 (0.745-0.847)	81.25	71.81			
F=4						0.7246	0.0988	0.0259
	FT	18.3	0.902 (0.858-0.935)	83.78	88.21			
	FS	17.1	0.913 (0.872-0.945)	82.35	88.84			
	ARFI	1.88	0.825 (0.773-0.870)	88.57	74.68			

Abbreviations:FT,FibroTouch; FS,FibroScan; ARFI,acoustic radiation force impulse.
AUROC, area under the receiver operating characteristics curve;CI,confidence interval.
P value: AUROC of FT versus FS,AUROC of FT versus ARFI,AUROC of FS versus ARFI→DeLong test

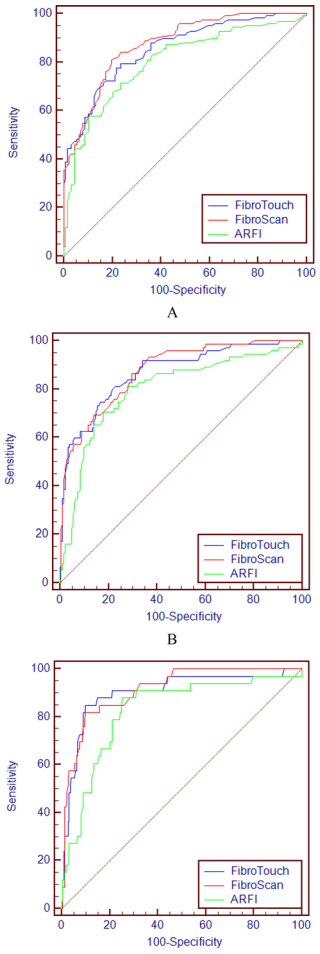


Figure 1. ROC curves for FibroTouch,FibroScan and ARFI for the diagnosis of F≥2(A), F≥3(B), F=4(C).

Abstract #333

Degree of liver fibrosis and viral load in patients with chronic hepatitis B infection undergoing transient elastography—a single center cross-sectional study

Junmay Giltendez Dacal[1], Enjel A. Gabriel[1], Jenny Lim Limquiaco[1], Lawrence U. Liu[1]

[1]CEBU Doctors' University Hospital

Significance: Presence of liver fibrosis in chronic hepatitis B infection influences management decisions. The immune tolerant phase and inactive carrier state of chronic HBV infection do not require treatment. However, studies looking into these seemingly quiescent stages have shown presence of moderate to severe degree of fibrosis. There has been no local data hence this study aims to determine the degree of liver fibrosis and viral load in this subgroup of patients.

Methodology: This is an observational cross-sectional study conducted in Cebu, Philippines. Patients with chronic hepatitis B infection undergoing transient elastography from January 2017 to September 2018 with complete data on viral hepatitis serology, viral load and ALT are enrolled. Descriptive statistics, frequency and percentages are employed. Spearman correlation coefficient is used to determine if a correlation exits between viral load and degree of fibrosis.

Results: Out of total 224 patients, 147 were enrolled for the study. Most of patients are male with mean age of 46 years and ALT level of 38.8 U/L. Mean HBV DNA level is 15,548,348 IU/ml. 83% of the patients have HBeAg negative status. Majority of patients have no evidence of fibrosis.13.6% have severe fibrosis and cirrhosis (8.1% in HBeAg- group; 5.5% in HBeAg + group). Although there is a significant relationship between HBV DNA and fibrosis, this is weak linear relationship (r + 0.343, P0.00).
Conclusion: Transient elastography identifies a proportion of patients with presence of severe fibrosis and cirrhosis even in dormant stages of chronic HBV infection. Treatment may be warranted in the presence of advanced fibrosis and especially cirrhosis.

Abstract #394

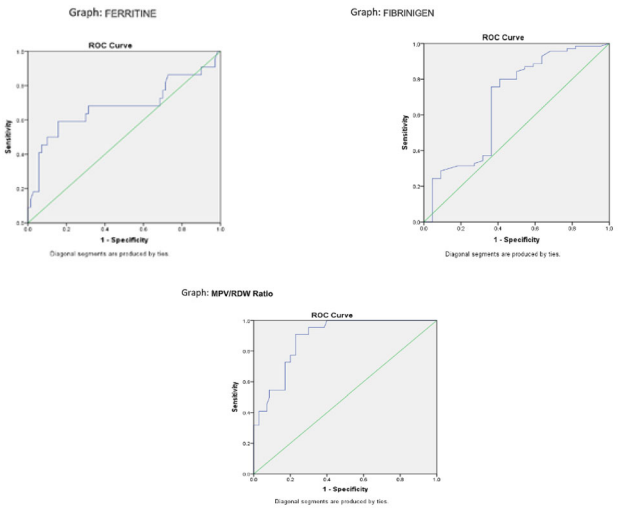
A study to evaluate prognostic biomarkers in decompensated cirrhosis (Ferritin, Fibrinogen and MPV/RDW)

Ekant Surendra Gupta[1], Sharath Putta Reddy[1], Sethu Babu[1]

[1]Krishna Institute of Medical Sciences, Hyderabad

Introduction: Chronic liver disease with its complications is associated with high morbidity and mortality. The disease progression and outcome is now being assessed using non invasive biomarkers. We studied ferritin, fibrinogen and mean platelet volume/red blood cell distribution width(MPV/RDW) as prognostic biomarkers.
Objectives: To study ferritin, fibrinogen, MPV/RDW and its association with early outcome(death, survival) in decompensated cirrhotic patients after one month.
Methodology: 100 patients aged 18–70 years, diagnosed as decompensated cirrhosis were enrolled in our study from June-2017 to May-2018. Patients with etiology of haemochromatosis were excluded.
Results: 100 patients (age 52 ± 10 years, M: F-78:22) were enrolled. In our study, 24% and 76% patients were in CTP class B and C respectively. Out of 100 patients, 70(70%) were alive, 22(22%) died and 8 (8%) were subjected to liver transplantation during one month. Ferritin (< 200, 200–400, > 400 ng/mL), fibrinogen (< 100, 100–200, > 200 mg/dL) and MPV/RDW(≤ 0.50, 0.51–0.60, > 0.60) were significantly different when considered both as continuous and categorical co-variate between death and survival ($p < 0.05$). In univariate logistic regression analysis, high ferritin (OR > 400 = 10.52, p = 0.030; RC: Ferritin < 200), high MPV/RDW ratio (OR > 0.6 = 26.82, p = 0.002; RC: MPV/RDW Ratio ≤ 0.50) and low fibrinogen(OR < 200 = 6.09, p = 0.027; RC Fibrinogen > 300) were the independent factors significantly associated with the outcome. In multivariate analysis, high MPV/RDW Ratio(> 0.60) was the only independent factor significantly associated with the outcome (p = 0.005). Area under the ROC curves showing that MPV/RDW had higher discriminative ability to negative outcome (AUC = 0.883) as compared to ferritin(AUC = 0.803) and fibrinogen (AUC = 0.678).
Conclusion: High Ferritin, high MPV/RDW and low fibrinogen is associated with poor outcome in patients with established decompensated cirrhosis.

	Alive (n=70)	Death (n=22)	p-value
MPV	10.1±1.9	13.1±2.4	< 0.0001*
RDW	18.9±2.6	18.6±3.3	0.647
MPV/RDW Ratio	0.54±0.11	0.70±0.09	< 0.0001*



Area Under the Curve					
	Area (AUC)	Std. Error	Asymptotic 95% Confidence Interval		p-value
			Lower Bound	Upper Bound	
FERRITINE	.678	.078	.525	.830	0.012*
FIBRINIGEN	.678	.073	.535	.822	0.012*
MPV/RDW Ratio	.883	.035	.815	.951	< 0.0001*

Abstract #475

Predictors for fibrosis regression in chronic HCV patients after treatment with DAAS: results of a real-world cohort study

Sherief M. Abd-Elsalam[1], Hanan H Soliman[1], Dina H Ziada[1]

[1]Tropical Medicine Department-Tanta University

Introduction: Direct-acting antivirals (DAAs) in treatment of chronic HCV patients have led to marvelous improvement of rates of sustained virological response (SVR). However, the main goal of therapy is obtaining histological and hemodynamic regression because this will reduce all-cause mortality and morbidity especially the risk of hepatocellular carcinoma and liver failure. The aim of this study was to detect the factors affecting fibrosis regression in Chronic HCV patients treated with DAAs.
Methods: This study was conducted in Tropical Medicine and Infectious Diseases department, Tanta University, Egypt. This was a Prospective observational cohort study conducted between October 2015 and December 2017. Transient elastography (FibroScan®) examination was performed as base line before therapy, at SVR12, 6 months and 1 year after completing therapy for cured patients.
Results: Nearly half of the patients with moderate fibrosis had fibrosis reduction by one grade or more by the end of the year. The percent was higher in advanced fibrosis, with 89% and 78.7% of the patients had at least one grade reduction in their fibrosis one year after interferon containing and interferon free regimens respectively. Using multiple regression analysis; BMI, degree of hepatic stiffness and degree of steatosis were related to regression of hepatic fibrosis after therapy.

Conclusions: DAAs resulted in a significant improvement in parameters of liver fibrosis. BMI, steatosis and LS were independent factors for fibrosis regression in chronic HCV patients treated with DAAs. We need more studies to explore the mechanism by which steatosis affects fibrosis regression especially in the era of DAAs.

Abstract #619

External validation in Asian non-alcoholic fatty liver disease (NAFLD) patients of the FibroScan-based FAST^{TM} score to identify at risk non-alcoholic steato-hepatitis (NASH) patients

Vincent Wai-Sun Wong[1], Ming-Hua Zheng[2], Atsushi Nakajima[3], Anthony Wing-Hung Chan[4], Yang–Yang Li[5], Shoji Yamanaka[6], Kento Imajo[7], Xiao-Yan Pan[8], Grace Lai-Hung Wong[9]

[1]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, [2]NAFLD Research Center, Department of Hepatology, The First Affiliated Hospital of Wenzhou Medical University & Wenzhou Key Laboratory of Hepatology & Institute of Hepatology, Wenzhou Medical University, [3]Department of Gastroenterology and Hepatology, Yokohama City University Graduate School of Medicine, [4]Department of Anatomical and Cellular Pathology, The Chinese University of Hong Kong, [5]Department of Pathology, The First Affiliated Hospital of Wenzhou Medical University, [6]Department of Pathology, Yokohama City University Graduate School of Medicine, [7]Department of Gastroenterology and Hepatology, Yokohama City University Graduate School of Medicine, [8]Department of Endocrinology, The First Affiliated Hospital of Wenzhou Medical University, [9]Department of Medicine and Therapeutics, The Chinese University of Hong Kong

Objectives: Recently a score named FAST^{TM} combining FibroScan liver stiffness measurement (LSM), controlled attenuation parameter (CAP) and AST has been proposed to identify NASH patients with significant fibrosis (NASH + NAS $\geq$ 4+F $\geq$ 2). This is to facilitate selection of patients for clinical trials and future treatment. The objective was to perform a validation of this score in Asian biopsy-proven NAFLD patients from independent cohorts.
Methodology: Consecutive patients from 3 liver units (Hong-Kong (N = 243), Wenzhou (N = 111) and Yokohama (N = 50)) who underwent a concomitant liver biopsy (LB) for suspicion of NAFLD, a FibroScan (LSM and CAP) and blood withdrawal were pooled. In each cohort, a single expert pathologist staged the LB using the NASH CRN scoring system. The FAST^{TM} performance was assessed using area under the receiver operating characteristics (AUC). Performance associated with cut-offs determined in the derivation cohort was assessed (0.40 for sensitivity (Se) $\geq$ 0.90 and 0.76 for specificity (Sp) $\geq$ 0.90).
Results: After excluding missing data, 263 patients were analyzed. 40% of the pooled cohort were female, median age was 51 [IQR = 20] years and body mass index was 27.2 [5.2] kg/m^2. 45% had fibrosis stage F $\geq$ 2, 11% were cirrhotic, 62% were NASH and 32% were NASH + NAS $\geq$ 4+F $\geq$ 2. The FAST^{TM} AUC to identify those patients was 0.85 (0.80–0.89). At 0.40 cutoff, Se = 0.92, Sp = 0.55 and negative predictive value = 0.93. At 0.76 cutoff, Sp = 0.88, Se = 0.54 and positive predictive value = 0.68. 35% of the patients were in between cutoffs.
Conclusion: The FAST^{TM} showed good performance in Asian NAFLD patients and can be used to identify patients eligible for potential pharmacologic therapy.

Abstract #659

A noninvasive diagnostic system for cirrhosis in patients with non-alcoholic fatty liver disease

Cailun Zou[1], Qianyi Wang[1], Xiaojuan Ou[1], Xinyan Zhao[1], Min Wang[1], Yameng Sun[1], Yu Wang[1], Weijia Duan[1], Xiaoming Wang[1], Ping Wang[1], Shanshan Wu[2], Yuanyuan Kong[2], Jidong Jia[1]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, [2]Clinical Epidemiology and Ebm Unit, Beijing Friendship Hospital, Capital Medical University

Introduction and Objectives: Presence of cirrhosis in patients with non-alcoholic fatty liver disease (NAFLD) is predictive of long-term liver-related outcome. However, the noninvasive diagnosis is still challenging. The aim of this study was to construct a noninvasive diagnostic scoring system consisting of demographic, anthropometric, laboratory and liver stiffness measurement (LSM) for NAFLD related cirrhosis.
Methods: Consecutive patients with histologically proven NAFLD were enrolled. The clinical and histological data were collected. A non-invasive scoring system was constructed by multivariate modeling with histological staging as the gold standard, and the diagnostic performance was compared with other four models using area under receiver operating characteristic (AUROC) curves.
Results: Of 107 NAFLD patients enrolled, 28% were histologically diagnosed with cirrhosis. History of diabetes mellitus, body mass index, platelet count, total bile acid level, and liver stiffness measurement were 5 independent indicators of cirrhosis by multivariate analysis. A scoring system (NAFLD cirrhosis score) with these 5 variables had an AUROC curve of 0.942 (95% CI: 0.870–0.981) for diagnosis of cirrhosis, which was superior to NAFLD fibrosis score (AUROC: 0.803; 95% CI: 0.704–0.880), FIB4 (AUROC: 0.866; 95% CI: 0.777–0.930), BARD (AUROC: 0.810; 95% CI: 0.712–0.886) and APRI (AUROC: 0.738; 95% CI: 0.633–0.827). An internal validation of the new score was addressed by bootstrapping and had a discrimination with AUROC of 0.950.
Conclusion: NAFLD cirrhosis score is a simple and reliable scoring system that may be used for the diagnosis of NAFLD related cirrhosis noninvasively.

Abstract #714

Diagnostic accuracy of gamma glutamyl transferase platelets ratio in predicting liver fibrosis and cirrhosis noninvasively in HCV patients

Muhammad Osama Tariq Butt[1], Abdul Nadir[1], Kamran Shafiq[1], Ahmed Zia[2]

[1]Department of Gastroenterology, Pakistan Kidney and Liver Institute and Research Centre, [2]Department of Radiology, Pakistan Kidney and Liver Institute and Research Centre

Introduction: Assessment of the presence or absence of cirrhosis is important which is most commonly undertaken by Hepatic Sheer Wave Elastography (SWE). A number of non-invasive hepatic fibrosis scoring algorithms have been developed to assess hepatic fibrosis.
Objective: This study was done to compare SWE to the non-invasive algorithms in adult HCV positive patients.
Methods: For each patient, the AST/ALT ratio, GGT Platelet Ratio (GPR), APRI and FIB 4 scores were calculated. Patients were divided into non cirrhotic (NCR) (F0–3) and cirrhotic (CR) (F4) groups based

on SWE readings (F0–1 $\leq$ 7.02 kPa and F4 $\geq$ 11.6 kPa). The diagnostic accuracy of fibrosis markers was estimated by using the receiver operating characteristic (ROC) curve.
Results: Total number of patients were 480, 27.5% had F0-F1 while 50.4% had F4 fibrosis on SWE. For the prediction of Cirrhosis ($\geq$ F4), AUROC of GPR (0.801) was significantly higher than FIB4 (0.794) and APRI (0.768) with the optimal cut off of GPR taken as 0.25. (sensitivity and specificity of 81.4% and 63.2% respectively). Fig. Similarly for the prediction of fibrosis ($\geq$ F2), AUROC of GPR (0.820) was significantly higher than FIB4 (0.729) and APRI (0.726) taking optimal cut off of GPR as 0.20. (sensitivity and specificity of 82.1% and 64.5% respectively).
Conclusion: For the identification of significant fibrosis and cirrhosis in HCV patients, GPR appears to be have better association than APRI and FIB4 and can be used in routine practice as an alternative to SWE especially in resource constrained country like Pakistan.

Abstract #715

Non-invasive assessment of Hepatic Steatosis using Controlled Attenuation Parameter (CAP) of FibroScan® in Patients from Yangon GI and Liver Centre (Single Centre Experience)

Soe Thiha Maung[1], Aung Hlaing Bwa[1], Si Thu Sein Win[1], Moe Pwint Oo[1], Khin Maung Win[1]

[1]Yangon Gi and Liver Centre

Introduction: Controlled Attentuation Parameter (CAP) is a non-invasive method for diagnosing hepatic steatosis. Since liver biopsy cannot be done routinely in Myanmar, CAP is used for detection and quantification of hepatic steatosis.
Objectives: Since NAFLD becomes an emerging disease in Myanmar population, this study aimed to evaluate the prevalence of hepatic steatosis of patients attending Yangon GI and Liver Centre.
Methodology: In this single-centre observational study, CAP of total 471 patients visited Yangon GI and Liver Centre were recorded and these patients were categorized into normal (S0), mild (S1), moderate (S2) or severe (S3) hepatic steatosis.
Results: Total of 471 patients were screened by using Echosens FibroScan® 530 Compact. The mean age of whole group was 47.4 years and 52% of patients were female (n = 245) and 48% were male (n = 226). The median BMI of the entire group was 26.8. Among all patients, 29% (n = 136) were HBs Ag positive, 36% (n = 170) were anti-HCV positive and the rest 35% (n = 165) were non-B non-C. CAP of all the patients were recorded and when these results were categorized, 26% (n = 122) had severe steatosis (S3), 25% (n = 119) had moderate steatosis (S2), 13% (n = 63) had mild steatosis (S1) and 36% (n = 167) had normal steatosis (S0).
Conclusion: According to this study, 64% of the study population had CAP score of more than normal value. Therefore, Myanmar population has a relatively high prevalence of fatty liver. CAP provides an immediate assessment of steatosis but longitudinal data are still needed to demonstrate how CAP relates to clinical outcomes.

Abstract #737

Spleen stiffness by shear wave elastography for the screening of varices in patients with compensated advanced chronic liver disease

Rathan Cyriac Joseph[1], Krishnadas Devadas[2], Sandeep Narayanan[3]

[1]Government Medical College Trivandrum

Introduction: With the increasing use of transient elastography, patients with compensated advanced chronic liver disease (cACLD) are on a rise, which in turn leads to the overburden of endoscopy units. Hence, simple, noninvasive tests are needed to identify patients at risk of having oesophageal varices prior to endoscopy. This study focuses on the performance of spleen-stiffness and other non-invasive indices like liver stiffness-spleen diameter-to-platelet ratio score (LSPS), liver Stiffness (LS), platelet- spleen ratio (PSR) in predicting high-risk oesophageal varices in patients with cACLD.
Methods: 202 consecutive patients with cACLD, defined by LS $\geq$ 10 kPa were included in the study. Those with history of decompensation, portal vein thrombosis, hepatocellular carcinoma or current beta-blocker therapy were excluded. Spleen-stiffness was measured with 2D-shear-wave elastography. LSPS and PSR were calculated based on established formulae. High-risk varices were defined as-large varices (diameter $>$ 5 mm) or small varices with red colour signs. Area under curve (AUC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were assessed.
Results: Spleen-stiffness with a cutoff value of 60 kPa yielded a AUC of 0.89, sensitivity of 75%, specificity of 93%, PPV of 60%, NPV of 97%, accuracy of 90%. Below the cut-off score of 60 kPa, there was $<$ 5% pooled risk of missing High-risk varices.
Conclusion: Spleen-stiffness $>$ 60 kPa by shear wave elastography had the best discrimination for high-risk varices and could spare most of the screening endoscopies with a low risk of missing high-risk varices.

Abstract #754

Comparison of diagnosis efficacy of FibroTouch and FibroScan for steatosis and fibrosis in patients with Non-alcoholic Fatty Liver Diseases

Min-Wang[1], Guanhua-Zhang[1], Yu-Wang[1]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University

Aims: To assess hepatic fibrosis and steatosis in patients with non-alcoholic fatty liver diseases by FibroTouch (FT) and FibroScan (FS).
Methods: The patients with biopsy-proven NAFLD were retrospectively enrolled from 2012 to 2018 in our hospital. Controlled attenuation parameter(CAP) and Liver stiffnesses (LS) were measured by FT and FS (M probe) before liver biopsy. Steatosis(S) and fibrosis(F) evaluated by histology was regarded as the gold standard. The performances of FT and FS for diagnosing steatosis and fibrosis were evaluated using area AUROCs. The risk factors for CAP and LS by FT were explored using multiple analysis.
Results: There were 111 patients with biopsy-proven NAFLD enrolled. The medium age and BMI were 52 years and 25.2 kg/m^2 (Table 1). For diagnosing S $\geq$ 2 and S = 3, the AUROC for FT and FS were 0.805, 0.834 (p = 0.34) and 0.851, 0.823 (p = 0.57); the cut-off values for FT and FS were 258 dB/m, 273 dB/m, and 287 dB/m, 284 dB/m, respectively (Figure 1, Table 2). For diagnosing F $\geq$ 2,

F ≥ 3 and F = 4, the AUROC for FT and FS were 0.916, 0.897 (p = 0.45), and 0.904, 0.918 (p = 0.54); and 0.869, 0.865 (p = 0.86); the cut-off values were 11.2 kPa, 7.8 kPa, and 13.0 kPa, 10.4 kPa, and 13.3 kPa, 13.1 kPa (Figure 2, Table 3); There was no significant difference between FT and FS in diagnosing efficacy of steatosis and fibrosis. Multivariate analysis demonstrated that BMI was an influencing factor for CAP values by FT; PLT, PTA, and BMI were associated with LS values by FT (Table 4).
Conclusions: FT has similar efficacy to FS in diagnosing steatosis and fibrosis in NAFLD patients.

Abstract #818

Comparison of the diagnostic value of FibroTouch and FibroScan in the degree of liver fibrosis

Zhenyu Li[1], Yinpeng Jin[2], Xiaojin Wang[2], Feng Zhou[2]

[1]Hospital of Pla Navy, [2]905 Hospital of Pla Navy

Objective: To evaluate the correlation between FibroTouch/FibroScan and liver pathological stage. Methods: 111 patients with chronic hepatitis B admitted to our department from March 2014 to July 2018 were enrolled, and the degree of liver fibrosis was measured by FibroTouch and FibroScan, respectively, and the consistency of the results of these two instruments was compared. Meanwhile, liver biopsy was performed to compare the consistency of the results of FibroTouch/FibroScan and the histopathological stage.
Results: FibroTouch and FibroSan were used to detect the degree of liver fibrosis in 111 patients, respectively. Person correlation analysis was used, and the correlation coefficient was 0.889 ($P < 0.05$), suggesting that there was a correlation between the two detected results. Based on the metavir's pathological fibrosis stage results, the area under the ROC curve of FibroTouch and FibroSan in the diagnosis of liver fibrosis was 0.934 and 0.932, with a sensitivity of 86.6% vs. 77.3% and a specificity of 100% vs. 100%. Based on the Ishark pathological fibrosis stage results, the area under the ROC curve of FibroTouch and FibroSan in the diagnosis of liver fibrosis was 0.922 and 0.945, and the sensitivity of FibroTouch and FibroSan in the diagnosis of liver fibrosis was 88.4% vs. 79.1%, and the specificity was 100% vs. 100%, but the difference was not statistically significant ($P > 0.05$).
Conclusion: FibroTouch and FibroScan have a good consistency with fibrosis stage of liver tissue, and can non-invasively detect liver hardness.

Abstract #855

A quantitative method (qVessel) analysis the characteristics of hepatic vascular changes in different causes

Zhengxin Li[1], Zhi-Min Zhao[1], Cheng-Hai Liu[1], Yayun Ren[2], Xiao Teng[2], Dean Tai[2]

[1]Institute of Liver Diseases, Shuguang Hospital, Shanghai University of Traditional Chinese Medicine, [2]Hangzhou Choutu Technology Co., Ltd.

Aims: To establish qVessel—a quantitative analysis method for hepatic vessels, and explore the characteristic of vascular changes along with the progression of fibrosis caused by three liver diseases.
Methods: 10 biopsy samples with chronic hepatitis B(CHB), 6 with primary biliary cholangitis (PBC) and 4 with non-alcoholic steatohepatitis (NASH) were collected as the training cohort. They were in different fibrosis stages evaluated by Metavir system. All slides were scanned with Genesis, then immunohistochemically stained with CD34, CK19, α-SMA to identify veins, bile ducts and arteries, respectively, the staining results were used as a reference for developing the qVessel algorithm. Then, 46 CHB, 51 PBC and 21 NASH and 11 normal liver samples were scanned and analyzed as the testing cohort.
Results: qVessel identify arteries, veins and bile ducts through discriminating elastin, thin less nucleus wall and thick rich nucleus wall, respectively. Numbers of arteries and central veins increased from S1 to S4 in all kinds of patients ($P < 0.05$). The number of arteries was the most relevant to fibrotic stages, Spearmen correlation-coefficients were 0.443, 0.334, 0.386 in CHB, PBC and NASH, respectively ($P < 0.05$). Circularity of central vein had lower numbers, while portal vein area and long axis portal vein had higher numbers in CHB than PBC in S4 stage ($P < 0.05$).
Conclusions: qVessel can be a useful tool to analyze vessels in liver biopsies. In our study, we found the numbers of arteries and central veins increased as fibrosis progress, with the most obvious change happened in arteries.

Abstract #864

Correlation Between Liver Stiffness Score by Fibroscan and Presence of Esophageal Varices Among Patients of Fatima University Medical Center

Jeriko Henry Bionat Aguirre[1], Diana Alcantara Payawal[1]

[1]Fatima University Medical Center

Background: Liver stiffness measured by transient elastography correlates with hepatic vein pressure gradient. Liver stiffness value of 21 kPa predicts significant portal hypertension.
Objective: The aim of the study is to predict presence of esophageal varices by Fibroscan and possible grading by degree of liver stiffness among patients of Fatima University Medical Center (FUMC).
Methods: A cross sectional study among FUMC patients with chronic liver disease was done. Demographic data, Fibroscan results and endoscopic findings of esophageal varices were correlated.
Results: A total of 52 patients were included in the study of which 42 were males (80.8%), and 10 (19.2%) were females. Hepatitis B is the most common etiology of patient with chronic liver disease. The mean stiffness of the study was found to be 43.5 kPa on Fibroscan. The scores obtained correlates well with the grading of esophageal varices as identified endoscopically and fits well when calculated statistically ($p < 0.05$).
Conclusion: Fibroscan is a good non-invasive method to predict the presence of esophageal varices and possible grading with high sensitivity and specificity.

Abstract #884

Correlation of the Level of Liver Fibrosis and Steatosis Using Transient Elastography (Fibroscan®) and Control of Blood Sugar in Patients with Diabetes Mellitus Type 2

Princess Joy Pagtalunan Casem[1], Diana Alcantara Payawal[1], Marilyn Talingdan Te[1]

[1]Fatima University Medical Center

Introduction: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of abnormalities in liver function and imaging detected by ultrasonography. Previous studies revealed the correlation

of NAFLD to patients with Diabetes Mellitus and severe NAFLD is prevalent in patients with Diabetes Mellitus type 2.
Objective: The aim of this study is to determine the correlation of liver steatosis and fibrosis in the blood sugar control of patients with type 2 DM.
Methods: This cross sectional study was done in patients with Type 2 DM who underwent Transient elastography (FibroScan®) at Fatima University Medical Center, Digestive unit to evaluate for liver fibrosis and steatosis. Demographic factors and HBa1c were correlated.
Results: A total of 141 patients were enrolled in the study to evaluate the association of liver fibrosis and steatosis using FibroScan® and HBa1C find in patients with Diabetes mellitus type 2. Patients with mild fibrosis (F0–F1) were grouped into Group I and those with higher fibrosis (F2–F4) were grouped into Group II. The following were the findings of this study: (1) Age and gender were not associated with liver fibrosis and steatosis. (2) There was no difference between HBa1C and liver steatosis and fibrosis in patients with type 2 DM.
Conclusion: Our results and analysis demonstrates that there was no difference between HBa1C and liver steatosis and fibrosis in patients with type 2 DM.

Abstract #885

Association of Type 2 Diabetes Mellitus with Severity of Liver Fibrosis and Steatosis Using Liver Stiffness Measurement and Controlled Attenuation Parameter in Transient Elastography (Fibroscan®)

Nezille Joy Reyes Lina[1], Diana Alcantara Payawal[1], Marilyn Talingdan Te[1]

[1]Fatima University Medical Center

Abstract
Introduction: Prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) and Diabetes Mellitus (DM) is increasing in the past decades. Diabetes Mellitus is considered as risk factor in developing NAFLD. Use of Transient Elastography (Fibroscan®) is now being employed in diagnosing early NAFLD.
Objectives: This study aims to determine the association of liver fibrosis and steatosis among Type 2 diabetic patients using non-invasive parameters of liver stiffness measurement (LSM) and controlled attenuation parameters (CAP). Furthermore, this aims to identify the risk factors associated with significant liver steatosis and fibrosis among Type 2 diabetic patients.
Methods: All patients with diabetes and impaired fasting glucose who underwent FibroScan for assessment of liver fibrosis by liver stiffness measurement (LSM), and steatosis by Controlled Attenuation Parameter (CAP) were included. Multivariate analysis on the association of Type 2 Diabetes Mellitus with severity of liver steatosis and fibrosis was done.
Results and Analysis: A total of 168 patients are included with a mean age of 57, with male predominance (78.2%). Type 2 Diabetes Mellitus is significantly associated with moderate and severe steatosis as evident by higher CAP values. Risk factors associated with significant steatosis and fibrosis include age > 50, increase BMI, higher waist circumference and dyslipidemia. However normal HbA1c, was not significantly correlated with CAP nor LSM.
Conclusion: Patients with Type 2 Diabetes Mellitus have higher steatosis and severe fibrosis. Higher BMI, age > 50, higher waist circumference and dyslipidemia are risk factors associated with staetosis and fibrosis among Type 2 Diabetic patients.

Abstract #887

Correlating Low Density Lipoprotein Levels with Steatosis and Level of Fibrosis through Transient Elastography (Fibroscan®) on Patients with Hypertension and Diabetes

Ivan William Agleham Tajan[1], Dianna Alcantara Payawal[2], Marilyn Talingdan Te[1]

[1]Fatima University Medical Center, [2]FUMC

Introduction: Lipid accumulation in the liver is a major hallmark of Non Alcoholic Fatty Liver disease which refers to a wide spectrum of liver disease ranging from simple fatty liver to non alcoholic steatohepatitis to cirrhosis. Low Density Lipoprotein Levels correlate well to development of Non alcoholic fatty Liver disease.
Objective: The aim of this study is to determine correlation between the Low Density Lipoprotein Levels and comorbid conditions with level of fibrosis and steatosis using transient elastography (Fibroscan®).
Methods: A cross sectional study was done amongst patients who undergone (Fibroscan®) in Fatima University Medical Center, Digestive health Unit and was evaluated for the presence of liver stiffness. Demographic Factors and laboratory results were correlated.
Results: A total of 71 patients fulfilled the inclusion criteria to evaluate the association of liver stiffness measurement using (Fibroscan®) with laboratory findings and demographics. Patients with mild fibrosis (F0–F1) were grouped into Group I and those with higher Fibrosis (F2–F4) were grouped into Group II. The following were the findings of the study (1) age and gender were not associated with liver stiffness amongst two groups. (2) There was no difference on the fibrosis between controlled LDL and uncontrolled LDL levels of the patients based on the target LDL per comorbid condition.
Conclusion: There is no significant difference on the level of fibrosis based on the LDL levels, however, the researcher would like to recommend adding more parameters such as the compliance and intensity and duration of Statin Level used.

Abstract #891

Correlation of Stages of Chronic Hepatitis B with Liver Stiffness and Controlled Attenuation Parameter using Fibroscan

Roda Forca Falcutila[1], Diana Alacantara Payawal[1], Marilyn Talingdan Te[1]

[1]Fatima University Medical Center

Introduction: Hepatitis B virus infection is a major health problem. Some develop acute HBV infection while others develop chronic hepatitis. Liver cirrhosis is a significant complication of chronic hepatitis. Non-invasive testing with fibroscan is now used to measure liver steatosis and stiffness.
Objective: This study aims to determine the relationship of phases of chronic hepatitis B with liver stiffness and controlled attenuation parameter using fibroscan among patient at Fatiima University Medical Center.
Methods: Patient diagnosed with chronic hepatitis B were stratified into three groups based on phases of chronic hepatitis (immune-tolerant phase, the immune-active phase, inactive hepatitis B phase). Liver stiffness and controlled attenuation parameter were determined in each group using the fibroscan. *P* value was measured to determine if the significant relationship between groups.
Results: According to the given data, it shows that there is no significant relationship between the three phases of chronic hepatitis B

and the measured liver stiffness and controlled attenuation parameter using fibroscan.
Conclusion: This study shows that no significant relationship between phases of chronic hepatitis b and the fibroscan findings of liver stiffness and controlled attenuation parameter.

Abstract #918

CCL5 expression correlates with the severity of hepatic inflammation of chronic hepatitis B

Xiang-An Zhao[1], Hai-Yan Chang[1], Yong Liu[2], Yuxin Chen[2], Yali Xiong[3], Yang Li[3], Jian Wang[3], Rui Huang[3], Chao Wu[3]

[1]Department of Infectious Diseases, Nanjing Drum Tower Hospital Clinical College of Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine, Nanjing, Jiangsu, China; [2]Department of Laboratory Medicine, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China; [3]Department of Infectious Diseases, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu, China

Background: Recent researches have revealed that C–C motif ligand 5 (CCL5) may play a key role in the acute and chronic liver disease. We aimed to clarify whether any increased CCL5 expression in CHB patients and the dynamic CCL5 expression among different stages of hepatic inflammation and fibrosis.
Methods: Fifty-one CHB patients who underwent liver biopsy and twelve healthy liver tissue samples which were obtained from donors of liver organ were recruited in the present study. CCL5 expression and CCL5+ cells in the liver tissues were analyzed using immunohistochemistry. The degree of hepatic inflammation and fibrosis of patients with chronic HBV infection was graded according to the modified histology activity index described by Scheuer.
Results: Livers in CHB patients exhibited a significantly accumulated CCL5+ cells when compared to that of healthy controls (42.80 ± 4.37 vs 7.25 ± 0.99/HPF, $P < 0.001$). Chronic HBV infected patients with higher inflammatory grading scores had more CCL5+ cells in their livers compared to those with lower scores ($P < 0.05$). However, there is no association between CCL5 expression and fibrotic staging scores in CHB patients ($r = 0.073$, $P = 0.61$). The number of CCL5+ cells in the liver tissues of CHB patients were also positively correlated with alanine transaminase ($r = 0.278$, $P = 0.041$) and aspartate aminotransferase ($r = 0.328$, $P = 0.009$).
Conclusion: CHB patients have a significant accumulation of CCL5 in the liver, and CCL5 may play a pathological role in hepatic inflammation in CHB patients.

Abstract #1019

Liver Stiffness Measurement by Fibroscan Predicts the Presence and Size of Esophageal Varices Among Patients with Chronic Liver Disease

Jeriko Henry Bionat Aguirre[1], Marilyn Talingdan Te[1], Diana Alcantara Payawal[1]

[1]Fatima University Medical Center

Background: Fibroscan is a novel, noninvasive, ultrasound-based technology that allows measurement of liverstiffness. It may be used as a noninvasive method for assessing esophageal varices, developed as an alternative toendoscopy.
Objective: To investigate the clinical value of FibroScan transient elastography for assessing portalhypertension in patients with chronic liver disease by determining the relationship between liver stiffness-measurement with the endoscopic findings of esophageal varices.
Methods: A cross sectional study among FUMC patients with chronic liver disease was done. Demographicdata, Fibroscan results and endoscopic findings of esophageal varices were correlated using Pearson's correlations.
Results: A total of 52 patients were included in the study of which 42 were males (80.8%), and 10 (19.2%) were females. Hepatitis B is the most common etiology of patient with chronic liver disease. The mean stiffness of the study was found to be 43.5 Kpa on Fibroscan. Liver stiffness was positively correlated with the presence of esophageal varices ($p < 0.05$). Liver stiffness also increased in conjunction with increased severity of esophageal varices.
Conclusion: FibroScan appears to be a clinically valuable non-invasive method to predict the presence of esophageal varices and possible grading with high sensitivity and specificity.
Keywords: FibroScan, endoscopy, esophageal varices, chronic liver disease

Liver Surgery and Transplantation

H01 - Liver resection

Abstract #568 Variation in the gut microbial community is associated with the progression of liver regeneration

Qiongling Bao[1], Lanjuan Li[1]

[1]State Key Laboratory for Diagnosis and Treatment of Infectious Disease, The First Affiliated Hospital, Zhejiang University, Hangzhou, P. R. China

Introductions: Gut flora is suggested to play a vital role in the progression of liver regeneration (LR).
Objectives: To highlight a potential dynamic interaction between intestinal bacteria (IB) and metabolites that might contribute to LR.
Methodology: Male SD rats were subjected to surgical removal of 2/3 of the liver and samples were collected over a 14-day period. Intestinal community and metabolic profiles were characterized to establish their potential interactions during LR.
Results: Partial hepatectomy caused fluctuating changes in gut microbiome, which paralleled the biological processes of LR. The enhanced cell proliferation occurring within 30–48 h was associated with a decreased ratio of Firmicutes to Bacteroidetes reflected by a reduction in Ruminococcaceae and Lachnospiraceae, while an increase in Bacteroidaceae, Rikenellaceae and Porphyromonadaceae, which was indicative of a lean phenotype. Whereas, the microbiota derived from 12–24 h and 3–14 day were characterized by elevated F/B ratios, suggesting the differing energy extract behaviors of microbiota during the course of LR. Functional changes of the shifted microbiota confirmed the pyrosequencing results. The microbiome derived from hour 12 rats showed over presentation of metabolism-related modules, while the microbiome derived from day 2 rats was functionally unique in replication-related modules. Upon examining the dynamic pattern of metabolic response, the specific pathways including glycerophospholipid metabolism, taurine and hypotaurine metabolism were identified to be attributable to the systemic alterations in LR related-metabolism. Moreover, several key functional bacteria were strongly related to the perturbations of above pathways.
Conclusion: Gut flora may play a central role in manipulating metabolic responses in LR.

Abstract #657

Non-curative surgical resection influences severe morbidity after extensive hepatobiliary resection for hepatobiliary disease

Norihisa Kimura[1], Keinosuke Ishido[1], Daisuke Kudo[1], Hayato Nagase[1], Yusuke Wakasa[1], Kenichi Hakamada[1]

[1]Hirosaki University Graduate School of Medicine

Background and Aim: Extensive hepatobiliary resection for hepatobiliary malignancies is the most effective treatment for acquiring negative margins and improved long-term survival. However, this procedure is more complex and difficult to perform compared to simple hepatectomy and can lead to severe morbidity. The aim of this study was to evaluate the short-term outcomes after extensive hepatobiliary resection for hepatobiliary disease.
Methods: One hundred twenty-seven consecutive patients who underwent major hepatectomy with biliary reconstruction between January 2001 and December 2017 were identified from a prospectively maintained institutional database. Three severe complications, such as biloma, infectious complications, and hepatic insufficiency were assessed in this analysis.
Results: Major morbidity ($\geq$ Grade 3) and mortality were 52.0% (n = 66) and 2.4% (n = 3), respectively. Biloma, infectious complications, and hepatic insufficiency occurred in 28 (22.0%), 80 (63.0%), and 25 (19.7%) patients, respectively. Cancer-positive margin was the only risk factor for biloma [odds ratio (OR) = 3.13, p = 0.023] and infectious complications (OR = 3.12, p = 0.044) in univariate analysis. Regarding hepatic insufficiency, male (p = 0.019), cancer-positive margin (p = 0.006), right side hepatectomy (p = 0.016), preoperative jaundice (p = 0.031), operative blood loss $>$ 1500 mL (p = 0.033), and perioperative blood transfusion (p = 0.007) were risk factors in univariate analysis, while, cancer-positive margin (OR = 3.29, p = 0.033) and blood transfusion (OR = 3.06, p = 0.047) were independent risk factors in multivariate analysis.
Conclusions: This study indicated that cancer-positive surgical margins influenced not only poor prognosis but also severe morbidity after extensive hepatobiliary resection. Non-curative surgical resection in addition to excessive surgical stress, such as extensive hepatobiliary resection, can lead to hypercytokinemia and worsen postoperative condition.

Abstract #756

Laparoscopic Repeat Liver Resection; Short-term Outcomes

Yang Won Nah[1], Hyung Woo Park[1], Soon Eun Park[1], Jin A. Kwon[1]

[1]Ulsan University Hospital

Background: Laparoscopic liver resection (LLR) is now accepted as a primary tool for many liver tumors including hepatocellular carcinoma (HCC) and metastatic liver tumors. Repeat LLR (R-LLR), however, is performed far less frequently. So the authors conducted this study to evaluate the short-term outcome of R-LLR.
Methods: We reviewed a prospectively collected database of 100 patients who underwent laparoscopic liver resections (LLR) from Aug 2008 to Oct 2018. Data of 10 patients undergoing R-LLR were analyzed and compared to (1) the primary LLR group (P-LLR, n = 90) and (2) repeat open liver resection group (R-OLR, n = 20).
Results: There was no perioperative mortality. 10 R-LLR's were performed for HCC (5), colorectal liver metastasis (3), prostatic cancer liver metastasis (1) and liver cyst (1). Open conversion rates were 20% for R-LLR and 3% for P-LLR (p = 0.077). Between the repeat and primary LLS groups, there was no significant difference in operative time, intraoperative bleeding amount, intraoperative transfusion rate, length of stay (LoS) and postoperative complication rates (Fig. 1). When compared R-LLS group to R-OLR group, operative time and length of stay were different significantly, favoring laparoscopic approach for repeat liver resection (Fig. 2).
Conclusion: Repeat liver resection can be done by laparoscopic approach safely and with shorter operative time and length of stay than by open approach in selected patients. More experiences are needed to define the role of repeat-LLR for recurrent liver tumors.

Abstract #842

Comparative outcomes of laparoscopic major liver resection with benchmark article and using propensity score matching

Hanisah Guiling Guro[1], Jai Young Cho[1], Ho-Seong Han[1], Yoo-Seok Yoon[1], Youngrok Choi[1]

[1]Amai Pakpak Medical Center and Seoul National University Bundang Hospital

Objective: To compare the outcomes of laparoscopic major liver resection(LLR) and open liver resection(OLR) in hepatocellular carcinoma using the "standard cohort" article method and propensity score matching method.
Methods: We retrospectively reviewed a data of 177 patients who underwent major liver resection for HCC(LLR; n = 67, OLR; n = 110). Propensity score matching method (PSM) was first used to compare outcomes between the LLR and OLR groups, 65 patients were included in this method. The second method of comparison used was Exclusion criteria method, 30 patients were included in the LLR group and 34 patients in the OLR group after exclusion was applied.
Results: After PSM, there were no significant differences in blood loss (1407.2 $\pm$ 2322.7 vs 1071.5 $\pm$ 1160.6 ml; P = 0.299), blood transfusion rate (32.2% vs 32%; P = 0.574), tumor size (4.4 $\pm$ 2.5 vs 4.7 $\pm$ 2.4 cm; P = 0.584), and complication rate (21.5% vs 33.8%; P = 0.085) in between the two groups. The mean operative time was significantly longer in the LLR than in the OLR group (418.7 $\pm$ 172 vs 335.1 $\pm$ 121.6 min; P = 0.002). The mean hospital stay was shorter in the LLR than in the OLR group (11.4 $\pm$ 8.5 vs 17.6 $\pm$ 21.4 days; P = 0.009). In the exclusion method, there were no significant differences in between the two groups in terms of blood loss (780 $\pm$ 822 vs 947 $\pm$ 660.5 ml; P = 0.382), blood transfusion rate (9 (30%) vs 11 (32.4%); P = 0.528), hospital stay (9 $\pm$ 3.7 vs 10.4 $\pm$ 3.59 days; P = 0.119), and complication rate (3 (10%) vs 7 (20.6%); P = 0.208). Operation time (395 $\pm$ 166.6 vs 296 $\pm$ 68.3 min; P = 0.002) was significantly longer in the LLR than in the OLR group. Tumor size (4.6 $\pm$ 2.6 vs 6.6 $\pm$ 3.7 cm; P = 0.016) was longer in the OLR group.
Conclusion: Both the propensity score matching method and the exclusion method are very effective in eliminating confounding factors in a given study.

H02 - Liver transplantation

Abstract #174

Excellent Outcomes for Polynesian (Maori and Pasifika) Patients Undergoing Orthotopic Liver Transplantation (OLT)

Hannah Giles[1], Ed John Gane[2], Stephen John Gerred[1]

[1]Counties Manukau Health, [2]New Zealand Liver Transplant Unit

Introduction: The Counties Manukau Health (CMH) Liver transplant recipients are unique with 40% being Polynesian. We hypothesised that outcomes post-transplant could be inferior to other groups due to higher rates of socioeconomic deprivation.
Objectives: Compare outcomes of Polynesian with non-Polynesian (NP) patients undergoing orthotopic liver transplant (OLT) at CMH.
Methods: Adult patients from CMH who underwent OLT at the New Zealand Liver Transplant Unit (NZLTU) between 1998-2018 were included. Analysis of clinical records was undertaken to obtain baseline clinical and demographic data. Follow up data was also obtained including complications and survival post-transplant. Analysis using log rank, t test and Fisher's exact. Institutional approval (#730-T04).
Results: Between 1998 and 2018, 103 CMH patients underwent OLT, 10(9.7%) were Maori, 30(29.1%) Pasifika, 35(34%) European, 17(16.5%) Asian, 9(8.7%) Indian and 2(1.9%) Other. The mean age was 47.9 years in the Polynesian cohort and 51.1 years in the NP group (p = 0.24). Most recipients were male, 70% Polynesian vs 75% NP. The most common underlying liver disease in both groups was Hepatitis B (83% Polynesian vs 24% NP); however the predominant indication for OLT in the Polynesian cohort was Hepatocellular Carcinoma (52.5%) versus end stage liver disease for NP (46%). There was no significant difference in rates of post-transplant diabetes (p = 0.30), hypertension (p = 0.10) or Calcineurin Inhibitor-induced renal impairment (p = 0.08). Survival was not significantly different between the Polynesian and NP CMH cohorts (Fig. 1) or NZLTU's national statistics at 10 years (Fig. 2).
Conclusions: The outcomes post-OLT are excellent in both Polynesian and Non-Polynesian patients.

Figure 1: Survival Polynesian vs NP

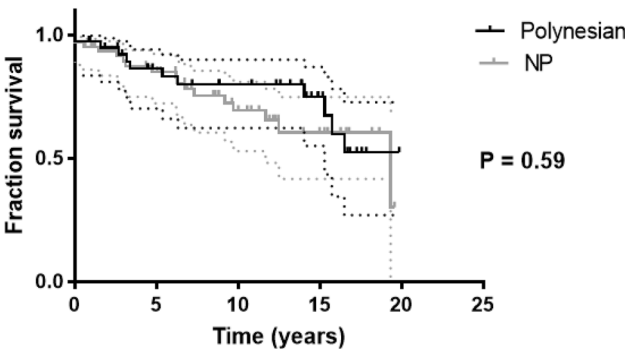
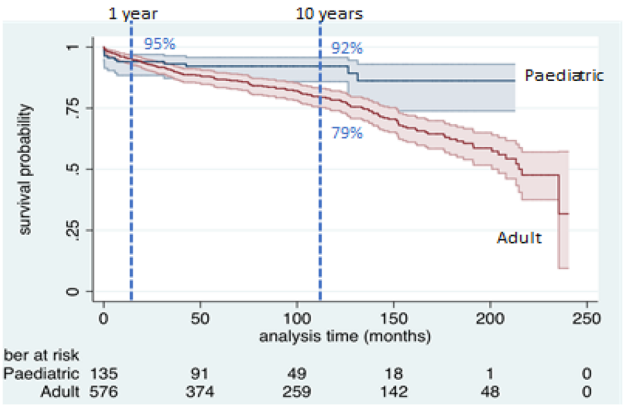


Figure 2: New Zealand Liver Transplant Unit Outcomes



Abstract #500

Sarcopenia and Chronic Liver Diseases

Ching-Sheng Hsu[1], Jia-Horng Kao[2]

[1]Liver Diseases Research Center, Taipei Tzu Chi Hospital and School of Post-Baccalaureate Chinese Medicine, Tzu Chi University, [2]Department of Internal Medicine, National Taiwan University College of Medicine and National Taiwan University Hospital and Hepatitis Research Center, National Taiwan University College of Medicine and National Taiwan University Hospital

Introduction: Growing lines of evidence indicate that sarcopenia not only correlates with the clinical outcomes and survival of patients undergoing liver transplant, but also serves as a prognostic factor for candidates of liver transplantation and patients with hepatocellular carcinoma.
Methods: We conducted a narrative review and search of literature from PubMed, Ovid MEDLINE, and the Cochrane Library database till August 2018. Studies relevant to the emerging data of sarcopenia and chronic liver diseases were examined and discussed.
Results: Sarcopenia may predict the mortality and morbidity of patients following transplantation, and recent pilot studies also demonstrated that sarcopenia may be a prognostic predictor for the outcomes of cirrhotic patients on the wait-list or with HCC. However, there is no enough data to support the use of sarcopenia as a prognostic predictor in patients with non-cirrhotic liver diseases. Lastly, a few studies has demonstrated the benefits of therapies, including nutritional (energy with/out protein) supplement and testosterone on sarcopenic cirrhosis patients.
Conclusions: Sarcopenia plays a vital role in the outcomes of cirrhotic patients with or without liver transplant. To develop an effective and practical measurement of sarcopenia has become an urgent issue in the management of patients with chronic liver diseases.

Abstract #652

Looking Through the Pipes: Role of Stent Insertion in a Post-Living Donor Liver Transplant Patient with Biliary Stricture

Enrik John Torres Aguila[1], Jonard Tan Co[1]

[1]St. Luke's Medical Center Global City

Introduction: Biliary complications are one of the major sources of morbidity for liver transplant recipients. With advances in therapeutic and diagnostic endoscopy, nonoperative management have become the preferred modality.

Methodology: This is a case of a 62-year-old male, Filipino, known cirrhotic diagnosed with hepatocellular carcinoma. He underwent right lobe living donor liver transplantation and had good recovery. 2 years post-transplant, he developed jaundice with generalized pruritus. Liver enzymes were elevated. ERCP revealed stricture in the biliary anastomosis. Cholangiogram showed a slightly dilated common bile duct (CBD) measuring 9 mm with a cutoff near the anastomotic site. Papillotomy was performed followed by dilatation of the stricture and insertion of a plastic stent with noted good egress of contrast post-procedure. Laboratory tests post-stenting revealed decreasing trends with resolution of symptoms. 6 months post-stenting, an MRCP done showed a nondilated CBD and an absent stent which was likely spontaneously passed out. Bilirubin levels were normal hence plan to replace stent to dilate stricture was aborted.

Results: The patient's late onset anastomotic stricture is likely because of fibrotic healing arising from ischemia at the anastomosed bile ducts. Therapeutic endoscopy serve as first-line where stents are inserted and replaced by larger stents every 3 months to prevent complications. Multiple stents provide greater dilatation for persistent strictures.

Conclusion: Post-liver transplant patients with biliary strictures affect graft survival. Preferred treatment is via endoscopy with repeated aggressive dilatation of the stricture and insertion of multiple plastic stents. With an over-all success rate at 70-100%, therapeutic endoscopy promises favorable outcomes.

Abstract #732

Successful Living Donor Liver Transplantation for Hepatic Encephalopathy Stage 4

Marianne Linley Loo Sy[1], Juliet Lingat Gopez-Cervantes[1], Ian Homer Yee Cua[1], Dante Allan Mayor Concejero[2], Siegfredo Ricerra Paloyo[2], Anthony Quezon Yap[2], Ma. Amornetta Jovita Padlan Jordan-Casupang[2]

[1]Institute of Digestive and Liver Diseases, St. Luke's Medical Center, Global City, [2]Center for Liver Disease and Transplantation, St. Luke's Medical Center-Global City

Significance: Historically, Living Donor Liver Transplantation (LDLT) is considered to be inferior to whole liver deceased donor liver transplantation. Improvements in surgical techniques, anesthesia, and post-operative care have made favorable outcomes with adult LDLT. LDLT has not been widely accepted as focused treatment for patient in hepatic encephalopathy stage 4.

Clinical Presentation: A 41-year-old, Filipino, male with end stage liver disease due to acute-on-top-of chronic hepatitis C related liver cirrhosis and hepatocellular carcinoma was being evaluated for liver transplantation (LT). While being prepared for the LT, his clinical status suddenly deteriorated as he had rapid decline in neurologic status in a span of few days. He was eventually intubated and slipped into hepatic encephalopathy stage 4. EEG findings (Figure 1) represent a diffuse cerebral dysfunction with intermittent runs of triphasic wave patterns most commonly seen in metabolic/toxic disturbances, such as in hepatic encephalopathy. At this time, his child–pugh score is C, iMELD 36, and UNOS status I.

Management: Emergency right lobe LDLT was done for the patient. Post-operative, there was reversal of hepatic encepalopathy, becoming GCS 15 at 3rd day post LDLT. His donor recovered without any post-operative complications.

Recommendation: Scarcity of deceased donor organs, specifically in the Philippines, is one of the major limiting factors in liver transplantation. LDLT may be the only recourse in areas where there is very low deceased donor organ donation rate. LDLT for hepatic coma is a viable option. The high iMELD and Child–pugh score do not preclude LDLT.

Abstract #771

Association of donor hepatic steatosis with ischemic reperfusion injury in liver transplant reciepent

Sunil Raviraj Kothakota[1], Prafulla Vishnurao Jadhav[2], Madhu Sasidharan[1], Harish Kareem[1], Ajith Kumar Nair[3]

[1]Senior Resident, [2]Consultant, [3]Chief Co-Ordinator

Introduction: Ischemic reperfusion injury (IRI) is an important complication of liver transplant (LT). The donor risk index (DRI), which does not incorporate steatosis, includes several variables known to impact on allograft survival. The purpose of this study was to report on donor liver allograft steatosis and its association with severity of IRI.

Aim: To determine effect of type and grade of donor liver steatosis on the occurrence and severity of IRI in LT recipients.

Methods: This was a bidirectional cohort study done at single center over a period of 37 months from July 2013 to August 2016. Liver biopsy was done twice, initially at the time of procurement before graft perfusion for steatosis assessment. Steatosis was classified as micro(MiS) or macro(MaS) with mild, moderate or severe grade. Second biopsy for IRI assessment was taken before skin closure in death donor LT (DDLT) and at the time of transaminitis in postoperative period in living donor LT (LDLT). IRI was graded as per neutrophilic infiltrate, apoptosis, and hepatocyte cell dropout. Prevalence of IRI and association steatosis was studied along with other factors.

Results: Among 53 subjects IRI was not seen in 12(22.6%). Mild IRI was seen in 26(49.1%), moderate in 13(24.5%) and severe in 2(3.8%) patients. Steatosis was not associated with IRI. DDLT and ischemic time were significantly associated with IRI. Child and MELD scores, gender and age were not associated with risk of IRI.

Conclusion: Type and grade of donor hepatic steatosis has no significant association with severity of IRI.

Abstract #876

Elizabethkingia meningosepticum blood infection in a liver transplant recipient – a case report

Avisnata Das[1], Indrajeet Kumar Tiwary[1], Mahesh Kumar Goenka[1]

[1]Apollo Gleneagles Hospital

Objectives: Preventing and managing opportunistic infections in post-transplant period in an immunosuppressed patient remains a major challenge globally in liver transplant units, including infections by less common and newly emerging organisms. Here we report a case of Elizabethkingia meningoseptica (a ubiquitous Gram negative

aerobic bacillus of the Chrysobacterium group and an emerging nosocomial pathogen) infection in a deceased donor liver transplant (DDLT) recipient.
Methodology (Clinical scenario): A 44 year old gentleman suffering from Cryptogenic Chronic Liver Disease (CLD) with Hepatocellular Carcinoma of Segment 4 (had undergone Transarterial chemoembolization and Radiofrequency ablation for the same) underwent DDLT in August 2018 at our centre. He was shifted to lIver ICU post-operatively and put on appropriate immunosuppression regime. Patient developed fever with rising procalcitonin level on post-operative Day 4, for which blood, urine, sputum cultures were sent and chest and abdominal imaging done. Blood culture showed growth of Elizabethkingia meningoseptica sensitive to Minocycline.
Results (Clinical outcome): After treatment with Intravenous Minocycline for 7 days (200 mg loading and 100 mg IV twice daily), patient became afebrile after 3 days while repeat blood culture after 5 days was sterile. He was discharged on post-operative Day 10.
Conclusion: Our literature search suggests this is the second -reported case in the world of Elizabethkingia infection in the perioperative setting of a liver transplant patient and probably the first such case from India/South Asia. The infection was successfully treated with sensitive antibiotic as per antibiogram.

Abstract #895

Portal venous stenosis after Deceased Donor Liver Transplant: A Case Report

Marianne Linley Loo Sy[1], Ian Homer Yee Cua[1], Juliet Lingat Gopez-Cervantes[1], Dante Allan Mayor Concejero[1]

[1]Institute of Digestive and Liver Diseases, St. Luke's Medical Center, Global City

Introduction: Liver transplantation (LT) is the treatment of choice for appropriately selected patients with end-stage liver disease. With evolving strategies, refinements in surgical techniques, and improved anesthesia and post-operative care, the number of liver transplant cases are expected to increase. Detection of complications post-operative is a significant component of long term management of LT patients. An important complication after LT is portal vein stenosis (PVS), a rare vascular complication but with severe sequela.
Objective: We present an adult case of deceased donor liver transplantation who developed late PVS.
Case Presentation: A 52-year-old, Filipino, male, with decompensated liver cirrhosis sec to non-alcoholic fatty liver disease, with portal hypertension, refractory ascites, hepatorenal syndrome type II, and child–pugh class B and iMELD score of 25, underwent successful deceased donor liver transplantation. One-year post LT, he had vague abdominal pain. Post operative imaging surveillance showed dilated portal venous system with focal severe stenosis. His liver function tests were normal. He underwent a portal vein stenting using a self-expandable 10 mm stent. Liver Doppler ultrasound post stenting showed patent portal venous flow.
Discussion: Portal vein stenosis (PVS) is a rare but serious vascular complication LT. As opposed to the presented case, it is frequently seen in living donor liver transplant, especially among pediatric population. Post-operative imaging surveillance plays a major role in the detection of this vascular complication.
Conclusion: Vascular complications post liver transplant are rare, and can be detected by different imaging modalities. Stent placement is a safe and effective management of PVS.

Abstract #996

Spectrum and Outcome of sepsis in Living donor Liver Transplant

Shashwat Sarin[1], Viniyendra Pamecha[1], Shridhar V. Sasturkar[1], Piyush Kumar Sinha[1]

[1]Institute of Liver and Biliary Sciences, New Delhi

Background: Sepsis is a leading cause of morbidity and mortality in patients undergoing living donor liver transplant (LDLT).
Aim: To describe the spectrum and outcome of sepsis in patients undergoing elective LDLT.
Methods: Prospectively collected data for consecutive patients who underwent LDLT at our institute from July 2012 to August 2018. Sepsis was defined as new onset bacteremia or presence of SIRS with infection post-transplant. All patients were culture negative prior to transplant. The spectrum, outcome, and predictors for mortality were calculated.
Results: A total of 342 adult patients underwent liver transplant for CLD/ACLF of which 301 (93.4%) were males with a mean age of 46.8 years (18–71), a median MELD of 25 and a median GRWR of 0.96. The most common etiologies indicating transplant were ethanol (n = 136, 39%), cryptogenic (n = 58, 16.9%) and NASH (n = 37, 10.8%). A total of 128 patients (37.4%) developed sepsis during their hospital admission, with 69 of 128 (53.9%) developing severe sepsis requiring vasopressor support. The median day of developing sepsis was 9. The incidence of bacteremia was 75/342 (21.9%). 15/128 (11.7%) patients developed fungal sepsis with culture positivity in blood or respiratory secretions.
An absolute graft weight of less than 600 gm ($p = 0.014$), re-exploration ($p < 0.001$) and post operative dialysis ($p < 0.001$) were independent predictors of sepsis ($p = 0.014$). The overall 90 day survival was 88.4%; 93.8% in the non septic group, 80.5% in the septic group and 65.8% in those with severe sepsis.
Conclusion: Sepsis is the leading cause for mortality in patients undergoing living donor liver transplant.

Abstract #1016

Single orifice venous outflow reconstruction in Living Donor Liver Transplantation using right lobe graft; Feasibility and outcome compared with the dual outflow technique

Bramhadatta Pattnaik[1], Piyush Kumar Sinha[1], Shridhar Vasantrao Sasturkar[1], Nihar Ranjan Mohapatra[1], Viniyendra Pamecha[1]

[1]Institute of Liver and Biliary Sciences

Introduction: Middle hepatic vein (MHV) reconstruction is crucial to avoid anterior sector congestion in living donor liver transplantation (LDLT) using modified right lobe graft.
Objective: To compare the single orifice outflow (RHV + MHV combined reconstruction on IVC) with dual outflow technique (RHV and MHV separate reconstruction on IVC).
Methodology: Analysis of 304 consecutive recipients who underwent LDLT using right lobe grafts at our institution from June 2011 to August 2018 was done. Group A (n = 109) received dual outflow and group B (n = 204) received single -orifice technique. The intraoperative and postoperative variables were compared.
Results: The graft recipient weight ratio (GRWR) was significantly lower in the single orifice group (0.97 vs 1.08, $p < 0.001$). The warm ischemia time (27.3 vs 46.1 min, $p < 0.001$), an hepatic phase (135.2 vs 158.3 min, $p < 0.001$) and duration of surgery (711.5 vs 857.8 min,

$p < 0.001$) were lesser. Group B had lower peak AST (164 vs 183 IU/L, $p = 0.01$), ALT (177 vs 209 IU/L, $p < 0.001$), creatinine level (0.96 vs 1.08, $p = 0.02$), severe sepsis (13.7% vs 22.9%, $p = 0.03$), grade III and above complications (50% vs 63.5%, $p = 0.03$), ICU/HDU stay (11.2 vs 14.7 days, $p < 0.001$) and hospital stay (24.6 vs 27.4 days, $p = 0.03$). Though statistically non-significant, group B had better neo-MHV patency rates (1 month 95.1% vs 92.6%, $p = 0.36$; 3 month 93.1% vs 89.95, $p = 0.19$). The 90 days (87.2 vs 88.7%, $p = 0.68$) and 1 year (87.2% vs 87.7%, $p = 0.88$) survival rates were comparable.

Conclusion: The single orifice technique leads to improved graft function and peri operative morbidity in spite of having low GRWR.

	Group A (n=203)	Group B (n=107)	p Value
Bilirubin(1st 7 days)	2.5	3.8	0.08
Peak AST (1st 7 days)	239	335	0.05
Peak ALT(1st 7 days)	230	385	0.03
Peak INR	2.51	2.46	0.73
Serum Urea	79.0	77.8	0.83
Serum Creatinine	1.03	1.16	0.05
Graft Dysfunction	29.5%	34.5%	0.34
Ascites	32.1%	37.3%	0.30
Sepsis	41.2%	46.1%	0.28
Hospital Stay	23.9	27.4	0.11
ICU Stay	12.8	13.8	0.63

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Serum Creatinine	1.03	1.16	0.05
Graft Dysfunction	29.5%	34.5%	0.34
Ascites	32.1%	37.3%	0.30
Sepsis	41.2%	46.1%	0.28
Hospital Stay	23.9	27.4	0.11
ICU Stay	12.8	13.8	0.63

Abstract #1028

The dynamicity of bone marrow derived stem and progenitor cells in liver regeneration in Living Donor Liver Transplantation Model

Imtiakum Jamir[1], Viniyendra Pamecha[1], Dananjay Mathur[1], Anupam Kumar[1]

[1]Institute of Liver and Biliary Sciences (ILBS)

The kinetics of bone marrow derived stem cells and progenitor cells in partial transplanted graft and partial hepatectomy model in humans is not known. To our knowledge this is the first study comparing the kinetics of bone marrow derived hematopoietic stem cells and endothelial progenitor cells in living donor liver transplantation model.

28 donor-recipient pairs were studied. PBMCs (peripheral blood mononuclear cells) from bone marrow derived Hematopoietic stem cells (HSCs) and Epithelial Progenitor cells (EPCs) were performed at baseline and on POD 1, 3, 5 and 7. PBMC's were isolated and flow cytometry was performed for characterization of the HSC(LIN1−, CD38− CD34+ CD90+) and EPC(CD34+, CD133, CD309). CT volumetry was done on POD7 for estimation of liver regeneration (LR).

In healthy donors (control) the remnant liver regenerated from 459.37 g ± 102.77 to 749.6 g ± 184.95 and in recipients from 718 ± 128.82 g to 1229.36 ± 207.35 g on POD7 (p-0.031). In six recipients the liver regeneration was < 50% and 22 recipients had > 50%. The kinetics of HSCs and EPCs were different between the recipients and the healthy donors. Also the overall baseline EPCs (p-ns), HSCs (p-ns) and CD34+ (p-< 0.01)were lower in the recipients compared to the donors suggesting an impaired bone marrow in the recipients. In recipients with > 50% LR the baseline HSCs (p-0.001) and EPCs (p-0.008) were significantly high and remained so during the first postoperative week.

Partial graft recipients with greater percentage of liver regeneration were characterized by a significantly higher number of circulating bone marrow derived HSCs and EPCs which continued to persist during the first week of liver regeneration.

Hepatocellular Carcinoma

I01 - Hepatocarcinogenesis

Abstract #90

Aspartate-β-hydroxylase, a rising star in the diagnosis of Glypican-3 negative hepatocellular carcinoma, is a prognostic biomarker for primary liver cancer

Ran Xue[1], Qinghua Meng[1]

[1]Beijing You-An Hospital, Capital Medical University

Aims: Glypican-3 (GPC3) has high sensitivity and specificity for the diagnosis of hepatocellular carcinoma (HCC). Aspartyl-(asparaginyl)-β-hydroxylase (ASPH) also highly expressed in liver cancer. Our aim was to investigate the correlation between ASPH and GPC3 expression in primary liver cancer (PLC) and to further define the significance of ASPH in the prognosis of PLC, as well as to explore the underlying cellular mechanisms of ASPH.

Methods: The expression of GPC3, ASPH and alpha-fetoprotein (AFP) was detected by immunohistochemical staining. The tumor size, lymph node involvement, and metastasis were determined by

pathological and imaging approaches. Protein–protein interaction (PPI) network by Gene MANIA Cytoscape app was used to estimate genes regulated by ASPH. Gene Ontology (GO) enrichment, Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment, Database for Annotation, as well as Visualization and Integrated Discovery (DAVID) enrichment were used to predict biological roles of ASPH target genes.
Results: The enrolled 139 cases were divided into two sub-types, namely ASPH + PLC and ASPH − PLC. There was no significant difference for ASPH expression in different hierarchical patterns of PLC or different histologic types of HCC. In all GPC3-HCC, 55% cases were ASPH positive. ASPH expression positively correlated with AFP level in PLC (P = 0.017). ASPH + PLC has a worse prognosis than ASPH-PLC (P = 0.016, log-rank test).
Conclusions: ASPH has diagnostic value in GPC3- HCC. ASPH immunophenotype is closely relevant to malignant behavior of PLC. ASPH + PLC may confer more aggressive subtype, compared to ASPH-PLC. Meanwhile, ASPH is a potential prognostic biomarker for PLC.

Abstract #98

Blood PIVKA-II (Prothrombin Induced by Vitamin K Absence) and AFP (Alpha Fetoprotein) on Patients with Chronic Hepatitis, Cirrhosis and Hepatocellular Carcinoma

Le Thi Thu Hien[1], Hoang Thi Minh[2], Nguyen Quang Duat[2]

[1]Thai Nguyen University of Medicine and Pharmacy, [2]Military Medical University

Introduction: Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death worldwide, and is highly prevalent in Eastern and South-Eastern Asia, with incidence rates of 31.9/100,000 and 22.2/100,000. The recommended noninvasive methods include computed tomography and magnetic resonance imaging and alpha-fetoprotein (AFP). AFP levels are normal in up to 40% of patients with HCC, particularly during the early stage of the disease, which reflects a low sensitivity. Another approach aimed at overcoming the limitations of AFP is to combine its measurement with that of a protein induced by vitamin K absence or antagonist-II (PIVKA-II).
Objectives: To survey AFP and PIVKA-II levels of chronic hepatitis, cirrhosis and HCC and determine the correlation between AFP and PIVKA-II levels in HCC patients.
Subjects and Methods: 89 patients were divided into four groups: healthy, chronic hepatitis, cirrhosis, and HCC. AFP and PIVKA-II concentrations were measured by chemiluminescence magnetic microparticale immunoassay on Architect ci16200 system of Abbott company. Results: The AFP median in the HCC group was 1286.28 ng/mL, the PIVKA-II median in the HCC group was 5742 mAU/mL, AFP and PIVKA-II levels in HCC groups are significantly higher than the healthy, chronic hepatitis and cirrhosis groups with $p < 0.001$. It has a very strong correlation between the concentration of AFP and PIVKA-II in the HCC group with the correlation equation: $y = 1.0653 + 17{,}820$ ($r = 0.49$, $p < 0.05$).
Conclusion: AFP was the most useful single biomarker for diagnosing HCC. Combining PIVKA-II with AFP improved the diagnostic performance.

Abstract #179

LncRNA XIST inhibits metastasis and EMT of Hepatocellular Carcinoma by acting as a ceRNA for miR-197-3p to regulate Wnt//β-catenin signaling

Zhi-Shuo Mo[1], Pei-Pei Wang[1], Ying Zhang[1], Chan Xie[1], Dong-Ying Xie[1]

[1]Department of Infectious Disease, The Third Affiliated Hospital, Sun Yat-Sen University, Guangzhou, China

Introduction: Long non-coding RNAs (LncRNAs) have emerged as critical regulators in a variety of diseases, such as hepatocellular carcinoma (HCC). However, the function and mechanisms responsible for these molecules in HCC are not thoroughly understood.
Objectives: The present study aimed to investigate the role of LncRNA X inactive-specific transcript (LncRNA XIST) in HCC metastasis progression.
Methodology: Quantitative reverse transcription polymerase chain reaction (qRT-PCR) was used to detect the expression of LncRNA XIST and miR-197 in HCC specimens from patients and HCC cell lines. The role of LncRNA XIST on HCC cell invasion and migration with in vitro experiments, including wound healing, Cell invasion and migration analysis, as well as in an HCC xenograft model in BALB/c nude mice.
Results: We found that LncRNA XIST was downregulated in metastatic HCC, compared with non- metastatic HCC, but miR-197-3p expression was significantly upregulated in metastatic HCC tissues, positively associated with invasiveness of HCC cell lines. LncRNA XIST was a negative regulator of miR-197-3p. Metastatic HCC cells with low LncRNA XIST/high miR-197 expression had Wnt/β-catenin signaling activation. High levels of LncRNA XIST expression inhibits EMT and invasive capability of HCC cells in vitro and in vivo. We also found that miR-197 directly targeted Axin2, NKD1, and DKK2 which can negative regulate Wnt/β-catenin signaling.
Conclusion: LncRNA XIST inhibits HCC metastasis by competitively binding miR-197-3p and regulating Wnt/β-catenin signal pathway and may be a new therapeutic target and predictive factor for HCC.

Abstract #187

Downward expression of long non-coding RNA XIST is associated with hepatocellular carcinomas metastasis and poor prognosis

Zhi-Shuo Mo[1], Pei-Pei Wang[1], Ying Zhang[1], Chan Xie[1], Dong-Ying Xie[1]

[1]Department of Infectious Disease, The Third Affiliated Hospital, Sun Yat-Sen University, Guangzhou, China

Introduction: Long non-coding RNA X inactive-specific transcript (LncRNA XIST) has been found to play an important role in the progression of tumors. However, the functional of LncRNA XIST in hepatocellular carcinomas (HCC) metastasis remains unknown.
Objectives: This study aimed to investigate the role of LncRNA XIST in HCC metastasis progression.
Methodology: We investigated LncRNA XIST expression in 23 liquid nitrogen preserved-archival HCC samples, 9 of which were metastasis, 14 were non- metastasis. LncRNA XIST expression in 16 HCC cell lines were detected by qPCR. Statistical analyses were applied to derive prognostic associations between LncRNA XIST and clinical characters.

Results: We found LncRNA XIST was significantly downregulated in metastatic samples, compared with non-metastatic samples. Downward expression of LncRNA XIST was observed in highly metastasis HCC cell lines MHCC97L, MHCC97H, HCCLM3, HCCLM6 compared with non-metastasis HCC cell lines THLE-3, QGY7703, QGY-7701 SMMC-7721, HepG2, Hep3B,HCCC-9810 and PLC/PRF 5, Huh7, HepG2.2.15, Bel-7402, BEL-7404. Statistical analysis suggested downregulation of LncRNA XIST was significantly correlated with clinical staging of the HCC patients ($P < 0.001$), TNM classification ($P < 0.001$), and numbers of metastatic organs/lymph nodes ($P = 0.015$) and patients with low LncRNA XIST levels exhibited shorter survival time ($P < 0.001$), Multivariate analysis indicated that LncRNA XIST expression might be an independent prognostic indicator of the survival of patients with HCC.
Conclusion: Our results suggest that LncRNA XIST is a potential therapeutic target for HCC and upregulation of LncRNA XIST expression might represent a novel strategy to inhibit HCC metastasis.

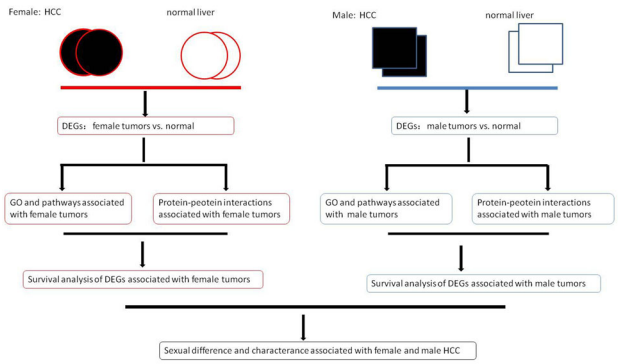


Figure 1 A work flow chart representing bioinformatic analysing gene chip dataset in HCC respect to sex. Primarily contains three steps: identification of DEGs in cancer related to patient sex; identification of gene functions and pathways differentially expressed between normal and tumor tissues separated by sex; and survival analysis sex related genes.

Abstract #206

Bioinformatic analysis in identifying sexual dimorphism linked characterization of hepatocellular carcinoma

Yali Feng[1], Yuchao Wu[2], Yingren Zhao[2], Yuan Yang[2]

[1]Department of Infection Disease and Hepatopathy, Xi'an Jiaotong University First Affiliated Hospital, [2]Department of Infectious Diseases, First Affiliated Hospital, School of Medicine, Xi'an Jiaotong University, Xi'an, Shanxi Province, China

Background/Aim: Hepatocellular carcinoma (HCC) is sexual disparity in humans, with significantly higher prevalence in male. The molecular mechanism of sex difference by which inhibits or promotes liver cancer is still unknown. Here, we aim to screen out functional signatures of differently expressed genes (DEGs) in both female tumors and male tumors with bioinformatic analysis.
Materials and Methods: Gene chip expression profiles: GSE19665, GSE 23342 and GSE 9843, consisted of carcinoma and non-cancerous HCC with critical sex feature, were downloaded from GEO dataset. Further evaluating selected DEGs in both sexual groups by hierarchical clustering analysis, Venn diagram analysis and functional PPI network constructure were performed. Afterwards, possible role of important genes were asscessed by utilizing KM Plotter database for post-survival analysis.
Results: Parts of DEGs were common in female and male tumor samples, wherever others were respective. Cell cycle in biological process is mainly enriched in both sex tumors, while metabolic pathways and drug metabolism were more significant in male cancer tissue. Several hug DEGs in significant PPI models, such as CDK1 and CCNB1, were both up-regulated in female and male tumors, leading poor prognosis in male patients. Other genes as CYP3A4 and SERPINA4, male-specific down-regulated, shew decreased survival rate in male but no obvious difference in female.
Conclusion: Some common and specific characterizations of gene expression were identified between two sex relative HCC samples. More suverys are needed to explore the molecular sexual difference in HCC clearly and develop precision therapy according sex-affected signature.

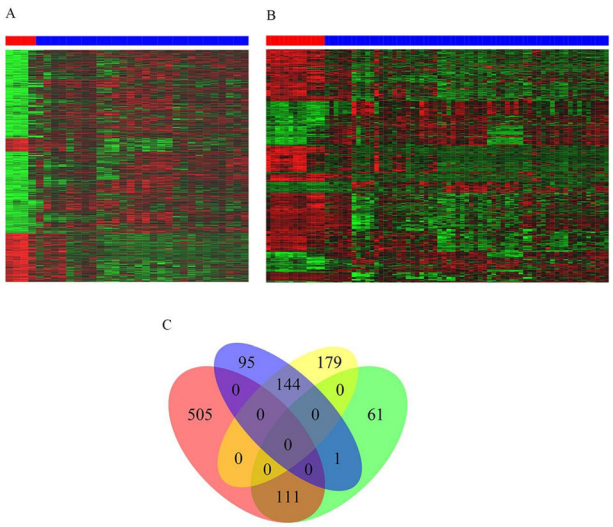


Figure 2 Differential gene expression analysis of HCC respect to sex. Heatmap of differentially expressed gene (DEG) clustering. Green represents downregulation and red represents upregulation. Top red represents normal liver.Top blue represents HCC tumor tissue. (**a**)female, (**b**)male (**c**)Venn diagram of DEGs in two sexes. Red and blue represents up-regulated and down-regulated DEGs respectively in female. Yellow and green represents up-regulated and down-regulated DEGs respectively in male.

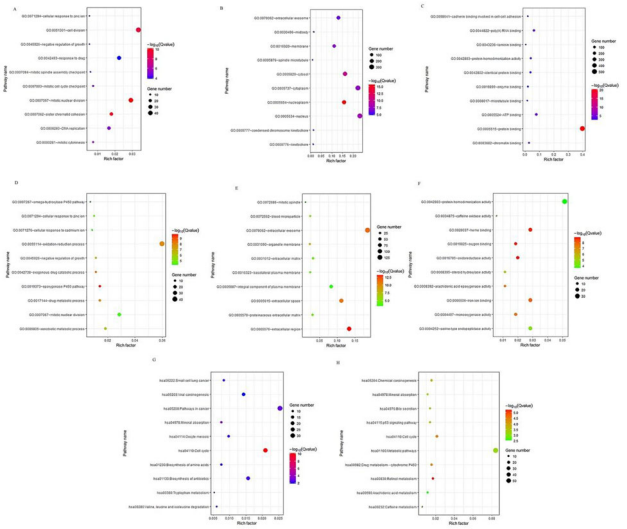


Figure 3 Bubble diagram of GO terms and pathways enrich in DEGs stratified by sex: **(a,d)** biological process, **(b,e)** cellular component and **(c,f)** molecular function, and **(g,h)** KEGG pathways.

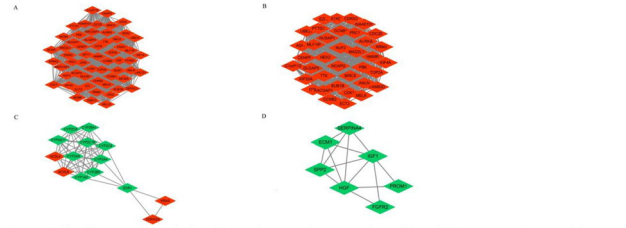


Figure 4 Significant sub-modules of protein-protein connection with MCODE score>4.**a** Module A. **b** Module B. **c** Module C. **d** Module D. Red represents up-regulated nodes in network and green represents down-regulated nodes.

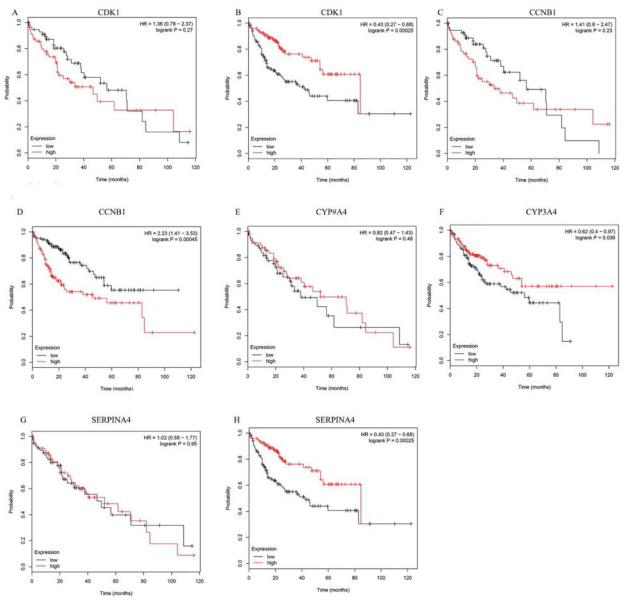


Figure 5 Survival analysis of differentially expressed genes in sex-specific HCC were performed by using KM Plotter database. P <0.05 was considered statistically significant. The Kaplan – Meier survival curves were plotted for CDK1(**a,b**),CCNB1(**c,d**),CYP3A4(**e,f**) and SERPINA4(**g,h**).

Table 1 The top hub genes in PPI network in terms of their degree between female and female.

Female	Gene name	Degree	Clustering Coefficient	Male	Gene name	Degree	Clustering Coefficient
	TOP2A	156	0.20239		TOP2A	78	0.26607
	CDK1	114	0.36625		CDK1	54	0.53948
	GAPDH1	111	0.11433		CCNB1	52	0.57919
	CCNB1	107	0.41474		CDKN3	47	0.66605
	ACLY	96	0.08794		BIRC5	46	0.68213
	CCNB2	91	0.52454		AURKA	46	0.69952
	BIRC5	89	0.49413		CCNB2	44	0.75159
	NDC80	88	0.54075		MAD2L1	44	0.75370
	CCNA2	87	0.53034		HMMR	44	0.72093
	CDC20	86	0.53844		TTK	43	0.78295
	CDKN3	86	0.54118		EZH2	42	0.60511
	MAD2L1	85	0.57843		CDC20	41	0.80610
	BUB1	84	0.60614		PTTG1	41	0.80488
	AURKA	82	0.56218		RACGAP1	41	0.83171
	KIF11	79	0.63746		NCAPG	41	0.85854

Table 2 Top five enriched pathways of hub genes in both female and male resrectively.

Sex	term	P value	genes
Female	cfa04110:Cell cycle	6.24E-09	CCNB1, CDK1, CCNB2, MAD2L1, BUB1, CDC20, CCNA2
	cfa04914:Progesterone-mediated oocyte maturation	7.00E-08	CCNB1, CDK1, CCNB2, MAD2L1, BUB1, CCNA2
	cfa04114:Oocyte meiosis	1.14E-05	CDK1, MAD2L1, BUB1, CDC20, AURKA
	cfa04115:p53 signaling pathway	0.003875	CCNB1, CDK1, CCNB2
	cfa05203:Viral carcinogenesis	0.030904	CDK1, CDC20, CCNA2
Male	bta04110:Cell cycle	8.73E-11	CCNB1, CDK1, MAD2L1, CCNB2, TTK, CDC20, PTTG1
	bta04114:Oocyte meiosis	2.77E-07	CDK1, MAD2L1, AURKA, CDC20, PTTG1
	bta04914:Progesterone-mediated oocyte maturation	2.33E-04	CCNB1, CDK1, MAD2L1, CCNB2
	bta04115:p53 signaling pathway	0.004502	CCNB1, CDK1, CCNB2
	bta05166:HTLV-I infection	0.005894	MAD2L1, CDC20, PTTG1

Abstract #246

Circulating cytokeratins of hepatic progenitor cells in the early and intermediate stages of hepatocellular carcinoma

Peter Andrew Camentil Reyes[1], Caecilia H. C. Sukowati[2], Claudio Tiribelli[3]

[1]Philippine Council for Health Research and Development and Italian Liver Foundation and The Doctors' Hospital Bacolod, Inc., [2]Fondazione Italiana Fegato and Dipartamento Di Area Medica, University of Udine, [3]Fondazione Italiana Fegato

Introduction: There were only few studies highlighting cytokeratins in different stages of HCC. This study aims to: (1) determine the expression of CK19, CK7, and CK18 in peripheral blood of HCC patients before and after treatment; (2) determine the positivity of circulating cells for OV-6 antigen, a marker that can detect hepatocytic differentiation; and (3) compare CK19 and CK18 expression between the tumor and its surrounding liver cirrhotic region

Methods: Peripheral blood mononuclear cells samples were isolated from 32 HCC patients receiving chemoembolization, radiofrequency ablation or hepatectomy. mRNA analysis of CK19, CK7, and CK18 were performed using reverse transcription quantitative real-time PCR. Six PBMC isolates were examined by flow cytometry for the presence of OV-6 positive cells. Changes of mRNA expressions at pre-treatment and at 1 month post-treatment were compared between complete responders and non-responders. RTqPCR analysis of CK19 and CK18 was performed for 38 liver tissues undergoing hepatectomy consisting of paired tumoral region versus the surrounding liver cirrhosis. Diagnosis of HCC was through EASL criteria and response was evaluated through mRECIST criteria. T-test was used and significance was set to $p < 0.05$.

Results: The presence of CK19 before treatment and the pattern of CK18 at before and 1-month post treatment can possibly be used as non-invasive markers in monitoring outcomes among post TACE and RFA patients in the early and intermediate stages of HCC. The difference in CK18 and CK19 mRNA expressions between the tumoral region and its SLC can be a potential marker for predicting early development of HCC.

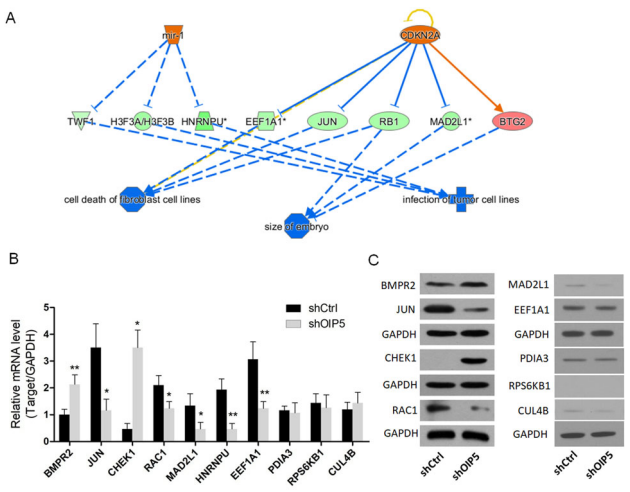
Abstract #311

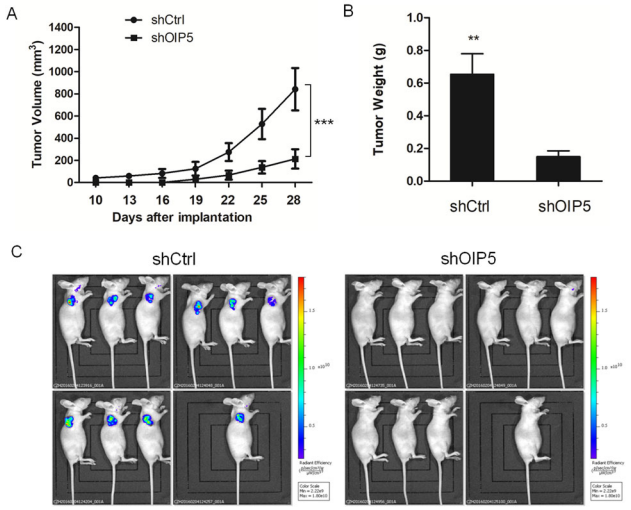
Overexpression of Opa interacting protein 5 increases the progression of liver cancer via BMPR2/JUN/CHEK1/RAC1 dysregulation

Chuanlong Zhu[1], Yuwen Li[2], Jun Li[1], Guimei Li[3]

[1]Department of Infectious Disease, The First Affiliated Hospital of Nanjing Medical University, [2]Department of Pediatrics, The First Affiliated Hospital of Nanjing Medical University, [4]Department of Pediatrics, Shandong Provincial Hospital Affiliated to Shandong University

Introduction: Opa interacting protein 5 (OIP5) overexpression is associated with human carcinoma. However, its biological function, underlying mechanism, and clinical significance in liver cancer remains unknown.
Objectives: In this study, we sought to explore the effects of OIP5 expression on liver cancer, and the mechanisms regulating these effects.
Methodology: OIP5 expression was measured in human hepatocellular carcinoma (HCC) tissues and liver cancer cell lines. The effect of OIP5 knockdown on tumorigenesis was also detected in nude mice, differentially expressed mRNAs (DEGs) were identified and their biological functions were identified.
Results: The results indicated that OIP5 expression was upregulated in HCC tissues and four liver cancer cell lines ($P < 0.01$). Higher OIP5 protein expression predicted shorter survival of HCC patients ($P < 0.01$). OIP5 knockdown led to suppression of proliferation and colony forming ability, cell cycle arrest at G0/G1 or G2/M phase, and promotion of cell apoptosis. A total of 628 DEGs including 87 up-regulated and 541 down-regulated genes were identified after OIP5 knockdown. Functional enrichment analysis suggested that DEGs were involved in RNA Post-Transcriptional Modification, and among which the expression of many genes, such as JUN, RAC1, BMPR2 and CHEK1 was markedly affected by OIP5 silencing.
Conclusion: OIP5 involvement in the progression of liver cancer via BMPR2/JUN/CHEK1/RAC1 dysregulation, providing a potential biomarker in liver cancer diagnosis and targeted therapy.





Abstract #372

Comparison of clinical judgement and genetic differentiation of multinodular HCC; Intrahepatic metastasis (IM) vs Multicentric occurrence (MC)

Yuji Iimuro[1], Atsushi Takano[2], Kenji Amemiya[3], Yosuke Hirotsu[4], Hitoshi Mochizuki[5], Toshio Oyama[6], Masao Omata[7]

[1]Dept of Surgery, Yamanashi Central Hospital, Kofu, Japan, [2]Dept of Surgery, Yamanashi Central Hospital, [3]Genome Analysis Center, Dept of Pathology, Yamanashi Central Hospital, [4]Genome Analysis Center, Yamanashi Central Hospital, [5]Genome Analysis Center, Dept of Medicine, Yamanashi Central Hospital, [6]Dept of Pathology, Yamanashi Central Hospital, [7]Dept of Medicine, Yamanashi Central Hospital and the University of Tokyo, Tokyo, Japan

Background: It is important to differentiate between IM and MC in multinodular HCC. The differentiation has been dependent on image finding or pathological observation of each tumor, while the criteria remains obscure. The AIMs of the present study were to elucidate genetic alterations in multinodular HCCs for differentiation between IM and MC, and to examine the accuracy of conventional criteria.
Methods: Forty HCC patients (30 solitary and 10 multinodular) were genetically investigated. Microdissected samples were analyzed employing a next generation sequencer (NGS). We performed targeted sequencing covering 72 SMGs associated with HCC. As a validation analysis, genetic clonality among pathologically distinct components within each HCC nodule was analyzed. Then, multinodular HCCs were tested whether each tumor possesses common genetic alterations or not (10 patients; 27 nodules). The genetic results were compared with conventional clinical judgement.
Results: Validation analysis revealed that pathologically distinct components within HCC nodule possessed common trunk mutations, such as TERT promoter, TP53, or CTNNB1, implying their monoclonal origin despite pathological heterogeneity. In internodular analysis, MC was identified in 2 cases without common genetic alterations, and IM was diagnosed in 7 cases. In a case with 4 nodules, 2 nodules had common mutations, while others not, being mixture of IM and MC. The concordance rate between these results and conventional clinical judgement was about 50%.

Conclusion: There is limitations in conventional diagnosis criteria for IM or MC in multinodular HCCs. Elucidation of genetic clonality in each tumor is critical for better understanding of pathophysiological features of multinodular HCCs.

Abstract #459

Aristolochic Acid I induced FLAP/CysLTs signaling and CYLD/Lin28B axis in premalignant liver tissue

Kunkai Su[1], Xin Huang[2], Christian Bréchot[3], Lanjuan Li[4], Yijia Lou[4]

[1]State Key Laboratory, Collaborative Innovation Center and National Clinical Research Center for Diagnosis and Treatment of Infectious Diseases, Zhejiang University, [2]Biotherapeutics Research Center, The 2nd Affiliated Hospital, Zhejiang University, [3]Pasteur Institute, Paris, France, [4]Institute of Pharmacology and Toxicology, College of Pharmaceutical Sciences, Zhejiang University

Introduction: Short-term aristolochic acid I (AAI) exposure displays potential hepatocarcinogenesis. However, the initiation mechanism is controversial. 5-lipoxygenase (5-LO) appears in some cancer types, but it has only been seldom investigated in hepatocellular carcinoma (HCC) pathogenesis. Reduced tumor suppressor gene cylindromatosis (CYLD) expression contributes to HCC development.
Objectives: This study aimed to evaluate 5-LO pathway associated CYLD downregulation and their prognostic significance in hepatic premalignancy.
Methodology: Canine livers receiving AAI were explored for the relevance of functional components in 5-LO pathway and Cyld transcription. Liver tissues from HCC patients or donors, and HCC patient-based large data were evaluated for 5-LO cysteinyl leukotrienes (CysLTs) signaling and CYLD expression. Human HCC cell lines were used to reveal the possible mechanism in vitro.
Results: In the livers of canine receiving AAI, 5-LO-activating protein (FLAP) overexpressed in prenuclear membrane of hepatocytes. Enhanced CysLTs biosynthesis, overexpressed CysLT receptor 2 (CysLTR2), and decreased Cyld transcription appeared in parallel, accompanied by miR-362 overexpression. Liver tissues from HCC patients exhibited FLAP and CysLTR2 overexpression in HCC cells, but membrane-embedded microsomal glutathione-S-transferase 2 mainly appeared in paracancerous tissue. HCC tissues from patients displayed little CYLD. High FLAP transcription significantly shortened the time of 50% survival rate of HCC patients. FLAP knockdown led to CYLD overexpression through a miR-362- or p-JNK signaling-independent mechanism in AAI-treated-human HCC cells.
Conclusion: Our findings highlight a novel mechanism in the initiation process of hepatocarcinogenesis, and FLAP-CysLTs signaling determines CYLD expression may be potential biomarkers for early HCC detection and be explored for anti-HCC therapy.

Abstract #494

Aspartate-β-hydroxylase regulates metabolic reprogramming in hepatocelluar carcinoma via P53/BNIP3L/NIX-dependent signaling pathway

Ran Xue[1], Jing Wu[2], Qinghua Meng[3]

[1]Beijing You-An Hospital, Capital Medical University, [2]Beijing You-An Hospital, Capital Medical University, [3]Beijing You-An Hospital, Capital Medical University

Aim: Metabolic reprogramming is widely observed during hepatocellular carcinoma (HCC) development. Aspartate-β-hydroxylase (ASPH) was one of the most differentially expressed genes in HCC. In the this study, we aimed to explore the relationship of ASPH in the P53/BNIP3/NIX-dependent mitophagy, characterized the impact of ASPH on metabolic reprogramming.
Methods: In this research, we constructed HCC animal model and anoxic autophagy model, using lentivirus to deliver ASPH to HepG2 cell line and the CRISPR/Cas9 system to knockout ASPH, so that we can assess the effect of ASPH on mitophagy, characterized metabolic reprogramming. Besides, we uncovered the mechanism of ASPH-induced mitophagy and metabolic reprogramming using western blotting, RT-PCR, electron microscopy, immunofluorescence and transient transfection of a GFP-LC3-expressing construct.
Results: In this study, ASPH down-regulated the expression of P62, and improved the expression of Atg5, Atg7 and LC3-II/LC3-I. Meanwhile, ASPH also inhibited the expression of TOMM20, which reflects the oxidative phosphorylation level of cells. In addition, ASPH regulated metabolic reprogramming in HCC, including increased levels of glycolysis and pentose phosphate pathways, with the up-regulation of GLUT1, PKM2 and G6PD. However, ASPH did not affect the level of lipid, lactic acid and glutamine metabolism based on the the expressions of MCT1, ACC, ACLY, and GLS1. Furthermore, ASPH also significantly inhibited the expression of P53 and increased the expressions of BNIP3 and NIX in HCC.
Conclusions: Our finding suggests that ASPH regulates metabolic reprogramming via P53/BNIP3L/NIX-dependent signaling pathway in HCC. This study will provide a theoretical basis of ASPH as an effective target for HCC treatment.

Abstract #573

MarvelD3 Inhibits Hepatocellular Carcinoma Epithelial-mesenchymal Transition and Invasion via Suppression of the NF-κB Signaling Pathway

Teng Li[1], Jia Wei[2], Saiping Qi[3], Yanmeng Li[4]

[1]Department of Oncology, Beijing Friendship Hospital, Capital Medical University, Beijing, [2]Department of Oncology, Beijing Friendship Hospital, Capital Medical University, Beijing, [3]Experimental Centre, Beijing Friendship Hospital, Capital Medical University, [4]Experimental Centre, Beijing Friendship Hospital, Capital Medical University

Introduction: Tight junction (TJ) imbalance is associated with hepatocellular carcinoma (HCC). MarvelD3 was the recently identified integral membrane protein forming TJ. However, little is known about the detailed role of marvelD3 in epithelial tight junctions and how it is regulated the metastasis of HCC.
Objectives: We aim to demonstrate the role of marvelD3 in inhibiting HCC invasion and the underlying molecular mechanisms.
Methodology: In this study, marvlD3 levels were assessed between 40 paired HCC tissues and adjacent normal tissues. The changes of marvelD3 were assessed during TGF-β-induced epithelial–mesenchymal transition (EMT). MarvelD3 knockdown HCC cell lines were constructed by using marvelD3-siRNAs to analyze the correlation among marvelD3 and EMT related proteins. Tumor cell behaviors were also analyzed in marvelD3 knockdown HCC cells. Association between marvelD3 and genes in nuclear factor NF-κB pathway were discussed.
Results: The loss of MarvelD3 expression was significantly correlated with the occurrence and TNM stage of liver disease. MarvelD3 is transcriptionally downregulated in TGF-β-induced EMT HCC cells. Expression of marvelD3 protein significantly associated with

E-cadherin and Vimentin in HCC tissue and cell lines. Knockdown of marvelD3 promoted tumor cell invasion, accompanied by activation of NF-κB signal pathways as well as increasing MMP-9 gene levels. **Conclusion:** The study demonstrated that marvelD3 inhibited HCC EMT and invasion via suppression of the NF-κB signaling pathway. This may suggest that marvelD3 could be further evaluated as a novel biomarker for predicting the prognosis of HCC and as a target for the treatment of HCC in the future.

Abstract #598

Prognostic and therapeutic value of aberrantly expressed methylation genes in human hepatocellular carcinoma

Limin Zhen[1], Gang Ning[2], Lina Wu[3], Fangji Yang[4], Yongyuan Zheng[5], Jie Song[6], Liang Peng[7]

[1]The Third Affiliated Hospital, Sun Yat-Sen University, [2]The Third Affiliated Hospital, Sun Yat-Sen University, [3]The Third Affiliated Hospital, Sun Yat-Sen University, [4]The Third Affiliated Hospital, Sun Yat-Sen University, [5]The Third Affiliated Hospital, Sun Yat-Sen University, [6]The Third Affiliated Hospital, Sun Yat-Sen University, [7]The Third Affiliated Hospital, Sun Yat-Sen University

Abstract

Introduction: Hepatocellular carcinoma (HCC) is a malignant disease and its incidence and mortality is increasing worldwide.

Objectives: The aim of the study was to identify the prognostic and therapeutic value of aberrantly methylated differentially expressed genes (DEGs) in HCC, and to explore the underlying mechanisms of tumorigenesis by using integrated bioinformatic analysis.

Methodology: Gene expression profiles (GSE65372 and GSE37988) were analyzed using the online tool, GEO2R to obtain aberrantly methylated DEGs. Functional enrichment analysis of screened genes was performed by the DAVID. Protein–protein interaction (PPI) networks were constructed using the STRING. Next, we used the Cytoscape software to analyze the network and select hub genes by cytoHubba. Finally, we validated the results with the Cancer Genome Atlas (TCGA) data.

Results: The mRNA and protein expression of four up-regulated and hypomethylated oncogenes were all significantly higher in HCC tissues than normal samples, while which were lower in 4 down-regulated and hypermethylated tumor suppress genes (TSGs) in HCC tissues than normal liver tissues. In up-regulated and hypomethylated oncogenes, higher methylated expression of CDC5L, RHOA and YBX1 showed favorable prognostic prediction values in HCC patients after adjustment of age, gender, stage, gender, height and weight. Similarly, HCC patients with lower methylated levels of BCR, DFFA, SCUBE2 and TP63 had better overall survival (OS).

Conclusion: Higher methylated expressions of CDC5L, RHOA, YBX1 and lower methylated levels of BCR, DFFA, SCUBE2 and TP63 were associated with better prognosis in HCC patients, which may be the therapeutic target of HCC.

Abstract #674

ARPP-19 Enhances Proliferation and Migration of HCC Cell through Promoting Epithelial–Mesenchymal Transition

Chunlei Zhang[1], Yifan Zhang[2], Kaiyue Tang[3], Guang Ji[4], Haiyan Song[5]

[1]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, [2]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, [3]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, [4]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, [5]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine

Background/objectives: HCC is one common malignant tumor worldwide. Previous research demonstrated ARPP-19 was over-expressed in HCC. This study aims to elucidate the relationship between ARPP-19 and HCC prognosis. Subsequently, the underlying mechanism of the role of ARPP-19 in HCC cell proliferation and migration will be explored.

Methods: The expression of ARPP-19 was examined in tissue microarray containing 92 HCC tissues. The expression rate was calculated. Kaplan–Meier method and Log-rank test were used for survival rate. Lentiviruses with ARPP-19 siRNA or ARPP-19 cDNA vectors were constructed and infected with HCC cell Huh7 and SMMC7721 to establish cells with different ARPP-19 level. Effects of ARPP-19 on proliferation were evaluated by CCK-8, DAPI staining and clone formation. F-actin staining was used to detect cell morphology. Wounding-healing assay and transwell assay was performed to detect cell migration. Epithelial–mesenchymal-transition (EMT) related molecules was measured.

Results: 71.7% of HCC tissues had high ARPP-19 expression, the overall survival time of patients with high ARPP-19 was lower than patients with low ARPP-19. Silencing ARPP-19 retarded cell proliferation, suppressed cell migration. Overexpression of ARPP-19 promoted proliferation and migration. Cells that inhibited ARPP-19 expression shrank to round shape, cells that overexpressed ARPP-19 stretched to spindle shape and pseudopods increased. ARPP-19 overexpression reduced the expression of E-cadherin and up-regulated the expression of vimentin.

Conclusion: ARPP-19 is highly expressed in most HCC patients and negatively correlated with survival. This molecule can enhance proliferation and migration of HCC cells by promoting EMT, which contributes to promote t HCC progression and leading to poor prognosis.

Abstract #776

RFX5 promotes hepatocellular carcinoma progression via transcriptional activation of KDM4A

Dong-Bo Chen[1], Xing-Wang Xie[2], Xue-Yan Wang[3], Pu Chen[4], Kangjian Deng[5], Lai Wei[6], Hong-Song Chen[7]

[1]Peking University People's Hospital, Peking University Hepatology Institute, Beijing Key Laboratory of Hepatitis C and Immunotherapy for Liver Disease, Beijing 100044, China, [2]Peking University People's Hospital, Peking University Hepatology Institute, Beijing Key Laboratory of Hepatitis C and Immunotherapy for Liver Disease, Beijing 100044, China, [3]Peking University People's Hospital, Peking University Hepatology Institute, Beijing Key Laboratory of Hepatitis C and Immunotherapy for Liver Disease, Beijing 100044, China, [4]Laboratory of Hepatobiliary and Pancreatic Surgery, Affiliated Hospital of Guilin Medical University, [5]Laboratory of Hepatobiliary and Pancreatic Surgery, Affiliated Hospital of Guilin Medical University, [6]Peking University People's Hospital, Peking University Hepatology Institute, Beijing Key Laboratory of Hepatitis C and Immunotherapy for Liver Disease, Beijing 100044, China, [7]Peking University People's Hospital, Peking University Hepatology Institute, Beijing Key Laboratory of Hepatitis C and Immunotherapy for Liver Disease, Beijing 100044, China

Background: We previously identified that RFX5 was significantly upregulated in hepatocellular carcinoma (HCC) tumors and cell lines. This study aims to reveal its biological significance and the underlying mechanism in HCC.
Methods: The significance of RFX5 in HCC was investigated by monitoring the colony formation and subcutaneous tumor growth after knocking down it with lentiviral shRNA and CRISPR/Cas9 system. The downstream target genes of RFX5 was determined with ChIP-seq analysis and then validated with ChIP-PCR and luciferase assay. The involvement of these down stream genes in HCC development was further studied by performing colony formation rescue and subcutaneous tumor growth rescue experiment, and by analyzing the expression pattern and clinical significance in HCC.
Results: We found that RFX5 was amplified, and overexpressed in HCC, which showed oncogene dependence in HCC cell lines. Moreover, we identified that KDM4A, a histone demethylase, was closely regulated by RFX5 both in HCC tissues and cell lines. Both mRNA and protein expression level of KDM4A in HCC tumor tissue are tightly correlated with that of RFX5, and linked to bad prognosis of HCC patients. Notably, KDM4A overexpression largely rescued the growth inhibitory effects of RFX5 depletion in HCC cells, indicating that KDM4A is a downstream effector of RFX5. We further proved that RFX5-KDM4A pathway could protect cells from apoptosis and promote cell cycle transition from G0/G1 to S phase by regulating the p53 and its downstream genes in HCC.
Conclusion: RFX5 could promote hepatocellular carcinoma progression via transcriptional activating KDM4A expression.

Abstract #790

Comprehensive liquid profiling of circulating tumor DNA and protein biomarkers in long-termed follow-up patients with hepatocellular carcinoma

Jingfeng Liu[1]

[1]Mengchao Hepatobiliary Hospital of Fujian Medical University

Introduction: Circulating tumor DNA (ctDNA) provides a novel approach for detecting tumor burden and predicting clinical outcomes of hepatocellular carcinoma (HCC).
Objectives: To thoroughly evaluate HCC circulating genetic features and further integrate them to build up a robust strategy for HCC surveillance and prognostic outcome assessment.
Methodology: Target sequencing and low coverage whole genome sequencing were performed on 168 plasma samples collected from 34 long-term follow-up HCC patients to capture tumor somatic SNVs and CNVs, respectively. Clinical information was also obtained to evaluate the prognostic performance of ctDNA comparing with clinically applied protein biomarkers.
Results: All plasma samples before surgery showed somatic genetic variations resembling corresponding tumor tissues. During follow-up, SNVs and CNVs dynamically changed correlating to patients' tumor burden. We integrated the comprehensive ctDNA mutation profiles to provide a robust strategy to accurately assess patients' tumor burden with high consistence with imaging results. This strategy could discover tumor occurrence in advance of imaging for an average of 4.6 months, and showed superior performance than serum biomarkers AFP, AFP-L3% and DCP. Furthermore, our strategy could precisely detect minimal residual disease in advance and predict patients' prognostic outcomes for both relapse-free survival and overall survival; further combining ctDNA with DCP could increase the sensitivity for MRD detection.
Conclusion: We demonstrated that plasma CNV and SNV levels dynamically correlated with patients' tumor burden in HCC. Our strategy of comprehensive mutation profile integration could accurately and better evaluate patients' prognostic risk and detect tumor occurrence in advance than traditional strategies.

Abstract #868

CD133 mediates epithelial to mesenchymal transition (EMT) in hepatoma cells

Preety Rawal[1], Hamda Siddiqui[2], Vikrant Nain[3], Savneet Kaur[4]

[1]Gautam Buddha University, Greater Noida, Uttar Pradesh, 201308, [2]Institute of Liver and Biliary Sciences, New Delhi, 110070, [3]Gautam Buddha University, Greater Noida, Uttar Pradesh, 201308, [4]Institue of Liver and Biliary Sciences, New Delhi, 110070

Introduction: Recent studies have shown that CD133 is a potent inducer of epithelial mesenchymal transition (EMT) in certain types of cancers. In the current study, the role of CD133 in EMT in liver cancer was addressed by transient inhibition of CD133 in hepatoma cell lines.
Methodology: Huh7 and Hep3B cells were cultured in vitro in presence of TGF- and then silenced by transfection with CD133 siRNAs or control siRNAs using lipofectamine. Subsequently, the role of CD133 in EMT was studied by real time PCRs and functional assays like chemotaxis, invasion and wound healing in the CD133 and control siRNA treated cells.
Results: Treatment of hepatoma cells with CD133 siRNA resulted in more than 60% inhibition of CD133 gene expression as compared to that observed in control siRNA transfected cells. Functional assays revealed that in comparison to the control siRNA transfected cells, CD133 inhibited cells showed about 50–55% reduction in chemotactic, migratory and invasive properties ($p < 0.05$ for each). Real time PCRs also showed significant downregulation in expression of mesenchymal genes like vimentin and N-cadherin in CD133 silenced hepatoma cells as compared to that observed in control cells ($p < 0.01$).
Conclusion: Incubation with CD133 significantly abrogates EMT properties and mesenchymal gene expression in both Huh7 and Hep3B cell types. The study highlights the role of CD133 as one of the important EMT regulators in HCC invasion.

Abstract #870

Hepatocellular Carcinoma with Scalp Metastasis : A Case Report

Yasmin Francesca Arriola Bautista[1], John Alfredo Raphael Perez Pangilinan[2], Prima Bianca Gaffud Chua[3], Diana Alcantara Payawal[4]

[1]Cardinal Santos Medical Center, [2]Cardinal Santos Medical Center, [3]Cardinal Santos Medical Center, [4]Cardinal Santos Medical Center

Introduction: Hepatocellular carcinoma (HCC) is the 5th most common cancer in the world. Metastasis is one of the most significant factors affecting prognosis. Common sites of extrahepatic metastases include lungs, regional lymph nodes and less commonly bone. Cutaneous metastases from hepatocellular carcinoma (HCC) are very rare. Here we present a case of Hepatocellular carcinoma with scalp metastasis.
Case Report: We report a case of a 56-year-old male, Diabetic and Hypertensive on medications. Patient presented with a 3-month history of abdominal pain, bloatedness and bipedal edema. Patient had Chronic Hepatitis B, with previous treatment with Adefovir in 2009. There was no history of increased abdominal girth, jaundice, fever,

weight loss. Imaging done showed a hepatic mass that was assessed as HCC. Patient underwent TACE and was started on Sorafenib. 3 weeks prior to admission, patient noted a palpable lump on the right parietal area of the head. There was no history of trauma. Interval showed increase in the size of the mass. Patient was admitted, CT scan done showed an enhancing expansile lytic lesion with a soft tissue component at the right parietal bone measuring 2.4 × 2.5 × 3.2 cm, most likely representing metastasis. Assessment was Hepaticellular Carcinoma with scalp metastasis, Child's Pugh C. Patient deteriorated, ultimately developing Hepatorenal syndrome and eventually expired. No histopathogy was done.

Conclusion: Cutaneous metastasis in primary malignancies are sparse, and with regards to Hepatocellular Carcinoma, an extreme rarity. This case is one of the few present, among other literature with similar findings.

Abstract #937

Dysregulation of PD-1/PD-Ls and 4-1BB/4-1BBL immune checkpoints in hepatocellular carcinoma tissue

Yong Liu[1], Guiyang Wang[1], Rui Huang[1], Yang Li[1], Haiyan Chang[1], Xiang-An Zhao[1], Yuxin Chen[1], Chao Wu[1]

[1]Nanjing Drum Tower Hospital, Nanjing University Medical School

Introduction: Immune checkpoints, such as the programmed death-1 (PD-1) and its ligands (PD-Ls), 4-1BB and 4-1BB ligand (4-1BBL), play an essential role in initiation and progression of hepatocarcinogenesis in tumor immune microenvironment.

Objectives: We aimed to explore the expression profile of PD-1/PD-Ls and 4-1BB/4-1BBL in liver tissues and serum from patients with hepatocellular carcinoma (HCC).

Methodology: Soluble PD-1 (sPD-1), sPD-L1, sPD-L2, 4-1BB, 4-1BBL in serum and pairs of primary human hepatocellular carcinomas tissues, paracancerous tissues and adjacent normal liver tissues from 21 patients with HCC and 22 subjects without HCC were detected by Luminex xMAP Technology.

Results: Dysregulated immune microenvironment of PD-1/PD-Ls and 4-1BB/4-1BBL was identified in the tumor tissues and adjacent non-tumor tissues. The correlation between PD-1, PD-L1 and 4-1BB levels increases successively in hepatocellular carcinomas tissues, paracancerous tissues and adjacent normal tissues. Meanwhile sPD-L2 and 4-1BBL had a positive correlation in the non-tumor liver tissues but no correlation in tumor tissues. sPD-1 and sPD-L1 levels within tumor tissues are negatively correlated with clinicopathological stages of HCC, while serological sPD-1 and sPD-L1 levels have positive correlation with the clinicopathological stages.

Conclusion: The immune imbalance of sPD-1/PD-Ls and 4-1BB/4-1BBL immune checkpoints in liver tumor microenvironment might play a significant role in tumor initiation tumor progression as well as immune escape, and higher serum sPD-1 and sPD-L1 levels may reflect a late clinicopathological stages and poor outcome in HCC patients.

Abstract #970

Serum miRNA 122 Level with HBV-related Hepatocellular Carcinoma

Khin Naing Thin[1], Win Naing[2], Yi Yi Kyaw[3], Ne Win[4]

[1]Department of Hepatology and Yangon Specialty Hospital, Myanmar and Ministry of Health, [2]Department of Hepatology and Yangon Specialty Hospital and Ministry of Health, [3]Advanced Molecular Research Centre and Department of Medial Research and Ministry of Health, [4]Nation Blood Bank and Yangon General Hospital and Ministry of Health

Introduction: Chronic hepatitis B is a major etiological factor for HCC. More than 60% of patients with HCC do not receive curative therapy as a result of late diagnosis. Alpha-fetoprotein (AFP) is widely used to detect primary HCC, whereas its sensitivity and specificity are not satisfying. Recently, circulating microRNAs (miRNAs) have been reported to be promising biomarkers for diagnosing and monitoring cancers. miRNAs are a group of small non-coding RNAs that can function as endogenous RNA to regulate expression of the targeted genes. The aim of this study was to study the role of serum miRNA 122 expression in patients with HBV-related HCC.

Method: Hospital based cross-sectional analytic study of 22 patients with HBV related HCC and 21 patients with HBV infection without HCC was done. The expression of serum miRNA 122 level was measured by using quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) method.

Results: The mean Ct value of HCC patient was 35.10 and that of non-HCC patients was 33.16. The mean standard deviation (SD) of serum miRNA level in patients with HCC was 2.09 and that in patients with non-HCC was 2.93. The serum miRNA 122 level in patients with HCC was significantly reduced in comparison with chronic HBV infected patients without HCC (p value 0.0286). The demographic data; age, sex, severity of liver disease did not show significant association with serum miRNA levels.

Conclusion: Serum miRNA 122 level can serve as a non-invasive biomarker for diagnosis of HBV-related HCC.

Abstract #1034

Occurrence of Hepatocellular Carcinoma after Direct Acting Antiviral Therapy in Hepatitis C infected Patients

Thandar Tun[1]

[1]Mandalay General Hospital

Introduction: Sustained virological response (SVR) in management of Hepatitis C Virus (HCV) infection reduces the incidence of Hepatocellular Carcinoma (HCC). However, Direct Acting Antiviral (DAA) based regimens on the occurrence of HCC in patients with cirrhosis is still controversial.

Objective: To evaluate the occurrence of HCC in HCV infected patients who received DAA.

Methodology: From Oct 2015 to Oct 2017, 696 HCV infected patients were retrospectically studied for onset of new HCC after DAA treatment. The median follow-up period was 11 months.

Results: A total of 652 patients were included in the DAA group. 18 patients were diagnosed with de novo HCC within the time of observation.

Newly diagnosed HCC patients were mostly male (1.6:1), Mean age was 61.72 years.

All patients had advanced cirrhosis of liver. 6 patients had esophageal varices and 2 patients were diabetic.

The median time to diagnosis of HCC was 9.7 months after DAA treatment.

2 patients failed to attend regular follow up.

12 patients achieved SVR however 4 patients did not obtain SVR. 2 patients has been changed HCC during DAA treatment.

Genotype 3 was the commonest (9 patients) followed by Genotype 6 (3 patients).

Most of patients(88%) were treated with Sofosbuvir/Daclatasvir/Ribavirin combination.
Conclusion: Monitoring for HCC should be performed indefinitely in patients with cirrhosis.
De novo HCC may be caused by age, advanced cirrhosis, decompensation and other comorbid diseases.

I02 - Epidemiology and Natural history

Abstract #220

Clinical and epidemiological characteristics of patients with hepatocellular carcinoma in North-East Asia population

Igor Malov[1], Oidov Baatarkhuu[2], Jazag Amarsanaa[3], Lkhagva-Ochir Tovuu[4], Evgeniy Savilov[5], Sergey Malov[6], Rodion Rasulov[7], Victorya Dvornichenko[8]

[1]Irkutsk State Medical University, [2]Mongolian National University of Medical Sciences, [3]Mongolian Association for the Study of Liver Diseases, [4]National Cancer Center of Mongolia, [5]Irkutsk State Medical Academy of Continuing Education, [6]Irkutsk State Medical University and Irkutsk State Medical Academy of Continuing Education, [7]Irkutsk State Medical Academy of Continuing Education, [8]Irkutsk State Medical University

Introduction: Among all oncological diseases, liver cancer is the 3th in Mongolian and 5th in Russian most common.
Objectives: We sought to describe the epidemiological and clinical characteristics and outcomes of HCC patients in North-East Asia from Mongolia and Asian region of Russia.
Patients and Methods: The studies were carried out in the cross-border regions of Mongolia and Asian part of Russia in the Lake Baikal region (Irkutsk region). 349 patients with hepatocellular carcinoma (HCC) of the Caucasian and Mongolian races were enrolled in the study.
Results: HCC incidence (2015) shows more unfavorable trends in the territory of Mongolia (74.5 per 100,000 total population) compared to Asian region of Russia (8.45 per 100,000). Patients from Mongolia often have a history of jaundice and acute hepatitis. HCC patients in Mongolia are related with HBV or HCV in 94.4% and 76.0% in Russia. Out of the etiological factors HCC is more often associated with the hepatitis B virus in Mongolia (34.4%) than in the Asian part of Russia (17.1%). At the same time, in Caucasians, HCC developed primarily on the background of liver cirrhosis.
Conclusion: Mongolia in terms of the incidence of HCC belongs to the hyperendemic regions of the world. In this country, among the risk factors, HBV continues to play a big role.
Due to the high incidence and late diagnosis in both countries, there is a need to develop a national strategy for early diagnosis and treatment of patients with HCC.

Abstract #387

Circulating cell-free HBV-human chimera DNA as new marker for HCC recurrence and clonality after curative resection

Chiao-Ling Li[1], Ming-Chih Ho[2], You-Yu Lin[3], Sheng-Tai Tzeng[4], Yun-Ju Chen[5], Hsin-Yung Pai[6], Ya-Chun Wang[7], Shiou-Hwei Yeh[8], Pei-Jer Chen[9]

[1]National Taiwan University College of Medicine, Taipei, Taiwan, [2]National Taiwan University College of Medicine, Taipei, Taiwan, [3]National Taiwan University College of Medicine, Taipei, Taiwan, [4]TCM Biotech International Corp., Taipei, Taiwan, [5]TCM Biotech International Corp., Taipei, Taiwan, [6]TCM Biotech International Corp., Taipei, Taiwan, [7]TCM Biotech International Corp., Taipei, Taiwan, [8]National Taiwan University College of Medicine, Taipei, Taiwan, [9]National Taiwan University College of Medicine, Taipei, Taiwan

Background and Aims: After curative resection of hepatocellular carcinoma (HCC), about 20–50% of patients develop tumor recurrence within the first year, indicating the frequent presence of minimal residual HCC. This study examined the HBV-human chimera DNA (vh-DNA) as a potential circulating biomarker in HBV-related HCC for monitoring the presence of residual HCC.
Method: We established a capture-NGS platform to identify the HBV integration sites in 42 resected HCC tissues. For individual HCC, the most dominant junction of HBV integration was chosen to design specific primers for droplet digital PCR (ddPCR). We used ddPCR to detect and quantify the HCC specific vh-DNA in plasma samples collected just before surgery and 2 months after surgery. Levels of vh-DNA were then correlated with HCC recurrence in one-year follow-up.
Results: We succeeded in detecting HBV integrations in 38 out of 42 HBV-related HCC ($\sim$ 91%), matching the performance of whole-genome sequencing. The copy number of vh-DNA in plasma at surgery correlated well with the size of HCC, with the detection limit at 1–2 cm (Fig. 1A). Among the plasma collected at 2 months after surgery, two-thirds of samples contained the same vh-DNA as baseline plasma, indicating a possible residual HCC. Consistently, they suffered HCC recurrence more frequently than those without vh-DNA in one year (Fig. 1B), suggesting recurrence of HCC originated from the residual HCC.
Conclusion: This study supported vh-DNA as a new circulating biomarker for detecting minimal residual HCC in HBV-related HCC after surgery and for monitoring recurrence within 1 year of surgical resection.

Abstract #399

Diagnostic Efficiency of Determination of Alpha-Fetoproteinin and Ostopontin for Early Diagnostics of Hepatocellular Carcinoma in the Output of Hepatitis B and C

Sergey Malov[1], Igor Malov[2], Evgeniy Savilov[3], Rodion Rasulov[4], Victorya Dvornichenko[5], Nikolay Yushchuk[6]

[1]Irkutsk State Medical University and Irkutsk State Medical Academy of Continuing Education, [2]Irkutsk State Medical University, [3]Irkutsk State Medical Academy of Continuing Education, [4]Irkutsk State Medical Academy of Continuing Education, [5]Irkutsk State Medical University, [6]Moscow State University of Medicine and Dentistry Named After A.I. Evdokimov

Every year, 7000–10000 cases of hepatocellular cancer (HCC) are registered in Russia.
Objective: To evaluate the diagnostic advantages of the combined determination of alpha-fetoprotein (AFP) and osteopontin (OPN) for detecting HCC in the outcome of hepatitis B (HB) and C (HC) in comparison with the use of AFP alone as a tumor marker common in clinical practice.
Materials and methods: Quantitative determination of AFP (Architect AFP) and OPN (ELISA, Bender MedSystems GmbH 2066) was carried out in 154 patients with HCC, 100 apparently healthy individuals, 95 patients with chronic hepatitis and 54 patients with cirrhosis of non-infectious etiology. The average age of patients with HCC was 63.1 years, the proportion of men 55.2%. HB markers were detected in 23.4% of patients, HC - 60.4%, and coinfection - 16.2%.

38 (24.7%) patients were diagnosed at stage I-IIIA of the disease according to the TNM classification.
Results: In apparently healthy individuals, the average level of AFP was 4.1 ng/ml; OPN - 18.4 ng/ml, which is significantly below the selected threshold (cut off), which was taken for AFP 20 ng/ml, for OPN 100 ng/ml. With this approach to the entire cohort of the examined, Se = 84.0%; Sp = 75.0%; Ac = 79.5%; +PV = 79.1; −PV = 93.8. When using AFP only: Se = 28.9%; Sp = 94.7%; Ac = 61.8%; +PV = 79.1; −PV = 93.8.
Conclusions: The joint determination of AFP and OPN increases the diagnostic efficiency of HCC detection due to a significant increase in the method sensitivity.

Abstract #498

Combined Use of WFA(+)-M2BP and AFP-L3 for the Prediction of HCV-Related Hepatocellular Carcinoma Development

Yu-Ju Lin[1], Yu-Han Huang[2], Liang-Chun Chen[3], Hui-Han Hu[4], Jessica Liu[5], Chin-Lan Jen[6], Sheng-Nan Lu[7], Masaya Sugiyama[8], Nao Nishida[9], Chien-Jen Chen[10], Masashi Mizokami[11], Hwai-I Yang[12], Mei-Hsuan Lee[13]

[1]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [2]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, [3]Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan, [4]Genomics Research Center, Academia Sinica, Taipei, Taiwan, [5]Genomics Research Center, Academia Sinica, Taipei, Taiwan and California Perinatal Quality Care Collaborative, Palo Alto, California, USA and Perinatal Epidemiology and Outcomes Research, Division of Neonatology, Department of Pediatrics, School of Medicine, Stanford University and Lucile Packard Children's Hospital, Palo Alto, California, USA, [6]Genomics Research Center, Academia Sinica, Taipei, Taiwan, [7]Department of Gastroenterology, Chang-Gung Memorial Hospital, Kaohsiung, Taiwan, [8]Genome Medical Sciences Project, National Center for Global Health and Medicine, Ichikawa, Japan, [9]Genome Medical Sciences Project, National Center for Global Health and Medicine, Ichikawa, Japan, [10]Academia Sinica, Taipei, Taiwan, [11]Genome Medical Sciences Project, National Center for Global Health and Medicine, Ichikawa, Japan, [12]Genomics Research Center, Academia Sinica, Taipei, Taiwan, [13]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan

Introduction: Serum Wisteria floribunda agglutinin-positive Mac-2-binding protein (WFA(+)-M2BP) and the ratio of lens culinaris agglutinin-reactive alpha-fetoprotein to total alpha-fetoprotein (AFP-L3%) were associated with hepatitis C virus (HCV)-related hepatocellular carcinoma (HCC).
Objectives: This study aimed to evaluate the use of WFA(+)-M2BP and AFP-L3% on the prediction of HCC.
Methodology: The REVEAL-HCV cohort enrolled participants residing in seven townships during 1991–1992. A total of 916 individuals seropositive for antibodies against HCV but seronegative for hepatitis B surface antigen had adequate serum or plasma samples at baseline for the measurements of both WFA(+)-M2BP and AFP-L3%. The ascertainment of HCC was by computerised data linkage with the national cancer registration and death certification systems until December 31, 2013. The sensitivities, specificities, positive predictive values (PPV), negative predictive values (NPV) and areas under receiver operating curves (AUROCs) were calculated.
Results: During a median follow-up of 21.7 years, 120 newly onset HCC cases were identified. The median value of WFA(+)-M2BP was 0.72 COI (range 0.08–12.84); and the median value of AFP-L3% was 3.6% (range 0.0–52.4%). By using the cut-offs of 2.5% for AFP-L3% and 2.86 for WFA(+)-M2BP, the sensitivity, specificity, PPV, NPV and AUROC were 0.600, 0.985, 0.177, 0.998, 0.785, respectively, for the 5-years prediction of HCC. The predictability for 10-years risk of HCC were 0.154, 0.985, 0.235, 0.976, 0.687 for the sensitivity, specificity, PPV, NPV and AUROC, in correspondingly.
Conclusions: The combined use of WFA(+)-M2BP and AFP-L3% may facilitate the surveillance of HCC among HCV-infected patients.

Abstract #577

Risk Factors, Clinical Aspects and Demogrphic Data of Hepatocellular Carcinoma (HCC) in Southeastern Europe During the Last Decade

Dimitrios Dimitroulopoulos[1], Dimitrios Kypreos[2], Nikolaos Saribeyoglou[3], Stavros Stavrinidis[4], Georgios Sofianidis[5], Eleni Manthopoulou[6], Dimitrios Katsinelos[7], Eleni Michalopoulou[8], Ioannis Marakis[9], Xenofon Tsamakidis[10], Klisthenis Tsamakidis[11]

[1]Gastroenterology Dpt, Agios Savvas Hospital, [2]Gastroenterology Dpt, Agios Savvas Hospital, [3]Gastroenterology Dpt, Agios Savvas Hospital, [4]Gastroenterology Dpt, Agios Savvas Hospital, [5]Gastroenterogy Dpt, Agios Savvas Hospital, [6]Gastroenterology Dpt, Agios Savvas Hospital, [7]Gastroenterology Dpt, Agios Savvas Hospital, [8]Gastroenterology Dpt, Agios Savvas Hospital, [9]Gastroenterology Dpt, Agios Savvas Hospital, [10]Gastroenterology Dpt, Agios Savvas Hospital, [11]Gastroenterology Dpt, Agios Savvas Hospital

Risk factors, clinical aspects and demographic data of HCC patients in Southeastern Europe are not yet well investigated.
Aim: Determination of demographic and clinical aspects and also the risk factors for HCC in Southeastern Europe during the last decade.
Patients/methods: Data of 328 HCC patients (years 2007–2017) were analyzed retrospectively.
Results: The median age of patients was 67 years (range 42–89). 242 (73.7%) were males. 179 (54.5%) were infected from HBV, 117 (35.6%) were infected from HCV, 7 (2.1%) were co-infected from the viruses reported above, 12 (3.6%) reported chronic alcohol abuse and for 13(3.9%) the cause of HCC was NASH/NAFLD. Of these that were infected from HBV and HCV, 33 (11.1%) reported also chronic alcohol abuse. 219 (66.7%) were diagnosed in advanced stage of HCC, 78 (23.7%) in intermediate and 31 (9.4%) in early. 144 (43.9%) presented elevated values of AFP, and 57 of these (17.3% of total) AFP $>$ 400 ng/ml. 99 (30.1%) were diagnosed with multinodular HCC, 20 (6.1%) with diffuse disease, 27 (8.2%) with local lymph node metastases and 13 (4.0%) with distant metastatic disease. With cirrhosis stage A were presented 189 (57.6%) patients, with stage B 79 (24.0%) and with stage C 34 (10.3%). Hepatectomy, RFA, chemoembolization and sorafenib administration were the main therapeutic approaches.
Conclusion: In Southeastern Europe HCC is threefold more common in males than in females. HBV and HCV infections and chronic alcohol abuse are the main etiological factors. Elevated AFP levels can be useful for early diagnosis in high risk patients.

Abstract #658

Influence of metabolic risk factors on recurrence of hepatocellular carcinoma after tumor resection

Yijin Wang[1], Li Mo[2], Hongyang Liu[3], Jingmin Zhao[4]

[1]The 5th Medical Center, Chinese PLA General Hospital, [2]The 5th Medical Center, Chinese PLA General Hospital, [3]The 5th Medical

Center, Chinese PLA General Hospital, [4]The 5th Medical Center, Chinese PLA General Hospital

Introduction: Metabolic syndrome (MS) has been increasingly recognized a risk factor for hepatocellular carcinoma (HCC), however, whether MS play roles in HCC recurrence after hepatic resection remains unknown.
Objective: To evaluate whether MS is a risk factor for HCC recurrence after resection.
Methods: 506 HCC patients undergoing liver resection between 2012 and 2017 were recruited. MS, defined as presenting 3 or more metabolic abnormalities, including obesity, diabetes, hypertriglyceridemia, hypercholesterolemia and hypertension, were assessed at the time of tumor resection.
Results: The median patient age was 49 and 83.8% were men. The median follow-up time was 26 months. Interestingly, univariate analysis showed that patients with MS had a lower risk for HCC relapse within 2 years than those without ($p = 0.081$). After adjusting for age, cirrhosis status, tumor diameter, tumor number and hypertension, MS showed no association with HCC recurrence. Further analysis of recurrence incidence at different time points showed that the probability of HCC recurrence in patients with MS was 3.4, 3.4 and 42.9% at 6 months, 12 months and 36 months, respectively. While the recurrence probability at the same time point in patients without MS was 13.3, 22.7 and 52.3%, respectively ($p = 0.0973$).In multivariate analysis, cirrhosis (odds ratio [OR], 3.21; 95% CI, 1.32–7.81; $p = 0.01$) large tumor size > 5 cm ([OR], 3.61; 95% CI, 2.29–5.69; $p < 0.001$), and multiple tumors (odds ratio [OR], 3.59; 95% CI, 1.51–8.55; $p = 0.004$) were found to be independent risk factors for HCC recurrence.
Conclusions: MS seems not associated with tumor recurrence in HCC patients with resection.

Abstract #707

Comparison of hepatocellular carcinoma prediction models using various analyzes in treatment naïve patients for chronic hepatitis B

Sang Bong-Ahn[1], Dae Won-Jun[2]

[1]Nowon Eulji Medical Center, Eulji Hospital, [2]Department Internal Medicine, Hanyang University College of Medicine

Introduction: This study aimed to compare the various hepatocellular carcinoma (HCC) prediction models in treatment-naïve patients receiving entecavir or tenofovir for chronic hepatitis B (CHB).
Methods: We enrolled 3184 patients treated with chronic hepatitis B. We analyzed 1350 patients who were treated with entecavir or tenofovir as initial treatment, those with initial clinical records, and those without cancer within 1 year after treatment. HCC prediction decision tree was constructed We constructed logistic regression, decision tree analysis, support vector machine (SVM) analysis and random forest analysis through using 90 variables including demographic, laboratory data, and cirrhosis.
Results: Eighty-four patients were diagnosed with hepatocellular carcinoma. Age (OR = 12.3, $p = 0.001$), family history of HBV (OR = 7.2, $p = 0.006$), cirrhosis (OR = 35.1, $p = 0.001$), diuretics use (OR = 4.1, $p = 0.04$), WBC count (OR = 4.1, $p = 0.04$), hemoglobin (OR = 4.6, $p = 0.03$), admission history (OR = 6.2, $p = 0.01$), and ascites (OR = 10.7, $p = 0.001$) were the significant predictors of hepatocellular carcinoma development. Cirrhosis, family history of HBV, serum albumin, serum alkaline phosphatase, smoking history, platelet count, and WBC count were selected to set up a decision tree as the prediction model. Decision tree algorithm showed high prediction accuracy [Accuracy: 96% (95% CI 93.0–98.0), AUC 0.825]. Random Forest analysis [Accuracy: 95% (92.5–97.2), AUC 0.877), support vector machine analysis [Accuracy: 96% (94.5–98.4), AUC 0.799) and logistic regression analysis [Accuracy: 94% (0.91–0.96), AUC 0.85] are also show good area under the curve (AUC).
Conclusion: Proposed HCC prediction models produces high accuracy and area under the curve (AUC) in chronic hepatitis B patients.

Abstract #727

The Evaluation of α-fetoprotein as a Biomarker for the Surveillance of Hepatocellular Carcinoma at Cipto Mangunkusumo National General Hospital and Dharmais National Cancer Hospital, Indonesia

Alessa Fahira[1], Chyntia Olivia Maurine Jasirwan[2], Lianda Siregar[3], Imelda Loho[4], Kemal Fariz Kalista[5], Irsan Hasan[6], Juferdy Kurniawan[7], Cosmas Rinaldi Adithya Lesmana[8], Andri Sanityoso Sulaiman[9], Rino Alvani Gani[10]

[1]Undergraduate Medical Student, Faculty of Medicine, Universitas Indonesia, [2]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [3]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Dharmais National Cancer Hospital, Jakarta, Indonesia, [4]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [5]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [6]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [7]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [8]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [9]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [10]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Background: Hepatocelullar carcinoma (HCC), the most common type of liver cancer, is one of the leading cause of cancer-related death worldwide with a very poor prognosis. In Indonesia, the average life of expectancy is less than three months with most patients being in an advanced stage—in which the survival rate is very low. Early detection through surveillance program is by thus crucial. HCC guidelines worldwide have given surveillance recommendation through the examination of α-fetoprotein (AFP) and ultrasound for patients at risk in developing HCC. However, there have been some controversies regarding the usage of AFP concerning its low sensitivity and specificity in detecting HCC.
Objectives: To evaluate the effectiveness of AFP in the surveillance of HCC patients and discover the parameters most associated with the increase of AFP $\geq$ 10 ng/ml in Indonesia.
Methods: Analyzing medical records of HCC patients and patients of high-risk in developing HCC of whom include cirrhosis, hepatitis B and C patients who undergo treatment at the Cipto Mangunkusumo National Hospital and Dharmais National Cancer Hospital, Indonesia.
Results: The sensitivity and specificity of AFP in the surveillance of HCC in Indonesia were 82.6% and 68.9%, respectively. The parameters most associated with the increase of AFP $\geq$ 10 ng/ml through multivariate analysis were the etiology of hepatitis B, in the stage of BCLC B & C, and the presence of cirrhosis.

Conclusion: AFP can still be used in the surveillance of HCC in Indonesia for its high sensitivity value.
Keywords: Hepatocelullar carcinoma, α-fetoprotein, Surveilance, and Biomarker.

Abstract #731

Synchronous Double Primary Malignancy: Hepatocellular Carcinoma and High Grade Urothelial Carcinoma: A Case Report

Gizelle Mica Makiputin Silla[1]

[1]Up-Philippine General Hospital

The occurrence of multiple primary malignant tumors in a single patient is rare, with an incidence rate of 0.73–11.7%. With screening programs' improvement comes increase in diagnoses of malignancies. Risk of having a second primary malignancy vary and range from 1% in primary liver cancer up to 16% in primary bladder cancer.

We present a 61 year old male with cirrhosis from chronic Hepatitis B presenting with abdominal pain, jaundice, weight loss, hematuria who underwent open cholecystectomy but had perioperative bleeding per JP drain with increasing severity of abdominal pain hence referral to our institution. On abdominal CT scan, a $6 \times 5 \times 4$ cm hypervascular mass in the right hepatic lobe segment VII and a concomitant urinary bladder mass was noted. Trans-arterial chemoembolization (TACE) was immediately done for possible tumor rupture and cystoscopy with transurethral resection of a 3×3 cm wide-based bladder mass which revealed to be high grade urothelial carcinoma, invasive with glandular differentiation and positive for lymphovascular invasion. He underwent radiation therapy and continued on a second TACE and is also being given Tenofovir treatment. He is presently well after the second chemoembolization with latest urinary cytology showing no malignant cells.

Invasive bladder cancer has been described with other second malignancies such as lung and renal cell cancer however, it has rarely been described concurrently with a primary liver cancer. A multidisciplinary approach would be warranted to address both and it is important to recognize them early and perform adequate investigations because of relevant implications on subsequent therapeutic interventions.

Abstract #831

Clinical Profile of Patients with Hepatocellular Carcinoma at St. Luke's Medical Center and Cardinal Santos Medical Center from 2003–July 2018

Nicodemus Lim Ong[1], John Alfredo Raphael Perez Pangilinan[2], Ian Homer Yee Cua[3], Diana Alcantara Payawal[4]

[1]St. Luke's Medical Center, [2]Cardinal Santos Medical Center, [3]St. Luke's Medical Center, [4]Cardinal Santos Medical Center

Background: In the Philippines, data is limited on the characteristics of patients with hepatocellular carcinoma (HCC). Recent studies from other neighboring Asian countries suggests a change in trend in the epidemiology of HCC. This study aims to update the data, describe the etiology and clinical profile of patients with HCC at 2 tertiary referral centers in the Philippines.

Methods: This is a two-center retrospective, descriptive study of all adult patients with hepatocellular carcinoma at St. Luke's Medical Center, Quezon City (SLMC-QC) and Cardinal Santos Medical Center (CSMC). Clinical profile data, specifically patient's age, gender, presence or absence of liver cirrhosis, Child's Pugh score, and registered etiology of HCC (HBV, HCV, alcoholic liver disease, nonalcoholic fatty liver disease, others) was obtained and recorded in a Microsoft Excel. Data were analyzed using descriptive statistics.
Results: A total of 1260 subjects were included in this study. Patients were predominantly male (76.1%) with mean age of 63. Majority (83.3%) developed HCC under a background of liver cirrhosis, with baseline liver function under Child–Pugh B at 51.8%, followed by Child's A (23%) and Child's C (17.6%). Hepatitis B (44.3%) is the most common etiology, followed by NAFLD (16%). Hepatitis B was also the most predominant etiology for HCC in noncirrhotic HCC patients.
Conclusion: Patients with HCC from both our centers are mostly males, with a mean age of 63. Majority developed HCC on a background of liver cirrhosis, with hepatitis B being the most common etiology followed by NAFLD.

Abstract #859

Hepatocellular Carcinoma Associated WITH Spontaneous Liver Abscess in a Patient with Chronic Hepatits B: A Case Report

Virgilio Jr. Sandico Lo[1], Melchor Mesa Chan[2]

[1]University of Sto. Tomas Hospital, [2]University of Sto. Tomas Hospital

Introduction: Hepatocellular carcinoma (HCC) associated with spontaneous concurrent liver abscess is extremely rare, with available literature reporting prevalence of only 0.9–2%. Most of the recorded cases of HCC presenting with liver abscess are due to invasive interventions.
Clinical Presentation: We present a case of a 65 year old male, Filipino, previously diagnosed case of Chronic Hepatitis B who was admitted due to 1 week history of intermittent fever and chills, accompanied by jaundice, epigastric pain, anorexia and weight loss. Abdominal exam revealed increased warmth in the right upper quadrant with no tenderness.
Management: White blood cell count and Alpha feto protein level were both elevated at 13.5×109/L and 443.4 ng/mL, respectively. Whole Abdominal Ultrasound revealed a 9 cm solid mass at Segment VI/VII of the right hepatic lobe with intralesional blood flow, which on subsequent triphasic contrast-enhanced CT scan demonstrated heterogenous enhancement with a large central area of necrosis and gas collection. Primary consideration was hepatic abscess, to rule out malignancy. Imipenem and Metronidazole were started. Patient subsequently underwent ultrasound guided percutaneous aspiration of the hepatic mass yielding 100 ml of dark red, non-clotting fluid as well as tissue cores and fragments. Cytology confirmed the presence of HCC and culture examination revealed *Eschericia coli* indicative of concomitant abscess formation.
Conclusion: Pyrexia, leucocytosis and appropriate imaging findings may signify red flags that may indicate an unusual case of HCC. Differential diagnosis of HCC with abscess is difficult and may require aspiration cytology or pathology.

Abstract #961

Transient Elastography Can Predict De Novo Hepatocellular Carcinoma (HCC) Development in Cirrhotic Patients Treated with Direct Acting Antiviral Drugs (DAAs)

Mohamed Kohla[1], Mohamed Rady[2], Maha Elsabaawy[3], Mahmoud Allam[4], Abdelaleem Helal[5]

[1]National Liver Institute, Menoufia University, [2]National Liver Institute, Menoufia University, [3]National Liver Institute, Menoufia University, [4]National Liver Institute, Menoufia University, [5]National Liver Institute, Menoufia University

Background: Hepatocellular carcinoma is a common health burden in cirrhotic patients.
Aim: To evaluate Transient Elastography as predictor of HCC after Direct acting antiviral drugs (DAAs).
Methods: Patients with HCV related fibrosis who did FibroScanTM before treatment with DAAs were included. Liver, renal function tests, CBC, INR, alpha-fetoprotien, abdominal ultrasonography, Triphasic CT, and FibroScanTM were performed. Patients who had a Transient Elastography measurement before treatment with DAAs were included and divided into two groups; Group (I) patients who developed De novo HCC and Group (II) are those who did not developed HCC after DAAs.
Results: Patients who developed de novo HCC after DAAs (group I, thirty patients) had higher serum AST levels (68.3 ± 38.2 vs. 48.7 ± 32.4 U/L), lower platelet count (131.5 ± 55.6 vs. $179.5 \pm 69.8 \times 103/\mu L$) and older age ($59.5 \pm 6.4$ vs. 51.3 ± 10.5 years) than patients who did not developed HCC (group II, ninety patients) with a p value < 0.05. Group I patients had a statistically significant higher liver stiffness measurement (LSM) by FibroscanTM (32.1 ± 10.7 vs 15.5 ± 11.5 kPa, p value = 0.001) than patients who did not developed HCC. With a cutoff value of 18.5 kPa being the most predictive value for de novo HCC development after DAAs (90.0% sensitivity, 80.0% specificity, 55.0% PPV, 97.3% NPV, 80.0% accuracy) as shown in figure 1.
Conclusion: The measurement of liver stiffness by FibroScanTM could be a reliable method for risk stratification and prediction of de novo HCC development after DAAs in cirrhotic patients.

Abstract #987

Impact of fibroblast growth factor-2 and its receptor gene polymorphisms on tumor progression and patient survival in patients with hepatitis B virus-associated hepatocellular carcinoma

Jae Youn Cheong[1], Soon Sun Kim[2], Chul Won Seo[3]

[1]Ajou University Hospital, [2]Ajou University Hospital, [3]Ajou University Hospital

Purpose: The fibroblast growth factor (FGF), vascular endothelial growth factor and hepatocyte growth factor play a critical role in hepatocellular carcinoma (HCC). We determined the association of single nucleotide polymorphisms (SNPs) of growth factor signaling related genes with the development and progression of tumor and overall survival in patients with hepatitis B virus (HBV)-associated HCC.
Patients and methods: We assessed 9 SNPs of FGF1, FGF2, FGF receptor (FGFR)-2, Flt-1 and c-MET gene in 245 patients with HCC and 483 chronic HBV carriers without HCC.
Results: None of all tested SNPs was associated with the risk of HCC in chronic HBV carriers. FGF2 rs308379 A allele was significantly associated with small tumor size, early tumor stage and less vascular invasion. Flt-1 rs4771249 C allele was associated with low alpha-fetoprotein level. In Kaplan–Meier analysis, the patients with FGF2 rs308447 TT genotype showed decreased survival than the patients with CC or CT genotype (P = 0.016) and FGF2 rs308379 A allele carrier had a shorter survival than TT genotype (P = 0.020). In addition, FGFR2 rs1219648 CC genotype was significantly associated with increased survival (P = 0.047). Multivariate Cox proportional analysis revealed that FGF2 rs308379 AA genotype [hazard ratio (HR) = 0.635, P = 0.033] and advanced tumor stage (HR = 2.819) were independent prognostic factors for overall survival in patients with HCC.
Conclusion: These observations suggest that the SNP of FGF2 and FGFR2 gene can be a potential indicator of the tumor progression and the survival in patients with HBV-associated HCC.

Abstract #1029

Fifteen Years of Hepatocellular Carcinoma, a paradigm shift from Infectious to non-infectious etiology

John Alfredo Raphael Perez Pangilinan[1], Diana Alcantara Payawal[2]

[1]Cardinal Santos Medical Center, [2]Cardinal Santos Medical Center

Introduction: Hepatocellular carcinoma (HCC) is the fifth most common cancer globally. The two most important risk factors are chronic HBV and HCV infection. Recent data suggests that non-communicable diseases are at the forefront of HCC etiology.
Methods: This is a single-center retrospective, descriptive study of patients with HCC at Cardinal Santos Medical Center from 2003 to 2018. Clinical data, including demographics were obtained.
Results: We obtained 674 subjects; 51% being male. Child's Pugh B was most common (67%). While majority of subjects (52%) had HBV as etiology of HCC, trends showed that in 2003–2010 (Time 1) and 2011–2018 (Time 2) the prominent shift to NAFLD as the etiology of HCC can be assumed. With a mean age of 64, it is evident that majority of subjects born without vaccination is key in recognizing HBV as the primary etiology. But as data suggests, NAFLD has taken a prominent role, encompassing 17% of the cases of HCC in Time 2 compared to Time 1 (3.9%). In total, Time 2 showed 30% with non-infectious etiology, versus 19% in time 1, representing a 63% increase over a 15 year span.
Conclusion: As eradication of preventable diseases improves, new obstacles emerge in healthcare. As results of vaccination and management of Hepatitis broadens, a trend towards developing HCC in inconspicuous settings emerges. The non-communicable and lifestyle aspect in developing this comes into focus, an important thrust in the next chapter in preventing and managing HCC.

I03 - Imaging and Histology

Abstract #155

Real B Score: An effective risk prediction tool for Hepatocellular carcinoma (HCC) in Polynesian patients on oral Anti-viral therapy (OAV) for Chronic Hepatitis B (CHB)

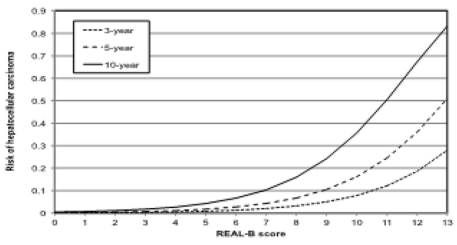
Hannah Margaret Giles[1], Sethu Elango Nagappan[2], Stephen John Gerred[3], Rebekah Jane Carey[4], Vrushali Ramakrishna Savant[5], Ed John Gane[6]

[1]Counties Manukau Health, [2]New Zealand Liver Transplant Unit (NZLTU), [3]Counties Manukau Health, [4]Counties Manukau Health, [5]Counties Manukau Health, [6]Counties Manukau Health

Introduction: CHB is the leading cause of HCC in New Zealand. Almost two-thirds of those infected are Polynesian ethnicity (Māori or Pasifika). Recently, the PAGE-B and REAL-B scores have been demonstrated effective in stratifying the HCC risk in Caucasian and Asian cohorts.
Objectives: To validate REAL-B and PAGE-B scores as predictors of HCC in Polynesians.
Methods: Polynesian patients on OAV were identified from databases at CMDHB and NZLTU. After excluding patients who had less than 12 months of OAV, viral co-infection or developed HCC within 12 months of starting OAV, 676 patients were analysed. The REAL-B and PAGE-B scores were calculated from baseline clinical data and outcomes obtained from clinical note review. Time-varying receiver operating characteristic (ROC) curves and the area under ROC (AUROC) assessed the discrimination of the risk scores. Approval (#731-T05, A+8155).
Results: The Real-B score was significantly better than Page-B score in predicting 3 years HCC risk with AUROC of 0.866 (95% CI 0.8147–0.9178) compared to AUROC of 0.7594 (95% CI 0.6584–0.864), (P = 0.01). The two models were equivalent at predicting the 5 and 10 years risk. A REAL-B score of 0–4 equates to a 10 years HCC risk of 2.5%, score 5–9: 15.5%, score 10–13: 61%.
Conclusion: The Real-B score is effective in predicting HCC risk at 3, 5 and 10 years in Polynesian patients with CHB on OAV therapy. A Real-B score of 5 equates to a 5% risk of HCC at 10 years which should be considered a threshold to commence ultrasound surveillance.

REAL-B scoring system derived from Cox regression analysis

Sex	Age	Cirrhosis at baseline	Diabetes	Platelet count	AFP
Female: 0	15-29: 0	No: 0	No: 0	≥200: 0	≤20: 0
Male: 1	30-39: 1	Yes: 2	Yes: 1	100-200: 1	>20: 1
	40-49: 2			<100: 2	
	50-59: 3				
	60-69: 4				
	70-79: 5				
	≥80: 6				



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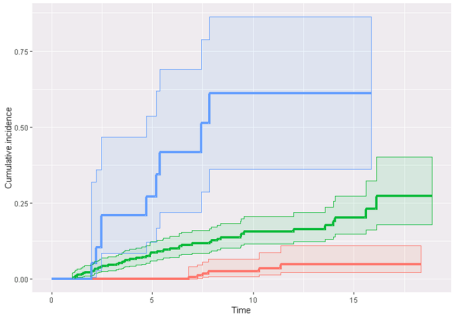
Cumulative Incidence of HCC - Polynesian Patients by Real B Score



Risk score group	Cumulative 10-year HCC incidence
0-4	2.5%
5-9	15.5%
10-13	61.1%

Abstract #528

FNAC of hepatic malignancy and its clinical co-relation

Abul Hayat Manik[1], Md Robed Amin[2], Muhammad Rafiqul Islam[3]

[1]Hepatology Dept, Dhaka Medical College Hospital, [2]Assoc Prof, Dept of Medicine, Dhaka Medical College Hospital, [3]Asst Professor, Dept of Medicine, Dhaka Medical College Hospital

Introduction: The clinical and radiological presentations of both primary and metastatic tumors can be similar—as a space occupying lesion (SOL). Fine needle aspiration cytology (FNAC) can play a major decisive diagnostic role. The specificity of FNAC of the liver approaches 100% and the sensitivity ranges from 67 to 100%, averaging about 85%.
Objectives: The present study was conducted to observe the diagnostic accuracy of FNAC in making a morphological diagnosis of these lesions by differentiating lesions from primary and metastatic neoplasm of the liver verified subsequently through their clinical co-relation.
Methodology: A total 100 patients with hepatic SOL were enrolled in a non random sampling method. Then USG guided FNA of hepatic lesion done and sent for cytological study. A structured case record form was applied for clinical profile.
Results: 42 patients were found having primary hepatocellular carcinoma and 58 patients has got secondary hepatic malignancy. FNAC confirmed secondary hepatic malignancy (n = 58) as metastatic adenocarcinoma 43(74.1%), metastatic small cell carcinoma 9(15.5%), Gastrointestinal stromal tumor 2(3.4%), squamous cell carcinoma 2(3.4%), Non Hodgkins lymphoma 2(3.4%). Both hepatocellular carcinoma and secondary hepatic malignancy predominantly presents with abdominal pain, 39(92.9%) cases of HCC and 47(81.0%) cases of secondaries. HBsAg found in 15(35.7%) cases, Anti HBc(total) 11(26.2%) cases, and Anti HCV 9(21.4%) cases of hepatocellular carcinoma. Tumor marker AFP was not statistically significant in this study.
Conclusion: Correlation with clinical, radiological, and cytological findings is helpful in arriving at the correct diagnosis of hepatic SOL and therefore increases overall accuracy and cost-effectiveness of the procedure.

Abstract #810

Artificial intelligence system for detection of focal liver lesions in ultrasonography images

Thodsawit Tiyarattanachai[1], Roongruedee Chaiteerakij[2], Sanparith Marukatat[3], Rungsun Rerknimitr[4]

[1]Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [2]Division of Gastroenterology, Department of Medicine, Chulalongkorn University, Bangkok, Thailand, [3]Image Technology Laboratory, National Electronics and Computer Technology Center (NECTEC), Pathum Thani, Thailand, [4]Division of Gastroenterology, Department of Medicine, Chulalongkorn University, Bangkok, Thailand

Introduction: Utilizing convolutional neural network (CNN) for radiologic images analysis has been of great interest. However, CNN-assisted analysis for ultrasonography (USG) images has not been well established.
Objective: To develop the CNN for detection of focal liver lesions (FLLs) in USG images.
Methodology: We developed a CNN using multi-step transfer learning method with 1378 liver USG images, including 758 with FLLs (177 hepatocellular carcinomas (HCCs), 112 cysts, 201 focal fatty changes (FFCs), 161 focal fatty sparings (FFSs), 67 hemangiomas and 40 others) and 620 without FLLs (Figure 1). Another set of 12,303 abdominal organ images (6538 livers, 3849 kidneys and 1916 gallbladders) were used to adapt the CNN to USG domain. Performance was evaluated on an independent set of 200 images with FLLs (44 HCCs, 40 cysts, 54 FFCs, 37 FFSs, 16 hemangiomas and 9 others) and 200 images without FLLs. ROC curves were generated using multiple decision thresholds.
Results: With the decision threshold of 0.2, the CNN had overall sensitivity and specificity of 81% and 82%, respectively, with an AUC of 0.89 (95% CI 0.85–0.92), for detection of FLLs. When stratified by FLLs size, the sensitivities were 83% and 65% for FLLs size $\geq$ 1 cm and $<$ 1 cm, respectively ($p = 0.064$), with equal specificity of 82% (Figure 2). Proportion of HCCs, cysts, FFCs, FFSs and hemangiomas detected were 84, 88, 80, 78 and 75%, respectively.
Conclusion: The CNN performed well in detection of FLLs. To expand its application, developing CNN for real-time detection and characterization of FLLs is warranted.

I04 - Treatment of HCC

Abstract #68

Transarterial Chemoembolization in Patients with Hepatocellular Carcinoma: Study of Different Outcomes and Their Predictive Factors

Mahmoud Zaki Elkadeem[1]

[1]faculty Of Medicine, Tanta University, Tropical Department

Abstract
Aim: To analyze the outcomes after transarterial chemoembolizaton (TACE) including radiological response and liver decompensation, and their predictive factors.
Methods: Sixty-two hepatocellular carcinoma patients underwent transarterial chemoembolizaton. Laboratory data, tumor criteria, and Child–Pugh score were recorded baseline and at one month post-procedure. Tumor response according to Modified Response Evaluation Criteria in Solid Tumors was evaluated. Results: Twenty-five patients (40.3%) showed complete response, 15 patients (24.2%) showed partial response, 2 patients (3.2%) showed stable disease, and 20 patients (32.3%) showed progressive disease. Significant difference was detected in patients with different radiological responses as regards tumor criteria (size, invasion of portal vein, Barcelona Clinic Liver Cancer stage), and technique of TACE. Thirty-six patients (58%) had liver decompensation after TACE. Tumor criteria, serum bilirubin, AST, INR, Model for End Stage Liver Disease, and low platelet count were detected to be predictors of as radiological response and liver decompensation after TACE.
Conclusion: Radiological response cannot be considered alone to determine the outcomes after transarterial chemoembolization. Also, tumor criteria, liver functions, and platelet count are predictors of the outcome.
Keywords: Hepatocellular carcinoma, Modified Response Evaluation Criteria in Solid Tumors Transarterial chemoembolization.

Abstract #69

Prognostic Value of Golgi Protein 73 as Marker for Follow up of Hepatocellular Carcinoma Patients After Locoregional ablation

Mahmoud Zaki Elkadeem[1]

[1]Faculty of Medicine Tanta University Tropical Department

Abstract
Background and aim: Hepatocellular carcinoma (HCC) is a global health problem. HCC diagnosis is based on abdominal ultrasound and alpha fetoprotei. Golgi protein 73 is a type-II membrane protein upregulated in liver cells. Serum Golgi protein 73 (sGP73) can be a promising biomarker for diagnosis and prognosis of HCC. The aim was to assess serum Golgi protein 73 as a marker for follow up of HCC patients who after radiofrequency or microwave ablation in comparison to alpha fetoprotein.
Methods: This study was performed on 80 subjects who were divided into three groups; Group 1: included 30 with HCC, Group 2: included 30 patients of liver cirrhosis without HCC, and Group 3: included 20 healthy individuals as control ones. GP73 levels were measured in all subjects and followed up in group I one, 3 and 6 months after tumor ablation.
Results: AFP level was significantly higher in group I than others, with a cut off value $>$ 20 ng/ml (sensitivity 86.67%, specificity 84%). Also, GP73 level was significantly higher in group I with a cut off value $>$ 79.2 ng/ml (sensitivity 96.67%, specificity 96%). Both GP 73 and AFP levels were significantly decreasing after ablation in different periods of follow up than before. GP73 correlated positively with AFP, ALT, and AST.
Conclusion: GP73 is a useful marker in early diagnosis of HCC, also in follow up after locoregional therapy to detect early recurrence.
Keywords: Hepatocellular carcinoma, Alphafetoprotein, Golgi protein 73, prognosis.

Abstract #71

Percutaneous microwave and radiofrequency ablation for hepatocellular carcinoma: a comparative study

Ali Ghweil[1], Heba Osman[2]

[1]South Valley University, [2]Lecturer of Gastroentrology South Valley University

Background: Percutaneous microwave ablation and radiofrequency ablation are two commonly used modalities for the treatment of

hepatocellular carcinoma; however, comparisons of them have not been documented adequately.
Methods: Of 55 patients with biopsy-proved hepatocellular carcinoma, 25were treated percutaneously with microwave ablation and 30 with radiofrequency ablation. The local tumor control, complications related to treatment, and long-term results of the two modalities were compared
Results: The complete ablation rates were 92% (21/25) using microwave ablation vs 90% (27/30) using radiofrequency ablation (P = 0.75), and no significant differences were found either in the ablation of tumors of 3.0 cm or less (P = 1.00) or in those of more than 3.0 cm (P = 1.00) between the two modalities. The local recurrence rates were 12% (3/25) using microwave ablation vs 20% (6/30) using radiofrequency ablation (P = 0.12), and there were no significant differences between the two modalities either in tumors of 3.0 cm or less (P = 0.36) or in those of more than 3.0 cm (P = 0.82). The rates of major complications associated with microwave ablation and radiofrequency ablation were 12% (3/25) vs 10% (3/30) P = 0.71). The disease-free survival rates in the microwave ablation group were 52, 40, 32, and 16% at 1, 2, 3, and 4 years, respectively, and those in the radiofrequency ablation group were 46.6, 36.6, 20 and 10% at 1, 2, 3 and 4 years, respectively (P = 0.53).

Abstract #81

Outcome of Transarterial Chemoembolization (TACE) in patientwith Hepatocellular Carcinoma

Ali Ghweil[1], Shamaradan Bazeed[2], Ahmed Elyan[3], Ahmed Okasha[4]

[1]South Valley University, [2]South Valley University, [3]Assistant Lecturer of Gastroentrology South Valley University, [4]Assistant Professor of Radiology South Valley University

Outcome of Transarterial Chemoembolization (TACE) in patientwith Hepatocellular Carcinoma.

Abstract
Background: Transarterial chemoembolization (TACE) is recommended as a treatment for unresectable hepatocellular carcinoma (HCC) in patients with normal underlying liver function. The efficacy of TACE in cirrhotic patients with compromised liver function is unknown Aim of the study: to evaluate the outcome following transarterial chemoembolization (TACE) in patients with unapplicable locoregional therapy in hepatocellular carcinoma (HCC).
Patients and methods: This Prospective Cohort study conducted on 50 patients with HCC at Tropical medicine and gastroenterology department Qena university hospital.
Results: 56% of patients reached complete remission within 1 month of ttt in mean duration of follow up 58.28 months, 66% of patients had recurrence 40% in < 1 year and 26% 1–2 years, 34% of recurrence were Target tumor progression, 20% Intrahepatic new lesion and 12% both, Total deaths were 46% of patients.
Conclusions: TACE offers a reasonable palliative therapy for HCC

Abstract #129

Multidisciplinary treatments using Cyber-Knife for advanced hepatocellular carcinoma

Takamasa Ohki[1], Mayuko Kondo[2], Yukiyo Fukumura[3], Makoto Imai[4], Ken Kurokawa[5], Junya Arai[6], Chikako Shibata[7], Kaoru Takagi[8], Kentaro Kojima[9], Michiharu Seki[10], Jun Kato[11], Nobuo Toda[12], Kazumi Tagawa[13]

[1]Mitsui Memorial Hospital, [2]Mitsui Memorial Hospital, [3]Mitsui Memorial Hospital, [4]Mitsui Memorial Hospital, [5]Mitsui Memorial Hospital, [6]Mitsui Memorial Hospital, [7]Mitsui Memorial Hospital, [8]Mitsui Memorial Hospital, [9]Mitsui Memorial Hospital, [10]Mitsui Memorial Hospital, [11]Mitsui Memorial Hospital, [12]Mitsui Memorial Hospital, [13]Mitsui Memorial Hospital

Background: Cyber-knife (CK) one of the stereotactic radiotherapy offers a treatment option for hepatocellular carcinoma (HCC) patients that are not eligible for surgery, transarterial chemoembolization, or radiofrequency ablation. We have evaluated the efficacy and safety of CK for advanced HCC (stage 4a or 4b).
Methods: Our 25 consecutive patients (mean age 72.4 years, with total 46 targets) receiving Cyber-knife are presented. Mean radiation dose was 38.6 Gy delivered over 5–6 fractions. The evaluation was made by enhanced CT after 3–4 months from radiation.
Results: The mean observational period was 480 days. Twenty-four patients (96%) were male and 16 patients (64%) were positive for HCV. Twenty patients (80%) were already treated with sorafenib. The mean diameter of the targets was 24.9 mm. The distribution of each target was as follows: lymph nodes 38, portal vein thrombosis 3, bone metastasis 2, bile duct invasion 1, vena cava inferior invasion 1, and lung metastasis 1. Overall response rate (CR + PR) according to mRECIST was 95.7% (CR 31 targets and PR 13 targets). There were no severe side effects exceeded CTCAE grade 2.
Conclusion: Our results showed that CK is a safe and effective local treatment. CK is considered to be useful for controlling advanced HCC.

Abstract #135

The prognostic factors of the viral and tumor status in Sorafenib treatment on Chinese patients with advanced hepatocellular carcinoma: A single-center study in Taiwan

Shao Wu Lee[1], Teng Yu Lee[2], Sheng Shun Yang[3], Hong Zen Yeh[4], Chi Sen Chang[5]

[1]Taichung Veterans General Hospital, [2]Taichung Veterans General Hospital, [3]Taichung Veterans General Hospital, [4]Taichung Veterans General Hospital, [5]Taichung Veterans General Hospital

Aim: Sorafenib is of proven efficacy in treating patients of hepatocellular carcinoma (HCC). Our study was aimed to determine the factors influence the sorafenib efficacy.
Methods: We evaluated data of HCC patients receiving sorafenib from June 2012 to October 2016. All HCC cases were of the BCLC classification stage C. The exclusion criteria: those of BCLC classification stage A or B, with the absence or co-infection of HBV and HCV, poor compliance to medication, or loss of follow-up within the following day. The presence of HBV, HCV, macoscopic vascular invasion (MVI) or extrahepatic spread (EHS) was recorded for each patient. Time-to-progression (TTP) and overall survival (OS) were analyzed.
Results: Among a total of 90 HCC patients, 48 (53.3%) had HBV infection, 42 (46.7%) had HCV infection, 51 (56.7%) had MVI, and 39 (43.3%) had EHS. Patients with HCV infection showed better TTP and OS than those with HBV infection. Patients with EHS had a longer TTP and OS than those with MVI. For patients with HBV infection, those with EHS had a longer TTP (mean 4.60 vs. 2.64 months, p = 0.002) and OS (mean 6.65 vs. 4.53 months, p = 0.045) compared to those with MVI. Among those with MVI, patients with HBV infection had a poorer TTP (mean 2.64 vs. 4.74 months, p = 0.019) and shorter OS (mean 4.53 vs. 7.00 months, p = 0.059) compared to those with HCV infection.

Conclusion: HCC patients with HCV infection or with the presence of EHS showed better sorafenib efficacy.

Abstract #173

Comparative long-term outcomes of laparoscopic liver resection and radiofrequency ablation for hepatocellular carcinoma: Location of tumor matters

Jai Young Cho[1], Sungho Kim[2]

[1]Seoul National University Bundang Hospital, [2]Seoul National University Bundang Hospital

Background: Laparoscopic liver resection (LLR) has been considered as standard surgery for small hepatocellular carcinoma (HCC) located in the anterolateral segments of the liver. However, there have been few reports comparing LLR and radiofrequency ablation (RFA) for HCC.

Method: We retrospectively compared short- and long-term outcomes of 105 patients with LLR and 272 patients with RFA for newly diagnosed single, < 4 cm size of HCC located on the anterolateral segments of the liver. We performed 1:1 propensity score matching (PSM) between two groups and matched 61 patients for both groups.

Results: After PSM, all variables including demographic, tumor factors and liver function were similar between two groups. There was no mortality in the two groups. The hospital stay was shorter in RFA group than LLR group (5.1 vs. 8.9 days; P = 0.001), however, there was no significant difference in complication rate between two groups (4.9 vs. 13.1%; P = 0.114). The 5-year overall survival rates were similar between two groups (83.6 vs. 84.5%; P = 0.913), but the 5-year disease-free survival rate was higher in LLR group (56.4%) than RFA group (41.8%; P = 0.009). In patients with alpha-fetoprotein > 100 ng/ml, LLR group showed better 5-year overall (100 vs. 80.0%; P = 0.022) and disease-free survival rates (76.6 vs. 45.5%; P = 0.006) than those in RFA group.

Conclusion: For single small HCC located in the anterolateral segments of the liver, LLR group showed similar complications and overall survival rate, but better disease-free survival rate compared to RFA group. LLR is recommended in patients with higher alpha-fetoprotein level.

Abstract #205

Effectiveness of Antiviral Therapy in Hepatitis B Virus-related Hepatocellular Carcinoma Initially Treated with Transarterial Chemoembolization: a Multicenter Retrospective Study

Baek Gyu Jun[1], Young Don Kim[2], Gab Jin Cheon[3], Sae Hwan Lee[4], Hong Soo Kim[5]

[1]University of Ulsan College of Medicine, Gangneung Asan Hospital, [2]University of Ulsan College of Medicine, Gangneung Asan Hospital, [3]University of Ulsan College of Medicine, Gangneung Asan Hospital, Gangneung, [4]Soonchunhyang University College of Medicine, Cheonan Hospital, [5]Soonchunhyang University College of Medicine, Cheonan Hospital

Background and Aim: It remains uncertain whether antiviral treatment improve surivival in hepatitis B virus (HBV)-hepatocellular carcinoma (HCC) patients receiving palliative therapy. The purpose of this study is to evaluate the role of antiviral therapy in HBV-HCC patients after diagnosis of HCC.

Methods: This retrospective study analyzed 113 HBV-HCC patients who underwent transarterial chemoembolization (TACE) in two university hospital. Overall survival (OS) was compared in patients treated with/without antiviral treatment after diagnosis of HCC. Subgroup analysis and Cox regression analysis were performed to determine the efficiency of antiviral treatment and prognostic factors for OS.

Results: OS was not different between the patients treated with antiviral treatment (n = 67) and the patients who received no antiviral treatment (n = 46) (p = 0.103). Barcelona Clinic Liver Cancer (BCLC) was independent prognostic factors for OS of HBV-related HCC patients who were treated with TACE. By subgroup analysis, antiviral therapy achieved better survival improvement in BCLC stage B and C (p < 0.001) but had no survival improvement in BCLC stage 0 and A (p = 0.605). Antiviral therapy was one of the independent prognostic factors for patients with BCLC stage B and C (HR 0.230, 95% CI 0.094–0.565, p = 0.001).

Conclusion: Antiviral therapy did not improve survival of HBV-related HCC patients treated with TACE. However, antiviral therapy shows survival benefit only in BCLC stage B and C disease.

Table 1. Baseline characteristics

Variable	Antiviral Treatment (n=67)	No treatment (n=46)	Total (n=113)	P-value
Sex				0.707
Male	55	39	94	
Female	12	7	19	
Mean age (mean ± SD)	60.36±8.95	59.76±9.82	60.12±9.278	0.738
Number of tumor				0.348
1	22	22	44	
2	20	9	29	
3	11	5	16	
>4	14	10	24	
Size of largest tumor (mean ± SD)	4.43±3.48	4.30±3.69	4.38±3.55	0.853
Child-pugh score (mean ± SD)	5.63±0.99	5.67±0.94	5.65±0.97	0.082
MELD score	9.61±6.45	9.40±3.73	9.52±5.49	0.845
HBeAg				0.500
Positive	5	2	7	
Negative	62	44	106	
Liver cirrhosis				0.054
Yes	48	40	88	
No	19	6	25	
mUICC stage				0.032
1	5	10	15	
2	24	13	37	
3	33	15	48	
4	5	8	13	
BCLC stage				0.082
0	6	11	17	
A	28	18	46	
B	27	11	38	
C	6	6	12	
HBV DNA (IU/mL)	3726±5786	1344±2897	2756±4948	0.011
ECOG performance status				0.425
0	51	34	85	
1	14	12	26	
2	2	0	2	

MELD, Model For End-Stage Liver Disease; mUICC, modified Union for International Cancer Control ; BCLC, Barcelona clinic liver cancer; ECOG, Eastern Cooperative Oncology Group

Table 2. Prognostic factors for overall survival

Variable		Univariate analysis			Multivariate anaylsis	
	HR	95% CI	P value	HR	95%CI	P value
Antiviral therapy						
No	1.000					
Yes	0.593	0.313-1.124	0.109			
Age	0.945	0.919-0.990	0.012	0.956	0.921-0.992	0.017
Sex, male	1.127	0.496-2.561	0.776			
HBeAg						
Negative	1.000					
Positive	0.699	0.415-1.178	0.179			
Child-pugh class						
A	1.000					
B	1.342	0.613-2.934	0.462			
MELD score	0.994	0.942-1.048	0.813			
Number of tumor			0.005			
1	1.000					
2	1.223	0.503-2.974	0.657			
≥3	3.372	1.535-7.410	0.002			
Size of largest tumor	1.183	1.095-1.279	<0.001			
BCLC stage						
0 and A	1.000			1.000		
B and C	2.873	1.482-5.573	0.002	2.773	1.431-5.376	0.003
Baseline HBV DNA						
<2000 IU/ml	1.000					
≥2000 IU/mL	1.318	0.680-2.554	0.413			

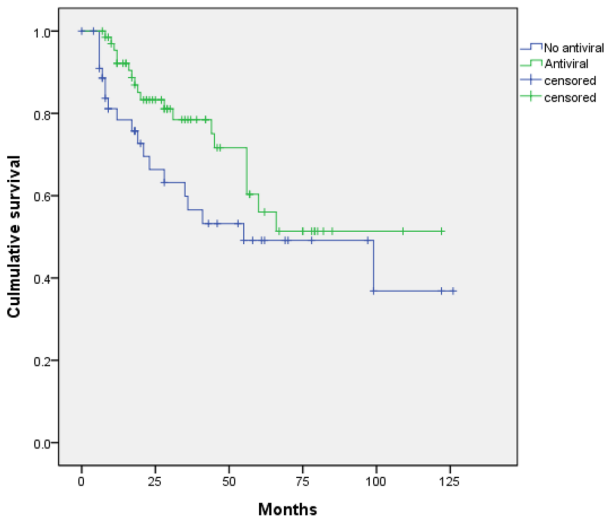
HR, hazard ratio; CI, confidence interval; MELD, Model For End-Stage Liver Disease; BCLC, Barcelona clinic liver cancer

Table 3. Prognostic factors for overall survival in BCLC B and C

Variable		Univariate analysis			Multivariate anaylsis	
	HR	95% CI	P value	HR	95%CI	P value
Nucleotide analogue						
No	1.000					
Yes	0.236	0.098-0.568	0.001	0.230	0.094-0.565	0.001
Age	0.955	0.910-1.003	0.068			
Sex, male	1.568	0.528-4.652	0.418			
HBeAg						
Negative	1.000					
Positive	2.689	0.650-12.661	0.164			
Child-pugh class						
A	1.000					
B	1.342	0.613-2.934	0.462			
MELD score	0.931	0.803-1.079	0.341			
Number of tumor			0.248			
1	1.000					
2	0.510	0.113-2.303	0.381			
≥3	1.321	0.367-4.571	0.670			
Size of largest tumor	1.135	1.024-1.257	0.016	1.148	1.026-1.285	0.016
Baseline HBV DNA						
<2000 IU/ml	1.000					
≥2000 IU/mL	1.381	0.558-3.419	0.486			

HR, hazard ratio; CI, confidence interval; MELD, Model For End-Stage Liver Disease; BCLC, Barcelona clinic liver cancer

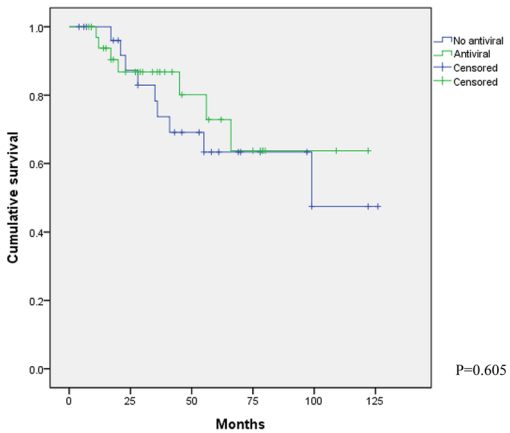
Fig. 1 Overall survival for patients with and without antiviral therapy



P = 0.103

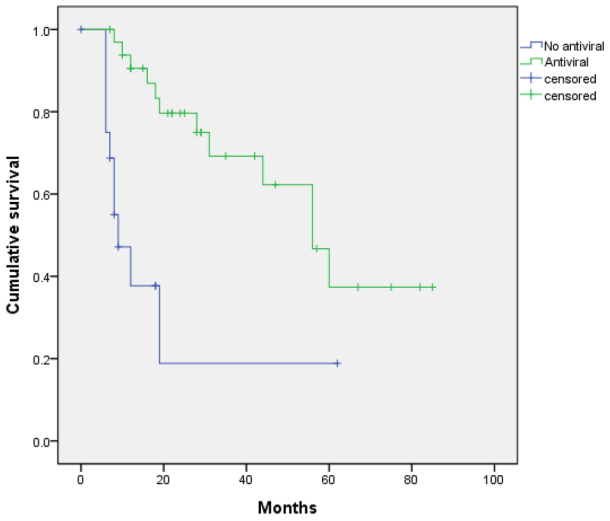
Fig. 2 Overall survival of antiviral therapy and non-antiviral therapy in subgroup analysis stratified by BCLC stage

(a) BLCL 0 and A



P=0.605

Figure 1. BCLC B and C



p<0.001

Clinical Parameter	Pre-MAT value		Post-MAT value		p-value
Platelet Count (10^12/L)	0.1133	± 0.1032	0.1547	± 0.1278	0.6854
Serum Albumin (g/L)	33.4567	± 7.3204	30.9033	± 9.6188	0.7330
AFP (ng/mL)	1012.8333	± 419.3973	99.19	± 136.5634	0.0230
SGPT (U/L)	40	± 28.2843	37.33	± 32.0602	0.9377
SGOT (U/L)	41.5	± 36.0625	39.83	± 38.4242	0.9683
INR	1.205	± 0.1485	1.155	± 0.2192	0.8144
Tumor size (cm)	3.7	± 2.2113	2.6333	± 2.5541	0.6135

Table 3. Comparison of mean laboratory parameters and mean tumor size on 30-day follow up of patients who underwent Microwave Ablation Therapy.

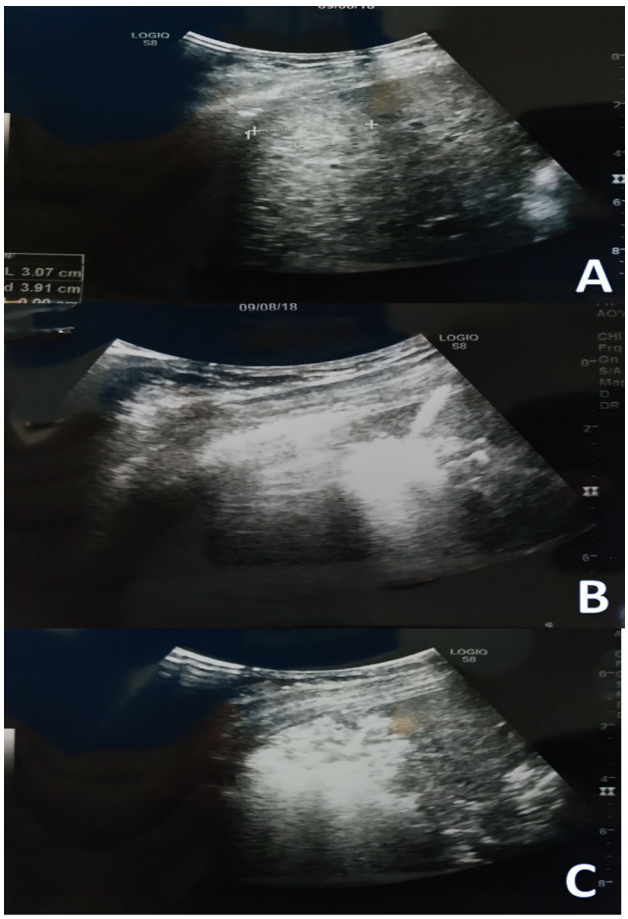


Figure 1. Ablation Method in a 41 year old male patient with Primary Hepatocellular Carcinoma secondary to Chronic Hepatitis B. Figure 1-A depicts the sonographic evaluation done prior to MAT. Figure 1-B presents the development of hyperechogenicity, representing the evolution of an ablation zone. Figure 1-C shows the hepatocellular tumor post-microwave ablation presenting as a hyperechogenic area with distinct borders.

Abstract #269

Microwave Ablation Therapy for Primary Hepatocellular Carcinoma: A Report on the Initial Institutional Experience in a Tertiary Hospital in the Philippines

Marco Angelo Dominguez Tongo[1], Diana Alcantara Payawal[1]

[1]Cardinal Santos Medical Center, San Juan City, Philippines

Liver cancer is among the leading causes of cancer deaths. In the Philippines, prevalence rate is 7.8% for hepatocellular carcinoma with mortality rate of 25%. Surgical resection has been commonly undertaken by Filipinos with hepatocellular carcinoma. However, with cases of poor residual post operative recovery and post resection complications, techniques of local ablation were developed. Currently, a novel thermogenic ablative method, Microwave Ablation Therapy, was recently introduced in a tertiary hospital in the Philippines.

This study aims to present the initial experience of a tertiary Philippine hospital in using Microwave Ablation Therapy. Secondarily, this study aims to describe the patient demographics, clinical outcomes and complications involving this procedure.

From July 2018 to October 2018, a total of 8 patients with Primary Hepatocellular carcinoma underwent MAT at Cardinal Santos Medical Center.

Mean hospital stay was 5.5 days, and mean number of days from MAT to discharge was 3.5 days. The most common complication post-procedure was fever, noted in 37.5%. There was significant decline of alpha fetoprotein on 30-day follow-up ($p = 0.023$). There was further note of an upward trend in platelet count and a downward trend in tumor size.

Although surgery and radiofrequency ablation therapy has been more commonly used, Microwave Ablation Therapy has shown potential as a viable treatment option for patients with primary hepatocellular carcinoma.

Abstract #271

Surgical resection significantly provides survival benefit of hepatocellular carcinoma patients in various BCLC stages

Chih-Wen Lin[1], Pei-Min Hsieh[2], Tsung-Chin Wu[3], Jen-Hao Yeh[3], Gin-Ho Lo[4], Pojen Hsiao[3], Yu-Chan Li[5], Kun-Chou Hsieh[6], Yaw-Sen Chen[6]

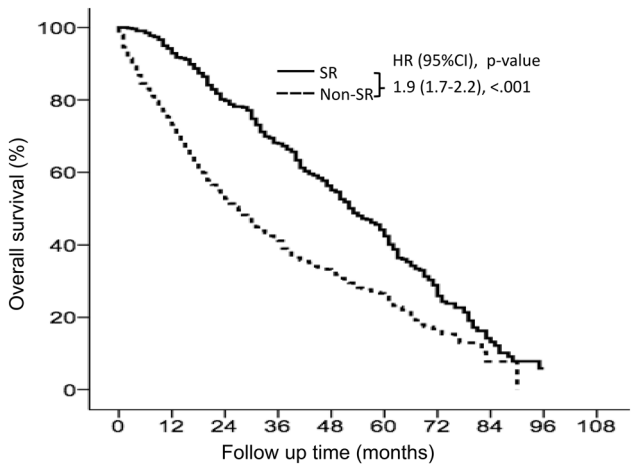
[1]Division of Gastroenterology and Hepatology, E-Da Dachang Hospital, I-Shou University and Division of Gastroenterology and Hepatology, Department of Medicine, E-Da Hospital, I-Shou University and School of Medicine, College of Medicine, I-Shou University, [2]E-Da Hospital, I-Shou University, [3]Division of Gastroenterology and Hepatology, E-Da Dachang Hospital, I-Shou University, [4]Division of Gastroenterology and Hepatology, Department of Medicine, E-Da Hospital, I-Shou University, [5]School of Medicine, College of Medicine, I-Shou University, [6]Department of Surgery, E-Da Hospital, I-Shou University

Background: The benefits of surgical resection (SR) for various Barcelona Clinic Liver Cancer (BCLC) stages of hepatocellular carcinoma (HCC) remain unclear. We investigated the risk factors of overall survival (OS) and survival benefits of SR over nonsurgical treatments in patients with HCC of various BCLC stages.

Methods: Overall, 2316 HCC patients were included, and their clinicopathological data and OS were recorded. OS was analyzed by the Kaplan–Meier method and Cox regression analysis.

Results: The median follow-up duration time was 20 (range 0–96) months for the total cohort and was subdivided into 52 (8–96), 32 (1–96), 19 (0–84), and 12 (0–79) months for BCLC stages 0, A, B, and C cohorts, respectively. The risk factors for OS were (1) SR and cirrhosis; (2) SR, cirrhosis, and Child–Pugh (C–P) class; (3) SR, hepatitis B virus (HBV) infection, and C–P class; and (4) SR, HBV infection, and C–P class for the BCLC stage 0, A, B, and C cohorts, respectively. Compared to non-SR treatment, SR resulted in significantly higher survival rates in all cohorts. The 5-year OS rates for SR vs non-SR were 44.0% vs 28.7%, 72.2% vs 42.6%, 42.6% vs 36.2, 44.6% vs 23.5%, and 41.4% vs 15.3% (all p values < 0.05) in the total and BCLC stage 0, A, B, and C cohorts, respectively.

Conclusion: SR conferred significant survival benefits to patients with HCC of various BCLC stages and should be considered a recommended treatment for select HCC patients, especially patients with BCLC stage B and C disease.



Abstract #316

Stereotactic body radiation therapy combined with transarterial chemoebolization for ≤ 5 cm hepatocellular carcinoma

Baek Gyu Jun[1], Soo Yong Choi[1], Young Don Kim[1], Gab Jin Cheon[1]

[1]University of Ulsan College of Medicine, Gangneung Asan Hospital

Background: We evaluated the efficacy of stereotactic body radiotherapy (SBRT) for hepatocellular carcinoma (HCC) patients treated in combination with transarterial chemoembolization (TACE).

Methods: We retrospectively reviewed 104 patients with HCC of ≤ 5 cm who underwent combined SBRT with TACE from August 2011 to December 2016. We evaluated local control (LC) rate and overall survival (OS) after combined treatment. Outcomes in patients with small (< 3 cm)-sized HCC (n = 77) were compared to with outcomes in patients with medium (3–5 cm)-sized HCC (n = 27). Radiation induced liver disease (RILD) was defined as worsening Child–Pugh score by two points.

Results: The median follow up duration after SBRT with TACE was 22.0 months (range 2–83 months). Mean size of tumors was 2.27 ± 1.13 cm Mean 52.1 ± 10.5 Gy in 3–5 fractions was prescribed. 1-, 2-, 3-year LC rates for all patients were 93.1, 89.9 and 88.8%, respectively. 1-year LC rate did not differ between small- and medium-sized HCC (93.2% vs 80.8%, log-rank p = 0.109). 1-, 3-, 5-year OS were 87.4, 56.7 and 45.4%, respectively. 3-year OS rate of small-HCC was better than that of medium-sized HCC (63.0% vs 37.1%, log-rank p = 0.047). RILD was observed in 20 (17.5%) patients. RILD did not differ between small- and medium-sized HCC (15.6% vs 29.6%, p = 0.111).

Conclusions: Treatment with SBRT + TACE can be an effective local therapeutic tool for ≤ 5 cm HCC patients, with good local tumor control and low treatment-related toxicity.

Table 1. Baseline characteristics in both small- and medium- sized hepatocellular carcinoma

Variable	Small HCC (<3cm) (n=77)	Medium sized HCC (3-5cm) (n=27)	Total (n=114)	P-value
Sex				
Male	61	19	80	0.348
Female	16	8	24	
Mean age (mean ± SD)	61.7 ± 10.04	62.78 ± 11.31	61.98 ± 10.34	0.644
Number				
1	51	16	67	0.862
2	16	8	24	
>3	10	3	13	
Mean tumor size (mean ± SD)	1.71 ± 0.55	3.86 ± 0.77	2.27 ± 1.13	<0.001
Child-pugh score (mean ± SD)	5.65 ± 0.98	5.52 ± 0.80	5.62 ± 0.93	0.535
BCLC stage on diagnosis (%)				0.013
0	21 (27.3)	5 (18.5)	26	
A	43 (55.8)	9 (33.3)	52	
B	10 (13.0)	11 (40.7)	21	
C	3 (3.9)	2 (7.4)	5	
BCLC stage on treatment (%)				0.009
A	54 (70.1)	10 (37.0)	64	
B	14 (18.2)	11 (40.7)	25	
C	9 (11.7)	6 (22.2)	15	
The etiology				0.357
Alcohol	18	9	27	
Hepatitis B virus	44	15	59	
Hepatitis C virus	8	3	11	
others	7	0	7	
Radiation dose	52.7±11.3	50.4±7.9	52.1±10.5	0.337
ALT	28.3 ± 27.1	30.7 ± 17.8	28.98 ± 24.99	0.679
Total bilirubin (mg/dl)	1.01 ± 0.64	1.03 ± 0.65	1.01 ± 0.64	0.878
Platelet count (x10^9/L)	125.4 + 65.5	130.3 ± 68.8	126.7 ± 65.7	0.7.9

Values are expressed as n only, mean±SD, n (%), ALT alanine transaminase,

Figure 1 local control rate

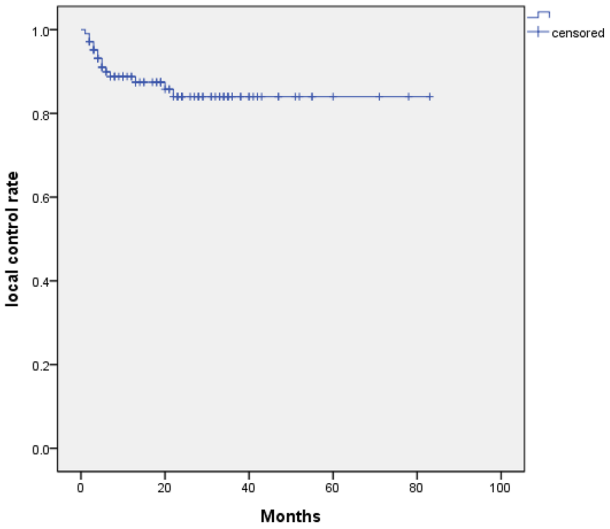


Figure 2 Local control rate according to tumor size

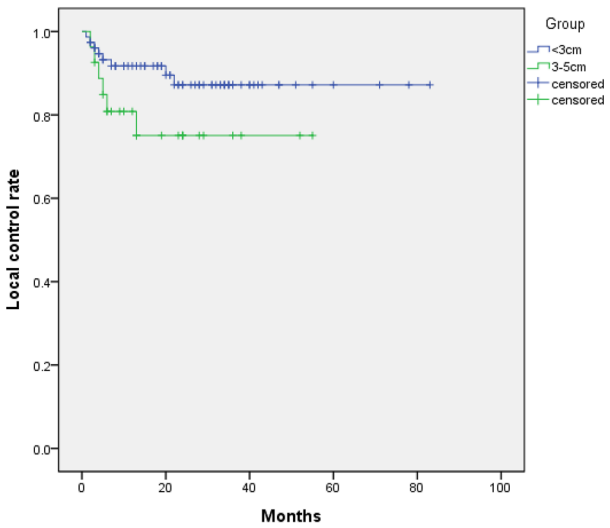


Figure 3 overall survival

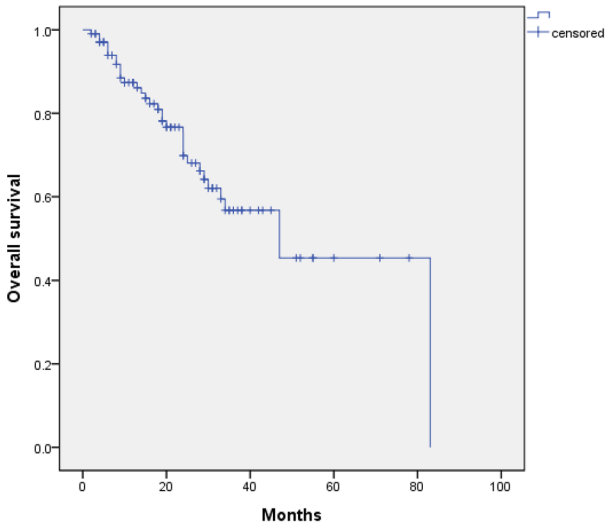


Figure 4 Overall surivival according to tumor size

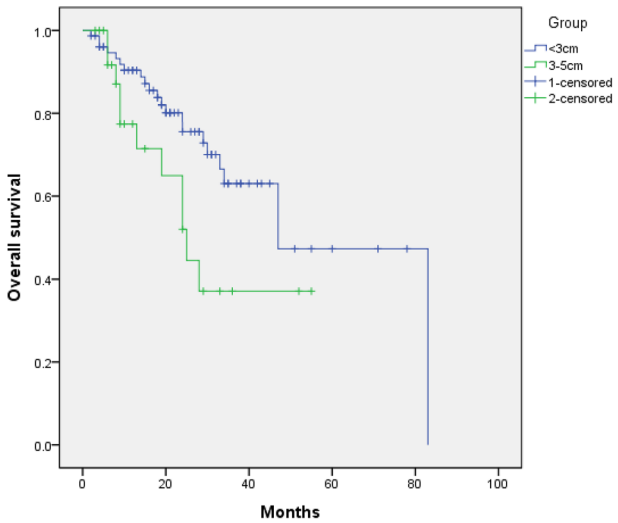


Table 2. Liver toxicity in both small- and medium- sized hepatocellular carcinoma

Variable	Small HCC (<3cm) (n=77)	Medium sized HCC (3-5cm) (n=27)	P-value
RILD (%)	12 (15.6)	8 (29.6)	0.111
Radiation induced hepatitis (%)	5 (6.5)	3 (2.1)	0.438

RILD, radiation induced liver disease

Abstract #319 Real-world data for preliminary evaluation of lenvatinib for unresectable hepatocellular carcinoma: comparison with the REFLECT study

Kohei Kotani[1], Maito Suoh[1], Sawako Uchida-Kobayashi[1], Atsushi Hagihara[1], Hiroyuki Motoyama[1], Hideki Fujii[1], Hiroyasu Morikawa[1], Masaru Enomoto[1], Yoshiki Murakami[1], Akihiro Tamori[1], Shogo Tanaka[2], Shigekazu Takemura[2], Shoji Kubo[2], Norifumi Kawada[1]

[1]Department of Hepatology, Graduate School of Medicine, Osaka City University, Osaka, Japan, [2]Department of Hepato-Biliary-Pancreatic Surgery, Graduate School of Medicine, Osaka City University, Osaka, Japan

Introduction: Lenvatinib was approved in Japan for unresectable hepatocellular carcinoma (uHCC) in March 2018 based on results of the REFLECT study. However, its real-world data have not been sufficiently evaluated.
Objectives: To describe and identify the real-world data of lenvatinib treatment for uHCC.
Methodology: We included 30 uHCC patients who received lenvatinib treatment from the date of approval to September 2018 and were followed-up until October 2018. Lenvatinib was used not only as the first-line treatment, but also as second- or third-line treatment. Clinical characteristics, adverse events (AEs), and efficacy were evaluated and compared with those of the lenvatinib administration cohort of the REFLECT study.
Results: In our cohort, the proportions of elderly patients ($\geq$ 75 years) (40% versus 12%, $p < 0.001$), Child–Pugh class B patients (17% versus 1%, $p < 0.001$), and previous anticancer procedures (93% versus 68%, $p = 0.004$) were greater than those in the REFLECT study cohort. The most common any-grade AEs in our cohort were hypertension (67%), palmar-plantar erythrodysesthesia (63%), and fatigue (63%). The proportions of these AEs were significantly greater in our cohort than in the REFLECT cohort, especially grade 3 or higher fatigue (20% versus 4%, $p < 0.001$). Regarding efficacy, disease control rate was lower in our cohort than in the REFLECT cohort (55% versus 76%, $p = 0.027$).
Conclusion: Lenvatinib was administered to not only uHCC patients within the REFLECT study eligibility criteria but also to patients outside this criteria in the real world. Further studies on management techniques for AEs are required to achieve good efficacy.

Abstract #380

Final analysis of serum biomarkers in patients from the phase 3 study of lenvatinib (LEN) vs sorafenib (SOR) in unresectable hepatocellular carcinoma (uHCC) [REFLECT]

Richard S. Finn[1], Masatoshi Kudo[2], Ann-Lii Cheng[3], Lucjan Wyrwicz[4], Roger Ngan[5], Jean Frederic Blanc[6], Ari D. Baron[7], Arndt Vogel[8], Masafumi Ikeda[9], Fabio Piscaglia[10], Kwang-Hyub Han[11], Shukui Qin[12], Yukinori Minoshima[13], Michio Kanekiyo[14], Min Ren[15], Ryo Dairiki[16], Toshiyuki Tamai[17], Corina Dutcus[18], Yasuhiro Funahashi[19], Jeffry Tr Evans[20]

[1]Division of Hematology/Oncology, Geffen School of Medicine, UCLA Medical Center, [2]Gastroenterology and Hepatology, Kindai University Faculty of Medicine, [3]National Taiwan University Hospital, [4]Centrum Onkologii-Instytut IM., M. Sklodowskiej Curie, [5]Queen Elizabeth Hospital, [6]University of Bordeaux, [7]California Pacific Medical Center, [8]Hannover Medical School, [9]Division of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital East, [10]Medical and Surgical Sciences, University of Bologna, [11]Severance Hospital, Yonsei University, [12]Nanjing Bayi Hospital, [13]EISAI Co., Ltd., [14]EISAI Inc., [15]EISAI Inc., [16]EISAI Co., Ltd., [17]EISAI Inc., [18]EISAI Inc., [19]EISAI Co., Ltd., [20]Beatson West of Scotland Cancer Centre, University of Glasgow

Introduction: In the phase 3 REFLECT study in uHCC, lenvatinib demonstrated a treatment effect on overall survival (OS) by statistical confirmation of noninferiority to sorafenib, and improved objective response rate (Kudo et al. Lancet. 2018).
Objective: Assess biomarker analyses from REFLECT.
Methods: 954 Patients with uHCC received lenvatinib or sorafenib. Serum samples (lenvatinib, n = 279; sorafenib, n = 128) were collected at baseline and during the study. Tumor response correlations (independent imaging review per mRECIST: complete/partial responses vs others) with pharmacodynamic biomarker changes used Wilcoxon rank-sum tests. VEGF, ANG2, FGF19, FGF21, and FGF23 levels (by ELISA) were analyzed by quartiles: low (0–25%), middle (25–75%), or high (75–100%). OS correlations were examined by Cox regression, Kaplan–Meier, and log-rank tests (all nominal P values).
Results: Both treatments increased VEGF levels; only lenvatinib increased FGF19 and FGF23. Lenvatinib-treated responders had greater increases in FGF19 and FGF23 vs others (FGF19: 55.2% vs 18.3%, $P = 0.0140$; FGF23: 48.4% vs 16.4%; $P = 0.0022$). Higher baseline VEGF, ANG2, and FGF21 correlated with worse OS in both arms, and for patients with high baseline FGF21 (lenvatinib, n = 70; sorafenib, n = 27), OS was longer for lenvatinib vs sorafenib (median, 10.9 vs 6.8 months; HR 0.528; 95% CI 0.328–0.849; $P = 0.0075$; $P_{interaction} = 0.0397$).
Conclusions: Differences in biomarker changes may reflect distinct target engagements for lenvatinib and sorafenib. Increased VEGF, ANG2, and FGF21 may be prognostic for shorter OS with both treatments; increased FGF21 may be predictive for reduced OS with sorafenib. Results are hypothesis-generating and warrant further study.

Abstract #403

Reduction of intrahepatic tumor by hepatic arterial infusion chemotherapy prolongs survival in hepatocellular carcinoma with portal vein tumor thrombus or distant metastasis

Hee Chul Nam[1], Pil Soo Sung[1], Keungmo Yang[1], Si Hyun Bae[1], Jung Suk Oh[1], Ho Jong Chun[1], Jeong Won Jang[1], Jong Young Choi[1], Seung Kew Yoon[1]

[1]The Catholic University of Korea and Department of Internal Medicine

Purpose: There are limited studies on the impact of intrahepatic tumor reduction in advanced hepatocellular carcinoma (HCC) with portal vein tumor thrombus (PVTT) or extrahepatic metastasis. We aimed to identify the survival benefit of intrahepatic tumor control by hepatic arterial infusion chemotherapy (HAIC) in patients with PVTT or extrahepatic metastasis.
Methods: Between 2010 and 2017, a total of 187 consecutive patients with advanced HCC were treated with HAIC. Of these, 154 patients (82.4%) had portal vein tumor thrombus and 47 patients (25.1%) had extrahepatic metastasis when HAIC began. The survival outcomes and responses rates by HAIC were analyzed. Multivariate analysis was performed to estimate the clinical factors associated with survival outcomes.
Results: The initial presence of extrahepatic metastasis had no significant effects on overall survival (OS) of the patients ($P = 0.068$). The intrahepatic objective response (OR) (complete response plus partial response) rate of all the enrolled patients was 18.7%. For the patients with OR, the survival outcome was significantly better than

for those without OR, irrespective of initial distant metastasis. Subgroup analyses for patients with Vp3 and Vp4 PVTT showed similar results with total patients. Two independent factors associated with better OS were identified, including the achievement of intrahepatic OR by HAIC and the favorable liver function at the time of best response evaluation.
Conclusion: HAIC-induced intrahepatic tumor reduction significantly prolongs patient survival, irrespective of PVTT or initial distant metastasis. It is critical that the intrahepatic tumor burden be reduced aggressively, even when patients have PVTT or extrahepatic metastasis.

Abstract #417

Safety and clinical activity results from atezolizumab (atezo) + bevacizumab (bev) in hepatocellular carcinoma (HCC): Updates from a Phase Ib study

Chih-Hung Hsu[1], Michael S. Lee[2], Baek-Yeol Ryoo[3], Stacey Stein[4], Kyung-Hun Lee[5], Wendy Verret[6], Jessica Spahn[7], Hui Shao[8], Bo Liu[9], Koho Iizuka[10], Michael J. Pishvaian[11]

[1]Department of Oncology, National Taiwan University Hospital, Taiwan, Taiwan, [2]UNC Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA, [3]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea, [4]Yale School of Medicine, Yale University, New Haven, CT, USA, [5]Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea, [6]Genentech, Inc, South San Francisco, CA, USA, [7]Genentech, Inc., South San Francisco, CA, USA, [8]F. Hoffmann-La Roche Ltd., Beijing, China, [9]Genentech, Inc., South San Francisco, CA, USA, [10]Genentech, Inc., South San Francisco, CA, USA, [11]Georgetown University Medical Center, Washington, DC, USA

Introduction: The current standard of care for advanced HCC include agents targeting angiogenesis (bev; anti-VEGF) or PD-L1/PD-1 signalling (atezo; anti–PD-L1). When combined, these agents exhibit complementary mechanisms of action and support the hypothesis for effective therapy in advanced HCC.
Objectives: Primary objectives were to examine safety and investigator-assessed ORR per RECIST v1.1. Secondary endpoints included PFS and DOR per RECIST v1.1 and OS.
Methodology: In a Phase Ib study, patients (pts) with unresectable or advanced 1L HCC received atezo 1200 mg + bev 15 mg/kg IV q3w until loss of clinical benefit/unacceptable toxicity.
Results: By July 26, 2018, 103 pts were safety evaluable. Any grade (Gr) tx-related AEs (TRAEs) occurred in 84 pts (82%) and Gr3-4 TRAEs in 28 pts (27%), most commonly hypertension (n = 10 [10%]). 19 pts (18%) experienced serious TRAEs and 2 pts had Gr5 TRAEs. There were 12 pts requiring systemic corticosteroid tx for immune-related AEs. 73 pts were efficacy evaluable (follow-up $\geq$ 16 weeks) and had an ORR of 32%. Responses occurred in all assessed clinically relevant subgroups, including AFP $\geq$ 400 ng/ml, EHS and/or MVI (Table). 19/23 confirmed responses were ongoing ($\geq$ 6 months, 12 pts), with a 65% 6-months PFS rate. Median DOR and OS have not yet been reached (DOR, range 1.6+ to 22.0+).
Conclusion: Encouraging response rates, durable responses and a tolerable safety profile support the use of atezo + bev as a potential 1L tx option in unresectable or advanced HCC. The Phase III IMbrave150 trial (NCT03434379) is currently recruiting.
NCT02715531.

Abstract #420

Control of intracranial disease is associated with improved survival for patients with brain metastases from hepatocellular carcinoma

Si Hyun Bae[1], Hee Chul Nam[1], Pil Soo Sung[1], Do Seon Song[1], Jung Hyun Kwon[1], Soon Woo Nam[1], Jeong Won Jang[1], Jong Young Choi[1], Seung Kew Yoon[1], Hong Seok Jang[1]

[1]The Catholic University of Korea

Purpose: We performed a retrospective study to identify prognostic factors and determine outcomes for patients with brain metastases from hepatocellular carcinoma (HCC).
Patients and Methods: A total of 86 patients with brain metastases from HCC were identified from two institutions; 32 of 86 patients received tumor-removing surgery or stereotactic radiosurgery (SRS) with or without whole-brain radiotherapy (WBRT), 30 of 86 received WBRT only, and 24 of 86 received conservative treatment.
Results: Median OS after development of brain metastases was 50 days (1–536 days). The median age at the time patients were diagnosed with brain metastasis was 54 years. Univariate analyses showed that treatment with curative intent (surgery or SRS), Child–Pugh classification A, Alpha-feto protein level less than 400 ng/mL, and recursive partitioning analysis (RPA) class I or II were associated with improved survival ($P < 0.001$, 0.002, 0.029 and 0.012, respectively. We further divided patients with three groups by the treatment modality; surgery or SRS (group1), WBRT (group 2), or conservative treatment (group 3). Group 1 showed best survival, followed by group 2 and group 3, sequentially ($P < 0.001$). Multivariate analysis showed that treatment modality and Child–Pugh classification are associated with improved OS ($P < 0.001$ and 0.009, respectively).
Conclusion: Although the overall prognosis of patients with brain metastases from HCC is extremely poor, patients actively treated with surgery or radiosurgery have prolonged survival, suggesting that interventions to control intracranial disease are important treatment modalities.

Abstract #431

Inflammatory cytokines and change of Th1/Th2 balance as prognostic indicators for hepatocellular carcinoma in patients treated with transarterial chemoembolization

Hae Lim Lee[1], Jeong Won Jang[2], Sung Won Lee[1], Jung Hyun Kwon[4], Soon Woo Nam[3], Si Hyun Bae[4], Jong Young Choi[2], Seung Kew Yoon[2]

[1]Bucheon St. Mary's Hospital, The Catholic University of Korea, [2]Seoul St. Mary's Hospital, The Catholic University of Korea, [3]Incheon St. Mary's Hospital, The Catholic University of Korea, [4]St. Paul's Hospital, The Catholic University of Korea

Introduction: HCC usually develops in chronic inflammation, suggesting that immune status influences the behavior of HCC. This study evaluated clinical implications of T cell cytokines and regulatory T cells (Tregs) in patients with HCC treated by TACE.
Methods: A total of 142 patients with newly diagnosed HCC treated by TACE were enrolled. Whole blood was obtained for analysis of CD4+ T cell cytokines (IL-1b, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-12p70, IL-13, IL-17A, IL-22, IFN-γ, and TNF-α) and regulatory T cells. The follow-up cytokine values were evaluated in 76 patients.
Results: Patients with CTP class A had a significantly lower proportion of detectable IL-4 or IL-6, but a higher proportion of detectable IL-22 than patients with CTP class B/C. Detectable IL-6

was significantly associated with advanced tumor characteristics. Undetectable IL-17A was significantly associated with extrahepatic metastasis. The cumulative overall survival (OS) rate was significantly higher in patients with undetectable IL-6 than in patients with detectable IL-6, and it was also higher in patients with detectable IL-22 than in patients with undetectable IL-22. In multivariate analysis, detectable IL-6 remained independently predictive of poor OS. Increased IFN-γ/IL-10 ratio and no increase in IL-6 level following TACE were associated with prolonged survival, and baseline Tregs could affect the Th1/Th2 cell balance.

Conclusion: T cell cytokines are associated with a variety of clinical aspects of HCC, and IL-6 is the most significant predictors of survival. A shift toward increased Th1 response and no increase in IL-6 level exert favorable immunologic effects on HCC prognosis.

Abstract #445

A phase 1b open-label, multicenter study of lenvatinib plus pembrolizumab in patients with unresectable hepatocellular carcinoma (uHCC)

Masafumi Ikeda[1], Max W. Sung[2], Masatoshi Kudo[3], Masahiro Kobayashi[4], Ari Baron[5], Richard Finn[6], Shuichi Kaneko[7], Andrew X. Zhu[8], Tomoki Kubota[9], Silvija Kraljevic[10], Kohei Ishikawa[11], Abby B. Siegel[12], Hiromitsu Kumada[13], Takuji Okusaka[14]

[1]Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital East, [2]Tisch Cancer Institute at Mount Sinai, [3]Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, [4]Department of Hepatology, Toranomon Hospital, [5]California Pacific Medical Center, Pacific Hematology Oncology Associates, [6]David Geffen School of Medicine, UCLA Medical Center, [7]Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University, [8]Massachusetts General Hospital, [9]EISAI Co. Ltd., [10]EISAI Ltd., [11]EISAI Co. Ltd., [12]Merck & Co. Inc., [13]Department of Hepatology, Toranomon Hospital, [14]Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital

Introduction: Lenvatinib showed noninferiority with respect to overall survival (OS) compared with sorafenib in the first-line treatment of patients with uHCC in a phase 3 trial (REFLECT).

Objective: To report preliminary results from a phase 1b trial of lenvatinib + pembrolizumab in patients with uHCC.

Methods: Patients with uHCC, BCLC stage B (not eligible for transarterial chemoembolization) or C, Child–Pugh class A, and ECOG PS $\leq$ 1 received lenvatinib (body weight $\geq$ 60 kg: 12 mg/day; $<$ 60 kg: 8 mg/day) daily and pembrolizumab 200 mg IV Q3 W. Dose-limiting toxicities (DLTs) were assessed during cycle 1 in patients ineligible for other therapies (3 + 3 design; Part 1). After confirming tolerability, patients with no prior systemic therapy were enrolled (Part 2). The primary end point was safety. Secondary/exploratory end points included objective response rate using modified RECIST. Complete or partial responses were confirmed $\geq$ 4 weeks after initial response.

Results: As of December 1, 2017, 18 patients had received lenvatinib + pembrolizumab (Part 1: n = 6; Part 2: n = 12). Patients had BCLC stage B (n = 6) or C (n = 12); Child–Pugh scores of 5 (n = 14) or 6 (n = 4); 4 patients (22%) had received sorafenib. No DLTs were reported in Part 1. All 18 patients remained on study. Treatment-emergent adverse events (TEAEs) occurred in 17 patients (94%); most common TEAEs were decreased appetite and hypertension (56% each). No new safety signals were identified. Efficacy outcomes are in the Table. At data cutoff, tumor reduction from baseline was observed in all evaluable patients except 1.

Conclusion: Lenvatinib + pembrolizumab was well-tolerated with encouraging antitumor activity in patients with uHCC.

Abstract #460

Subgroup analysis of Chinese patients in a phase 3 study of lenvatinib vs sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma

Shukui Qin[1], Xuenong Ouyang[2], Yuxian Bai[3], Ying Cheng[4], Zhendong Chen[5], Zhenggang Ren[6], Tianqiang Song[7], Corina Dutcus[8], Kenichi Saito[9], Toshiyuki Tamai[10], Thomas Chung Cheung Yau[11], Kun-Ming Rau[12], Ann-Lii Cheng[13], Guohong Han[14]

[1]Bayi Hospital of Nanjing University of Chinese Medicine, [2]Nanjing Military Fuzhou General Hospital, [3]The Tumor Hospital of Harbin Medical University, [4]Jilin Cancer Hospital, [5]The Second Hospital Affiliated to Anhui Medical University, [6]Zhongshan Hospital Fudan University, [7]Cancer Hospital, Tianjin Medical University, [8]EISAI Inc., [9]EISAI Inc., [10]EISAI Inc., [11]The University of Hong Kong, [12]Kaohsiung Chang Gung Memorial Hospital, [13]National Taiwan University Hospital, [14]Xijing Hospital, Fourth Military Medical University

Introduction: In the phase 3 REFLECT study in patients with unresectable hepatocellular carcinoma (uHCC), lenvatinib demonstrated statistical confirmation of noninferiority vs sorafenib in terms of overall survival (OS).

Objective: To report efficacy and safety data of Chinese patients from mainland China, Taiwan, and Hong Kong.

Methods: In the open-label, randomized, global, multicenter, phase 3 study, 954 patients with uHCC, $\geq$ 1 measurable target lesion, BCLC Stage B or C, Child–Pugh class A, ECOG performance status $\leq$ 1, and no prior systemic therapy were randomized 1:1 to lenvatinib (body weight $\geq$ 60 kg: 12 mg/day; $<$ 60 kg: 8 mg/day) or sorafenib 400 mg BID. The primary end point was OS. Secondary end points included progression-free survival (PFS), time to progression (TTP), objective response rate (ORR; by modified Response Evaluation Criteria in Solid Tumors), and safety (by NCI CTCAE 4.03). The subgroup analysis was performed for all patients randomized from mainland China (n = 213), Taiwan (n = 54), and Hong Kong (n = 21).

Results: For the 288 Chinese patients (lenvatinib, n = 144; sorafenib, n = 144), efficacy results are presented in Table 1. The most common treatment-emergent adverse events (all grades; grade $\geq$ 3) were hypertension (40%; 22%), decreased weight (32%; 6%), and diarrhea (32%; 2%) for lenvatinib, and palmar-plantar erythrodysesthesia syndrome (49%; 7%), diarrhea (42%; 3%), and hypertension (30%; 15%) for sorafenib.

Conclusions: Consistent with the overall study population, these findings suggest encouraging benefits with a manageable safety profile for lenvatinib in Chinese patients with uHCC from mainland China, Taiwan, and Hong Kong.

Abstract #485

A Comparison of Prognosis between Surgical Resection and Radiofrequency Ablation Therapy for Patients with Hepatocellular Carcinoma and with Esophagogastric Varices

Cheng-Yi Wei[1], Chien-Wei Su[1,2], Yi-Hsiang Huang[1,3], Teh-Ia Huo[1,4], Ming-Chih Hou[1,2], Han-Chieh Lin[1], Jaw-Ching Wu[3,5]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, [2]Faculty of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan, [3]Institute of Clinical Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan, [4]Department and Institute of Pharmacology, School of Medicine, National Yang-Ming University, Taipei, Taiwan, Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, [5]Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan

Background: Surgical Resection (SR) is not recommended for hepatocellular carcinoma (HCC) patients with esophagogastric varices (EV) due to risk of post-hepatectomy liver failure by current HCC practice guidelines. Radiofrequency ablation (RFA) therapy is suggested. We aimed to compare the long-term prognosis between SR and RFA for HCC patients with EV.
Methods: This retrospective study enrolled 251 patients with treatment-naïve HCC with EV who underwent SR or RFA as first-line treatment from 2003 to 2017. EV was diagnosed by an esophagogastroduodenoscopy at the time of HCC diagnosis. Prognostic factors were analyzed by the Cox proportional hazards model.
Results: Total 68 patients underwent SR and 183 patients received RFA. SR patients were younger, more male, more presence of hepatitis B surface antigen, larger sized tumor, lower alpha-fetoprotein, higher albumin, lower total bilirubin, shorter prothrombin time, and higher platelet counts. After a median follow-up duration of 45.1 months, 151 patients died. The cumulative 5-year overall survival (OS) rate was significantly higher in RS group than RFA (66.7% vs. 36.8%, $p < 0.001$). Multivariate analysis showed age > 65 years (hazard ratio HR 1.791, 95% confidence interval CI 1.268–2.531, $p = 0.01$), RFA (HR 2.100, 95% CI 1.320–3.341, $p = 0.002$), and serum albumin level less than 3.5 g/dL (HR 1.502, 95% CI 1.068–2.112, $p = 0.019$) were the independent risk factors predictive of poor OS for HCC patients with EV.
Conclusions: HCC patients with EV received SR had a significantly higher OS than RFA. SR could be recommended as first-line treatment modality for HCC patient with EV.

Abstract #502

Microwave Ablation in Hepatocellular Carcinoma: Case Series

Prima Bianca Gaffud Chua[1], John Alfredo Raphael Perez Pangilinan[1], Diana Alcantara Payawal[1]

[1]Cardinal Santos Medical Center

Introduction: Hepatocellular Carcinoma (HCC) is one of the most common cancers and second leading cause of cancer death worldwide (1–2). Current treatment guidelines recommend surgical resection or liver transplantation as the gold standard treatment for very early and early-stage HCC patients with well-conserved liver function (3–5). However, majority of patients who are diagnosed with liver malignancies are not eligible for resection or transplantation due to inadequate functional liver function, multifocal or advanced disease, prohibitive tumor location (6). As a result, thermal ablative therapies have emerged as a well-accepted alternative and is becoming increasingly utilized in the recent decades for treatment of primary and metastatic liver tumors (6–9).
Objective: To provide an alternative option in thermal ablative therapy with the use of Microwave Ablation (MWA) among patients with HCC.
Methodology: Case series.
Result and Conclusion: Presently in the Philippines, RFA is still the technique done by most interventionalists. Here we present 6 cases of MWA in HCC done for the first time in the country with the following data summary shown in table 1. All subjects underwent MWA therapy with no complications and were sent home stable. These cases represent the possibility of a more refined approach to management of HCC. This presents an opportunity to possibly improve interventional care provided to each patient, ensuring the best possible results with minimally invasive therapy. This paper would provide opportunities to evaluate this technique and compare it to conventional RF ablative management.

Abstract #509

Practice patterns, response rates, and deterioration of liver function after transarterial chemoembolization (TACE) in unresectable hepatocellular carcinoma (uHCC): Final analysis of OPTIMIS in China

Hong Shan[1], Han Chu Lee[2], Jean-Luc Raoul[3], Markus Peck-Radosavljevic[4], Masatoshi Kudo[5], Keiko Nakajima[6], Inga Bayh[7], Yefa Yang[8], Wenhui Wang[9], Ann-Lii Cheng[10]

[1]Department of Radiology, The Third Affiliated Hospital, Sun Yat-Sen University, Guangzhou, Guangdong, China, [2]Asan Medical Center, Seoul, South Korea, [3]Digestive Oncology, Institut De Cancérologie De L'ouest, Nantes, France, [4]Medical University of Vienna, Vienna, Austria and Klinikum Klagenfurt Am Wörthersee, Klagenfurt, Austria, [5]Kindai University Faculty of Medicine, Osaka, Japan, [6]Bayer Healthcare Pharmaceuticals, Whippany, NJ, USA, [7]Bayer AG, SBU Oncology, Pharmaceuticals, Wuppertal, Germany, [8]Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, China, [9]Lanzhou University First Affiliated Hospital, Lanzhou, China, [10]National Taiwan University Hospital, Taipei, Taiwan

Introduction: There is no global consensus on the use of TACE in patients with uHCC.
Objective: The primary objective of OPTIMIS was to assess overall survival (OS) from time of TACE ineligibility in patients with versus without early start of sorafenib at time of TACE ineligibility.
Methodology: OPTIMIS was an international, prospective, non-interventional study of uHCC patients for whom the decision to treat with TACE was made prior to enrollment. TACE ineligibility was determined using a protocol-specified criteria.
Results: Globally, 1650 patients received TACE, including 150 from China. Of those, 114 (76%) from China and 636 (39%) globally were TACE ineligible at inclusion. Of patients eligible for TACE at inclusion, 19/36 (53%) in China and 507/1014 (50%) globally became ineligible during the study. The median time from first to second TACE was 49 days (IQR 39–91) in China and 80 days (IQR 50–160) globally. In TACE-administered patients, complete and partial response rates to first TACE were 1% and 17% in China and 14% and 26% globally, respectively. Chronic bilirubin deterioration after first TACE was noted in China (18%) and globally (11%). In a propensity score matched global population, a trend towards longer OS was

observed in patients with versus without early start of sorafenib at time of TACE ineligibility.
Conclusions: Based on limited patients from China (n = 150), a higher proportion were treated with TACE despite not being adequately indicated versus the global population. The global data suggest that continuing TACE after ineligibility may not benefit patients.

Abstract #549

Fufang Banmao Capsule, a traditional Chinese medicinal formulation, improved the survival of patients with hepatocellular carcinoma and Vp3-4 portal vein tumor thrombosis on supportive treatment

Liu Yao[1], Wang Xiaojing[1], Huang Yunyi[2], Jiang Yuyong[1], Wang Xianbo[1]

[1]Center of Integrative Medicine, Beijing Ditan Hospital, Capital Medical University, [2]Department of Gastroenterology, Dongzhimen Hospital, Beijing University of Chinese Medicine

Introduction: Fufang Banmao (FFBM) capsule, which represents one of the Chinese medicinal formulations, has been used for several decades to treat hepatocellular carcinoma (HCC).
Objectives: To retrospectively observe the effects of FFBM capsule on the 6-month survival of patients with advanced HCC and Vp3-4 portal vein tumor thrombosis (PVTT) who only received supportive therapy.
Methodology: 232 patients with HCC and Vp3-4 PVTT who were treated with supportive therapy were enrolled. Of 232 patients, 43 received FFBM capsule and supportive therapy (FFBM group) and 189 received supportive therapy alone (control group). Propensity score matching (PSM) was used to balance the characteristics between the individuals of the two groups.
Results: Cox multivariate analysis identified γ-glutamyl transpeptidase, Child-Puge class, α-fetoprotein, largest tumor diameter, and FFBM capsule to be independent predictive factors of overall survival (OS). After one-to-three PSM, 34 pairs of patients were included in the FFBM versus control analysis; for these patients the OS probability was significantly higher in the FFBM group than in the control group at 6 months ($p = 0.0200$). The median survival time was 5 months in the FFBM cohort and 3 months in the control cohort. FFBM capsule may be recommended for patients with HCC and Vp3-4 PVTT in the high-risk group (score 4–7) because of better survival outcome.
Conclusion: FFBM capsule has the potential to effectively and safely improve the survival time of patients with advanced HCC with Vp3-4 PVTT who only received supportive therapy, especially those in the high-risk group (score 4–7).

Abstract #580

Sorafenib and Regorafenib After Chemoembolization in Intermediate Stage Hepatocellular Carcinoma Patients

Dimitrios Dimitroulopoulos[1], Dimitrios Kypreos[1], Georgios Sofianidis[1], Eleni Manthopoulou[1], Ioannis Marakis[1], Xenofon Tsamakidis[1], Klisthenis Tsamakidis[1]

[1]Gastroenterology Dpt, Agios Savvas Hospital

The benefits of Sorafenib as first line and Regorafenib as second line treatment to HCC patients after recurrence to TACE is not yet adequate studied.
Aim: To estimate the efficacy of Sorafenib as first line treatment and Regorafenib as second line in HCC, intermediate stage, patients after recurrence to previous TACE treatment.
Patients/Methods: Retrospectively was estimated the efficacy of Sorafenib and Regrafenib administration, when under Sorafenib progression disease was observed, (overall survival [OS] and time to disease progression [TTDP]) in 12 patients (Group A) with intermediate stage HCC after recurrence to treatment with TACE (1–3 TACEs, median 2). The results were compared with these of an historical and similar group of 15 HCC patients treated only with TACE (Group B).
Results: There were not significant differences in disease characteristics between the two studied groups. The index of disease control for group A was 67.2% and the mean TTDP was 4.2 months during the Sorafenib administration. Regorafenib was administered when progression of HCC was observed. The OS was 31.2 months. For Group B the index of the disease control was 30.6% ($P = 0.001$), the mean TTDP was 2.3 months (hazard ratio 0.44, $P < 0.01$) and the OS 13.4 months (hazard ratio 0.57, $P < 0.001$). The multivariate analysis revealed that the addition of Sorafenib and Regorafenib was the most important factor for the OS and the prolongation of the TTDP.
Conclusion: The administration of Sorafenib and Regorafenib seems to be an attractive therapeutic approach for intermediate stage HCC patients after recurrence to previous TACE treatment.

Abstract #599

Safe Radiofrequency ablation for low platelet count patients with novel platelet count raising drug (Lusutrombopag)

Hideo Yoshida[1], Takamasa Ohki[2], Mineo Kanezaki[3], Takuma Teratani[3], Shinpei Sato[4], Shuntaro Obi[5], Takahisa Sato[5], Masatoshi Akamatsu[6]

[1]Japanese Red Cross Medical Center, [2]Mitsui Memorial Hospital, [3]NTT Medical Center Tokyo, [4]Kyoundo Hospital, [5]Teikyo University Medical Center, [6]JR Tokyo General Hospital

Background: Blood transfusion of platelet was the practical way to increase the number of platelet count before invasive hepatic procedure such as radiofrequency ablation (RFA) for liver cancer. Recently, novel drug which raises platelet count by acting on thrombopoietin receptor has become available.
Methods: Lusutrombopag was orally administered 3 mg daily for 7 days for the patients underwent RFA for liver tumor with low platelet count (mainly less than 50 thousands/μL). Medication was started 7–19 days before procedure. We collected demographic data, liver function, and platelet count of the patients.
Results: Lustrombopag was administered for 71 patients. Twenty-six were females and 45 were males. Median age was 71 yo (range 51–85). Thirty-two patients had HCV, 11 had HBV, 16 had alcoholic liver disease, 7 had NASH, and 4 had other disease as background liver disease. Median Child–Pugh score was 7 (range 5–11). Twenty-seven patients were Child A Class, 40 were Child B, and 4 was Child C. Twenty-two patients had stage I tumor, 34 had Stage II, 10 had stage III, and 5 had no data. Platelet count was elevated from $4.3 \times 104 \pm 1.4 \times 104$ to $8.3 \times 104 \pm 2.6 \times 104$. Sixty-three patients (89%) out of 71 need not platelet blood transfusion by Lustrombopag administration. No patients had bleeding complication after RFA procedure. One had portal thrombosis after lustrombopag taking.
Conclusions: Lustrombopag administration made the number of patients who need platelet blood transfusion lower at the time of RFA procedure for liver cancer.

Abstract #630

Clinical efficacy and safety of apatinib in first-line treatment for hepatocellular carcinoma: a prospective study

Jian Huai Zhang[1]

[1]Huai'an First People's Hospital, Huai'an, China

Introduction: Apatinib, an oral VEGFR-2 inhibitor, has been approved as third line treatment for metastatic gastric cancer in China.
Objectives: The aim of this study was to evaluate the efficacy and safety of apatinib, in first-line treatment for hepatocellular carcinoma (HCC).
Methodology: This is a prospective, single-center clinical study. Apatinib was administered at 500 mg/day continuously. The primary endpoint was progression-free-survival (PFS), the secondary endpoint was overall survival (OS), disease control rate (DCR), objective response rate (ORR) and safety. The tumor response was determined according to the Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1.
Results: From April 2017 to July 2018, 16 patients with advanced HCC were enrolled. The first evaluation of complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD) was 6.25% (n = 1), 31.25% (n = 5), 43.75% (n = 7) and 18.75% (n = 3), respectively. The ORR was 37.5% (6/16) and the DCR was 81.25% (13/16). The most frequently observed drug-related adverse events were myelosuppression (50%, n = 8), hypertension (50%, n = 8), anorexia (31.25%, n = 5), oral ulcer (43.75%, n = 7), hand-foot syndrome (56.25%, n = 9). The most common grade 3–4 adverse events were hand-foot syndrome and hypertension, grade 3–4 hematologic toxicities were rare. Toxicities were tolerable or could be clinically managed. mPFS has not been reached yet.
Conclusion: In summary, results of this small study indicate that apatinib is well tolerated and extremely effective for the treatment of advanced HCC.

Abstract #708

Incidence and Risk Factors of Postembolization Syndrome after Transcatheter Arterial Chemoembolization for Hepatocellular Carcinoma

Hyun Jin Baek[1], Suk Bae Kim[1], Il Han Song[1]

[1]Department of Internal Medicine, Dankook University College of Medicine

Introduction: Transcatheter arterial chemoembolization (TACE) is the most common therapeutic option for hepatocellular carcinoma (HCC). Postembolization syndrome (PES), which is defined as fever, upper abdominal pain, and nausea/vomiting after TACE, is a main cause of patient discomfort.
Objectives: The aims of this study were to investigate the incidence and to assess pre- or intra-procedural risk factors of PES.
Methodology: Single-center retrospective analysis of prospectively maintained medical reports was performed in 559 TACE episodes of 214 HCC patients between March 2013 and June 2018.
Results: The incidence of PES was 32.9% (abdominal pain 16.8%, fever 9.3%, nausea/vomiting 6.8%). Younger patients had a higher incidence of PES (63.0 ± 9.3 years vs. 65.9 ± 9.7 years, respectively, $p < 0.05$). Patients who developed PES had more advanced stage (stage I vs. II vs. III, 18.6% vs. 29.4% vs. 57.8%, respectively, $p < 0.001$), larger size of tumor (3.4 ± 2.7 cm vs. 2.1 ± 1.5 cm, respectively, $p < 0.05$), and more dosage of lipiodol (6.2 ± 3.8 mL vs. 4.1 ± 2.7 mL, respectively, $p < 0.05$) compared to those without PES. There was no statistical significance in the incidence of PES in Child–Pugh classification, ECOG performance status, the number of tumor, past therapeutic modality, and biochemical liver tests. Multivariate analysis by logistic regression demonstrated that age was the most independent predictive factor of PES (odds ratio: 0.961, 95% CI 0.934–0.990, $p < 0.05$).
Conclusion: PES is not rare in TACE-treated HCC patients. Recognition of the risk factors is important for timely proper management of PES. In the future, the prospective study for the PES prophylaxis is required.

Abstract #743

Meta-analysis on effects of Antiviral therapy prior to Hepatectomy on Viral Reactivation, Overall survival and Disease-free survival among patients with Chronic Hepatitis B-related Hepatocellular Carcinoma

Lariza Marie Luna Canseco[1], Hashamiiya M. Babaran[1], Carlos C. Cuano[1], Julius Christian S. Sunglao[1], Angela Domingo Salvana[1]

[1]Philippine General Hospital

Introduction: Liver cancer is the second most common cause of cancer death. Hepatic resection is favored over radiofrequency ablation for HCC with Child–Pugh A cirrhosis or T1 or T2 status.
Objectives: This study will investigate benefits of early Antiviral treatment, in terms of overall survival, disease-free survival and viral reactivation among Chronic Hepatitis B-related HCC prior to hepatectomy.
Methodology: Systematic literature search done using electronic database. Inclusion criteria: (1) Chronic Hepatitis B-related Hepatocellular Carcinoma patients ≥ 18 years old, (2) Curative resection, (3) Antiviral prior to hepatectomy for experimental arm versus no antiviral control, (4) With data on viral recurrence or survival on follow-up. Exclusion criteria (1) co-infection with other viral hepatitis or HIV, (2) Main form of therapy other than hepatectomy. Relevant data were compared and analyzed using Review Manager 5.3 software.
Results: Four studies were included, having a total of 833 study population, 417 in the antiviral arm and 416 under the control. Patients given nucleoside analogues prior to liver resection had a significantly reduced risk of viral reactivation by 88% compared to the control. For the 1, 3 and 5-year disease-free survival, treating with nucleoside analogues prior to surgery, showed a trend towards increased survival rate. In terms of overall survival, there was a significant increase in the Antiviral arm compared to the control group.
Conclusion: For Chronic Hepatitis B-related HCC patients, giving nucleoside analogues prior to liver resection significantly decreases viral reactivation and improves disease-free and overall survival.
Correspondence:
1 lariza.canseco@gmail.com
2 hashamiiyababaran@gmail.com
3 koa_blupen@yahoo.com
4 jsunglao2000@gmail.com
5 angela.salvana@yahoo.com

Abstract #749

Percutaneous Radiofrequency Ablation versus Transarterial Chemoembolization for Intermediate Stage (5.0–8.0 cm) Hepatocellular Carcinoma

Dennis Franco Fernandez[1], Stephen Ng Wong[1], Jose Decena Sollano[1]

[1]University of Santo Tomas Hospital

Significance: Transarterial chemoembolization(TACE) is the recommended treatment by most guidelines for unresectable hepatocellular carcinoma(HCC) 5–8 cm in size. However, complete response to TACE is low and it needs to be repeated to extend survival. Radiofrequency ablation (RFA) has been shown to be effective for larger HCC. We aimed to compare outcomes in patients with HCC 5–8 cm treated with RFA or TACE. Methodology: From September 2006–October 2018, patients with HCC 5–8 cm size had RFA (n = 50), TACE (n = 17) or TACE followed by RFA (TACE-RFA) (n = 18). Baseline characteristics and overall survival were compared between the three groups. Complete response rates were assessed in patients undergoing RFA and TACE-RFA while those undergoing TACE were not routinely assessed for radiologic response. Survival was estimated using Kaplan–Meier and multivariate analysis of survival predictors were analyzed using cox regression. Results: TACE patients had significantly higher bilirubin (TACE = 2.4 + 2.3 mg/dLvs.RFA = 1.3 + 1.2 mg/dLvs.TACE-RFA = 0.8 + 0.5 mg/dL; p = 0.007), creatinine (TACE = 1.2 + 0.4 mg/dLvs.RFA = 1 + 0.3 mg/dL vs. TACE-RFA = 1.1 + 0.3 mg/dL; p = 0.045), tumor number (TACE = 1.9 + 1.9 vs. RFA = 1.2 + 0.4 vs. TACE-RFA = 1.4 + 0.6; p = 0.013), and were more likely to be cirrhotic (TACE = 98.3% vs. RFA = 54% vs. TACE-RFA = 61.1%; p = 0.001). After a median follow-up of 15.5 months, RFA and TACE-RFA patients had better survival compared to TACE alone(1, 2 and 3 years: RFA = 78.1%, 67%, 59.9% vs. TACE-RFA = 94.4%, 94.4%, 64.8% vs. TACE = 48.4%, 16.1%, 16.1%; p = 0.001). Type of progression (p = 0.026), cirrhosis (p = 0.001), ascites (p = 0.05) BCLC subclass ($p < 0.0001$) Child–pugh score (p = 0.000129), serum albumin (p = 0.000383), bilirubin ($p < 0.0001$), INR (p = 0.005),and AFP levels (p = 0.018) were found to be predictors of survival on univariate analysis. On multivariate analysis, only albumin (OR = 2.64; 95% CI 4.38–1.59; $p < 0.001$) and treatment group (OR = 5.8; 95% CI 1.984–17.249; p = 0.001) were independent predictors of survival. Conclusion: In patients with hepatocellular carcinoma 5–8 cm in size, RFA or in combination with TACE appear to result in better survival compared to TACE alone, and may be an attractive treatment option for these patients.

Abstract #755

Safety and efficacy of lenvatinib in patients with advanced hepatocellular carcinoma; initial experience from Japanese field practice

Sadahisa Ogasawara[1], Susumu Maruta[1], Yoshihiko Ooka[1], Takahiro Maeda[1], Hiroaki Kanzaki[1], Kengo Kanayama[1], Yuko Kusakabe[1], Kazufumi Kobayashi[1], Souichiro Kiyono[1], Masato Nakamura[1], Tomoko Saito[1], Eiichiro Suzuki[1], Shingo Nakamoto[1], Shin Yasui[1], Akinobu Tawada[1], Tetsuhiro Chiba[1], Makoto Arai[1], Tatsuo Kanda[1], Naoya Kato[1], Hitoshi Maruyama[1]

[1]Chiba University, Graduate School of Medicine and Department of Gastroenterology

Background and aim: Lenvatinib has been used advanced hepatocellular carcinoma (HCC) patients in Japan since March 2018. The aim of this study was to assess the safety and efficacy of lenvatinib in patients with advanced HCC.
Methods: We retrieved medical records of patients with advanced HCC receiving lenvatinib in Chiba University Hospital. Radiological responses were evaluated using both RECIST version 1.1 and modified RECIST (mRECIST). CTCAE version 4.0 was used for assessments of adverse events.
Results: Between March 2018 and October 2018, 56 patients were administered lenvatinib for advanced HCC. According to baseline radiological assessments, 16 and 25 patients had macrovascular invasion and extrahepatic metastasis, respectively. Of 56 patients, 34 patients and 22 patients received lenvatinib as 1st line and 2nd line or later, respectively. During the follow-up period, 23 patients (41%) achieved objective response (complete response or partial response) according to mRECIST. This objective response rate was similar between 1st line group (44%) and 2nd line or later group (36%). Of 40 patients (71%) required dose modification, the most common adverse events due to dose modifications were anorexia (12 patients, 21%), fatigue (9 patients, 16%), and encephalopathy (6 patients, 11%). During the end of the observation period, 8 patients (16%) discontinued treatments due to adverse events.
Conclusion: ORR of lenvatinib in advanced HCC patients who had previous history of systemic therapies was similar with advanced HCC patients who received 1st line. Lenvatinib was generally tolerated in Japanese advanced HCC patients.

Abstract #799

Efficacy of Percutaneous Microwave Ablation Therapy Compared to Radiofrequency Ablation Among Patients with Intermediate Hepatocellular Carcinoma

Marco Angelo Dominguez Tongo[1], Diana Alcantara Payawal[1]

[1]Cardinal Santos Medical Center

Introduction: Liver Cancer is among the leading causes of Cancer deaths. In the Philippines, prevalence rate is 7.8% for Hepatocellular Carcinoma (HCC) with mortality rate of 25%. Radiofrequency ablation has been the recommended image-guided percutaneous ablation technique for the management of Hepatocellular Carcinoma however, with reports of skin burns. Percutaneous Microwave Ablation Therapy (PMAT) was recently introduced in a tertiary hospital in the Philippines.
Objectives: To compare the liver function tests and alpha-fetoprotein (AFP) levels among patients with Intermediate Hepatocellular Carcinoma who underwent PMAT versus those who underwent Radiofrequency ablation (RFA); To describe the demographics, and complications involving those who underwent PMAT or RFA.
Methods: Review of records from January 2018 to October 2018 was done wherein data including pre- and post procedural liver function tests, Alpha-feto protein (AFP), and imaging studies were recorded.
Results: Among patients with intermediate hepatocellular carcinoma, there was statistically significant decline of alpha fetoprotein among those who underwent MAT compared to those who underwent RFA (p = 0.0266). On the other hand, there was a trend towards greater decline in tumor size and levels of SGPT and SGOT among patients who underwent RFA, however, not statistically significant.
Conclusion: Although radiofrequency ablation therapy has been used for a longer period of time, PMAT has shown potential as a viable treatment option for patients with Intermediate Hepatocellular Carcinoma. The statistically significant decline of alpha fetoprotein is suggestive of improvement in prognosis for patients who underwent

PMAT among patients with Intermediate Hepatocellular Carcinoma however, further investigation is still warranted.

Abstract #845

Outcome of Locally Advanced Hepatocellular Carcinoma treated with Selective Internal Radiation Therapy compared to Sorafenib: A Multicentre Experience in the Philippines

Leila B. Sawadjaan[1], Janus Po Ong[1], Pierce Kaw HOE Chow[2], Mihir Gandhi[3], Ian Homer Y. Cua[4], Rolley R. Lobo[5], Catherine S. C. Teh[6]

[1]The Medical City, [2]National Cancer Center Singapore, [3]Singapore Clinical Research Institute, [4]St. Luke's Medical Center, [5]Davao Doctors Hospital, [6]Makati Medical Center

Introduction: Sorafenib is the recommended first-line therapy for patients with advanced hepatocellular carcinoma (HCC). Limited data compared the benefit of selective internal radiation therapy yttrium-90 (SIRT) to sorafenib in HCC patients. Objectives: To compare the efficacy and safety of SIRT and Sorafenib in patients with locally advanced HCC.
Methodology: This patient population represent the patients from the Philippines included in the SIRveNIB trial. Patients were randomly assigned 1:1 ratio. Primary end point was overall survival (OS). Analysis of efficacy of treatment was performed in the intention-to-treat population. Patients included were age ≥ 18 with locally advanced HCC $\pm$ portal vein thrombosis, not amenable to curative treatment options, and excluded if previously received Sorafenib. 18-month survival rates were estimated using Kaplan–Meier plots and compared using the log-rank test
Results: 57 patients were randomly assigned from 4 tertiary centres in the Philippines. 48% were male with a mean age of 56. 54.4% had Chronic Hepatitis B infection, 91.2% were Child A, 58% had BCLC B, and 1/3 had PVT. 21 from SIRT group and 25 from Sorafenib group received assigned treatment. Disease control rate was better with SIRT [86% (95% CI 64%, 97%) versus 32% (95% CI 14.9%, 53.5%). Median OS was 8.31 months with SIRT and 5.75 months with Sorafenib (HR 0.75; 95% CI 0.41–1.36; $p = 0.34$). Fewer patients receiving SIRT experienced treatment-related adverse events [SIRT, 9/21 (42.9%) versus Sorafenib, 21/25 (84%)] or treatment-related serious adverse events [SIRT, 2/21 (9.5%) versus Sorafenib, 14/25 (56%)].
Conclusion: Difference in overall survival among locally advanced HCC treated with SIRT compared to Sorafenib is not significant. Fewer adverse events were noted in patients treated with SIRT.

Abstract #862

Regorafenib in patients with progression after sorafenib can be effective in both group (initial responder and primary nonresponder)

Sangyoun-Hwang[1], Jungwoo-Im[1], Seonmi-Lee[1], Kijung-Jeon[1]

[1]Dongnam Institute of Radiological and Medical Sciences

Regorafenib is approved as second line therapy in sorafenib refractory patients in the basis of RESORCE study, but that was performed in patients with minimal duration of sorafenib usage above 4 months (initial responder, IR), then did not include patients with progression within 3 months (primary nonresponder; PN). We aimed to evaluate the efficacy and safety of regorafenib in patients with progressive disease after sorafenib monotherapy; IR versus PN.

Eligible patients with documented disease progression with sorafenib treatment were recruited in our hospital from 2017 to 2018. All patients received regorafenib 160 mg every 3 weeks.

Sixteen patients (IR group; 5 patients, PN group; 11 patients) were enrolled in the study. OS and PFS in whole patients was 5 months and 3 months. The median OS was 5 months in IR group, 6 months in PN group and the median PFS was 3 months in IR group, 3 months in PN group. The OS and PFS in IR group and PN group were not different significantly (p value = 0.481 and 0.648). 1 patients achieved SD, and 4 patients had PD in IR group, 1 patients had PR, 2 patients had SD, 8 patients had PD in PN group. In IR group, only one patients (20%) experienced HFSR, however in PN group, 8 patient (72%) experienced HFSR (p value = 0.0343) and 4 patient (36.3%) experienced gastrointestinal toxicity.

Our study suggests that regorafenib can be available second line treatment despite of primary responsiveness for sorafenib although more adverse reaction of regorafenib was showed in PN group.

Abstract #916

The immunological anti-tumour response of radiofrequency ablation and PD-1 inhibition in a pre-clinical HCC model

Kaiwen Huang[1]

[1]National Taiwan University

Background: Radiofrequency ablation (RFA) is standard treatment for some tumour types such as liver cancer and induces modulation of both innate and adaptive immune systems.
Methods: To investigate any synergistic effect of RFA and immune checkpoint inhibition, we initiated a translation experiment, where syngeneic hepatocellular carcinoma cells were injected in the two opposite flanks of immunocompetent BALB/c mice ($n = 8$ in each group). Treatments for hepatoma bearing mice included (1) RFA on one flank, (2) Immunotherapy (PD-1 inhibition).
Results: Tumour control on the opposite flank was augmented by addition of RFA, in which 2/8 animals showed a complete response and 5/8 a partial response. This was also the only group that showed a statistically significant increase in CD8+ (Cytotoxic) as well as CD49b+/CD45+ (Natural Killer) tumour infiltrating lymphocytes.
Conclusions: These data suggest a clinical role for combination treatment with checkpoint blockade and RFA through synergistic priming of the immune tumour response, enabling RFA to have an abscopal effect.

Abstract #941

Predictors for Refractoriness and Survival after Transarterial Chemoembolization among Hepatocellular Cancer Patients: Outcomes from a six-year retrospective cohort

Rudolf Villanueva Kuhn[1], Glenn Marc G. Ignacio[1], Jade Dequina Jamias[1]

[1]Department of Medical Imaging and Therapeutic Radiology, National Kidney and Transplant Institute

Introduction: Patients with hepatocellular carcinoma become refractory to repeated sessions of transarterial chemoembolization. Predictors associated with refractoriness and survival are however poorly defined and lack consensus.
Objectives: The aim of this study was to identify predictors associated with overall survival and refractoriness of HCC patients undergoing repetitive TACE. The secondary aim was to validate the

ART score, neutrophil–lymphocyte ratio and radiologic response using the mRECIST and CHOI criteria for the first time in a South-East Asian setting.
Methodology: The clinical and laboratory characteristics and radiologic response of 39 patients treated with repetitive conventional TACE from January 2012 to June 2018 were analyzed in a retrospective cohort.
Results: The median overall survival of patients was 23.2 months and overall mortality was 36%. Multivariate Cox regression analysis revealed that Child–Pugh score (Hazard ratio = 3.47, p = 0.044), AST (HR = 7.6, p = 0.021), tumour size (HR = 5.47, p = 0.033), progressive disease using CHOI criteria (HR = 5.47, CI 1.15–25.99, p = 0.033), neutrophil–lymphocyte ratio (HR = 1.25, p = 0.049) and enhancement on follow-up CT imaging (HR = 1.98, p = 0.034) were independent risk factors for poor survival. Multivariate analysis also showed that ALT (p = 0.005), enhancement (p = 0.003), Child–Pugh score (p = 0.010), and progressive disease using CHOI criteria (p = 0.022) were predictive of TACE refractoriness/failure.
Conclusion: Predictors for poorer survival and TACE failure/refractoriness were identified. A rational treatment strategy and the decision to switch therapy should be individualized considering the patient's clinical condition and aforementioned clinical and laboratory parameters and response on radiologic follow-up.
Keywords: TACE, liver cancer, response, survival

Abstract #958

TACE in HCC with Portal vein thrombosis

Wasey Mahmud Jilani[1], Zahid Azam[1]

[1]South City Hospital

Background: Portal vein tumor thrombosis (PVTT) is relative contraindication for transarterial chemoembolization (TACE) in hepatocellular carcinoma (HCC). Consensus policies for managing HCC with PVTT have not been established.
Aim: The purpose of our study was to evaluate the efficacy, safety and survival post-TACE in HCC patients with PVT.
Methods: From January 2017 to October 2018, 25 patients with unresectable HCC with PVT were offered TACE. Patients were assessed for tumor response by imaging at regular intervals and the data compared with the baseline laboratory and imaging characteristics obtained pre-TACE and survival was studied.
Results: 18 Patients (72%) had HCV, 5 patients (20%) had HBV and 2 patients (8%) had NASH cirrhosis. 8 (32%) Patients were Childs' A and 17 patients (68%) were Childs B. All patients underwent selective TACE. The study is continued but at the end of the follow up in October 2018, 20 patients (80%) were alive and 5 patients had died. Median survival time in patients who expired was 7 months. Clinical progression was observed in 9 patients (36%). Partial response according to mRECIST was seen in 8 patients (32%), with an average of 1.8 TACE sessions. Complete response with normalization of CT features and AFP levels was seen 3 patients (12%), 2 after the first session and 1 after the second session of TACE. One patient had ACLF which settled after 3.5 weeks.
Conclusion: TACE is a relatively safe and effective therapy in unresectable HCC with PVT with survival benefit compared with historical controls.

Abstract #985

The efficacy and safety of Lenvatinib for advanced hepatocellular carcinoma in a real world setting

Shuntaro Obi[1]

[1]Teikyo Univ. Chiba Medical Center

Background/purpose: In phase 3 trial, Lenvatinib (an inhibitor of vascular endothelial growth factor (GF) receptors 1–3, fibroblast GF receptors 1–4, platelet-derived GF receptor α, rearranged during transfection, and stem cell factor receptor) is non-inferior to Sorafenib in advanced hepatocellular carcinoma. This study examined the efficacy and safety of Lenvatinib in a real world setting.
Methods: This was a retrospective, multicenter, observational study. Inclusion and exclusion criteria were based on phase 3 trial, and participants were observed for at least 12 weeks. Therapeutic effect was determined using the modified Response Evaluation Criteria In Solid Tumors (m-RECIST) by the eighth week. Patients received oral Lenvatinib 12 mg/day (> 60 kg bodyweight) or 8 mg/day (< 60 kg bodyweight). Dose interruptions followed by reductions for Lenvatinib-related toxicities were permitted. Grades of adverse events (AEs) complied with the Common terminology criteria for adverse events version 4.0.
Results: All 16 cases included in this study had prior treatment history, and a median of 3.9 years had passed since the first treatment. Fatigue, hypertension, and proteinuria were identified as AEs with the highest frequencies, and were more than Grade 2. AEs could be controlled by carrying out appropriate dose reduction, interruption, and symptomatic treatment according to the protocol. In the m-RECIST evaluation at the eighth week, complete response, partial response, stable disease, and disease progression involved 0, 6, 8, and 1 case, respectively. Objective response rate was 40%.
Conclusion: Lenvatinib treatment could be accomplished with safety and good response in a real world setting.

Abstract #986

Radiofrequency Ablation versus Repeated Resection for Hepatitis B Recurrent Hepatocellular Carcinoma (≤ 5 cm) after Initial Curative Resection: A Retrospective Study

Yuemin Feng[1], Chenghui Xu[1], Hang Zheng[1], Tiantian Liu[1], Chengyong Qin[1], Qiang Zhu[1]

[1]Department of Gastroenterology, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, China

Introduction: The risk of recurrent hepatocellular carcinoma (rHCC) after curative resection is up to 70% at 5 years. The management of rHCC remains unclear.
Objectives: To compare radiofrequency ablation (RFA) and repeated resection as first-line treatment in hepatitis B rHCC patients and to evaluate the long-term outcomes of both therapies.
Methodology: Between January 2006 and December 2016, a total of 158 consecutive patients with rHCC (≤ 3 tumor nodules, ≤ 5 cm, Child–Pugh A or B) underwent re-resection or RFA. The overall survival (OS), progression-free survival (PFS) and complication were compared before and after propensity score matching (PSM). Subgroup analysis was conducted according to Child–Pugh class, tumor size and tumor number.
Results: The 1, 3 and 5 years OS rates for RFA group and re-resection group (before: 88.0%, 60.0%, 53.5% vs 84.3%, 61.7%, 39.8%, P = 0.567; after: 87.2%, 63.9%, 63.9% vs 82.2%, 60.9%, 40.6%, P = 0.263) and PFS rates (before: 61.2%, 31.7%, 19.1% vs 49.6%,

23.9%, 15.5%, P = 0.383; after: 66.3%, 25.9%, 12.9% vs 52.6%, 19.9%, 15.9%, P = 0.505) were comparable. RFA was superior to re-resection for complication rate and length of hospital stay ($P < 0.001$). Subgroup analysis indicated that, for rHCC with 2 or 3 tumor nodules, OS of RFA group was significantly better than re-resection groups ($P < 0.001$).
Conclusion: In total, RFA was the same effective as re-resection but safer. For rHCC with 2 or 3 tumor nodules, RFA is more efficient and safer than re-resection.

Abstract #1008

Frequency and Risk Factors for Complications After Ultrasound-guided Percutaneous Liver Radiofrequency Ablation in 363 Sessions

Engelbert Simon Sy Perillo[1], Virgilio J. R. Sandico Lo[1], Stephen N. Wong[2]

[1]University of Santo Tomas Hospital, [2]University of Santo Tomas Hospital and Chinese General Hospital and St. Lukes Medical Center, Quezon City

Introduction: Radiofrequency ablation (RFA) has become a common treatment of patients with unresectable primary and secondary hepatic malignancies. Investigation of its complications has been limited. Major complications from percutaneous RFA are low(3.1%) in the study of Kong et al. involving 255 patients in 2009. We aimed to determine frequency and factors that predict complications after RFA.
Methods: This was a retrospective study done over an 11-year period, 363 sessions of percutaneous radiofrequency ablation for the treatment of 812 liver tumors were included (297 sessions were done for the treatment of hepatocellular carcinoma and 66 for metastatic liver tumor). Sessions where > 1 tumor was within 5 mm of a vital structure or > 3 mm vessel were considered high-risk.
Results: An average number ($2.14 + 1.56$ vs $2.69 + 1.84$, $p = 0.026$) of primary and secondary hepatic malignancies with tumor size ($3.64 + 1.78$ vs $3.08 + 1.77$, $p = 0.021$) were included. There were 33% minor and 7.4% major complications. The most common major complications are liver abscess (1.9%) followed by organ damage (1.4%) and tumor bleeding (1.4%). 5 (0.01%) died in the immediate post-RFA period. 3 patients died due to RFA-related complications: intestinal perforation, hemothorax and tumor hemorrhage while 2 died due to RFA-unrelated complications: massive upper GI bleeding and acute coronary syndrome. Preoperative antibiotic use ($p = 0.00$), electrode type ($p = 0.01$), largest tumor size ($p = 0.00$) and total RFA time ($p = 0.00$) were found to be associated with major complication. On multivariate analysis, only the total RFA time was identified to be the significant risk factor for major (OR 1.03; 95% CI 0.954–0.984) complications.
Conclusion: RFA of liver malignancies is a safe procedure with acceptable complication rates. However, prudence is needed in trying to decrease RFA time in a single session. Staged procedures may decrease complication rates.

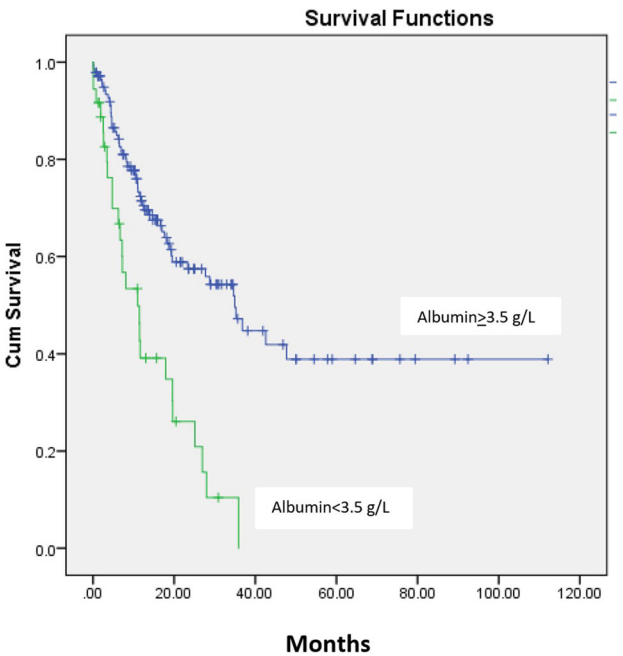
Abstract #1012

Predictors of Survival for Hepatocellular Carcinoma Treated with Ultrasound-guided Percutaneous Radiofrequency Ablation

Virgilio Jr. Sandico Lo[1], Engelbert Simon Sy Perillo[1], Stephen Ng Wong[1]

[1]University of Sto. Tomas Hospital

Introduction: Radiofrequency ablation (RFA) is a widely used technique for treating hepatocellular carcinoma (HCC). However, data regarding predictors of survival are lacking.
Objectives: We aimed to determine the independent predictors of survival for HCC treated with RFA.
Methods: RFA was performed on 181 index HCC patients from June 2007 to November 2018. Survival was estimated using Kaplan–Meier and multivariate analysis of survival predictors were analyzed using cox regression.
Results: After a median follow-up of 19.9 months, the 1-, 3- and 5-year overall survival rates were 86.5, 50.15 and 30.05%, respectively. Local tumor progression and intrahepatic distant recurrence were observed in 42.5% (77/181) and 30.9% (56/181), respectively. Patients with serum albumin > 3.5 g/L had better survival compared to serum albumin < 3.5 g/L (1, 3 and 5 years: = 69.5%, 47.2%, 38.9% vs 39.1%, 0%, 0%; $p < 0.001$). Other factors associated with survival on univariate analysis included: Cirrhosis ($p = 0.0001$), Child–pugh class ($p = 0.026$), RFA time ($p = 0.011$), Platelet count $< 150 \times 109$/L ($p = 0.002$), INR ($p < 0.001$) and total bilirubin ($p = 0.026$). The sole independent predictor of survival on multivariate analysis was serum albumin (OR = 3.40; 95% CI = 0.196–0.442; $p < 0.001$).
Conclusion: In patients with HCC treated with RFA, serum albumin > 3.5 g/L appear to result in better survival.



Abstract #1014

Predictors of Technique Effectiveness for Ultrasound-guided Percutaneous Radiofrequency Ablation for Hepatocellular Carcinoma

Virgilio Jr. Sandico Lo[1], Engelbert Simon Sy Perillo[1], Stephen Ng Wong[2]

[1]University of Sto. Tomas Hospital, [2]University of Sto. Tomas Hospital and Chinese General Hospital and Medical Center and St. Lukes Medical Center, Quezon City

Introduction: Radiofrequency ablation (RFA) is a widely used technique for treating hepatocellular carcinoma (HCC). However, not all HCC is completely ablated in 1 session. We aimed to determine the independent predictors of complete ablation (CA1) and primary technique effectives (PTE) of RFA.

Methods: RFA was performed on 298 consecutive HCC patients from June 2007 to November 2018. CA1 was defined as the absence of contrast enhancement (enhancing tumors) or hypodensity that encompasses the original tumor location (non-enhancing tumors) on CT-scan performed 1 month post-RFA. PTE pertains to the ability to completely ablate a tumor after > 1 session. Tumors that were within 5 mm of a large vessel or vital structure were considered high-risk. Multiple logistic regression analysis was used to determine independent predictors.

Results: A total of 540 tumors were ablated with a mean size of 2.9 + 1.7 cm. CA1 (< 3 cm = 94.3%; 3.1–5 cm = 85.2%; > 5 cm = 70.7%) and PTE rates (< 3 cm = 95.9%; 3.1–5 cm = 91.2%; > 5 cm = 90.4%) were higher for smaller tumors ($p < 0.001$). Isoechoic tumors had the highest CA1 (93.9%; $p < 0.001$) and PTE rates (96.9%; $p = 0.017$), while mixed echoic tumors had the lowest CA1 (76%; $p < 0.001$) and PTE rates (86.6%; $p = 0.017$). Other associated factors for CA1 on univariate analysis include tumor size, high risk tumor, tumors near a vital structure, and RFA time. However, the only independent predictor of both CA1 (OR [95% CI] = <3 cm = 13.15[0.02–0.25]; 3.1–5 cm = 2.03[0.21–1.13]) and PTE rates (OR[95% CI] = < 3 cm = 2.7[0.13–1.05]; 3.1–5 cm = 0.99[0.36–2.81]) on multivariate analysis was tumor size ($p < 0.001$).

Conclusion: RFA results in satisfactory local tumor control of HCC. Complete tumor ablation is substantial in lesions that do not exceed 5 cm.

Other Hepatobiliary Neoplasia

J01 - Cholangiocarcinoma

Abstract #284

A case of Klebsiella Pneumoniae septicemia and multiple liver abscesses co-infected with Enterococcus faecium and Escherichia coli

Xinchun Zheng[1], Mingxing Huang[1], Chunna Li[1], Jinyu Xia[1]

[1]Department of Infectious Diseases, The Fifth Affiliated Hospital of Sun Yat-Sen University

Background: Pyogenic liver abscess (PLA) is a major infectious disease in the hepatobiliary system and threaten life in Southeast Asia with a rising incidence. Most of such cases are polymicrobial and are commonly caused by seeding of infection from the biliary system. We herein present a rare case of Klebsiella *Pneumoniae septicemia* and multiple liver abscess co-infected with *Enterococcus faecium* and *Escherichia coli*.

Case presentation: A 45-year-old woman, who had an operation history of resection of hilar cholangicarcinoma, Intrahepatic metastatic tumor resection, bilioenteric anastomosis and cholecystectomy, presented with an iterative fever lasting over 3 months and aggravated within 1 week. Blood cultures from bilateral forearm vein were positive cultures for *K. pneumoniae*. Multiple hepatic occupying lesions were found in the liver by ultrasonography (US) that were considered as metastatic tumors. Contrast-enhanced CT of the abdomen disclosed multiple hypodense nodules in liver, which became much more greater when compared with previous CT results and were suspected of obstructive biliary multiple liver abscesses. PLA was confirmed by ultrasound guided liver puncture and drainage of pus and pus culture revealed the presence of *Enterococcus faecium* and *Escherichia coli* species from the abscess.

Conclusion: Increased awareness of the manifestations and subsequent management of patients with operation for hepatobiliary malignancies by clinicians is important to assist early recognition and help avoid serious sequelae. These patients are prone to multiple microbial infections and septicemia due to their low immunity, so treatments with the appropriate antibiotics and thoroughly drainage of pus are the key to cure liver abscess.

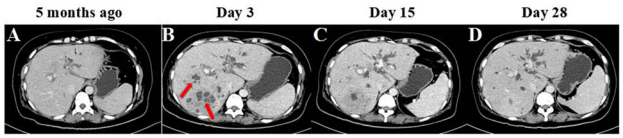


Figure 1 Abdnormal CT scan demonstrated a multiple pyogenic liver abscesses (B) (red arrow) proven by aspiration and pathology when compared to CT result in 5 months ago(A) and revealed that the size of abscess had become gratually reduced in diameter with virtually no lumen on day 15(C) and day 28(D) after antibiotic treatment and liver puncture and drainage of pus.

Abstract #694

Clinical research of primary hepatic intraductal papillary neoplasm of bile duct (IPNB) focusing on the preoperative characteristics and surgical outcomes

Satoru Tsuruta[1], Norihisa Kimura[1], Keinosuke Ishido[1], Daisuke Kudo[1], Kenichi Hakamada[1]

[1]Department of Gastroenterological Surgery, Hirosaki University Graduate School of Medicine

Background: Intraductal papillary neoplasm of bile duct (IPNB) was introduced as a precancerous and early neoplastic lesion by WHO in 2010. In 2018 meeting by Japan and Korea expert pathologists, it was described that IPNB can be subclassified into two types. Each of these two types has a different tendency in the anatomical location (intrahepatic or extrahepatic bile duct) and invasiveness. In this study, we reviewed the preoperative clinical features and surgical outcomes of primary hepatic IPNB retrospectively.
Methods: We examined the features of 7 cases of primary hepatic IPNB compared with 26 cases with intrahepatic cholangiocarcinoma (ICC).
Results: In intrahepatic IPNB cases, all tumors were confined to left hepatic lobe. Histopathologically, 5 cases had invasive components and 6 cases had mucus production. All cases had no recurrence. As compared with 26 cases of ICC, preoperative intrahepatic ($p = 0.026$) and extrahepatic ($p < 0.01$) biliary dilatation and histological mucus production ($p < 0.01$) were significantly found in primary hepatic IPNB. ICC group significantly showed CA 19-9 > 100 ($p = 0.043$), portal invasion ($p < 0.01$) and recurrence (20 cases) ($p < 0.01$).
Conclusion: Considering the possibility of high-malignant cases in tumor marker elevated cases and vascular invasive cases, adequate biliary resection with systematic hepatectomy and intraoperative rapid diagnosis would be desirable in intrahepatic IPNB cases. We also found that the prognosis of moderately and poorly differentiated ICC cases was significantly poor. The progression of preoperative diagnosis of intrahepatic bile duct tumor would enable us to give more selective treatment.

J02 - Other primary hepatobiliary neoplasia

Abstract #210

The Optimal Management of Pleural Effusion in Liver Abscess?

Jae Young Jang[1], Hong Soo Kim[2], Soung Won Jeong[1], Young Seok Kim[3], Sang Gyune Kim[3], Sae Hwan Lee[2]

[1]Institute for Digestive Research, Digestive Disease Center, Department of Internal Medicine, Soonchunhyang University College of Medicine, Seoul, Korea, [2]Department of Internal Medicine, Soonchunhyang University College of Medicine, Cheonan, Korea, [3]Department of Internal Medicine, Soonchunhyang University College of Medicine, Bucheon, Korea

Aims: We investigated clinical features of pleural effusion in patients with liver abscess.
Methods: This is a retrospective study conducted to evaluate the characteristics and management of pleural effusion in patients with liver abscess at Soonchunhyang University Seoul Hospital. A total of 526 patients were collected. Of these, 156 patients were excluded from the analysis. Finally, the clinical, radiological, and laboratory findings were analyzed in total of 370 patients in liver abscess.
Results: One hundred ten (29.7%) patients had pleural effusion. Among of these, 56.4% occurred in right, 5.5% in left and 35.5% in both. When pleural effusion was present, age (older age, $p = 0.046$), liver abscess size (43.01 vs. 59.48 mm, $p = 0.000$) and location (right superior segment, $p = 0.000$) were significantly different from those without. Most of patients (96 patients) were treated with only antibiotics and 14 patients underwent intervention with antibiotics for pleural effusion. Of the 13 patients who were able to perform fluid analysis, 11 (84.6%) were exudate and 2 (15.4%) were transudate. Duration of pleural effusion showed no significant difference between the groups that performed intervention and those who were treated with antibiotics only (17.79 vs. 12.35 days, $p = 0.112$).
Conclusions: The pleural effusion was more frequent in older patients, larger size and right superior segment. There was no statistically significant difference in duration of pleural effusion between intervention and non-intervention group. Therefore, treatment of pleural effusion is thought to be sufficient for antibiotics without special intervention in patients with liver abscess.

Abstract #216

Severe Intrahepatic Bile Duct Dilatation Caused by Clonorchis Sinensis Infection: A Case Report

Chong Jie Gan[1], Wen Tao Luo[1], Ruo Man Ke[1], Peng Yuan He[1], Li Juan Ouyang[1], Ming Xing Huang[1], Zhong Dao Wu[2], Jin Yu Xia[1]

[1]The Fifth Affiliated Hospital of Sun Yat-Sen University, [2]Department of Parasitology, Zhongshan School of Medicine

Introduction: Clonorchis sinensis has been clearly identified as a carcinogen in hepatic cholangiocarcinoma (Type I). The epidemic area is mainly distributed in China, South Korea, and other Asian countries,causing up to 5591 deaths and 275,370 DALYs per year. Herein, we present a case of severe intrahepatic bile duct dilatation caused by Clonorchis sinensis infection.
Methodology: Case description.
Results: A 46-year-old man who lived in Guangdong province of China for more than 10 years was admitted to hospital on June 18, 2018 because of sudden hemoptysis for 3 days. The patient had a long and clear history of eating finely sliced raw fish. Laboratory results showed that eosinophil counts and proportions increased significantly, up to 1.26 × 10^9/L (reference 0.02–0.52/L), with a ratio of 14.20% (reference 0.4–8.0%). The *Clonorchis sinensis* egg was found in the stool. Magnetic resonance cholangiopancreatography (MRCP) showed intrahepatic bile duct diffuse dilatation and peripheral bile duct cholestatic, adjacent liver tissue inflammation, considering parasitic infection (Figure 1). Pulmonary CT showed changes in the lower lung and left lung segments, considering hemorrhagic alveolitis. The cause of pulmonary hemorrhage is still a mystery, but it does not exclude that the eggs might return to the lungs and cause rupture of blood vessels.
Conclusion: Although typical liver imaging findings of infection caused by *Clonorchis sinensis* are very rare, clonorchiasis should be taken into consideration when exploring the causes of the dilatation of bile ducts, especially in the epidemic area.

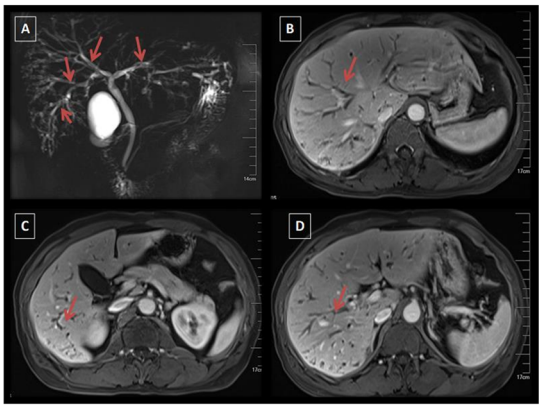


Figure 1. Intrahepatic bile duct diffuse dilatation and peripheral bile duct cholestatic, adjacent liver tissue inflammation. Figure A: MRCP showed proximal inflammatory stenosis, distal bile duct dilatation. Figures B, C, and D are partial levels of liver in MRCP, respectively(red arrow).

Abstract #264

Primary Hepatic Neuroendocrine Tumor Diagnosed as Hepatocellular Carcinoma: A Double Jeopardy?

Clint Lumba Becaldo[1], Arlene Matute Kuan[2], Leslee Yap Ong[3], Dennis Aranas Entera[3]

[1]Vicente Sotto Memorial Medical Center, [2]Vicente Sotto Memorial Medical Center and Chong Hua Hospital and Visayas Community Medical Center, [3]Vicente Sotto Memorial Medical Center and Chong Hua Hospital and Cebu Velez General Hospital

Introduction: Primary hepatic neuroendocrine tumors are extremely rare and difficult to distinguish from other liver tumors such as hepatocellular carcinoma particularly in a setting of hepatitis B coinfection.
Case Presentation: This case report aims to describe a case of primary hepatic neuroendocrine tumor with spinal metastases, on a 52-year-old man with chronic hepatitis B, who presented with intermittent abdominal pain with no other symptoms. Transarterial chemoembolization was planned prior to resection. The case presented is a medical challenge requiring meticulous radiological, histopathological, and immunohistochemical work-up to rule out an extrahepatic malignancy with hepatic metastasis to confirm the primary nature of hepatic tumors.
Conclusion: Given the background of chronic hepatitis B infection, we speculated that liver tumors do not always emerge as hepatocellular carcinoma, even in hepatitis B prevalent area, and that neuroendocrine tumors are often overlooked. Hence, a multiple approach to diagnose primary neuroendocrine tumors is implied.

Abstract #358

Pancreatic Adenocarcinoma in Young and Middle Aged Adult

Shih-Ting Huang[1], Tsang-En Wang[2], Cheng-Yu Ho[3], Ming-Jen Chen[4]

[1]Nurse Practitioner, Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan, [2]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan and Department of Medicine, Mackay Medical College, New Taipei City, Taiwan, [3]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan, [4]Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan and Department of Medicine, Mackay Medical College, New Taipei City, Taiwan

Introduction: Most of pancreatic cancer is adenocarcinoma (PAC). The epidemiologic studies showed PAC with high prevalence in elderly and infrequently in young and middle-aged. Those younger PAC patients might have different characteristics. However, very few papers discussed this topic in east world.
Aims: In this report, we shared our experience PAC patients below 50 years of age. Their clinical features, manifestation and prognosis were analyzed.
Methods: A retrospective studied the patients with PCA, < 50 years old. The patients were identified by pathology in our hospital from 2004 to 2015. The data was reviewed included gender, clinic manifestation and prognosis.
Results: Twenty-two patients were enrolled. Eighteen patients (82%) were males. The mean age of patients was 44.1-year-old. Three (17%) patients were below 41 years. The most symptoms were abdominal pain (68%), following by nausea, jaundice and weight loss. Four patients had diabetes and four patients had heavy alcohol use. Mean size of cancer was 4.2 cm and 82% were TMN stage IV at diagnosis. Two-third cancer (68%) was at the head. The mean survival time was 8.75 months. Only three patients live more than 1 year.
Conclusions: The PAC in middle age was not common and its' rate in all PCA is same in the west world. Some patients had risk factors as elderly, such as DM and alcohol use. However, they were found with more advanced stage and poor prognosis. We should pay attention about the possibility of PCA in middle age and their genetic characteristics in future.

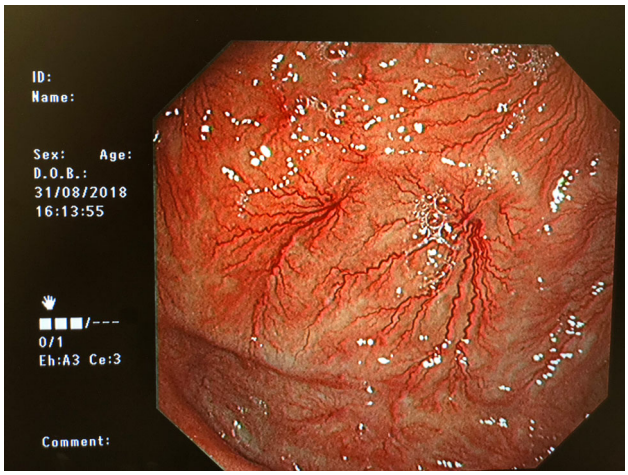
Abstract #401

An unusual cause of upper gastrointestinal bleeding – a diagnosis you cannot MISS!

Ivan Pui Kei Yuen[1], Steven Wc Tsang[1]

[1]Tseung Kwan O Hospital

A 77-year-old woman was admitted for anemic symptoms with low hemoglobin. Esophagogastroduodenoscopy found highly vascularized mucosa in the greater curvature of stomach with streaks of fresh blood without gastric varix (Figure 1). Computerized tomography revealed a large contrast enhanced mass (8.7×5.9 cm) in pancreatic body, causing compression of splenic vein with large amount of collateral vessels in mesentry of upper abdomen (Figure 2). Main portal vein and superior mesenteric vein were patent and spleen was not enlarged. Multiple metastatic hyper-enhancing masses in liver were also found. Therefore, the final diagnosis was metastatic pancreatic carcinoma causing splenic vein compression and hence left-sided segmental portal hypertension with upper gastrointestinal bleeding. This case demonstrated that gastric varix or splenomegaly may not appear even in late stage pancreatic cancer with isolated splenic vein thrombosis or obstruction. The splenic vein runs in close proximity along the pancreas. Any mass or inflammation (e.g. pancreatic cancer, chronic pancreatitis, pancreatic pseudocyst or retroperitoneal fibrosis) may result in spasm or compression of the splenic vein with subsequent thrombosis. Any blockage of the splenic vein could cause high pressure in left side portal venous circulation. We need to be aware and suspect of pancreatic cancer in patients with left-sided congested mucosa of stomach even without gastric varix.



Abstract #470

High-grade Hepatic Neuroendocrine Cancer Presenting as Hepatocellular Carcinoma in a Neurofibromatosis Patient: A Case Report

Fatimin Leila Sawadjaan[1], Janus Po Ong[1], Ryan De Gracia[1]

[1]The Medical City

Introduction: Hepatic neuroendocrine cancers are rare, representing 0.3% of all carcinoids, and are more rarely, diagnosed as high-grade malignancies.
Case: We report the case of a male patient with congenital neurofibromatosis (NF) who presented with a large solitary right lobe liver mass. He had no clinical evidence of chronic liver disease and had a normal serum alpha- fetoprotein. Two previous fine needle biopsies of the liver mass showed hepatocellular carcinoma (HCC). On CT scan, a concomitant left upper abdominal mass which was possibly matted lymphadenopathies led to repeat biopsy of the liver mass along with the left upper abdominal mass (Figure 1, 2). Immunohistomorphologic features lead to the diagnosis of a high-grade neuroendocrine carcinoma in both tumors (Figure 3, 4). This patient did not have symptoms of carcinoid syndrome but had an elevated serum chromogranin A which supported the diagnosis of a primary hepatic neuroendocrine cancer. The liver mass was considered unresectable as it encased the superior mesenteric artery, mimicking the hypervascularity of a locally advanced hepatocellular carcinoma. A 68 Ga-DOTATATE PET scan determined the masses to be non DOTATATE-avid, hence palliative salvage chemotherapy was the therapeutic consideration.
Conclusion: Primary hepatic neuroendocrine cancer presenting as hepatocellular carcinoma involves diagnostic and therapeutic dilemmas. Repeated biopsies and advanced imaging should be considered in unusual presentations of HCC and/or advanced HCC with mesenteric lymph node involvement that do not respond to conventional therapies.

Abstract #766

Periampullary choledochoduodenal fistula with ampulla of Vater Carcinoma

Fandy Albert Gosal[1], Luciana Sophie Rotty[1], Bradley Jimmy Waleleng[1]

[1]Gastroenterohepatology, Department of Internal Medicine, Sam Ratulangi University, Manado, Indonesia

Introduction: Most patients with ampullary carcinoma have obstructive jaundice without cholangitis. We experienced a patient with ampullary carcinoma without obstructive jaundice and cholangitis. This case report discusses a patient who presented with main complaint uncomfortable in right upper abdomen dan multiple lithiasis stone in left and right hepatic duct after 3 years post cholecystectomy.
Case report: A 64-year-old male patient was referred with to Hepatology department of Prof R.D. dr. Kandou Hospital in November 2018 with main complaint uncomfortable in right abdomen quadrant. Laboratory result normal in bilirubin and alkaline phosphatase. Ultrasonography results multiple stone in left and right hepatic duct with dilated common bile duct. Endoscopic ultrasonography results dilated common bile duct without stone acoustic. Endoscopic retrograde cholangio-pancreatography revealed a 2-cm polypoid mass located at the ampulla of Vater (duodenal papilla) with choledochoduodenalis fistula. A double pig tail stent was inserted for temporary biliary drainage.
Conclusion: Multiple stone post cholecystectomy is uncommon case, need some evaluation to reveal the causes.

Abstract #968

Double primary malignancies with hepatobiliary carcinoma: Clinical and survival profile of 13 patients in 5 years at a tertiary cancer care centre in India

Rupal Tripathi[1], Swarnima Jaitley[1], Deepak Negi[2], Dc Doval[3]

[1]Department of Research, Rajiv Gandhi Cancer Institute and Research Centre, Delhi, India, [2]Medical Records Department, Rajiv Gandhi Cancer Institute and Research Centre, Delhi, India, [3]Department of Medical Oncology, Rajiv Gandhi Cancer Institute and Research Centre, Delhi, India

Introduction: Patients with a confirmed diagnosis of cancer have a lifetime risk of developing a second primary malignancy. This includes both synchronous and metachronous second primary malignancies.
Objectives: The present study evaluated the clinical and survival profile of patients diagnosed with double primary malignancies with hepatobiliary carcinoma at a tertiary cancer care centre in India.
Methodology: All patients with a confirmed diagnosis of double primary malignancies with hepatobiliary carcinoma during the period 2012–2016 were included in the study. Details of each patient related to their clinical and survival profile were recorded.
Results: Among the 13 enrolled patients (61.5% males), first and second primary hepatobiliary carcinoma was observed in 15.4% and 61.6% patients, respectively, with metastasis in one patient each in both the groups. In 23.1% patients, both the primary malignancies were diagnosed together. The median age at the time of diagnosis of first and second primary malignancies was 59 (32–74 years) and 66 (32–74) years, respectively. Breast, urinary bladder and tongue were the most common sites of first primary malignancy (15.4% each) in cases with hepatobiliary carcinoma as second primary malignancy.

Altogether, 54% patients were dead while the rest were lost to follow up. The median follow up of the patients was 6 (0–240) months.
Conclusion: Early detection and treatment are the key to better management of patients with double primary malignancies. Regular screening and follow up visits may help in the early detection of both synchronous and metachronous double primary malignancies.

Abstract #971

Metastatic Neuroendocrine Tumour masquerading as Orbital Apex Syndrome; a Rare Case with Good Therapeutic Response

Madhumita Premkumar[1], Aswath Venkitaraman[1], Saurabh Mishra[1], Aakash Roy[1], Ashim Das[1]

[1]Postgraduate Institute of Medical Education and Research

Background: We report the rare case of a 53-year old obese hypertensive lady who presented with painful erythematous, progressive swelling of right eye, who received high dose methylprednisolone from ophthalmology services for orbital apex syndrome for 1 year. She was referred to hepatology for evaluation of deranged liver function tests with a presumptive diagnosis of steroid precipitated diabetes and nonalcoholic steatohepatitis.
Results: Her tests revealed normal hemogram, aspartate transaminase (AST) 78 IU/L, alanine transaminase (ALT) 108 IU/L and alkaline phosphatase (ALP) 188 IU/L. Tumour markers revealed an AFP of 3.8 IU/ml, CA 19-9 of 151.8U/ml and CEA of 1.29 ng/ml. Her viral serologies, autoimmune panel, thyroid function, cANCA, pANCA and ACE level were unremarkable. Fibroscan showed a CAP value of 306 dB/m with liver stiffness of 10 kPa. Ultrasound revealed small nodules in the liver and spleen along with grade 1 fatty liver. Computed tomography showed multiple nodules, largest 3 cm, with delayed enhancement in the liver and spleen. Biopsies from the showed monomorphic nesting round to oval tumour cells with eccentric nuclei, stippled chromatin, eosinophilic cytoplasm. Immunohistochemistry showed Synaptophysin and chromogranin positivity with Ki-67 of 4.5%. Consistent with neuroendocrine tumour (NET). DOTA PET scan confirmed the diagnosis of a metastatic NET involving the orbit, liver, spleen and multiple abdominal lymph nodes (Figure 1).
Conclusion: The patient was started on long acting octreotide and everolimus. Over a period of 3 months, chromogranin level has reduced from 244 ng/l to 48 ng/l. This is a rare presentation of NET as orbital apex syndrome.

J03 - Liver metastasis

Abstract #183

Age as a Predictor Factor for Unfavorable Outcome of Liver Associated Colorectal Cancer Metastasis Receiving Targeted Anti VEGF Chemotheraphy: Single Centre Teaching Hospital Experience

Budhi Bagus Ida[1], Metria Bagus Ida[2], Darmawan Ismail Ismail[1], Yuliyarsa Kristanto Kristanto[1], Soewoto Widyanti Widyanti[1]

[1]Department of Surgery Sebelas Maret University, [2]Medical Faculty Sebelas Maret University

Background: The incidence of stage IV (metastasis) colorectal cancer is remain high and has poor 5 year survival rate. Although we already given those patients with targeted chemotherapy regiment such bevacizumab as a palliative treatment, the results was still unfavorable. R status of resection suggested as predictor of recurrence and survival in all group of age. We evaluated, whether age factor has implication on the outcome of metastasis colorectal cancer.
Methods: We evaluated 10 patients of metastasis colorectal cancer (stage IV) whose had been given 4 regiments chometheraphy, FOLFOX 6 (5-Fluorouracyl, Leucovorin, Oxaliplatin) regiment + Bevacizumab (anti-VEGF regiment) from January until December 2017 and only resectable tumor would be included. We would reported the 1 year survival of those patients, included sex, age, R status, tumor site also been evaluated. Patients whose can not completed the chemotherapy has been excluded.
Results: 5 patients were younger than 40 years old, 6 patients were male (60%). Rectum was the commonest site of tumor which has been found in 7 cases, the others were left colon site tumor. 4 patients has R2 resection status, the others were R 0. After 1 year evaluation and chemotheraphy cycle completed, 4 patients were not survived, all of patients whose not survive were young colorectal cancer patients. Gastrointestinal related symptoms were the only side effect during this chemotherapy cycle.
Conclusion: Age factor was one of the unfavorable outcome predictor of liver and pulmonal metastasis colorectal cancer.
Keywords: age, metastasis colorectal cancer, outcome.

Charactheristic		n (patients)
Age	< 40 y o	5
	40 – 60 y o	5
Sex	Male	6
	Female	4
Resection	R 0	6
	R 1	-
	R 2	4
Site	Ascending Colon	-
	Transverse Colon	-
	Descending Colon	3
	Sigmoid Colon	-
	Rectal	7
1 y Survival	Survive	6
	Not Survive	4

Metabolic and Genetic Disease

K01 - Hemochromatosis, Wilson's disease

Abstract #146

Lipid profile changes in Egyptian patients with liver cirrhosis

Tamer Refaat Fouad[1]

[1]National Liver Institute, Menofia University

Background: Lipid changes are common in cirrhotic patients due to the important role of liver in their synthesis and transport. Objective: To test lipid profile changes in Egyptian cirrhotic patients and to examine the effect of liver disease severity on these changes.
Methodology: Hundred twenty-two cirrhotic patients (> 18 years) recruited from liver cirrhosis clinic at the National Liver Institute, University of Menofia were reviewed to identify their lipid profile changes.
Results: Median age was 56 years (40–75 years) and 63% were men. The primary cause of liver disease was hepatitis C; 86.1%. All tested lipid profile variables, except triglycerides, i.e., total cholesterol, high

density lipoprotein (HDL) and low density lipoprotein (LDL) showed a highly significant negative correlation with the liver dysfunction degree tested by MELD and MELD-Na scores (all p values were < 0.0001). Also, after grouping patients in four groups according to their MELD score, we again found that the more hepatic dysfunction was associated with more decline in total cholesterol (the four groups means were 161, 139.7, 130.5 and 103.4; $p < 0.0001$), HDL (52.5, 51, 44.9 and 29.3; $p < 0.0001$) and LDL (100.5, 81.2, 76.5 and 66.9; $p = 0.004$).
Conclusion: Serum total cholesterol, HDL and LDL decrease with liver cirrhosis and their degree of decrease increases with the advancement of liver disease.

Abstract #432

A novel SLC40A1 p.Y333H mutation with gain-of-function of ferroportin: a recurrent cause of hemochromatosis in China

Wei Zhang[1], Anjian Xu[1], Lina Wu[1], Xinyan Zhao[1], Yu Wang[1], Xiaoming Wang[1], Weijia Duan[1], Hong You[1], Jidong Jia[1], Xiaojuan Ou[1], Jian Huang[2]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, [2]Experimental Center, Beijing Friendship Hospital, Capital Medical University

Background and Aims: Hemochromatosis type 4, also known as ferroportin disease (FD), is an autosomal dominant genetic disorder caused by pathogenic mutations in the SLC40A1 gene, which encodes ferroportin 1 (FPN1). We have identified a novel SCL40A1 p.Y333H mutation in our previous study. In the present study, we tried to investigate the frequency and pathogenicity of the SCL40A1 p.Y333H mutation in hemochromatosis in China.
Methods: Patients were analyzed for SCL40A1 p.Y333H as well as mutations in the other classic hemochromatosis-related genes by Sanger sequencing. To analyze iron export capacity of the SLC40A1 p.Y333H mutant, the 293T cells were transfected with the SLC40A1 p.Y333H construct, and then treated with hepcidin after exposure to ferric ammonium citrate. Cellular localization of mutant FPN1, expression of FPN1 and intracellular ferritin were analyzed by immunofluorescence and Western-blotting.
Results: Of 22 unrelated cases with primary iron overload, three cases (3/22, 13.6%) harbored the SLC40A1 p.Y333H, with no missense mutations identified in any other classical hemochromatosis-related genes including HFE, HJV, HAMP, and TFR2. Pedigree analysis showed that three probands and the son of one proband had hemochromatosis of stage 3, while the son of another proband with age of 16 showed elevated transferrin saturation but normal serum ferritin level. In vitro studies showed the mutant p.Y333H ferroportin was resistant to hepcidin, affecting the subsequent internalization and degradation of FPN1, and was associated with ferroportin gain-of-function.
Conclusions: The SLC40A1 p.Y333H mutation is associated with gain-of-function of ferroportin, representing one of the major etiological factors of hemochromatosis in China.

Abstract #540

Genetic causes underlying undiagnosed iron overloaded cases in Han ethnicity

Yue Han[1], Qi Ming Gong[2], Xin Xin Zhang[3]

[1]Research Laboratory of Clinical Virology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine and Sino-French Research Center For Life Sciences And Genomics, Ruijin Hospital, [2]Department of Infectious Diseases, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, [3]Research Laboratory of Clinical Virology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine and Sino-French Research Center For Life Sciences And Genomics, Ruijin Hospital and Translational Medicine Research Center, Ruijin Hospital North, Shanghai Jiao Tong University School of Medicine

Introduction: International guidelines recommend HFE genotyping in iron overloaded patients, based on the fact that C282Y homozygosity for hemochromatosis is seen in 1/250 Caucasians. However, Asian data was scarce.
Objectives: To test the accountability of HFE and other non-HFE genes in Han cases.
Methodology: Liver disease patients with persistently elevated serum ferritin and transferrin saturation from year 2017 to 2018 were enrolled. Exclusion criteria included concurrent infection, anemia of chronic disease, non alcoholic fatty liver disease and alcohol abuse. Other undiagnosed liver disease patients were taken as disease control. Healthy controls were also included. Exome sequencing and Sanger validation were carried out in cases and both controls. Iron-copper genes were analyzed and statistically compared.
Results: Among 352 liver disease patients, 36 iron overloaded cases were initially enrolled, 18 cases were excluded after careful review. 48 liver disease controls and 19 healthy controls were also included. Age and sex were comparable among groups. None of the cases had HFE biallelic mutations. Further analysis demonstrated that non-HFE gene biallelic mutation accounted for 33.3% of the cases. In one severe case, in addition to the non-HFE mutation, copper gene was also mutated. No iron-copper gene mutation was found in the control.
Conclusion: In sharp contrast to the Caucasian situation, non-HFE genes accounted for most of the cases herein studied, while the occurrence of hemochromatosis is low. Copper gene defeats might influence the phenotypic expression. Rather than testing HFE alone, we suggest iron-copper panel screening in undiagnosed iron overloaded liver disease cases in Asian group.

Abstract #994

A Case Report of Noncirrhotic Hyperammonemic Encephalopathy in an AdulT

Eternity Dizon Labio[1], Maria Andrea Macalintal Vergara[1]

[1]Makati Medical Center

Significance: Noncirrhotic hyperammonemia is a rare cause of acute deterioration of mental status where a late-onset inborn error of metabolism (IEM) is an important consideration because therapeutic outcome is promising.
Clinical Presentation: We report a 68 year old male with ventricular tachycardia with an implantable cardioverter defibrillator, chronic kidney disease and subclinical hypothyroidism, with a 1 week history of acute mental status deterioration. His maintenance medications include amiodarone, furosemide, ketoanalogues, carvedilol,

rivaroxaban, levothyroxine. Patient had unsustained regard with no abdominal pathology nor stigmata of chronic liver disease.
Management: Baseline serum ammonia was 209 μg/dL (normal 30–122 μg/dL), seronegative for Hepatitis B, C with adequate synthetic liver function and unremarkable triphasic CT scan of the abdomen. CT scan of the Brain and EEG were compatible with metabolic encephalopathy. Patient slowly improved on hepatic encephalopathic management and upon starting L-ornithine-L-arginine (LOLA), he exhibited sustained wakefulness and sent home stable. Patient was readmitted after a month due to cellulitis causing poor compliance to oral medications with relapse of altered sensorium and hyperammonemia at 190 μg/dL. Once LOLA was resumed and infection resolved, patient regained alertness at serum ammonia of 104 μg/dL and was discharged stable.
Recommendations: Primary causes of noncirrhotic hyperammonemia are aberrations in the urea cycle. Our patient showing a sustained response to ammonia lowering management and LOLA has led us to suspect that hyperammonemia may have accounted for his presentation. Plans for urea cycle enzyme deficiency evaluation is underway.
Keywords: Case report, noncirrhotic hyperammonemia, encephalopathy, inborn error of metabolism

Nonalcoholic Fatty Liver Disease

L01 - Epidemiology and natural history

Abstract #100

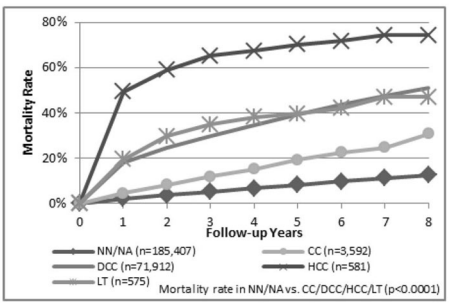
Increased Risk of Mortality in Nonalcoholic Fatty Liver Disease/ Nonalcoholic Steatohepatitis (NAFLD/NASH) Patients: Real-World Analysis of 2007–2015 Medicare Data

Rohit Loomba[1], Jeremy Fraysse[2], Suying Li[3], Stephen Harrison[4]

[1]Univ of California San Diego, San Diego, CA, [2]Gilead Sciences, Inc., Foster City, CA, [3]Chronic Disease Research Group, MN, [4]Pinnacle Clinical Research, San Antonio, TX

Objective: To quantify all-cause-mortality in NAFLD/NASH patients with advanced-liver-disease (ALD): compensated cirrhosis (CC), decompensated cirrhosis (DCC), hepatocellular carcinoma (HCC), and liver transplant (LT) in USA.
Method: We retrospectively sampled 20% of 2007–2015 Medicare-beneficiaries and included NAFLD/NASH-patients (ICD-9/10-CM codes) aged ≥ 18 years, classified as: (1) NAFLD/NASH overall, (2) NAFLD/NASH non-ALD (NN/NA) without diagnosis of ALD, and NAFLD/NASH with (3) CC, (4) DCC, (5) HCC, and (6) LT. Cohorts were not mutually exclusive and maximum follow-up was 8 years. Survival-analyses performed via Kaplan–Meier curves.
Results: 260,950 NAFLD/NASH patients (mean age 67.4 years; 60% female) included 185,407 NN/NA (71.1%), 3592 CC (1.4%), 71,912 DCC (27.6%), 581 HCC (0.2%), and 575 LT (0.2%). In 1 year of follow-up, mortality was up to 20-times significantly higher in ALD patients than in NN/NA ($p < 0.0001$), including 4.0% in NAFLD/NASH overall, 2.1% in NN/NA, 4.5% in CC, 17.8% in DCC, 49.9% in HCC, and 19% in LT (Figure). This trend continued over 8 years, with significantly higher mortality in ALD patients than NN/NA: 26.3% in NAFLD/NASH overall, 12.6% in NN/NA, 30.8% in CC, 51.0% in DCC, 74.4% in HCC, and 47% in LT ($p < 0.0001$ in NN/NA vs. ALD patients). In the NAFLD/NASH overall cohort, 28.9% of patients had at least 1 change to a different liver disease severity cohort over 8 years. For CC patients, 9.1, 17.7, and 52.6% had a diagnosis of DCC over 1, 2, and 8 years, respectively.
Conclusion: Early identification and effective treatments for NAFLD/NASH patients are needed to reduce the rate of mortality.

Figure. NAFLD/NASH Patients Cumulative Incidence of Death by Liver Disease Cohorts



Abstract #104

Clinical Outcomes in biopsy-proven NAFLD Patients from the HEPAmet Spanish Registry

Javier Ampuero[1], Rocío Aller[2], Rocío Gallego-Durán[3], Jesús Bañales[4], Javier Crespo[5], Natalia Mora-Cuadrado[6], Carmelo García-Monzón[7], María Jesús Pareja[8], Eduardo Vilar-Gómez[9], Manuel Romero-Gómez[3]

[1]Hospital Universitario Virgen del Rocio, Sevilla. Instituto de Biomedicina de Sevilla. Ciberehd., [2]Hospital Clínico Universitario de Valladolid. Centro de Investigación de Endocrinología y Nutrición. Universidad de Valladolid., [3]Hospital Universitario Virgen del Rocio, Sevilla. Instituto de Biomedicina de Sevilla. Ciberehd., [4]Department of Liver and Gastrointestinal Diseases, Biodonostia Health Research Institute, Donostia University Hospital, University of the Basque Country (UPV/EHU), Ikerbasque, Ciberehd, San Sebastián, Spain, [5]Hospital Universitario Marqués de Valdecilla, Santander., [6]Hospital Clínico Universitario de Valladolid. Centro de Investigación de Endocrinología y Nutrición. Universidad de Valladolid., [7]Liver Research Unit Hospital Universitario Santa Cristina Instituto de Investigación Sanitaria Princesa Madrid, Spain, [8]Hospital Universitario Juan Ramón Jiménez, Huelva., [9]Instituto Nacional de Gastroenterología, la Habana, Cuba

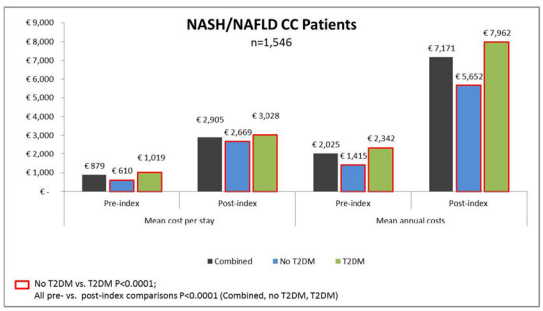
Introduction/Objectives: To examine clinical outcomes in biopsy-proven NAFLD-patients by fibrosis-score.
Methods: This prospective multicentre-study included 568 Spanish patients with biopsy-proven NAFLD from the Spanish Registry HepaMET from 2015 to 2017. NASH/fibrosis was defined according to Steatosis, Activity, and Fibrosis (SAF) score. Outcomes evaluated were: (a) mortality, (b) fibrosis progression (by FIB-4), (c) decompensated cirrhosis, (d) cardiovascular events, (e) chronic kidney disease, (f) development of metabolic comorbidities like type-2-diabetes (T2DM), dyslipidemia (low HDL), arterial hypertension; and (g) neoplastic processes. Mean follow-up time was 2.6 ± 2.7 years.
Results: Half of the study patients were males. Mean age was 50 ± 11 years old and average BMI: 35.7 ± 9 kg/m^2. NASH was identified in 46.7% (265/568) of patients. Fibrosis stage distribution was: F0 36.6% (208/568), F1 26.8% (152/568), F2 18.3% (104/568), F3 11.1% (63/568) and F4 7.2% (41/568). Prevalence of NAFLD-related risk factors was: obesity 56.7% (322/496), hypertension 46.3% (260/562), hypertriglyceridemia 38.8% (215/554), dyslipemia 32.4%

(159/490), and T2DM 31.7% (178/562). During the follow-up period, clinical outcomes were: (a) death 1.2% (7/568), (b) fibrosis progression 12% (39/325), (c) decompensated cirrhosis 12.2% (5/41), (d) cardiovascular events 3.9% (16/417), (e) chronic kidney disease 3.8% (14/368), (f) development of T2DM 5% (19/384), low HDL 22.2% (50/225), hypertriglyceridemia 8.3% (28/339), hypertension 7.3% (22/302), and (g) neoplastic processes 3.2% (18/568) (Table 1).
Conclusion: Over 3% of advanced fibrosis (F3–F4) patients died during the study period. Fibrosis was strongly related to progression to cirrhosis, neoplasms, renal insufficiency, and development of new onset of T2DM. NASH was associated with increased risk of developing dyslipidemia during follow-up.

	Death	CVD events	Kidney disease	Neoplastic processes	DM	Low HDL	Hypertriglyceridemia	AHT
F0	0,5%	2,7%	2%	3,4%	5,3%	17,6%	7,2%	4,5%
F1	0%	5,2%	3,6%	0,7%	3,9%	25,9%	10,2%	8,3%
F2	1,9%	7,8%	3,8%	1,9%	3,1%	28,6%	6,1%	11,4%
F3	4,8%	3,8%	6%	4,8%	16,1%	30,4%	2,8%	4,5%
F4	2,4%	0%	10,3%	12,2%	28,6%	16,7%	20%	17,6%
P	0.041	0.271	0.366	0.030	0.072	0.530	0.155	0.122
LogRank	9.950	5.161	4.309	10.743	8.592	3.170	6.664	7.286
	Death	CVD events	Kidney disease	Neoplastic processes	DM	Low HDL	Hypertriglyceridemia	AHT
F0-2	0,6%	4,2%	2,8%	2,2%	4,4%	21,6%	8%	6,9%
F3-4	3,8%	2,4%	7,6%	7,7%	20%	25,7%	9,8%	10,3%
P	0.040	0.485	0.334	0.030	0.007	0.883	0.911	0.542
LogRank	4.200	0.488	0.993	4.728	7.218	0.022	0.012	0.372
	Death	CVD events	Kidney disease	Neoplastic processes	DM	Low HDL	Hypertriglyceridemia	AHT
No NASH	0,8%	2,7%	2,7%	3%	6,1%	17,1%	9,6%	0%
NASH	1,5%	5,2%	4,4%	2,7%	6%	32,1%	5,8%	2,3%
P	0.149	0.431	0.343	0.885	0.985	0.141	0.465	0.756
LogRank	2.086	0.619	0.898	0.021	0.001	2.172	0.533	0.097

(mean time 22.8 months). Comorbidities were: hypertension (67%), hyperlipidemia (40%), obesity (57%), T2DM (68%). The number of annual hospitalizations-per-patient and length-of-stay significantly increased following CC diagnosis (0.5 ± 1.0 to 2.2 ± 2.6 and 1.5 ± 4.2 to 4.4 ± 6.8 days, respectively, both $P < 0.0001$). Mean cost per hospitalization and annual hospitalization costs significantly increased following CC diagnosis and these costs were higher for T2DM patients.
Conclusion: NAFLD/NASH CC patients experienced > 15% progression to ESLD and > 8% died over study period. Following CC diagnosis, there was a 300% increase in annual number of hospitalizations and > 250% increase in annual hospitalization costs. Improved treatment options are needed to decrease disease progression.

Figure: Mean cost per hospital stay and mean annual hospitalization costs for NASH/NAFLD CC patients pre- and post-index and stratified by T2DM and no T2DM patients



Abstract #105

NAFLD/NASH patients with compensated cirrhosis (CC) had high prevalence of comorbidities, liver disease progression, and number of hospitalizations and costs in France: PMSI database analysis

Jérôme Boursier[1], Cécile Fabron[2], Antoine Lafuma[2], Isabelle Bureau[2]

[1]Angers Hospital University, France, [2]Cemka, Bourg La Reine, France

Introduction/Objectives: Non-alcoholic-fatty-liver-disease (NAFLD)/nonalcoholic steatohepatitis (NASH) can progress to fibrosis, CC, and end stage liver disease (ESLD). This study evaluated liver disease progression and hospitalization costs in French NASH/NAFLD CC patients.
Method: Patients ≥ 18 years with NAFLD/NASH (ICD-10: K76.0, K75.8) were identified from the French National Database (PMSI) between 2009 and 2015. Patients with other causes of liver disease were excluded. All hospitalizations with CC diagnosis were extracted. The index dates were first dates of CC diagnosis in the study period.
Results: 131,898 NAFLD/NASH patients were identified. During the study period, 11.2% (n = 14,822) experienced CC, ESLD, and/or death. For the 1.2% (n = 1546) patients diagnosed with CC in the study period, mean age was 62.4 ± 12.9 years and 54.3% were female. Mean time to progression from NAFLD/NASH to CC was 22.4 months; 16.2% (n = 251) of CC patients progressed to ESLD (mean time 20.0 months); and 8.3% of CC patients (n = 128) died

Abstract #108

High Healthcare Costs in Non-alcoholic Fatty Liver Disease (NAFLD)/Nonalcoholic Steatohepatitis (NASH) Compensated Cirrhosis (CC) Patients with and without Type-2 Diabetes Mellitus (DM) in Germany

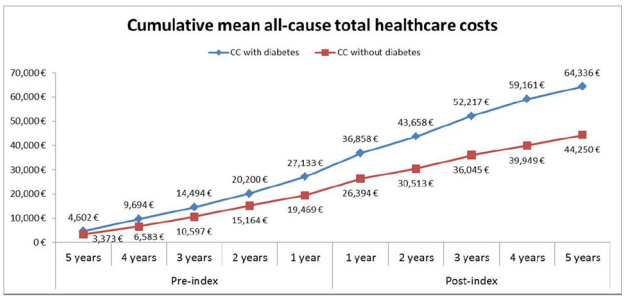
Ali Canbay[1], Julia Altevers[2], Sebastian Braun[3]

[1]Department of Gastroenterology, Hepatology and Infectiology, University of Magdeburg Medical School, [2]Xcenda GmbH, [3]Xcenda GmbH

Introduction/Objectives: This study examined comorbidities and healthcare costs among German NALFD/NASH DM and non-DM patients with CC.
Methods: Patients aged ≥ 18 years with a NAFLD/NASH diagnosis from 2011 to 2016 were identified from the InGef database and stratified by DM status. The first CC diagnosis was the index date. Patients were excluded if they had < 1 year of continuous enrolment (CE) pre- and post-index or had other causes of liver disease.
Results: The study population included 555 NAFLD/NASH CC patients with 1-year of CE pre- and post-index—307 with DM (mean age 68.1 ± 10.9; 56% male) and 248 non-DM (mean age 63.7 ± 13.9; 59% male). NAFLD/NASH CC DM vs. non-DM patients had a high prevalence of comorbidities: hypertension (90% vs. 67%), obesity (53% vs. 25%), and dyslipidaemia (61% vs. 42%). DM patients cumulated €2985,320 and the non-DM patients cumulated €1717,607 all-cause annual healthcare costs in the 1-year post-index period. Prior to cirrhosis index, DM patients had mean annual all-cause healthcare costs of €6934 and non-DM of €4305

($P < 0.001$). Following index, these costs increased to €9724 (DM) and €6926 (non-DM) ($P < 0.001$ for DM vs. non-DM and pre- and post-index). DM patients' cumulative mean annual all-cause total costs increased 137% over a five-year period, from €27,133 (pre-year 1) to €64,336 (year 5), while non-DM patients increased 127% from €19,469 (pre-year 1) to €44,250 (year 5) (Figure).

Conclusions: In the 5 years following cirrhosis diagnosis German NAFLD/NASH DM patients experienced substantial increase in cumulative costs, suggesting a need for improved patient management and treatment options.



Abstract #112

Fibrosis-4 score (FIB-4) provides consistent assessment of healthcare costs and healthcare resource utilization (HCRU) among Nonalcoholic Fatty Liver Disease/Nonalcoholic Steatohepatitis (NAFLD/NASH) patients with advanced fibrosis

Stuart Gordon[1], Burak Ozbay[2], Emily Parker[3], Stephanie Korrer[3], Robert Wong[4]

[1]Henry Ford Hospital, Detroit, MI, [2]Gilead Sciences, Health Economics Outcomes Research (HEOR), Foster City, CA, [3]Optum, Eden Prairie, MN, [4]Division of Gastroenterology and Hepatology, Alameda Health System, Highland Hospital, Oakland, CA

Objectives: To characterize total healthcare costs/HCRU among NAFLD/NASH patients with F3/F4 using FIB-4 index.

Methods: NAFLD/NASH patients ≥ 18 years were identified (ICD-9/10-CM codes) from 2008 to 2016 using Optum Database. Patients with no history of cirrhosis or hepatocellular carcinoma or liver transplant, having AST, ALT and platelet results within 180 days of each other were identified to calculate their FIB-4. A comprehensive FIB-4 based F3/F4 identification algorithm with 3 separate criteria was developed—(Criteria 1 [C1], Criteria 2 [C2], Criteria 3 [C3]. (Table) The first encounter of C1, C2 and C3 were assigned as F3/F4 index dates. Mean annual total healthcare costs/HCRU was calculated through per member per month values in 2016 USD.

Results: Among 91,122 NAFLD/NASH patients with FIB-4 scores, 3251 (3.6%) had F3/F4 based on C1. When using C2, 2482 (2.7%) had F3 and 939 (1.0%) had F4, and when using C3, 363 (0.4%) had F3 and 1463 (1.6%) had F4. The mean age (56–58 years) and sex distribution (45–48% females) were comparable between criteria. A high comorbidity burden was similar across all cohorts—hypertension (57–59%), hyperlipidemia (50–54%), type-2 diabetes (35–37%). Total healthcare costs increased significantly from pre-index to post-index periods for all criteria (Table). The annual mean number of ambulatory visits for F3/F4, F3, and F4 using all criteria indicated a 26%, 21–26% and 29–34% significant increase.

Conclusions: NAFLD/NASH patients experienced an increase in healthcare costs (11–48%) post-development of advanced fibrosis. FIB-4 may be a useful tool in assessing economic and clinical burden in NASH/NAFLD patients.

FIGURE:

F3 and F4 Cohorts with FIB-4 Cut-off values		N	% of total NAFLD/NASH cohorts (N=91,122)	Annual Mean Healthcare Costs		% increase
				Pre-Index	Post-Index	
C1 - F3/F4	Fib-4 > 2.67	3,251	3.6%	$ 28,983	$ 39,658	37%
C2 - F3	2.67 < Fib-4 ≤ 4.12	2,482	2.7%	$ 26,949	$ 34,013	26%
C2 - F4	Fib-4 > 4.12	939	1.0%	$ 37,101	$ 54,852	48%
C3 - F3	3.25 < Fib-4 ≤ 3.5	363	0.4%	$ 21,828	$ 24,150	11%
C3 - F4	Fib-4 > 3.5	1,463	1.6%	$ 33,836	$ 49,591	47%

Abstract #113

Substantial Healthcare Utilization (HCU) and Costs among Nonalcoholic Steatohepatitis (NASH) Patients with Comorbid Diabetes Mellitus (DM): Real-World Analysis of 2007–2015 US Medicare Data

Stuart Gordon[1], Suying Li[2], Yi Peng[3], Xinyue Wang[4], Robert Wong[5]

[1]Henry Ford Hospital, Detroit, MI, [2]Chronic Disease Research Group, MN, [3]Chronic Disease Research Group, MN, [4]Chronic Disease Research Group, MN, [5]Highland Hospital, Oakland, CA

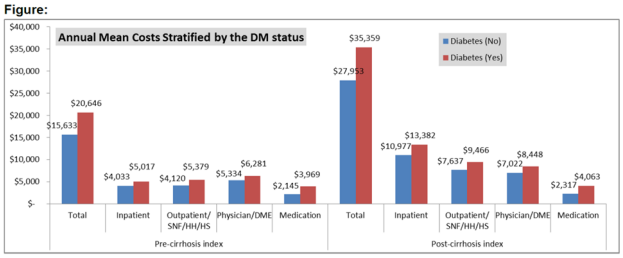
Introduction/Objectives: This study aimed to evaluate the impact of concurrent DM on HCU and costs among NASH patients with CC.

Method: NASH/Non-Alcoholic Fatty Liver Disease (NAFLD) patients with CC aged ≥ 18 years were extracted from 2007 to 2015 US Medicare 20% sample data via ICD codes. Index date was first CC diagnosis. Other liver diseases were excluded. Comorbidities were defined during 6 months pre-index period (pre). HCU and costs were analyzed during 6 months pre- and post-index period (post), and adjusted to per patient (PP) annual values in 2015 USD.

Results: 3775 NASH/NAFLD CC patients with mean age 67.0 (± 10.9) years and 63.3% females were included. More than 98% had ≥ 1 comorbidities: DM (74.8%), hyperlipidemia (91.6%), and hypertension (93.9%). Annual mean visits (inpatient/outpatient/physician) for CC cohort were 33.9 (pre) vs. 40.7 (post) ($p < 0.001$). Total costs for CC cohort was $19,385 (pre) vs. $33,504 (post) ($p < 0.001$). Comorbidity burden was high in both CC DM patients and CC non-DM patients: hypertension 97.1% (DM) and 84.7% (non-DM); hyperlipidemia 95.3% (DM) and 80.7% (non-DM). For CC DM patients, mean inpatient visits were 0.52 (pre) vs. 0.99 (post) ($p < 0.001$), and for CC non-DM patients, mean inpatient visits were 0.37 (pre) vs. 0.76 (post) ($p < 0.001$). The total costs for CC DM patients were $20,646 (pre) vs. $35,359 (post) ($p < 0.001$), and for CC non-DM patients were $15,633 (pre) vs. $27,953 (post) ($p < 0.001$).

Conclusion: Medicare patients with NASH/NAFLD and CC with/without DM reported a high comorbidity and HCU burden, suggesting early identification and effective treatment is needed.

Figure:



Durable medical equipment (DME); Skilled nursing facility (SNF); Home health (HH); Hospice (HS)

Abstract #114

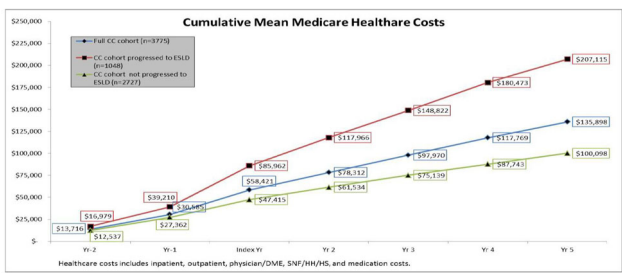
Health care costs are double for Nonalcoholic Fatty Liver Disease (NAFLD)/Nonalcoholic steatohepatitis (NASH) patients with compensated cirrhosis (CC) who progress to end-stage liver disease (ESLD)

Rohit Loomba[1], Suying Li[2], Yi Peng[2], Xinyue Wang[2], Stephen Harrison[3]

[1]Univ of California San Diego, San Diego, CA, [2]Chronic Disease Research Group, MN, [3]Pinnacle Clinical Research, San Antonio, TX

Introduction/Objectives: NAFLD/NASH is one of the most common causes of CC in the USA, which may advance to ESLD. We aimed to characterize long-term economic burden in NAFLD/NASH CC patients who progressed to ESLD compared to those who did not.
Methods: NAFLD/NASH patients with CC aged ≥ 18 years were extracted from the 2007–2015 US Medicare 20% sample data. The first CC diagnosis date was the index date. Medicare costs were estimated during 2-year pre-index and 1-year pre-index with 5 years of annual follow-up post-index. Total 7-year cumulative costs were calculated per patient (PP) annually and adjusted to 2015 USD.
Results: The study identified 3775 NAFLD/NASH patients with CC having 67 (± 10.9) years mean age, 63.3% females and a high comorbidity burden: with DM (74.8%); hyperlipidemia (91.6%); hypertension (93.9%). Cumulative Medicare costs increased 890.8% over 7 years, from $13,716 (2-year pre-index) to $135,898 (5-year post-index). 27.8% (1048) patients progressed to ESLD (progressors) and 72.2% (2727) remained in CC (non-progressors) during the study period. Comorbidity burden was high for both progressors and non-progressors: DM 79.1% (progressors) and 73.2% (non-progressors); hyperlipidemia 92.7% (progressors) and 91.3% (non-progressors); hypertension 96.4% (progressors) and 93.1% (non-progressors). The 7-year cumulative increase in Medicare costs was found to be 1120% for progressors [$16,979 (2-year pre-index) to $207,115 (5-year post-index)] and 698% for non-progressors [$12,537 (2-year pre-index) to $100,098 (5-year post-index)].
Conclusion: NASH/NAFLD Progressors experienced 1120% increase and non-progressors experienced 698% increase in health care costs. This study underscores the need for effective treatments for patients with NAFLD/NASH with CC.

Figure:



Abstract #115

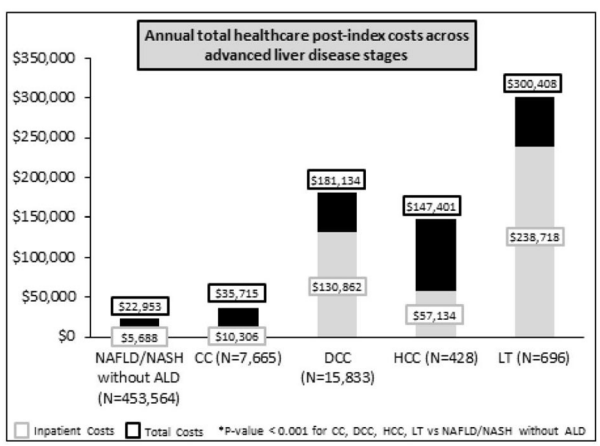
Rising and higher healthcare-resource-utilization (HCRU) and costs of Nonalcoholic Fatty Liver Disease (NAFLD)/ Nonalcoholic Steatohepatitis (NASH) patients with advanced liver disease – a US real-world-analysis

Robert Wong[1], Nandita Kachru[2], Nicole Meyer[3], Stuart Gordon[4]

[1]Division of Gastroenterology and Hepatology, Alameda Health System, Highland Hospital, Oakland, CA, [2]Gilead Sciences, Health Economics Outcomes Research (HEOR), Foster City, CA, [3]Truven Health Analytics, An IBM Company, Cambridge, MA, [4]Henry Ford Hospital, Detroit, MI

Background: NAFLD/NASH may progress to advanced-liver-diseases (ALD): compensated-cirrhosis (CC), decompensated-cirrhosis (DCC), hepatocellular-carcinoma (HCC) and liver-transplant (LT). We characterize the comorbidities, HCRU and costs among NAFLD/NASH ALD patients.
Methods: NAFLD/NASH patients aged ≥ 18 years from 2006 to 2016 were identified retrospectively from a large US commercial and Medicare healthcare claims database using ICD-9/10-CM codes. Following the initial NAFLD/NASH diagnosis, development of ALD was identified using first diagnosis date for each severity cohort (index date). Eligible patients were followed from index date to earliest of 6 months, progression to different cohort, end of coverage, or end of study period. Within each severity cohort, per member per month values were annualized to calculate the mean annual all-cause HCRU/costs as per 2016 USD.
Results: Of 468,017 NAFLD/NASH patients, 1.6% (7665) had CC, 3.4% (15,833) had DCC, 0.09% (428) had HCC, and 0.1% (696) had LT. Comorbidities were high across all ALD cohorts—hypertension (36–50%), hyperlipidemia (36–45%), abdominal pain (34–57%), type 2-diabetes (21–42%). All-cause inpatient (IP) admissions and outpatient (OP) services were significantly higher for NAFLD/NASH patients with ALD than those without ALD ($p < 0.001$), with > 50% of DCC and LT patients requiring IP admissions post diagnosis of liver-stage. Mean annual costs post-index among NAFLD/NASH with ALD patients were more than 150% higher compared to NAFLD/NASH without ALD ($35,715 (CC), $181,134 (DCC), $147,401 (HCC), and $300,408 (LT) vs. $22,953 (NAFLD/NASH without ALD) [$p < 0.001$].
Conclusion: Early identification and effective management among NAFLD/NASH patients are needed to reduce the risk of disease progression and subsequent healthcare costs.

FIGURE:



Abstract #116

Identification and Characterization of Nonalcoholic-Fatty Liver Disease/Nonalcoholic Steatohepatitis (NAFLD/NASH) Patients with Advanced Liver Fibrosis Identified Using Noninvasive-Test (NIT) of Hepatic Fibrosis

Zobair M. Younossi[1], Sanatan Shreay[2], Emily Parker[3], Rohit Loomba[4]

[1]Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, VA, USA and Center For Liver Disease, Department of Medicine, Inova Fairfax Medical Campus, Falls Church, VA, USA, [2]Gilead Sciences, Health Economics Outcomes Research (HEOR), Foster City, CA, [3]Optum, Eden Prairie, MN, [4]University of California San Diego, San Diego, CA

Objective: This study aimed to identify and characterize F3/F4 NAFLD/NASH patients using fibrosis-4 (FIB-4) score.
Method: NAFLD/NASH adults were identified from 2008 to 2016 using Optum-Research-Database. Patients without a history of advanced liver diseases (ALD), who had available AST, ALT and platelet values (180 days of each other) were identified to calculate FIB-4 scores. Based on the literature, F3/F4 patients were identified as > 2.67 to ≤ 4.12 and > 4.12; respectively. The first encounter of F3/F4 was assigned as the index date. Development of CC, DCC, HCC, and LT was identified using their first diagnosis (ICD-9/10-CM) codes.
Results: The algorithm identified 2482 likely NAFLD/NASH patients with F3 (mean age 57 $\pm$ 9 years. Following the presumed F3 NASH patients, 7.3% (n = 182) had an increase in FIB-4 > 4.12 (F4) over a mean duration of 16 months. 4.8% had a diagnosis of ALD, with DCC (3.3%; n = 83) followed by CC (1.2%; n = 30), LT or HCC (0.3%; n = 7). There were 939 likely F4 patients (mean age 56 $\pm$ 10 years). Following these presumed F4 NASH patients, only 3% (n = 28) had a CC diagnosis over mean duration of 12 months, while 7% had a first diagnosis of ESLD: 6.3% (n = 59) DCC patients and 0.7% (n = 7) patients who received a LT over mean duration of 18 months and 3 months, respectively.
Conclusion: Following NAFLD/NASH patients with F3/F4 according to FIB-4 scores for a mean duration of 18 months, 5.7% developed DCC indicating a missed opportunity to timely screen/diagnose/manage prior to ESLD. NITs may be used to risk stratify some patients with NAFLD/NASH.

Abstract #122

Bone mineral density with non-alcoholic liver disease in Korean healthcare center

Min Seong Kim[1], Jun Ha Roh[2]

[1]Department of Internal Medicine, Seoul Joeun Hospital, [2]Department of Orthopaedic Surgery, Seoul Joeun Hospital

Introduction: Low bone mineral density (BMD) has been reported in patients with non-alcoholic liver disease (NAFLD). To investigate bone metabolic characteristics in Korea primary clinic with NAFLD.
Methodology: We examined the medical records of 541 patients who performed Dual energy X-ray absorptiometry (DEXA) from October 2014 to September 2018. We excluded other causes of liver disease such as viral hepatitis and excessive drinking. Abdominal ultrasonography was performed to determine the fatty liver.
Results: In this study, we retrospectively analyzed 130 patients under the criteria. BMD was higher in the NAFLD group ($-$ 2.49 vs $-$ 2.01, p = 0.087). NAFLD was not significantly associated with BMD, adjusted for age, body weight and biochemical markers.
Conclusion: Overall, no significant association between NAFLD and BMD was found in the present study. It is nessesary to approach endocrinologic aspests such as muscle mass, BMI and metabolic syndrome as well as liver function.

Abstract #123 Bone mineral density in Korean healthcare center related with non-alcholic liver disease

Min Seong Kim[1], Jun Ha Roh[2]

[1]Department of Internal Medicine, Seoul Joeun Hospital, [2]Department of Orthopaedic Surgery, Seoul Joeun Hospital

Introduction: Low bone mineral density (BMD) has been reported in patients with non-alcoholic liver disease (NAFLD). To investigate bone metabolic characteristics in Korea primary clinic with NAFLD.
Methodology: We examined the medical records of 541 patients who performed Dual energy X-ray absorptiometry (DEXA) from October 2014 to September 2018. We excluded other causes of liver disease such as viral hepatitis and excessive drinking. Abdominal ultrasonography was performed to determine the fatty liver.
Results: In this study, we retrospectively analyzed 110 patients under the criteria. BMD was higher in the NAFLD group ($-$ 2.49 vs $-$ 2.01, p = 0.087). NAFLD was not significantly associated with BMD, adjusted for age, body weight and biochemical markers.
Conclusion: Overall, no significant association between NAFLD and BMD was found in the present study. However, it is nessesary to approach endocrinologic aspests such as muscle mass and metabolic syndrome as well as liver function.

Abstract #168

Study of Clinical Profile of Non Alcoholic Fatty Liver Disease and its association with Metabolic Syndrome

Zubin Pradeep Sharma[1], Ravindra Sharma[2]

[1]Department of Gastroenterology, Aditya Gastro Centre, [2]Aditya Gastro Centre

Aim: Recent epidemic of obesity, which the WHO reports to be 13.9% has its manifestations not only as increased prevalence of hypertension and diabetes type 2, but its effect on liver has been of such a magnitude that non alcoholic fatty liver disease (NAFLD) is now increasingly being recognized as a major cause of morbidity and mortality. NAFLD effecting about 15–40% of the western population is being considered hepatic manifestation of metabolic syndrome. Our study is aimed to see the association of NAFLD with metabolic syndrome.
Methods: Study conducted on 600 patients, both diagnosed as NAFLD and then graded on ultrasonographic findings. Fibroscan is done to establish the degree of fibrosis in cases of NAFLD. Patients were diagnosed as metabolic syndrome as per NCEP ATP 3 criteria.
Results: Prevalence of metabolic syndrome in our study was 77.4%. The prevalence of type 2 diabetes was 40% and dyslipidemia was found in 74.2% of patients and transaminitis was found in 58.3% of patients. Most of the patients were in the early stages of fatty liver and fibroscan findings were not showing association with the USG grades of fatty liver.
Conclusions: The results of our study are indicative of the findings that patients with NAFLD should be screened for all the components of metabolic syndrome such that the complications of metabolic syndrome can be prevented and managed.

Abstract #196

Impact of tamoxifen on development of NAFLD

Yong Seok Lim[1], Jeong-Ju Yoo[1], Sang Gyune Kim[1], Young Seok Kim[1]

[1]Department of Gastroenterology and Hepatology, Soonchunhyang University Bucheon Hospital, Bucheon, Korea

Background: Tamoxifen (TMX) and aromatase inhibitors (AI) suppress the action of estrogen and are used in the adjuvant therapy of breast cancer patients. Recently, the use of these drugs is increasing, there are still few studies between the incidences of nonalcoholic fatty liver disease (NAFLD) and these drugs. The aim of this study was to investigate the incidence of NAFLD after TMX and AI use.
Methods: This retrospective study included consecutive 702 patients taking TMX or AI more than 2 years between 2007 and 2017 in a tertiary hospital. The occurrence of NAFLD was determined by ultrasound or pre-contrast CT. The primary outcome was the incidence of de novo NAFLD.
Results: 466 patients (66.4%) received TMX, and 236 patients (33.6%) received AI. The incidence or worsening of NAFLD was 35.0% during the median 37 months observational period, which was significantly higher in TMX group than AI group (40.8% vs. 23.7%, $p = 0.039$). In multivariate analysis, TMX increased the risk or severity of NAFLD 1.50 times than AI [hazard ratio (HR) 1.50, 95% confidence interval (CI) 1.11–2.03, $p = 0.009$] as well as body mass index (HR 1.07, 95% CI 1.03–1.11, $p < 0.001$). However, when analyzed for diabetic patients, TMX did not significantly exacerbate NAFLD compared to AI.
Conclusion: TMX significantly increases the incidence of de-novo NAFLD or severity of NAFLD, especially in non-diabetic breast cancer patients. Therefore, when TMX is used for a long-term period, it is necessary to investigate and careful consideration the above side effects.

Abstract #340

Association between smoking and fatty liver: a longitudinal study

Akio Moriya[1], Yoshiaki Iwasaki[2], Eizo Kayashima[3], Tadahiko Mitsumune[3], Masaharu Ando[1]

[1]Department of Gastroenterology, Mitoyo General Hospital, [2]Health Service Center, Okayama University, [3]Junpukai Health Maintenance Center

Background and aims: Smoking is associated with various health problems. After smoking cessation, however, smokers are apt to gain weight and, consequently, may be also at risk of developing fatty liver.
Objectives: To determine the association between smoking and fatty liver.
Methodology: We analyzed those who underwent ultrasonography as a part of the systemic health checkup in 2007 and follow-up studies at least once during 2008–2010. We used logistic regression analysis to explore the association between smoking and fatty liver and generalized estimating equation to estimate the influence of smoking cessation on fatty liver, adjusting for other metabolic syndrome-related factors.
Results: We analyzed 4349 individuals (2623 men and 1726 women) with a total of 13957 observations. At baseline, 1310 cases had fatty liver (30.1%) and 1122 cases were smokers (25.8%). Although the prevalence of fatty liver was higher in smokers than in non-smokers (37.4% vs. 27.6%), the association between smoking and fatty liver was not significant in the cross-sectional study (adjusted odds ratio, 0.96; 95% confidence interval 0.79–1.16). At the latest follow-up, 156 cases (13.9%) out of 1122 smokers at baseline had given up smoking. In those who quitted smoking, the prevalence of fatty liver increased from 35 to 51%. The longitudinal analysis in smokers at baseline indicated that smoking cessation was directly associated with liver (adjusted odds ratio, 1.40; 95% confidence interval 1.11–1.76).
Conclusion: Smoking cessation was a significant risk factor of the incidence of fatty liver independent of obesity and other metabolic syndrome-related factors.

Abstract #414

Burden of Hepatocellular Carcinoma (HCC) and Mortality in Nonalcoholic fatty liver disease/non-alcoholic steatohepatitis NAFLD/NASH in Japan: a Targeted Literature Review

Yoshio Sumida[1], Omar Akhtar[2], Ricardo Lopes[2], Gabriel Wong[3], I-Heng Lee[3], Yuchiro Eguchi[4]

[1]Division of Hepatology and Pancreatology, Department of Internal Medicine, Aichi Medical University, [2]Amaris Ltd., [3]Gilead Sciences, Inc., [4]Liver Center, Saga University Hospital, Saga, Japan, Department of Internal Medicine, Saga University

Introduction: HCC is a significant cause of mortality in Japan. As the treatment and management of viral hepatitis improves, NAFLD and NASH are rapidly becoming the leading causes of HCC in Japan.
Methods: An English and Japanese literature search was conducted in Pubmed, Embase and ICHUSHI Web, identifying 2792 articles, with 192 included for full-text review. 66 studies were extracted.
Results: We found that HCC is the most common incident malignancy among NAFLD/NASH patients, with higher cumulative incidence seen in patients in later fibrotic stages (F3/F4) [10.5–20.0%] While NASH results in less HCC cumulative incidence than HCV (11.30% vs. 30.50%), they display similar deleterious impact on health outcomes including overall mortality rates. HCC frequently arises in NASH patients with advanced fibrosis with prevalence ranging from 10.5 to 20%. NASH-HCC patients experience high rates of recurrence (5-year recurrence rate: 70%). Among Japanese NASH patients, it was found that HCC is the main driver of mortality (40% in 2.7 years in NASH + HCC). With increasing length of follow-up, higher rates of mortality are observed in patients with more severe disease (F3/F4) [25% mortality in NASH F3/F4 vs. 0% in NASH F0–F2 over 7.7 years]. NASH-HCC patients also have a higher post-operative mortality than HCV-HCC patients.
Conclusion: HCC is the most common malignancy and cause of death among NAFLD/NASH patients in Japan, with higher mortality observed among those with advanced disease and complications. Early identification and effective treatments are needed.

Abstract #415

Epidemiology and Comorbidity Burden of Nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) in Japan: a Targeted Literature Review

Yuchiro Eguchi[1], Gabriel Wong[2], I-Heng Lee[2], Omar Akhtar[3], Ricardo Lopes[3], Yoshio Sumida[4]

[1]Liver Center, Saga University Hospital, Saga, Japan, Department of Internal Medicine, Saga University, [2]Gilead Sciences, Inc., [3]Amaris, Ltd., [4]Division of Hepatology and Pancreatology, Department of Internal Medicine, Aichi Medical University

Introduction: NAFLD and NASH represent a growing unmet medical need and an increasingly prevalent cause of end-stage liver disease, HCC and death in Japan.
Methods: An English and Japanese literature search was conducted in Pubmed, Embase and ICHUSHI Web, identifying 2792 articles, with 192 included for full-text review. 66 studies were extracted.
Results: Prevalence of NAFLD in the Japanese population rose from the early 1990s (12.6–12.9%) to the early 2000s (24.6–34.7% of the population). NASH prevalence is estimated to be 1.9–2.7%. NAFLD and NASH are more common among males than females, however females experience more severe disease than males. Older patients also demonstrate more severe disease than younger patients. While obese patients had higher prevalence of NAFLD/NASH, non-obese individuals (BMI < 25) consistently comprised 30 to $> 50\%$ of NAFLD and NASH patients. The evidence shows that despite obesity being linked with worse disease stages, "lean-NASH" also plays an important role in NASH epidemiology. Overall prevalence of comorbidities such as hypertension (13–86%), diabetes mellitus (33–71%), and chronic kidney disease (6–21%) was high in the Japanese NAFLD/NASH population. NAFLD was also a strong predictor of cardiovascular events, with 5% of NAFLD patients experiencing cardiovascular events over 2 years vs. 1% of healthy controls.
Conclusion: NAFLD/NASH is common in the Japanese population and the prevalence of these conditions has tripled in the last two decades. Furthermore, these NAFLD/NASH patients have a high comorbidity burden. Early and efficient identification and safe and effective treatments for NAFLD/NASH patients are urgently needed.

Abstract #416

Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis (NAFLD/NASH) in Japan – a retrospective database analysis of the characteristics of 86,706 patients

Shuji Terai[1], Gabriel Wong[2], I-Heng Lee[2], Aimee Hall[3], Craig Brooks-Rooney[4]

[1]Division of Gastroenterology and Hepatology, Graduate School of Medical and Dental Sciences, Niigata University, [2]Gilead Sciences, Inc., [3]Costello Medical, UK, [4]Costello Medical, Singapore

Introduction/Objectives: To describe demographics and prevalence of major comorbidities in Japanese NASH/NAFLD patients.
Methods: In this retrospective, cross-sectional study, data for NASH/NAFLD patients included in the Medical Data Vision database from Japan from January 2011 to March 2018 were analyzed. Patients with ≥ 1 claim for NASH/NAFLD (ICD-10 K758 and K760), ≥ 18 years old at index date and who had ≥ 6 months continuous enrolment prior to, and ≥ 3 months after, the index date were eligible. Demographic characteristics and major comorbidities were captured ± 6 months around index date; comorbidities were stratified by age group. A subset of patients with height and weight data was analyzed for BMI.
Results: We identified 86,706 NASH/NAFLD patients; 55.54% male with mean $\pm$ SD age 61.21 ± 14.43: 4.79% were 18–34 years old, 9.79% were 35–44 yo, 15.32% were 45–54 yo, 23.48% were 55–64 yo, 28.35% were 65–74 yo and 18.28% were ≥ 75 yo. In the overall population, 19.69% had renal impairment, 33.59% had cardiovascular disease, 43.22% had hyperlipidemia, 51.30% had hypertension and 65.32% had diabetes. The overall prevalence of comorbidities increased with age (Table 1). In 20,552 (23.70% of total study) patients with BMI data available, $> 55\%$ of the NAFLD/NASH population was obese (BMI ≥ 25) (Table 2).
Conclusion: The Japanese NASH/NAFLD patient population is elderly and spans the weight spectrum—almost half are aged ≥ 65 years and BMI ≥ 25—and have a high prevalence of comorbidities, which generally increase with age. Interestingly, a quarter of the population is non-obese, suggesting lean NASH may also play a role in Japan.

Abstract #421

Non-obese NAFLD patients with biopsy for abnormal liver function test has more advanced fibrosis and cirrhosis

Qianyi Wang[1], Hong You[1], Min Wang[1], Xiaojuan Ou[1], Xinyan Zhao[1], Yu Wang[1], Weijia Duan[1], Xiaoming Wang[1], Ping Wang[1], Yameng Sun[1], Yuanyuan Kong[2], Romil Saxena[3], Annette S. H. Gouw[4], Jidong Jia[1], Wu Shanshan[2]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing Key Laboratory of Translational Medicine in Liver Cirrhosis, National Clinical Research Center of Digestive Diseases, Beijing, China, [2]Clinical Epidemiology and EBM Unit, Beijing Friendship Hospital, Capital Medical University; National Clinical Research Center for Digestive Disease, Beijing, China, [3]Indiana University School of Medicine, Department of Pathology and Laboratory Medicine, Virginia Mason Medical Center, Seattle, WA, USA, [4]Department of Pathology Medical Biology, Pathology Section, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Background: Nonalcoholic fatty liver disease (NAFLD) commonly affects subjects with obesity and related metabolic abnormalities, yet non-obese NAFLD is increasingly being recognized although the characteristics of the latter group are less established.
Methods: We investigated the clinical, histological characteristics and the genetic background of 84 obese and non-obese NAFLD patients with biopsy for abnormal liver function test. Both the NAS-CRN and the SAF scoring systems were applied for the histopathological evaluation. Genetic analysis was performed to establish the PNPLA3 and TMS6F2 genotypes.
Results: Of 84 patients with NAFLD, 42.9% were categorized as non-obese (BMI < 25 kg/m^2), who were predominantly females (88.9% vs 52.1%, $P < 0.001$), with higher prevalence of diabetes and higher triglyceride. Histologically, there was a significant higher prevalence of advanced fibrosis and cirrhosis in nonobese patients (58.3% vs 29.2%, $P = 0.013$), as well a trend of higher degree of ballooning ($P = 0.061$). Accordingly, using noninvasive method, LSM value was significantly higher in non-obese group (12.1 kPa vs 8.1 kPa, $P = 0.032$). Higher fasting glucose ($P = 0.034$) and lower serum platelets ($P = 0.026$) were the two independent predictors of advanced fibrosis. The genotypic studies showed no significant differences in the proportion of patients carrying the PNPLA3 G allele between the two groups.
Conclusions: Non-obese NAFLD patients have a female preponderance and more advanced fibrosis and cirrhosis. Liver biopsy is crucial to establish correct diagnosis and evaluate the severity of disease in nonobese patients presented with abnormal LFTs.

Abstract #464

Role of TNF-α and IL-10 in patients with non alcoholic fatty liver disease

Raed Fanoukh Aboqader[1], Saba Muhammed Jassim[2]

[1]Al-Qasim Green University, [2]Babylon Uuniversity/College of Medicine

Introduction: Emerging evidence suggests that the severity of non alcoholic fatty liver disease (NAFLD) may associate with increased serum levels of inflammatory markers as well as decreased concentration of mediators with anti-inflammatory actions, such as tumor necrosis factor alpha (TNF-α) and interleukin (IL) 10, respectively.
Objective: To investigate the role of serum levels of TNF-α and IL-10 in patients with NAFLD.
Methodology: A total number of 49 morbidly obese patients with no history of alcohol were enrolled in this study. Ultrasonography was used to divided patients into two groups: those who had NAFLD and those without NAFLD. Five ml blood was aspirated from each patients and serum sample was used for assessment of TNF-α and IL-10 by ELISA technique T test was used to compare mean and p value less than 0.05 was considered statistically significant.
Results: The results of this study showed that the TNF TNF-α was significantly increased (12.44 ± 3.28 pg/ml) in patients with morbid obesity with NAFLD in comparison to those patients with morbid obesity without NAFLD (7.6 ± 2.86) (P value < 0.05). In addition to that IL-10 was significantly decreased (4.66 ± 1.94 pg/ml) in patients with NAFLD in comparison to those without NAFLD (9.14 ± 2.58 pg/ml) (P value < 0.05).
Conclusions: Both TNF-α and IL-10 might have a role in immunopathogenesis of NAFLD in morbidly obese patients. Further clinical prospective studies are essential to elucidate TNF-α and IL-10 role in NAFLD development in addition to clinical usefulness in the evaluation of morbidly obese patients at higher risk to develop steatosis.

Abstract #468

Physical activities among patients with nonalcoholic fatty liver disease in Hong Kong, Shanghai, Singapore and Malaysia

Vincent Wai Sun Wong[1], George Bb Goh[2], Jiangao Fan[3], Wah Kheong Chan[4], Wai Kay Seto[5], Wan Cheng Chow[2]

[1]The Chinese University of Hong Kong, [2]Singapore General Hospital, [3]Shanghai Jiaotong University, [4]University of Malaya, [5]University of Hong Kong

Introduction: Physical exercise is an important component in the management of nonalcoholic fatty liver disease (NAFLD), but physical activity habits in Asian patients have not been clearly documented. The CAP-Asia study is a multicenter study capturing clinical features and natural history of NAFLD patients across different Asian countries.
Objectives: To compare physical activity patterns among NAFLD patients in four regions.
Methods: Consecutive NAFLD patients attending five clinics underwent clinical assessment and transient elastography (FibroScan) examination, and completed the International Physical Activity Questionnaire. The magnitude of physical activities was classified according to standard recommendations.
Results: The analysis included 446 patients with complete data (Hong Kong, n = 240; Shanghai, n = 61; Singapore, n = 93; Malaysia, n = 52; age 54 ± 11 years; 53% males; body mass index 28.0 ± 4.3 kg/m^2; liver stiffness measurement 6.6 [interquartile range 5.1–8.7] kPa; controlled attenuation parameter 319 [288–344] dB/m). The time spent on vigorous exercise was the lowest in Singapore and Shanghai, and the highest in Malaysia (Table). Patients from all four regions spent similar amount of time on walking and sitting. Importantly, the mean sitting time was 2425 ± 1498 min per week. 30–52% of patients in each region had low physical activity level.
Conclusions: Despite regional variations, a significant proportion of Asian NAFLD patients spends long hours on sitting and have low physical activity level. Healthcare providers should recognize this problem and devise strategies to promote physical activities.

Abstract #503

Algorithms Using Noninvasive Tests Can Accurately Identify Patients with Advanced Fibrosis due to NASH: Data from the STELLAR Clinical Trials

Vincent Wai-Sun Wong[1], Zobair M. Younossi[2], Eric J. Lawitz[3], Naim Alkhouri[4], Manuel Romero-Gomez[5], Takeshi Okanoue[6], Michael Trauner[7], Stephen Djedjos, On Behalf Of Gilead[8], Stephen A. Harrison[9], Zachary Goodman[10], Quentin M. Anstee[11]

[1]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, [2]Inova Fairfax Hospital, [3]Texas Liver Institute, University of Texas Health San Antonio, [4]Texas Liver Institute, University of Texas Health San Antonio, [5]Hospital Universitario Virgen Del Rocio, [6]Saiseikai Suita Hospital, [7]Division of Gastroenterology and Hepatology, Medical University of Vienna, [8]Gilead Sciences, Inc., [9]Pinnacle Clinical Research, [10]Inova Fairfax Hospital, [11]Institute of Cellular Medicine, Newcastle University

Introduction/Objectives: Our goal was to evaluate sequential NIT algorithms to minimize the requirement for biopsy and improve accuracy over use of single tests.
Methodology: Baseline liver biopsies from the STELLAR NASH studies were read using the NASH CRN fibrosis classification and noninvasive fibrosis markers, including Fibrosis-4 (FIB-4) index, Enhanced Liver Fibrosis (ELF) test, and FibroScan® (FS). Test performance was evaluated using AUROCs with fivefold cross-validation repeated 100×. Thresholds were obtained by maximizing specificity given ≥ 85% sensitivity (and vice versa). The cohort was divided into evaluation/validation sets. The evaluation set was further stratified 250× into training and test sets. Optimal thresholds were derived as the average across training sets, and applied sequentially (FIB-4 followed by ELF and/or FS) to the validation set. 3202 patients (71% F3–F4) were included in this interim analysis on 26 July 2018.
Results: While FIB-4, ELF, and FS were able to discriminate advanced fibrosis (AUROCs 0.78, 0.80, and 0.80, respectively), up to 32% of patients experienced indeterminate results. Using STELLAR-derived thresholds, FIB-4 followed by FS or ELF in those with indeterminate FIB-4 values reduced indeterminate results to 13%. Published NIT thresholds yielded similar results. Adding a third test (FIB-4, ELF, then FS) reduced indeterminate results to 8%. Misclassification occurred at rates similar to biopsy (15–21%). Most misclassifications (63–81%) were false negatives; among false positive cases (19–27% of misclassifications), up to 70% had F2 fibrosis.
Conclusion: Using STELLAR-derived thresholds, FIB-4 followed by ELF and/or FS identified patients with NASH-related advanced fibrosis with misclassification rates similar to liver biopsy.

Abstract #523

Comparison of serological panels of fibrosis with transient elastography in patients with non-alcoholic fatty liver disease

Shoukat Ali Samejo[1], Dr Zaigham Abbas[1], Muhammad Asim Sharif[1]

[1]Dr. Ziauddin Hospital Clifton Campus Karachi

Background: Transient elastography measures the liver stiffness and fibrosis but is not available everywhere. The aim of this study was to compare the accuracy of non-patented serum panels; FIB-4 and AST-platelets ration index (APRI) and NAFLD fibrosis score with the transient elastography.
Aims: The aim of this study was to compare the accuracy of non-patented serum panels; FIB-4 and AST-platelets ration index (APRI) and NAFLD fibrosis score with the transient elastography.
Methods: In this prospective study patients who were found to have fatty liver on ultrasound examination of liver were further evaluated by clinical parameters, and serum tests to calculate the fibrosis scores and transient elastography was done. The performance of different scoring systems for fibrosis was judged taking transient elastography as gold standard using area under the receiver operator characteristic curves (AUROC). Only those patients were analyzed who had elasticity IQR/Median value up to 20.
Results: Total number of patients assessed were 192; male 140, age 43.9 ± 12.1. Twenty-three (12%) had diabetes and 16 (8.3%) were hypertensive. AUROC data is given in the table.
Conclusions: Fib-4 and APRI fibrosis tests could not show good accuracy in predicting significant fibrosis when compared to transient elastography as determined by AUROC. NAFLD fibrosis score may be used in predicting significant fibrosis in NAFLD patients where elastography facility is not available.

Abstract #555

Nutritional status and characteristics of energy metabolism in patients with obese and non-obese nonalcoholic fatty liver disease

Qing Ye[1], Tao Han[1]

[1]Department of Gastroenterology and Hepatology, Tianjin Third Central Hospital and The Third Central Clinical College of Tianjin Medical University

Objective: This study aimed to investigate nutritional status and characteristics of energy metabolism in patients with obese and non-obese nonalcoholic fatty liver disease.
Methods: The study enrolled 278 NAFLD patients with moderate to severe fatty liver disease. The patients with NAFLD were divided into the obese group (205 cases with body mass index (BMI) $\geq$ 25), the non-obese group (73 cases with BMI $<$ 25), as well as 50 healthy people as control group. Changes of intracellular water (ICW), extracellular water (ECW), body fat, skeletal muscle, protein content, and visceral fat area (VFA) in those three groups were analyzed. Energy metabolism indicators were measured, including resting energy expenditure (REE), respiratory quotient (RQ), and oxidation rate of three major nutrients (carbohydrate, fat, and protein).
Results: Compared to the control group, ALT, TG, LDL, FBS, and UA increased significantly in the non-obese NAFLD group (all $P < 0.01$). Compared to the obese NAFLD group, LDL and UA increased significantly ($P < 0.01$) in the non-obese NAFLD group. Body composition analysis showed that VFA was significantly higher in the non-obese NAFLD group than that in the control group ($P < 0.01$). Results showed that REE in the non-obese NAFLD group was not statistically different compared to the obese NAFLD group, however, that was significantly higher than that of the control group (both $P < 0.001$).
Conclusion: Patients with obese/non-obese NAFLD had different degrees of nutritional imbalance and disorder of energy metabolism. In addition, LDL, UA, VFA, and REE were the sensitive indicators.

Abstract #563

MACK-3 (Combination of hoMa, Ast, CK18): a promising novel biomarker for fibrotic non-alcoholic steatohepatitis

Kee Huat Chuah[1], Wan Nur Illyana Wan Yusoff[1], Pavai Sthaneshwar[2], Nik Raihan Nik Mustapha[3], Sanjiv Mahadeva[1], Wah Kheong Chan[1]

[1]Gastroenterology and Hepatology Unit, Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, [2]Clinical Diagnostic Laboratory, Department of Pathology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia, [3]Department of Pathology, Hospital Sultanah Bahiyah, Alor Setar, Kedah, Malaysia

Introduction: MACK-3 (combination of hoMa, Ast and CK18) was reported to be a good biomarker for the diagnosis of fibrotic non-alcoholic steatohepatitis (NASH). However, there is no external validation of this test to date.
Aim: To evaluate the accuracy of MACK-3 for the diagnosis of fibrotic NASH.
Methodology: Consecutive adult non-alcoholic fatty liver disease (NAFLD) patients who had liver biopsy in a university hospital were included. MACK-3 was calculated using the online calculator using the following variables: fasting glucose, fasting insulin, aspartate aminotransferase (AST) and cytokeratin 18 (CK18). MACK-3 cut-offs $\leq$ 0.134 and $\geq$ 0.550 were used to predict absence and presence of fibrotic NASH, respectively. Histopathological examination of liver biopsy specimen was reported according to Non-Alcoholic Steatohepatitis (NASH) Clinical Research Network Scoring System.
Results: Data for 196 subjects were analysed. MACK-3 was good for diagnosis of fibrotic NASH (AUROC 0.80), comparable to the Fibrosis-4 index (FIB4) and the NAFLD fibrosis score (NFS) and superior to the BARD score and CK18. MACK-3 was good for diagnosis of active NASH (AUROC 0.81) and was superior to other blood fibrosis tests. The overall accuracy, percentage of subjects in grey zone, sensitivity, specificity, positive predictive value, negative predictive value of MACK-3 for diagnosis of fibrotic NASH was 79.1, 46.9, 100, 43.8, 43.1 and 100%, respectively, while for diagnosis of active NASH was 90.0, 39.2, 84.2, 81.4, 88.9 and 74.5%, respectively.
Conclusion: MACK-3 is promising as a non-invasive test for active NASH and fibrotic NASH and may be useful identify patients who need more aggressive intervention.

Abstract #583

MRE: Non-invasive assessment of liver fibrosis, steatosis, and NASH in biopsy-proven NAFLD patients

Minjin Lee[1], Youngsun Lee[1], Chanuk Lee[1], Sehwa Kim[1], Haein Bak[1], Haseok Lee[1], Sangjun Suh[1], Youngkul Jung[1], Jihoon Kim[1], Yeonseok Seo[1], Hyungjoon Yim[1], Jongeun Yeon[1], Kwansoo Byun[1]

[1]Department of Internal Medicine, Korea University College of Medicine, Seoul, South Korea

In this study, we compared hepatic fibrosis and steatosis using MR imaging and transient elastography (TE) and tried to find non-invasive diagnostic marker for NASH and advanced fibrosis. This is a multicenter prospective study of patients with biopsy-proven NAFLD. The patients were underwent laboratory test, liver biopsy, MRI and TE 6 months before enrollment. MRI examination included mDIXON, MR spectroscopy (MRS), and MR elastography (MRE). TE measured liver stiffness and controlled attenuation parameter (CAP). Ninety-four patients with biopsy-proven NAFLD patients were enrolled from October 2016 to March 2018. Mean age and BMI were 51.29 ± 13.38 years and 29.12 ± 5.64 kg/m^2, respectively. Female was dominant (58, 61.7%) and other co-morbidities were diabetes (n = 37, 39.4%), hypertension (n = 39, 41.5%) and dyslipidemia (n = 28, 29.8%). For diagnosis of advanced fibrosis (stage 3–4), the AUROC of MRE tended to be superior (0.844; 95% CI, 0.748–0.915) comparing with TE (0.787; 95% CI 0.683–0.870) (P = 0.272). For diagnosis of severe steatosis (stage 2–3), CAP (0.706; 95% CI 0.595–0.802) showed lower AUROC compared with mDIXON (0.832; 95% CI 0.733–0.905; P = 0.027) and MRS (0.842; 95% CI 0.744–0.913; P = 0.029), respectively. Age, BMI, DM, dyslipidemia, AST, platelet are associated with NASH in univariate. In multivariate analysis AST, and MRE were significant factor for diagnosis of NASH. MRI (mDIXON, MRS and MRE) tended to identify more severe steatosis and fibrosis compared to TE in patients with biopsy-proven NAFLD. AST and MRE were significant factor for diagnosis of NASH. Non-invasive modalities using platelet, and MRI could be potential tools for diagnosis of NASH.

Abstract #601

Nonalcoholic Fatty Liver Disease is Associated with Coronary Artery Calcification in Asymptomatic Individuals

Kyoung Min Sohn[1]

[1]Gastroenterology, Hansol Hospital

Background and Aims: Nonalcoholic fatty liver disease (NAFLD) is related closely to risk factors for coronary artery disease (CAD), but it is unclear whether NAFLD independently contributes to asymptomatic individuals. Coronary artery calcium (CAC) scanning is the predictor of coronary events. We investigated the association of coronary artery calcification with NAFLD in asymptomatic adults.
Method: This is the cross-sectional study performed in Hansol Hospital Healthcare Center. NAFLD was defined as cases with the typical ultrasonographic findings without excessive alcohol consumption, medications causing hepatic steatosis or other chronic liver diseases. CAC was evaluated using the Agatston method.
Results: We enrolled 312 subjects (mean age 46.8 ± 8.7 years; 60.7% males) without known liver disease or a history of ischemic heart disease. NAFLD was found in 27% of the enrolled 312 subjects and CAC > 100 with moderate-high risk of CAD was found in 10.3% of subjects. Male gender (odds ratios (OR) 2.857; 95% confidence intervals (CI) 1.169–6.147), diabetes mellitus (OR 2.739; 95% CI 1.092–5.638), increased age (OR 1.208; 95% CI 1.071–1.316), and NAFLD (OR 1.862; 95% CI 1.065–3.592) were the independent factors that increased the risk of CAC > 100 in binary logistic regression.
Conclusion: NAFLD is associated with increased coronary artery calcification independent of traditional risk factors. The assessment of CAC may be useful in identifying NAFLD patients at risk of future cardiovascular events even in asymptomatic individuals.

Abstract #602

Noninvasive diagnosis of different fibrosis stages by transient elastography (Fibroscan) in patients with biopsy-proven non-alcoholic fatty liver disease: the quest for optimal cut-off values

Fuad Jafarov[1], Eda Kaya[2], Alev Bakir[3], Haluk Tarik Kani[4], Coskun Ozer Demirtas[4], Aybuke Fatma Sapmaz[5], Asli Ciftaslan[5], Tasnim Alkayyali[5], Lubna Quatranji[5], Yusuf Yilmaz[4]

[1]Department of Internal Medicine, Marmara University, Istanbul, Turkey, [2]Cerrahpasa School of Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey, [3]Department of Biostatistics and Medical Informatics, Halic University, Istanbul, Turkey, [4]Department of Gastroenterology, Marmara University, [5]School of Medicine, Marmara University, Istanbul, Turkey

Introduction: The optimal cut-off values for liver stiffness measurement (LSM) by transient elastography (TE) remain to be established owing to different thresholds in identifying fibrosis stages reported in the literature.
Objectives: Here, we sought to investigate the optimal cut-off values for LSM in identifying significant fibrosis ($F \geq 2$), advanced fibrosis ($F \geq 3$), and cirrhosis ($F = 4$). The thresholds of the current study were compared with those reported in a published pooled analysis.
Methodology: We enrolled 141 biopsy-proven NAFLD patients (mean age 48.13 ± 11.59 years; men/women: 76/65) who were followed-up in our outpatient clinic between 2016 and 2018 (Table 1). LSM was measured on TE by an experienced operator.
Results: Table 1 shows the general characteristics of the patients. The AUROC for the diagnosis of significant fibrosis, advanced fibrosis, and cirrhosis were 0.789 (95% confidence interval [CI], 0.714–0.864), 0.810 (95% CI 0.736–0.884), and 0.911 (95% CI 0.843–0.980), respectively. A LSM cut-off of 11.85 kPa ruled out the presence of advanced fibrosis with a negative predictive value (NPV) of 0.740, whereas a cut-off of 14.15 kPa ruled out the presence of cirrhosis with a NPV of 0.99. The positive predictive values of LSM for the detection of advanced fibrosis and cirrhosis were 0.633 and 0.31, respectively. In light of the relatively high kappa values, our cut-offs were generally compatible with those reported in the literature (Table 2).
Conclusion: Further studies with larger sample sizes are needed to establish the optimal cut-off values for LSM in identifying different stages of hepatic fibrosis.

Abstract #612

Modified AST to Platelet Ratio Index (m-APRI) is better predictor of Advanced Fibrosis in patients with Non-alcoholic Fatty Liver Disease (NAFLD) than other non-invasive scores

Cheryl Yu Wei Huang[1], Jun Jie Seah[1], Jia Wen Kam[2], Tiing Leong Ang[3], Kwong Ming Fock[3], Eng Kiong Teo[3], Jessica Tan[3], Daphne Shih Wen Ang[3], Jeannie Peng Lan Ong[3], Andrew Boon Eu Kwek[3], Malcolm Teck Kiang Tan[3], Yu Jun Wong[3], Rahul Kumar[3]

[1]Yong Loo Lin School of Medicine, National University of Singapore and Department of Gastroenterology and Hepatology, Changi General Hospital, [2]Clinical Trials and Research Unit, Changi General Hospital, [3]Department of Gastroenterology and Hepatology, Changi General Hospital

Introduction: As the prognosis of patients with NAFLD is inversely proportional to stage of liver fibrosis (LF), accurately staging and dichotomizing them into with/without advanced fibrosis (AF) is critical. For this purpose, Transient Elastography (TE) has become the clinical standard and non-invasive scoring systems like m-APRI; APRI; Fibrosis-4 Score (FIB-4); NAFLD Fibrosis Score (NFS) and BARD scores are essential tools in primary care.
Objectives: Compare diagnostic performance of m-APRI, APRI, FIB-4, NFS and BARD in predicting AF in a Singaporean NAFLD cohort.
Methodology: Consecutive (N = 161), NAFLD patients undergoing TE for staging LF were included. The cut-off for AF ($\geq$ F3) on TE was set at 7.9 kPa. Laboratory and anthropometric parameters done within 3 months of TE were used to calculate scores. Diagnostic performances of these scores in predicting AF was then analyzed.
Results: Mean age was 60 $\pm$ 14 years. The mean BMI was 26.8 $\pm$ 4.65 kg/m^2. M-probe was used in 113 patients; 48 needed XL probe for TE. Area under receiver operator characteristic curve of the different scores for AF was: m-APRI: 0.84 (95% CI 0.78–0.91), APRI: 0.80 (95% CI 0.73–0.88), FIB-4: 0.77 (95% CI 0.70–0.85), NFS: 0.77 (95% CI 0.69–0.84) and BARD: 0.65 (95% CI 0.56–0.73). The optimal cut-off of m-APRI for AF was 5.84, which has a sensitivity of 77.8%, specificity 79.8%, PPV 75.7%, NPV: 81.6% and accuracy of 79.0%. The difference between m-APRI and APRI ($p = 0.100$) or NFS ($p = 0.053$) was not significant, but was significant ($p < 0.001$) with FIB-4 ($p = 0.004$) and BARD ($p = 0.000$).
Conclusions: For prediction of AF in patients with NAFLD, m-APRI outperforms APRI, FIB-4, NFS, and BARD in Singaporean NAFLD cohort.

Abstract #614

For prediction of Non-alcoholic Fatty Liver Disease (NAFLD) induced Liver Cirrhosis, modified AST to Platelet Ratio Index (m-APRI) performs better than other non-invasive scores

Cheryl Yu Wei Huang[1], Jun Jie Seah[1], Jia Wen Kam[2], Tiing Leong Ang[2], Kwong Ming Fock[2], Eng Kiong Teo[2], Jessica Tan[2], Daphne Shih Wen Ang[2], Jeannie Peng Lan Ong[2], Andrew Boon Eu Kwek[2], Malcolm Teck Kiang Tan[2], Yu Jun Wong[2], Rahul Kumar[2]

[1]Yong Loo Lin School of Medicine, National University of Singapore and Department of Gastroenterology and Hepatology, Changi General Hospital, [2]Clinical Trials and Research Unit, Changi General Hospital

Introduction: The development of liver cirrhosis (LC) is the most important clinical milestone in the natural history of NAFLD. In clinical practice, Transient Elastography (TE) confirms presence of LC. Non-invasive simple scoring systems like m-APRI; Fibrosis-4 Index (FIB-4); APRI; NAFLD Fibrosis Score (NFS) and BARD score can predict presence of cirrhosis, and are useful decision-making tools in primary care.
Objectives: To compare the diagnostic performance of m-APRI, FIB-4, APRI, NFS and BARD scores in predicting LC in Singaporean NAFLD cohort.
Methodology: Consecutive patients with NAFLD, undergoing TE for staging of liver fibrosis were included. The cut-off point for cirrhosis (F4) on TE was 11.5 kPa. Anthropometric and laboratory tests done within 3 months of TE were used to calculate m-APRI, FIB-4, APRI, NFS and BARD score. Analysis was done to determine the diagnostic performances of these scores in predicting LC.
Results: 161 patients qualified for the study with mean age of 60 $\pm$ 14 years. The mean BMI was 26.8 $\pm$ 4.65 kg/m^2. TE assessment was carried out using M-probe(113 patients) and XL-probe(48 patients). The area under receiver operator characteristic curve for non-invasive scores predicting LC was—m-APRI: 0.83 (95% CI 0.77–0.90), FIB-4: 0.81 (95% CI 0.73–0.88), APRI: 0.78 (95% CI 0.70–0.86), NFS: 0.77 (95% CI 0.69–0.85) and BARD: 0.66 (95% CI 0.57–0.75). The optimal cut-off of m-APRI for cirrhosis was 9, with sensitivity 67.3%, specificity 85.7%, PPV 67.3%, NPV 85.7% and accuracy 80.0%. M-APRI was statistically superior in predicting LC compared to APRI ($p = 0.040$) and BARD ($p = 0.005$), but not FIB-4 ($p = 0.750$) and NFS ($p = 0.220$).
Conclusions: m-APRI outperforms FIB-4, APRI, NFS and BARD scores in predicting liver cirrhosis in patients with NAFLD.

Abstract #628

Enhancing FibroMeter VCTE availability by using a INR/prothrombin index conversion: validation in a Chinese NAFLD population

Grace Lai-Hung Wong[1], Anthony Wing-Hung Chan[2], Paul Cheung-Lung Choi[2], Henry Lik-Yuen Chan[3], Paul Calès[4], Vincent Wai-Sun Wong[3]

[1]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, [2]Department of Anatomical and Cellular Pathology, The Chinese University of Hong Kong, [3]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, [4]Hepato-Gastroenterology Department, University Hospital, Angers

Introduction: FibroMeter VCTE (FMVCTE) is a score combining blood markers and liver stiffness measurement (LSM) by VCTE (Fibroscan) that was shown to outperform other non-invasive fibrosis tests. Until today, FMVCTE calculation required the prothrombin index (PI, % vs normal) which is not widely available. Recently, a direct conversion method from international normalized ratio (INR) to PI was developed to enable using INR.
Objective: The objective was to validate INR use for FMVCTE calculation.
Method: Chinese patients with nonalcoholic fatty liver disease (NAFLD) proven by liver biopsy performed within 1 day from LSM were included. FMVCTE with PI (original formula) or using INR conversion were calculated. Area under receiver operating characteristics curves (AUC) were compared using Delong's test.
Results: 193 NAFLD patients were included. Diagnostic targets, according to Kleiner fibrosis stages, were F2–4: 31%, F3–4: 21% and F4: 10%. FMVCTE calculated with PI and INR had respectively AUC F2–F4: 0.85 (0.79–0.92) and 0.85 (0.79–0.91); AUC F3–F4: 0.91 (0.86–0.97) and 0.91 (0.87–0.96); and AUC F4: 0.96 (0.92–0.99) and 0.94 (0.90–0.98) (p value: 0.05). FMVCTE tests significantly

outperformed FIB4 and NAFLD fibrosis score for all diagnostic targets (p value < 0.05) with, respectively, AUC F2–4: 0.69 (0.60–0.78) and 0.70 (0.62–0.79); AUC F3–F4: 0.68 (0.57–0.79) and 0.69 (0.59–0.77); and AUC F4: 0.80 (0.69–0.91) and 0.80 (0.69–0.90).
Conclusion: FMVCTE calculated with INR, using a conversion formula between PI and INR (freely available on a calculator), provides similar accuracy to FMVCTE calculated with PI which enhances FMVCTE availability worldwide.

Abstract #636

Association of sarcopenia with fibrosis in patients with NAFLD

Tharun Tom Oommen[1], Krishnadas Devadas[1], Atul Hareendran[1], Rathan Cyriac[1], Jijo Varghese[1], Simna Lubina[1]

[1]Department of Medical Gastroenterology, Government Medical College, Thiruvanthapuram, Kerala

Introduction: Non Alcoholic Fatty Liver Disease (NAFLD) is seen in a quarter of the adult population worldwide. Sarcopenia is the loss of muscle mass,strength and performance. Mid arm muscle circumference (MAMC) and Handgrip are measures of muscle mass and strength, respectively. Transient Elastography (TEE) is a validated non invasive estimate of fibrosis in liver disease. It has been postulated that sarcopenia is a risk factor of NAFLD.
Objectives: To assess the correlation of muscle mass and strength with fibrosis in patients with NAFLD.
Methodology: 689 patients with Ultrasound evidence of fatty liver, without significant alcohol use or intake of steatogenic drugs were enrolled into the study. Right mid arm circumference (MAC) and Triceps skin fold thickness (TSF) were measured. MAMC was derived. Handgrips of the dominant and non dominant hands were measured.TEE score was estimated with Fibroscan.TEE was compared with MAMC and handgrip using Chi Square Analysis.
Results: TEE inversely correlated with the hangrips of dominant and non dominant hands (Chi Square = 4.75, p = 0.018 and Chi square = 8.61, p = 0.002, respectively). There was also inverse correlation between TEE and MAMC (Chi square = 15.6, p = 0.001).
Discussion: Postulated mechanisms of sarcopenia leading to fibrosis are (1) Perturbation in the levels of myostatin, a myokine which is thought to activate the hepatic stellate cells and initiate fibrosis. (2) Muscle is a site for glucose disposal in the body, and reduction in muscle mass can lead to worsening of insulin resistance.
Conclusion: There is an inverse correlation between sarcopenia and fibrosis. However prospective studies are required to establish causality.

Abstract #646

Exosomal miRNA analysis for classifying severity of disease in petients with biopsy-proven NAFLD

Young-Sun Lee[1], Sung Won Chang[1], Ha Seok Lee[1], Haein Bak[1], Sehwa Kim[1], Young Kul Jung[1], Ji Hoon Kim[1], Yeon Seok Seo[1], Hyung Joon Yim[1], Jong Eun Yeon[1], Soon Ho Um[1], Kwan Soo Byun[1]

[1]Korea University

Background and Aims: Although determining the exact mechanisms that lead to NAFLD and NASH is important for disease identification, factors that regulate disease progression are largely unknown. In this study, we analyzed serum exosomal miRNA from biopsy-proven NAFLD patients and compared miRNA expression according to disease severity.
Method: Sera were collected from 41 patients with biopsy-proven NAFLD without other chronic liver disease from November 2016 to January 2018. Sera were stored at − 20 °C and thawed for isolation of the exosome. Exosomes were isolated from sera using an exosome isolation kit. Total RNA was extracted from exosomes and microarray was performed.
Results: In microarray analysis, total 2578 miRNAs were identified. We classified patients into non-significant fibrosis group (F0–2, n = 25) and significant fibrosis group (F3–4, n = 16). 40 miRNAs expression were significantly increased in advanced fibrosis group comparing with non-advanced fibrosis group. Among them, miRNA4668 and miRNA3613 were increased more than 8 times in advanced fibrosis group comparing with non-advanced fibrosis group. Whereas 22 miRNAs expression were significantly increased in non-advanced fibrosis group comparing with advanced fibrosis group. When patients were classified into NASH group (n = 19) and non-NASH group (n = 22), 4 miRNAs showed higher expression comparing with NAFL group, whereas 1 miRNAs showed lower expression in NASH group comparing with NAFL group.
Conclusion: miRNA expression analysis showed significant differences according to status of fibrosis, NASH, and inflammation. These results mean miRNA expression might be important factor for disease progression in NALFD patients.

Abstract #676

Non-invasive Tests (NITS) for the Diagnosis of Non-alcoholic Fatty Liver and Steatohepatitis (NAFLD/NASH) with Advanced Fibrosis (AF) in Japan - a Targeted Literature Review

Yuchiro Eguchi[1], Gabriel Wong[2], I-Heng Lee[2], Omar Akhtar[3], Raina Jia[3], Yoshio Sumida[4]

[1]Liver Center, Saga University Hospital and Department of Internal Medicine, Saga University, [2]Gilead Sciences, Inc., [3]Amaris Ltd., [4]Division of Hepatology and Pancreatology, Department of Internal Medicine, Aichi Medical University

Background: Liver biopsy is the standard for fibrosis staging, but is an invasive procedure. Due to an elderly population and rising prevalence of NAFLD/NASH in Japan, there is a need for reliable NITs to accurately predict NASH fibrosis staging and progression.
Methodology: English and Japanese literature search was conducted in Pubmed, Embase and ICHUSHI Web. From 2792 articles, 25 were extracted assessing diagnostic characteristics of NITs in biopsy-proven Japanese NAFLD/NASH patients. Diagnostic characteristics included sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area-under-receiver-operating-characteristic (AUROC).
Results: Serum biomarkers, in particular CK18-F and Mac-2 bp have substantial evidence for diagnosing NASH (Table 1). PPVs reported are high (0.7–0.9, n = 4) and NPVs are low (< 0.7, n = 4), suggesting utility of in distinguishing high risk NASH cases. Type-IV collagen and platelet count have been associated with AF (Table 2). Scoring systems such as APRI, FIB-4 and NAFLD-fibrosis score, have shown utility in predicting AF stages. Trends of high NPV (> 0.8, n = 12) and low PPV (< 0.8, n = 12) implies that these models may exclude patients with low risk of advanced fibrosis from receiving invasive liver biopsies. Imaging-techniques, especially TE (Fibroscan), are useful for diagnosing AF.
Conclusion: FIB-4, NAFLD-Fibrosis score, Type-IV collagen, and Fibroscan have high utility in prediction of NASH AF. These NITs have been extensively studied in Japan and may be useful for in early

annual screening of NASH patients to predict prognosis. In addition, novel screens with high diagnostic accuracy such as the Enhanced Liver Fibrosis (ELF) Score, could be of future value.

Abstract #699

The optimal controlled attenuation parameter cut-offs in hepatic steatosis grade differentiation by transient elastography (Fibroscan) in a sample of biopsy-proven non-alcoholic fatty liver disease patients

Eda Kaya[1], Alev Bakir[2], Aybuke Fatma Sapmaz[3], Tasnim Kayyali[3], Lubna Quatranji[3], Asli Ciftaslan[3], Coskun Ozer Demirtas[4], Haluk Tarik Kani[4], Yusuf Yilmaz[4]

[1]Cerrahpasa School of Medicine, Istanbul University-Cerrahpasa, Istanbul, Turkey, [2]Department of Biostatistics and Medical Informatics, Halic University, Istanbul, Turkey, [3]Marmara University School of Medicine, [4]Marmara University Department Of Gastroenterology

Introduction: Controlled attenuation parameter (CAP) by transient elastography (TE) is an accurate method to detect hepatic steatosis in non-alcoholic fatty liver disease (NAFLD). However, the optimal thresholds of CAP in identifying hepatic steatosis grade are uncertain.
Objectives: Here, we aimed to investigate the optimal thresholds for CAP in identifying moderate (Steatosis grade (S) $\geq$ 2) and severe steatosis (S = 3). We compared the thresholds revealed in our study with those reported in a meta-analysis.
Methodology: We included 140 biopsy-proven NAFLD patients. According to liver histology S = 1, S = 2 and S = 3 were 19 (13.6%), 52 (37.1%) and 69 (49.3%) patients, respectively. CAP was measured by an experienced operator on TE.
Results: The general characteristics of the patients are summarized in Table 1. The optimal cut-offs for identifying moderate and severe steatosis revealed as 319.5 dB/m for both of them, and the AUROC 0.677 (95% confidence interval [CI] 0.548–0.807) and 0623 (95% CI 0.530–0.715), respectively. The CAP cut-off of 319.5 dB/m excluded the presence of moderate steatosis with a negative predictive value (NPV) of 0.283, whereas the presence of severe steatosis with a NPV of 0.633. The positive predictive values of CAP for the detection of moderate and severe steatosis were 0.950 and 0.600, respectively. Overall, our cut-off was more compatible considering relatively higher Kappa values. However, it could not differentiate moderate and severe steatosis (Table 2).
Conclusion: Despite good diagnostic performance of CAP further studies are needed to establish optimal cut-offs for differentiation of steatosis grade.

Abstract #705

Prescription of statin and treatment targets in non-alcoholic fatty liver disease patients

Stanley Khoo[1], Vincent Wai-Sun Wong[2], George Goh[3], Jiangao Fan[4], Wah Kheong Chan[1], Wai-Kay Seto[5], Wan Cheng Chow[3]

[1]University of Malaya, [2]The Chinese University of Hong Kong, [3]Singapore General Hospital, [4]Shanghai Jiaotong University School of Medicine, [5]The University of Hong Kong

Introduction: Cardiovascular disease is the leading cause of mortality in non-alcoholic fatty liver disease (NAFLD) patients. NAFLD patients often have dyslipidemia, and optimal treatment of dyslipidemia lowers the risk of cardiovascular disease. We aimed to study the prescription of statin and treatment targets in NAFLD patients.
Methods: Consecutive NAFLD patients attending five clinics in Asia were included in this study. The 10-year cardiovascular disease risk was calculated based on the Framingham Heart Study, and patients were categorized as moderate, high or very high risk for cardiovascular disease based on the American Association of Clinical Endocrinologist 2017 Guidelines. The low-density lipoprotein treatment goal for the risk groups was 3.4 mmol/l, 2.6 mmol/l and 1.8 mmol/l, respectively.
Results: The data for 439 patients were analyzed (mean age 56 $\pm$ 11 years, 51.7% males). Dyslipidemia was seen in 58.8% (258/439) but only 18.9% (83/439) were on statin. The percentage of patients who were at moderate, high and very high risk for cardiovascular disease was 42.8% (188/439), 26.9% (118/439) and 30.3% (133/439), respectively. Among patients who were on statin, 48.2% (40/83) did not achieve treatment target. Among patients who were not on statin, 49.2% (175/356) should be receiving statin. The percentages of patients who did not achieve treatment target and who should be receiving statin according to their cardiovascular disease risk are shown in Table 1.
Conclusion: This study highlights the suboptimal treatment of dyslipidemia in NAFLD patients and call for action to improve the treatment of dyslipidemia in NAFLD patients.

Abstract #709

Severity of NAFLD across Asian countries and predictors of severe disease

Chao Sun[1], Wah-Kheong Chan[2], George Boon-Bee Goh[3], Wan-Cheng Chow[3], Wai-Kay Seto[4], Jian-Gao Fan[5], Vincent Wai-Sun Wong[6]

[1]Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, [2]University of Malaya, [3]Singapore General Hospital, [4]The University of Hong Kong, [5]Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, [6]The Chinese University of Hong Kong

Introduction: Since liver fibrosis has emerged as the strongest predictor of liver-related mortality in patients with non-alcoholic fatty liver disease (NAFLD), early prediction and detection of hepatic fibrosis by non-invasive approaches are important.
Objectives: Our study aimed to assess the severity of NAFLD and predictors of significant or advanced fibrosis in NAFLD patients across Asia countries.
Methodology: We prospectively recruited 206 adult patients who underwent liver biopsy and FibroScan for NAFLD from five Asian centers between July 2016 and June 2018. The stage of fibrosis and routine laboratory values were evaluated with univariable and multivariable analyses.
Results: The percentage of significant fibrosis (F2–4) and advanced fibrosis (F3–4) was 32% (65/206) and 19% (40/206), respectively. By univariate analysis, waist circumference, body mass index (BMI), aspartate transaminase (AST), AST/alanine aminotransferase (ALT), fasting plasma glucose, glycosylated hemoglobin A1c (HbA1c) and liver stiffness measurement (LSM) were associated with significant or advanced fibrosis ($P < 0.05$). By multivariable analysis, diabetes, BMI, AST or AST/ALT and low platelet count were independently associated with significant or advanced fibrosis (Table 1, 2).
Conclusion: NAFLD patients with diabetes, higher BMI, AST or AST/ALT and lower platelet count were likely to have significant or

advanced liver fibrosis, who might require treatment and intensive follow-up to halt the development of cirrhosis.

Abstract #728

Reality Check: Prevalence of Non-Alcoholic Fatty Liver Disease in a Third-World Country

Enrik John Torres Aguila[1], Juliet Lingat Gopez-Cervantes[1], Ian Homer Yee Cua[1]

[1]St. Luke's Medical Center Global City

Introduction: Non-alcoholic fatty liver disease (NAFLD) is now recognized as one of the most common liver disease worldwide. It has a prevalence of 25% in Asia like many western countries. A previous local study in the Philippine General Hospital 10 years ago showed prevalence of NAFLD at 12.2%. With an increasing prevalence of obesity, diabetes and hypertension in the Philippines, we expect the population of NAFLD patients to increase as well.
Methodology: Patients diagnosed with NAFLD from 2010 to 2017 were identified from the databank of the Liver Disease and Transplant Center of St. Luke's Medical Center (SLMC) Quezon City and Global City. A descriptive analysis was done on the demographic profile of these patients.
Results: NAFLD was diagnosed in 971 (19.31%) out of 5028 patients with liver disease based on the databank. There has been an increasing trend with time. NAFLD serves as the second most common liver disease behind from hepatitis B infection. 56.6% were males while 43.3% were females with a mean age of 60 years and an increasing incidence starting at 40 years of age. In terms of treatment, majority were on lifestyle modification followed by statin therapy.
Conclusion: The prevalence of NAFLD at SLMC is 19.31% and is the second most common liver disease in an 8-year period. Male sex and age > 40 years appear to be characteristic features of our NAFLD patients. Prevalence appears to be increasing with time. The increasing cases of preventable chronic diseases could explain this pattern.

Abstract #729

Association between the components of metabolic syndrome and histological severities in patients with non-alcoholic fatty liver disease

Rui-Xu Yang[1], Wah-Kheong Chan[2], George Boon-Bee Goh[3], Wan-Cheng Chow[3], Wai-Kay Seto[4], Jian-Gao Fan[1], Vincent Wai-Sun Wong[5]

[1]Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China, [2]University of Malaya, Kuala Lumpur, Malaysia, [3]Singapore General Hospital, Singapore, [4]The University of Hong Kong, Hong Kong, [5]The Chinese University of Hong Kong, Hong Kong

Introduction and objectives: Metabolic syndrome (MetS) and its components are closely associated with nonalcoholic fatty liver disease (NAFLD). NAFLD patients with MetS were at high risk of liver histological progression. This study is aimed to analyze each MetS component and its relation to the histologic severity of NAFLD.
Methodology: Consecutive biopsy-proven NAFLD patients in five centers were included in this study. The diagnosis of MetS was based on the 2005 IDF consensus. The histological severities of NAFLD was evaluated by steatosis grade, presence of NASH and significant fibrosis. MetS components (central obesity, type 2 diabetes (T2DM), hypertension, dyslipidemia) and other comorbidities (obstructive sleep apnea, ischemic heart disease and stroke) were analyzed to elucidate the association of comorbidities and the severity of NAFLD.
Results: A total of 206 NAFLD patients with liver biopsy were enrolled in this study (109 non-NASH, 97 (47.1%) NASH, 65 (31.6%) with significant fibrosis). Within all the MetS and comorbidities, dyslipidemia was associated with higher grade of steatosis in NAFLD patients ($P = 0.033$). NAFLD patients with T2DM had higher proportion of NASH ($P = 0.017$) and significant fibrosis ($P = 0.000$). Most diabetic patients were under treatment (120 in 129 T2DM). Regardless of past history of T2DM, elevation of fasting plasma glucose (≥ 5.6 mmol/L) at baseline was associated with NASH and significant fibrosis.
Conclusion: Among the MetS components, dyslipidemia was associated with the steatosis in NAFLD development. However, the T2DM and the glucose control might be more essential in the progression of NASH and significant fibrosis.

Abstract #752

Factors Associated with Weight Loss on Follow-up of Patients with Nonalcoholic Fatty Liver Disease

Ann Margaret Caraan Navarroza[1], Maria Roselle Evangelista Guzman[1], Jason Yu Lim[1], Stephen Ng Wong[1]

[1]University of Sto. Tomas Hospital

Background: Nonalcoholic fatty liver disease (NAFLD) patients are expected to have poor compliance to weight loss outside of clinical trials. We aimed to determine the proportion of NAFLD patients who lost weight on follow-up and the factors associated with it.
Methods: Consecutive patients diagnosed with NAFLD on ultrasound at a single outpatient clinic from February 2007 to January 2017 with at least 1 follow-up visit were included. Patients with significant alcohol intake, secondary causes of NAFLD and hepatocellular carcinoma were excluded. Patients were asked to lose weight and follow-up every 6–12 months. Independent t test was used for continuous and Chi square for categorical variables.
Results: Included were 302(72.6%) overweight/obese and 114(27.4%) underweight/normal patients. After a median follow-up of 11 months, there was no difference in the proportion of patients who lost (38.7% vs 30.7%), maintained (29.1% vs. 34.2%), or gained weight (32.1% vs. 35.1%) in the overweight/obese and underweight/normal groups ($p = 0.304$). An average of $4.3 + 4.07\%$ change was seen in those who lost weight while $6.01 + 49.1\%$ change was seen in those who gained weight. Patients with diabetes (43.5% vs. 30.7%; $p = 0.008$), coronary artery/cerebrovascular diseases (48.6% vs. 34%; $p = 0.022$), lower LDL ($121.6 + 42.2$ vs. $128.6 + 40.7$; $p = 0.101$) and higher number of follow-ups ($5.08 + 4.2$ vs. $4.06 + 3.3$; $p = 0.012$) were more likely to lose weight. On multivariate analysis, only diabetes (OR = 1.7; 95% CI = 2.59–1.15; $p = 0.008$) and higher number of follow-ups (OR = 1.07; 95% CI = 1.13–1.01; $p = 0.011$) were independent predictors of weight loss.
Conclusions: Despite frequent reminders to lose weight, 63.5% of NAFLD patients gained/maintained weight instead. Surprisingly, none of the liver parameters influenced weight change. Instead, the presence of comorbid metabolic conditions strongly influenced weight loss and suggests a higher incentive level to lose weight in patients with comorbid conditions.

Abstract #760

Comparison of Lean versus Overweight/obese Patients with Nonalcoholic Fatty Liver Disease

Ann Margaret Caraan Navarroza[1], Stephen Ng Wong[2], Maria Roselle Evangelista Guzman[3], Jason Yu Lim[4]

[1]University of Sto. Tomas Hospital

Compare the clinical and biochemical profiles of normal/underweight (lean) versus overweight/obese NAFLD patients. Methods: Consecutive patients diagnosed with NAFLD on ultrasound in a single outpatient hepatology clinic from February 2007 to January 2017 were included. Patients with significant alcohol intake, secondary causes of steatosis, and incomplete data were excluded. Demographics, liver enzymes, albumin, International normalized ratio (INR), hepatitis and metabolic biochemical profiles were recorded. Normal alanine aminotransferase (ALT) was pegged at 24 IU/mL and 19 IU/mL for males and females, respectively. Logistic regression was used to determine independent predictors. Results: We included 663 patients (58.1% male). Most patients were overweight/obese(74.2%) while 82.1% had an elevated ALT. Cirrhosis or hepatocellular carcinoma (HCC) were already present on initial consult in 4.4% and 5.9%, respectively. Concomitant hepatitis B was equally common in patients with and without cirrhosis (20.7% vs. 17.5%; $p = 0.660$) or HCC (17.9% vs. 12.8%, $p = 0.415$). Compared to Lean NAFLD patients, overweight/obese patients were more likely to be younger ($50.9 + 14.2$ vs. $54.6 + 14.2$; $p = 0.004$), and have higher ALT ($57 + 52.8$ vs. $43.5 + 36.4$, $p < 0.0001$) and INR($1.9 + 9.3$ vs. $0.98 + 0.12$, $p = 0.025$). Overweight/obese patients were also more likely to have DM (49.8% vs. 33.9%; $p < 0.0001$), hypertension (58.3% vs 47.1%, $p = 0.007$), dyslipidemia (73.6% vs 63.2%; $p = 0.011$) and metabolic syndrome (63.6% vs 36.8%; $p < 0.0001$), and less likely to be cirrhotic (3.3% vs. 7.6%; $p = 0.0265$). Independent factors associated with over weightedness and obesity in NAFLD patients were younger age (OR = 1.02; 95% Cl = 1.02–1.003; $p = 0.014$), metabolic syndrome (OR = 0.358; 95% Cl = 0.5232–0.245; $p < 0.0001$), lower HDL (OR = 1.02; 95% Cl = 1.029–1.005; $p = 0.005$), and absence of cirrhosis (OR = 2.493; 95% Cl = 5.586–1.116; $p = 0.026$). Conclusions: Majority of NAFLD patients are overweight/obese, with elevated ALT, and with a significant proportion (7.8%) already with cirrhosis/HCC on initial presentation. Overweight/obese NAFLD patients are more likely to have metabolic derangements and its consequences compared to lean patients.

Abstract #869

Feasibility and stability of liver biopsy before treatment for preclinical nonalcoholic fatty liver studies

Hyunwoo Oh[1], Dae Won Jun[1]

[1]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea

Background: The heterogeneity of histological findings in preclinical diet-induced nonalcoholic fatty liver disease (NAFLD) animal models is highly challenging. Here, we aimed to evaluate the feasibility and stability of repeated liver biopsy in NAFLD animal models.
Methods: Heterogeneity of diet-induced NAFLD was evaluated at different time points in 52 high-fat diet (HFD), 35 methionine choline–deficiency diet (MCD), and 166 Western diet (WD) induced NAFLD mice. Serial liver biopsies (left lateral, right medial, and left medial lobes) were performed monthly for up to 3 months. Mortality rates and changes in food intake, body weight, and liver enzymes were assessed.
Results: At 12 weeks, of the HFD animals, 14% and 30% did not develop steatosis and lobular inflammation, respectively; of the MCD animals, 7% did not develop lobular inflammation; and of the WD animals, 14% and 51% did not develop steatosis and lobular inflammation, respectively. The mortality rate of repeated liver biopsy was 1.62% (2/123 mice died). Repeated liver biopsy can be used to trace disease progression. Although body weight, food intake, and liver enzymes slightly changed after biopsy, all recovered within a week. Repeated liver biopsy did not affect the degrees of inflammation and steatosis of the other liver lobes.
Conclusion: The diet-induced NAFLD models were quite heterogeneous. Our results suggest that the repeated liver biopsy before treatment was applicable and stable in this NAFLD animal study.

Abstract #897

Saga of an Outlier: Lean Nonalcoholic Fatty Liver Disease in Urban, Population of Karachi, Pakistan

Amna Subhan Butt[1], Saeed Hamid[2], Asma Ahmed[2], Waseem Memon[2], Safia Awan[2]

[1]Section of Gastroenterology, Department of Medicine, The Aga Khan University Hospital, Karachi, Pakistan, [2]Aga Khan University Hospital, Karachi, Pakistan

Background: Lean NAFLD is unique where in the absence of obesity and unrecognized traditional risk factors, diagnosis is either get delayed or even overlooked; hence resulting in compromised effectiveness or complete absence of required treatment. We aim to investigate the prevalence of lean NAFLD and to compare the clinical, metabolic characteristics of lean and obese NAFLD in urban, adult population of Karachi, Pakistan.
Methods: This was population based cross-sectional study piggyback with a large community based trial "Pakistan Diabetes Prevention Programme" conducted in collaboration with the University of Helsinki in "Karachi", Pakistan during 2013–2016. Approximately 20,000 residents of Karachi were screened for diabetes using systematic sampling. Individuals aged 35–75 years, having Indian Diabetes Risk Score score ≥ 60 were enrolled. Ultrasound liver was performed by an experienced sonologist to identify NAFLD. Anthropometric measurements, laboratory investigations were carried out. Lean NAFLD was defined if BMI was < 25 kg/m^2. Obese NAFLD defined if BMI was ≥ 25 kg/m^2. The study was funded by IDF, URC, AKUH, Pakistan.
Results: Out of 1225 individuals 741(60.5%) had NAFLD. Lean NAFLD was found in 128(17.2%). Comparing lean NAFLD with obese NAFLD higher proportion of males, smaller waist circumferences and lower ranges of metabolic factors were found in lean NAFLD (Table 1). The risk estimates for lean NAFLD were higher among smokers, subjects having larger waist circumference, HTN, elevated LDL and ALT (Table 2).
Conclusion: Lean NAFLD common in South Asian urban community of Pakistan. In the absence of significant metabolic derangement, early detection of lean NAFLD is challenging.

Abstract #903

Demographic and Metabolic Profiles of Non-alcoholic Fatty Liver Disease among Lean Filipino Patients: A Retrospective Cross-Sectional Study

Angelique Elga Cano Lo[1], Juliet Lingat Gopez-Cervantes[1]

[1]St. Luke's Medical Center, Global City

Introduction: Non-alcoholic fatty liver disease (NAFLD) is now the most common chronic liver disease in the world [1]. Obesity is considered a key player in its development [2]. However, NAFLD has been reported in lean subjects. If we are able to establish the association of certain levels of blood chemistries to its development, then clinicians would be able to do measures for prevention.
Objectives: This study aims to establish the demographic and metabolic profiles of non-alcoholic fatty liver disease among lean Filipino patients.
Methodology: This was a descriptive, cross-sectional study. All lean patients diagnosed to have fatty liver but with normal metabolic profile were included. The primary endpoint was to establish an association between the metabolic parameters and the development of fatty liver among lean population. Crude odds ratio and the corresponding 95% confidence interval from exact logistic regression was computed to determine the factors associated with NAFLD.
Results: Thirty-three lean patients were included, 28 of whom had NAFLD and 5 without. Overall, we had insufficient evidence to determine a significant association between age, sex, BMI, and blood chemistries with the presence of NAFLD among lean patients.
Conclusion: There is insufficient evidence to establish a significant association between the metabolic parameters and presence of NAFLD among lean Filipino patients with normal blood chemistries. However, large, comparative studies are still needed and further investigation with genetic testing for PNPLA3 may be warranted to establish etiology.

Abstract #922

Ophthalmic Complications of Non Alcoholic Fatty Liver disease: A cross sectional Observational clinical study

Patrick Basu[1], Nimy John[2], Mark Aloysius[3]

[1]Weill Cornell Medicine, [2]St. Vincent Hospital, [3]James J. Peters VA Medical Center

Objective: Non Alcoholic Fatty Liver disease (NAFLD) is a global epidemic with a multifactorial heterogeneous etiology. Insulin resistance is the hallmark of NAFLD. Multi-organ morbidities including Cardiac complications, Atheroma formations, Sleep Apnea, Degenerative joint disease (DJD), and Liver complications are well recognized. This study reveals a unique ocular complication of NAFLD—Premature Cataract formation in a Non-Diabetic cohort of NAFLD.
Method: Four Hundred (n = 400) NAFLD patients were initially recruited from age group 50–60 with BMI > 30%. The mean HbA1c was less than 7.1. The mean weekly Alcohol consumption was less than 30 g. Patients underwent Serum NAFLD score analysis, abdomen sonogram, ECHO, Carotid Doppler for atheroma Volume, Fibroscan for Base Line fibrosis and Ophthalmic Evaluations. All patients were placed on strict regulated Weight loss and exercise for 6 months. All patients had measurement of Leptin, Adiponectin, Retinol Binding Protein 4, Triglyceride, HOMA score, TNF Alfa levels prior to the study. Patients also underwent a sleep study to look for sleep apnea.

Table 1
Results: Table 2
Conclusion: Our study showed that NAFLD is associated with early development of Cataract formation in NAFLD, especially in the subgroup of high Inflammatory markers (High levels of TNF Alfa and Leptin, Sleep apnea, High Triglyceride levels, Elevated HOMA score and Moderate Atheroma load with normal Glucose Homeostasis). Patients with NAFLD will benefit with regular ophthalmologic evaluations to screen for premature cataract development.

Abstract #929

Non-alcoholic fatty liver disease and thyroid function in adult patients

Sakkarin Chirapongsathorn[1], Tassimon Pattaropong [2]

[1]Division of Gastroenterology and Hepatology, Phramongkutklao Hospital, College of Medicine, [2]Division of Endocrinology, Department of Medicine, Chiang Mai University

Background: A possible association between nonalcoholic fatty liver disease (NAFLD) and hypothyroidism has been suggested. The recognized link between hypothyroidism and elements of the metabolic syndrome may explain this association.
Aim: The purpose of this study was to determine the prevalence of hypothyroidism in a cohort of patients with NAFLD and analyze the potential factors associated with hypothyroidism in this patient population.
Methods: Two hundred and four patients with diagnosis of NAFLD by biopsy-proven or other criteria attending hepatology clinics at the Phramongkutklao hospital between October 2014 and June 2016.
Result: The number of data showed 206 cases diagnosed NAFLD but found to be hypothyroid only 2 cases, so the prevalence was 1%. The risk factors of NAFLD are diabetes mellitus 43.2%, hypertension 72.82%, dyslipidemia 80.1%. Mean of BMI was 28.44 ± 4.81 and obesity was found 75% of case that support the evidence base these were risk factors for NAFLD.
Conclusions: The study found that the incidence of hypothyroid in NAFLD patient was 1% unlike the previous research and might not support the hypothesis that hypothyroid was one of the risk factor. However we should increased sample sizes and added controlled-group in further research.

Abstract #936

Nonalcoholic fatty liver disease is associated with cardiac remodeling and LV diastolic dysfunction among non-obese diabetic patients

Jirran Caluscusin Cabatingan[1], Oscar Perez Payawal[2]

[1]Fatima University Medical Center

Objective: The aim of this study is to evaluate whether nonalcoholic fatty liver disease (NAFLD), being an independent factor, is associated with diastolic dysfunction and cardiac remodeling among non-obese type 2 diabetes mellitus (DM).
Methods: A total of 97 filipino, non-obese, type 2 diabetic patients, were gathered for this study. Of the 97 patients, 50 of them were diagnosed with NAFLD using abdominal ultrasonography, and 47 having none. All subjects then, underwent tissue doppler echocardiography to screen the presence of diastolic dysfunction and cardiac remodeling.

Results: Results show that non-obese diabetics with NAFLD is 7.24 times more likely to end up with abnormal LV End diastolic volume as compared to those with normal liver ($p = 0.00028$). Likewise, those with NAFLD is 3.37 times more likely to end up with abnormal values of LV mass index ($p = 0.0061$). Similarly, those with NAFLD is 7.88 times more likely to end up with either moderate or severe values of E/A Ratio. Lastly, those with NAFLD is 3 times more likely to have abnormal E/e' ratio as compared to those with normal liver.
Conclusion: NAFLD in non-obese diabetic patients displayed features of cardiac remodeling and LV diastolic dysfunction.

Abstract #975

Surveillance of Carotid Atherosclerosis and Coronary Artery Stenosis Using Carotid Ultrasonography and Coronary CT Angiography in Nonalcoholic Fatty Liver Disease

Yoshihito Kubotsu[1], Chika Inadomi[1], Takumi Akiyama[1], Hirokazu Takahashi[1], Shinichi Aishima[2], Keizo Anzai[1], Yuichiro Eguchi[3]

[1]Department of Metabolism and Endocrinology, Faculty of Medicine, Saga University, [2]Department of Pathology and Microbiology, Faculty of Medicine, Saga University, [3]Liver Center, Faculty of Medicine, Saga University

Background: Nonalcoholic fatty liver disease (NAFLD) is independent risk of developing cardiovascular diseases (CVD) and associates with increased overall mortality of CVD; however, surveillance of atherosclerosis and coronary artery stenosis (CAS) has not been well established in NAFLD. We aimed to determine the efficacy of carotid ultrasonography to identify.
Method: A total of 101 patients with NAFLD diagnosed with liver biopsy were retrospectively enrolled in this study. Mean and max intima-media thickness (IMT) was measured using carotid ultrasonography. Coronary CT angiography was suggested for all patients with mean or max IMT > 1.0 mm. Correlation between hepatic pathogenesis of NAFLD and atherosclerosis/CAS was also examined.
Result: Max IMT significantly correlated with age ($r = 0.039$, $p < 0.001$) whereas there was no correlation with histological hepatic fibrosis and liver stiffness. In the 37 patients who received coronary CT angiography, significant CAS was found in 15 patients (40.5%). All patients with significant CAS showed max IMT > 1.5 mm, and median max IMT was more developed in the patients with significant CAS than the patients without CAS (2.2 mm vs. 1.9 mm, $p < 0.05$). In the multivariate analysis, max IMT was risk for significant CAS independent to diabetes and statin use.
Conclusion: As other lifestyle related diseases including diabetes, dyslipidemia and hypertension, measurement of max IMT is useful to evaluate the risk of significant CAS in NAFLD and cut-off value might be around 1.5 mm. Opposite to our hypothesis, correlation between severity of hepatic fibrosis and atherosclerosis/CAS is not significant.

Abstract #998

The Difference of Sucrose Intake between High and Low Non-alcoholic Fatty Liver Disease Score among Indonesian Obese Adults in Jakarta

Ayu Diandra Sari[1], Cosmas Rinaldi Lesmana[2], Levina S. Pakasi[3], Laurentius A. Lesmana[4], Rina Agustina[5]

[1]Department of Nutrition, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia and Human Nutrition Research Center, Indonesian Medical Education and Research Institute, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia, [2]Department of Internal Medicine, Hepatobiliary Division, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia and Digestive Disease and Gi Oncology Center, Medistra Hospital, Jakarta, Indonesia, [3]Digestive Disease and Gi Oncology Center, Medistra Hospital, Jakarta, Indonesia, [4]Department of Internal Medicine, Hepatobiliary Division, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia and Digestive Disease and Gi Oncology Center, Medistra Hospital, Jakarta, Indonesia, [5]Department of Nutrition, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia and Human Nutrition Research Center, Indonesian Medical Education And Research Institute, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

A scoring system to detect non-alcoholic fatty liver disease (NAFLD) non-invasively in adult population has been developed and validated in Indonesia. However, dietary assessment of added sugar (sucrose) in typical Indonesian dishes that may become a risk factor of NAFLD has been limitedly evaluated. The aim of this study was to evaluate the difference of sucrose intake between high and low NAFLD score among Indonesian obese adults in Jakarta. This was a community-based, cross-sectional study among 102 adults with body mass index (BMI) > 25 kg/m^2 between September and November 2018 in Jakarta. Sucrose intake were assessed using 2×24-h food recall, calculated based on Indonesian and American food composition tables with dietary software. The NAFLD scoring system consisted of six risk factors, i.e. BMI > 25 kg/m^2, male sex, age > 35 years, triglycerides > 150 mg/dL, high density lipoprotein cholesterol levels < 40 mg/dL for men or < 50 mg/dL for women, and alanine aminotransferase levels > 35 U/L. The result research indicate that 75 (73.5%) subjects were women. The median of total NAFLD scores was 6.7. The median of total sucrose intake was 47.0 (13.7–220.5) g/day. Sucrose intake was significantly higher in subjects with NAFLD score of > 6.7 than < 6.7 (52.7 vs. 71.9 g; $p = 0.042$: Mann–Whitney U test). Sucrose intake is higher in obese adults with high NAFLD score than in low score. Sucrose, a disaccharide consisted of glucose and fructose, may be responsible for higher fat accumulation in the liver.

Keywords: carbohydrate intake, non-alcoholic fatty liver disease, obesity, sucrose intake

Abstract #1025

Non Alcoholic Fatty Liver Disease among lean adults in East Avenue Medical Center: A Prevalence Study

Alvin Nino Valentin De Aquino[1], Lovell Balute Gatchalian[1], Karla Mia Garcia Villena[1], Charisse Que Ignacio[1], Jan Erikson Tanada Tullas[1], Sarah P. Preza[1], Felix L. Domingo Jr.[1], Michael P. Chu[1]

[1]East Avenue Medical Center

Significance: Nonalcoholic fatty liver disease (NAFLD) is usually associated with metabolic syndrome. Little attention has been given to NAFLD in lean individuals, and many clinicians have a perception of it being benign in nature. Global prevalence of lean NAFLD varies widely, ranging from 3 to 30%. The main objective of this study to determine prevalence of NAFLD among lean patients in EAMC.
Methodology: Study Design: Analytical cross-sectional study. Study Population: All patients with diagnosed with NAFLD. Statistical

Analysis. Shapiro–Wilks test was used to check for normality assumption of continuous patient demographic and clinical characteristics. Kruskal–Wallis test was used to compare three averages. Chi square test, Fisher's exact test or Yates' Chi square test was used to compare proportions. Data processing and analysis were performed using STATA v13.
Results: From a total of 260 patients, 247 patients were diagnosed with NAFLD, based on ultrasonography suggestive of fatty liver and exclusion of other causes of steatosis. Of 247 adults, 42.1% had lean NAFLD. Identified factors associated with lean NAFLD were elevated FBS and smoking (p value < 0.05).
Conclusion: Lean NAFLD was more common in our patients with a prevalence rate of 42.1% as compared to other studies from other countries. In our study, the associated risk factor for lean NAFLD in a univariate and multivariate analysis was smoking. On the other hand, FBS $\geq$ 126 mg/dl was the associated risk factor for lean NAFLD in a univariate analysis. We suggest to be more vigilant in working up lean NAFLD patients who presents with fatty liver.

Abstract #1026

Fibrosis in Pediatric NAFLD - An Overveiw

Nibin Nahaz[1], Krishnadas Devadas[1], Jijo Varghese[1], S. Swetha[1], Nibin Nahaz[1]

[1]Medical College, Trivandrum

Introduction: Pediatric NAFLD prevalence is on the rise owing to the sedentary life style and change in the socioeconomic status. Pediatric NAFLD poses risk for significant fibrosis and eventual cirrhosis in adulthood. This aspect is largely neglected mainly due to the lack of awareness and concerns regarding the risk of liver biopsy. VCTE fairly asses the level of fibrosis.
Aim: To predict the risk factors for fibrosis in pediatric NAFLD.
Materials and Methods: Children (less than 18) who are attending the out patient clinic with Ultrasound diagnosed fatty liver are enrolled. Necessary blood investigations and anthropometric measurements are obtained. Liver stiffness measurement is assessed using VCTE (Vibration controlled Transient elastography) and SWE (Shear wave elastography). Hepatic steatosis is quantified with hepatorenal index (HRI/B mode ratio) and continuous attenuating parameter (CAP).
Results: Out of the 41 children enrolled for the study 20 were obese and 9 were overweight. The mean LSM was 5.53 ($\pm$ 1.485) which was well above the childhood population mean of 3.8. LSM measured by VCTE and SWE had a GOOD CORRELATION(R = 0.56). SGOT was raised in 28 (68%) and SGPT in 20 (48%). Raised SGPT (r = 0.503), BMI (r = 0.342) and more screen time (r = 0.32) were significant risk factors of fibrosis. Average B Mode ratio was 1.33. Waist–Hip ratio (r = 0.38) was a risk factor for higher B mode ratio.
Conclusions: Pediatric NAFLD posses risk for fibrosis. Children diagnosed with fatty liver or or transaminitis should be evaluated for fibrosis. A higher BMI and inactivity are risk factors for fibrosis.

L02 - Treatment

Abstract #225

Prevalence and risk factors for nonalcoholic fatty liver disease in island and mainland residents in Zhuhai city

Zong Ping Han[1], Ming Xing Huang[1]

[1]The Fifth Affiliated Hospital of Sun Yat-Sen University

Aim: To investigate the prevalence of and risk factors for nonalcoholic fatty liver disease (NAFLD) among community residents in Zhuhai in order to provide evidence for the prevention and treatment in the future.
Methods: Cluster sampling method was adopted in this study. Questionnaire survey, physical measurement, blood biochemistry (including liver function, fasting blood sugar) examination, Fibrotouch as well as liver B ultrasound were used to investigate the situation of NAFLD.
Results: A total of 513 people met the inclusion criteria for community residents, including 301 men and 212 women, with an average age of 47.66 years $\pm$ 7.01 years, of whom 63 lived in mainland and 37% in island. The overall prevalence rate of NAFLD was 43%. The prevalence rate of NAFLD among island residents was much higher than that of in mainland (P = 0.002). Body mass index, systolic blood pressure, waist circumference, diastolic blood pressure, hip circumference, neck circumference, subcutaneous fat thickness, fasting blood glucose, uric acid, alanine aminotransferase, fatty liver ultrasonic attenuation and aspartate aminotransferase levels were significantly higher in NAFLD than in the normal group (all $P < 0.05$).
Conclusion: The prevalence rate of NAFLD in island residents is much higher than in mainland. BMI, waist circumference, subcutaneous fat, fasting blood glucose, and alanine aminotransferase are risk factors for NAFLD.

Abstract #277

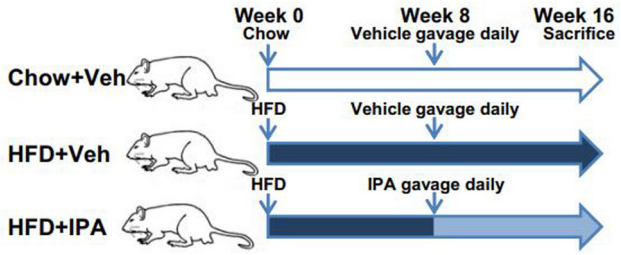
Indole-3-Propionic Acid Inhibits Gut Dysbiosis and Endotoxin Leakage to Attenuate Steatohepatitis in Rats

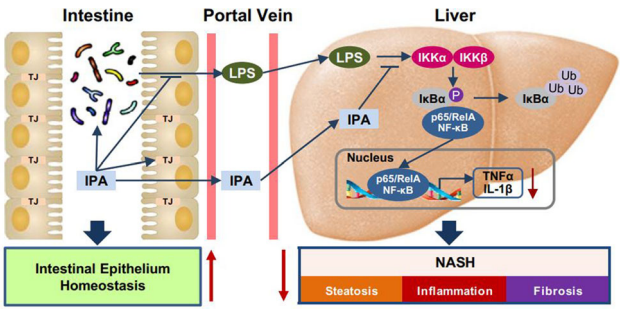
Ze-Hua Zhao[1], Feng-Zhi Xin[1], Yaqian Xue[2], Zhimin Hu[2], Yamei Han[2], Fengguang Ma[2], Da Zhou[1], Xiao-Lin Liu[1], Aoyuan Cui[2], Zhengshuai Liu[2], Yuxiao Liu[2], Jing Gao[2], Qin Pan[1], Yu Li[2], Jian-Gao Fan[1]

[1]Department of Gastroenterology, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China, [2]Shanghai Institutes for Biological Sciences, University of Chinese Academy of Sciences, Chinese Academy of Sciences, Shanghai, China

Introduction: The microbial metabolite has emerged as a critical component that mediates the metabolic effects of gut microbiota.
Objectives: To investigate the role of indole-3-propionic acid (IPA), a tryptophan metabolite produced by gut bacteria, in nonalcoholic steatohepatitis (NASH).
Methodology: Rats were fed a high-fat diet (HFD) and treated with IPA by daily gavage for 8 weeks. Murine macrophages pretreated with IPA were stimulated with LPS and then subjected to immunoblotting and quantitative RT-PCR analysis.
Results: We demonstrate that administration of IPA modulates microbiota composition in the gut and inhibits microbial dysbiosis in rats fed with high-fat diet. IPA induces the expression of tight junction proteins such as ZO-1 and Occludin and maintains intestinal epithelium homeostasis, and leads to a reduction of plasma endotoxin levels. Interestingly, IPA inhibits NF-κB signaling and reduces the proinflammatory cytokines such as TNFα, IL-1β and IL-6 in response to endotoxin in the macrophage to repress hepatic inflammation and liver injury. Moreover, IPA is sufficient to inhibit the expression of fibrogenic and collagen genes and attenuate diet-induced NASH phenotypes. The beneficial effects of IPA on the liver are likely through inhibiting the production of endotoxin in the gut.
Conclusion: These findings suggest a protective role of IPA on the control of metabolism, and uncover the gut microbiome and liver

cross-talk in regulating intestinal microenvironment and liver pathology via a novel dietary nutrient metabolite. IPA may provide a new therapeutic strategy for treating NASH.





Results: The majority of subjects were female (62%), obese (79%), and diabetic (55%). BL median MRI-PDFF and MRE were 16.3% and 3.27 kPa, respectively; 34% of subjects had MRE > 3.64 kPa, indicating ≥ F3 fibrosis. At W24, both GS-9674 100 mg and 30 mg resulted in statistically significant decreases in MRI-PDFF compared with placebo. At W24, ≥ 30% decline in MRI-PDFF was observed in 39% of subjects treated with GS-9674 100 mg, 14% treated with GS-9674 30 mg, and 12.5% with placebo. Statistically significant reductions in serum GGT, markers of FXR activation, C4 and total bile acids, were observed in GS-09674-treated subjects. GS-9674 was well-tolerated. Moderate/severe pruritus was more common with GS-9674 100 mg (14.3%) compared with GS-9674 30 mg (3.6%) and placebo (3.6%). Changes in lipid profile and glycemic parameters did not differ between groups.
Conclusion: Non-steroidal FXR agonist GS-9674 improves hepatic steatosis, serum bile acids, and liver biochemistry in patients with NASH.

Table: Median Relative (%) Changes in Imaging, ALT, and Serum Fibrosis Markers from Baseline to W24*

	GS-9674 100 mg (n=56)	GS-9674 30 mg (n=56)	Placebo (n=28)	P-values	
				100 mg vs. Placebo	30mg vs. Placebo
MRI-PDFF	-22.7	-1.8	1.9	**<0.001‡**	**0.029‡**
≥30% reduction in MRI-PDFF, % (n/N)	38.9% (21/54)	14% (7/50)	12.5% (3/24)	**0.011†**	0.87†
MRE-stiffness	0.4	-5.7	-0.4	0.92	0.42
Liver stiffness by FibroScan	-4.6	-4.2	3.2	0.65	0.49
ALT	-17.7	-19.0	-5.7	0.11	0.41
GGT	-37.1	-19.4	-4.3	**<0.001**	**0.042**
Fasting FGF19	0	2.4	10.9	0.83	0.91
C4	-37.7	-38.3	7.1	**0.01**	**0.008**
Total bile acids	-16.6	-36.5	2.2	0.14	**0.009**
Total cholesterol	1.9	1.3	-3.1	0.14	0.48
LDL cholesterol	5.7	5.3	-4.5	0.13	0.28
HDL cholesterol	-6.4	-2.7	-8.2	0.68	0.59
Triglycerides	2.8	-2.0	-1.5	0.47	0.79
Glucose	2.9	4.5	4.2	0.52	0.74

* Unless indicated, all data are median relative (%) changes from baseline and P-values from Wilcoxon rank-sum test.
‡ P-value by ANCOVA adjusted for baseline MRI-PDFF and diabetes status.
† P-value by Mantel-Haenszel test adjusted for baseline diabetes status.

Abstract #306

Non-steroidal FXR agonist GS-9674 significantly reduces hepatic steatosis, serum bile acids, and liver biochemistry in a phase 2, randomized, placebo-controlled trial of patients with NASH

Keyur Patel[1], Stephen A Harrison[2], James F Trotter[3], Robert Herring[4], Sergio Rojter[5], Zeid Kayali[6], Mitchell L Shiffman[7], Bradley Freilich[8], Eric J Lawitz[9], Chuhan Chung, On Behalf Of Gilead[10], Michael S Middleton[11], Mary Rinella[12], Mazen Noureddin[13]

[1]University of Toronto, [2]Pinnacle Clinical Research, [3]Texas Digestive Disease Consultants, [4]Quality Medical Research, [5]Ruane Clinical Research, [6]Inland Empire Liver Foundation, [7]Bon Secours Liver Institute of Virginia, [8]Kansas City Research Institute, [9]Texas Liver Institute, University of Texas Health San Antonio, [10]Gilead Sciences, Inc., [11]University of California San Diego, [12]Feinberg School of Medicine, Northwestern University, [13]Cedars-Sinai Medical Center

Introduction/Objectives: Here, we describe the safety and efficacy of GS-9674, a non-steroidal farnesoid X receptor (FXR) agonist, in a phase 2 trial of NASH patients.
Methodology: 140 non-cirrhotic subjects with NASH diagnosed by MRI proton density fat fraction (PDFF) ≥ 8% and liver stiffness ≥ 2.5 kPa by MR elastography (MRE), or historical biopsy consistent with NASH and F1-F3 fibrosis, were randomized 2:2:1 to receive GS-9674 100 mg (n = 56), GS-9674 30 mg (n = 56), or placebo (n = 28) orally QD for 24 weeks (W24). MRI-PDFF, MRE, FibroScan, and serum markers of fibrosis were measured at baseline (BL) and W24.

Abstract #329

Fibrinogen-like protein 2 aggravates non-alcoholic steatohepatitis by enhancing inflammatory signaling in macrophages

Junjian Hu[1], Hongwu Wang[1], Xitang Li[1], Xiaojing Wang[1], Qin Ning[1]

[1]Tongji Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology

Introduction: Fibrinogen-like protein 2 (fgl2), which is critical for immune regulation in inflammatory state, leads to production of proinflammatory cytokines and hepatic injury. Objectives: This study aims to investigate the role of fgl2 in the pathogenesis of non-alcoholic steatohepatitis (NASH) and to explore the mechanisms.
Methods: The wild type and fgl2(–/–)C57BL/6 mice were subjected to methionine/choline-deficient (MCD) diet or high fat diet (HFD) for establishing NASH models. Liver injury and steatosis, were detected by Hematoxylin–eosin staining and Oil-red staining. Bone marrow-derived macrophages were stimulated with LPS or free fatty acids (FFA). The NF-kappaB, p38-MAPK and NLRP3 inflamasome signaling pathways as well as lipid metabolism related molecules were tested both in vivo and in vitro using RT-PCR and western blotting. The levels of proinflammatory cytokines in cell supernatant and homogenate of liver tissues were tested by ELISA.

Results: Compared with WT mice NASH models, inflammatory liver injury and steatosis were dramatically attenuated in fgl2-deficient test groups. In both liver tissues and bone marrow-derived macrophages from the NASH models, fgl2 deficiency resulted in reduced secretion of proinflammatory cytokines including TNF-alpha, IL-1beta, MCP-1 and IL-6. Meanwhile, activation of NF-kappaB and p38-MAPK signaling pathways as well as expression of NLRP3, pro-caspase-1, caspase-1 and pro-IL-1beta were significantly decreased. Genes involved in lipogenesis (SREBP-1c, HMGCR) were downregulated while those involved in lipometabolism (PPAR-gamma, PGC-1alpha) were upregulated in fgl2-deficient test groups.
Conclusion: Fgl2 promotes inflammation and steatosis in NASH by enhancing inflammatory activity of macrophages via multiple signaling pathways.

Abstract #349

Effect of vitamin E and telmisartan on liver histopathology in nonalcoholic steatohepatitis: a randomized open labeled head to head study

Shahinul Alam[1], Mushfiqul Abrar[1], Golam Mustafa[1], Mohammad Kamal[2], Nooruddin Ahmad[1]

[1]Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, [2]Department of Pathology, Bangabandhu Sheikh Mujib Medical University

Introduction: Vitamin E and telmisartan resulted significant improvement in nonalcoholic steatohepatitis (NASH) patient.
Objective: Compare effect of vitamin E and telmisartan on histopathology of NASH.
Methodology: This is randomized open level head to head clinical trial. Nonalcoholic fatty liver disease (NAFLD) activity score (NAS) ≥ 5 were selected. Forty patients were divided into two groups: telmisartan (T) and vitamin-E (E) were followed up for 1 year. They were advised for life style change to reduce the weight. In E 14 and in T 16 patients completed the study.
Results: In E, NAS was improved from 6 ± 0.8 to 4.36 ± 1.4 ($p = 0.000$) and in T from $5.6 \pm 0.7$to 4.9 ± 1.2 ($p = 0.029$). Fibrosis was insignificantly changed in E from 1.6 ± 0.5 to 1.5 ± 0.5 and in T from 1.7 ± 0.9 to 1.5 ± 0.7 ($p = 0.671$ and 0.423, respectively). Steatosis improved significantly in group E from 2.07 ± 0.6 to 1.14 ± 0.66 ($p = 0.000$) but not in T from 1.94 ± 0.57t o 1.56 ± 0.8 ($p = 0.054$). Lobular inflammation was significantly improved in E from 2.0 ± 0.4 to 1.6 ± 0.5 ($p = 0.019$) but in T from 8 ± 0.3 to 1.8 ± 0.4 ($p = 0.580$). Ballooning was significantly attenuated from 1.9 ± 0.3 to 1.7 ± 0.5 (p value 0.029) in E but not in T from 1.9 ± 0.1 to 1.5 ± 0.5 ($p = 0.189$) (Table I). In comparative analysis of improvement NAS improvement was significantly higher in the group E (1.6 ± 1.2) than that of group T (0.6 ± 1.1) $p = 0.026$, independent of weight reduction.
Conclusion: Vitamin E is superior to telmisartan in improvement of NAS. Vitamin E decreases steatosis, lobular inflammation and ballooning but not telmisartan. Fibrosis was unaffected in both groups.

Table 1 Changes in anthropometry, biochemistry and histology after 12 months

Variable	Group E (N=14) Mean ± SD			Group T (N= 16) Mean ± SD		
	Base line	After 12 months	p	Base line	After 12 months	p
Anthropometric changes						
Weight (kg)	71.2 ± 13.0	68.0 ± 13.2	**.002**[b]	68.5 ± 13.1	62.2 ± 8.5	**.008**[b]
BMI (kg/m^2)	28.8 ± 3.55	27.05 ± 3.9	**.000**[b]	28.9 ± 5.4	27.9 ± 5.9	**.010**[a]
Liver Histology						
Steatosis	2.1 ± 0.6	1.1 ± 0.6	**.000**[b]	1.9 ± 0.5	1.6 ± 0.8	.054
Ballooning	1.9± 0.3	1.5 ± 0.5	.055	1.9 ± 0.3	1.5 ± 0.5	**.029**[a]
Lobular inflammation	2.0± 0.4	1.6 ± 0.5	**.019**[a]	1.9 ± 0.3	1.8 ± 0.4	.580
NAS	5.9 ± 0.8	4.3 ± 1.4	**.000**[b]	5.6 ± 0.7	4.9 ± 1.2	**.029**[a]
Fibrosis	1.6 ± 0.5	1.5 ± 0.5	.671	1.7 ± 0.9	1.5 ± 0.7	.423
Liver Biochemistry						
ALT (U/L)	58.2 ± 39.2	27.1 ± 14.4	**.010**[a]	60.7 ± 37.2	39.2 ± 34.1	.090
AST (U/L)	42 ± 16.6	22.8 ± 7.07	**.001**[b]	48.5 ± 28.3	33.6 ± 24.5	**.046**[a]
GGT (U/L)	43.3 ± 20.8	39.8 ± 26.7	.606	41.8 ± 24.1	48.6 ± 58.0	.483
Blood Biochemistry						
FBS (mmol/L)	6.1± 1.6	5.5 ± 1.5	.047	6.3 ± 3.0	5.3 ± 1.1	.285
Insulin resistance index (HOMA-IR)	2.4± 1.5	1.9 ± 0.5	.201	2.5 ± 1.7	1.7 ± 0.8	.097
S. cholesterol (mg/dl)	202.5 ± 33.7	170.0 ± 34.8	.325	213.7 ± 41.4	186.4 ± 39.9	**.028**[a]
LDL (mg/dl)	120.1 ± 28.7	114.4 ± 33.1	.619	130.9 ± 34.7	117.1 ± 35	.125
HDL (mg/dl)	37.0 ± 5.7	36.6 ± 7.8	.819	39.1 ± 9.8	38.0 ± 7.6	.483
Triglyceride (mg/dl)	212.2 ± 87	202.9± 68.5	.657	241.7± 138.1	187.6± 110.2	.053

For paired samples *t*-test, [a]P< 0.05, [b]P< 0.01 within group comparisons. BMI: Body mass index; NAS: NAFLD activity score;ALT: Alanine transaminase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; GGT; Gamma-glutamyltrasferase;FBS: Fasting blood sugar; HOMA-IR: Homeostasis model assessment insulin resistance; HDL: High density lipoprotein; LDL: Low density lipoprotein

Abstract #364

Cenicriviroc treatment for adults with nonalcoholic steatohepatitis: Year 2 analysis of the Phase 2b CENTAUR study

Vlad Ratziu[1], Arun Sanyal[2], Sven Francque[3], Vincent Wai-Sun Wong[4], Rohit Loomba[5], Zachary Goodman[6], Eric Lefebvre[7], Guruprasad P. Aithal[8], Stephen Harrison[9], Manal F. Abdelmalek[10], Frank Tacke[11]

[1]Hôpital Pitié Salpêtrière and Université Pierre Et Marie Curie, Paris, France, [2]Department of Gastroenterology, Virginia Commonwealth University, Richmond, VA, USA, [3]Gastroenterology and Hepatology, Antwerp University Hospital, University of Antwerp, Antwerp, Belgium, [4]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, The People's Republic Of China, [5]Division of Gastroenterology, Department of Medicine, University of California, San Diego, La Jolla, CA, USA; Nafld Research Center, Department of Medicine, University of California, San Diego, La Jolla, CA, USA, [6]Center for Liver Diseases, Inova Fairfax Medical Campus, Falls Church, VA, USA, [7]Former Employee of Allergan PLC, South San Francisco, CA, USA, [8]NIHR Nottingham Biomedical Research Centre, Nottingham University Hospitals NHS Trust and University of Nottingham, Nottingham, UK, [9]Pinnacle Clinical Research, San Antonio, TX, USA, [10]Division of Gastroenterology and Hepatology, Department of Medicine, Duke University, Durham, NC, USA, [11]Department of Medicine III, University Hospital Aachen, Aachen, Germany

Introduction: Cenicriviroc is a once-daily oral CCR2/5 antagonist, under evaluation in adults with nonalcoholic steatohepatitis (NASH).
Objective: To report Year (Y)2 data from the Phase 2b CENTAUR study (NCT02217475).
Methodology: Adults with histologically confirmed NASH, nonalcoholic fatty liver disease activity score ≥ 4, and liver fibrosis (NASH Clinical Research Network Stage 1–3) were randomized 2:1:1 for 2 years to Arms A, B, or C: cenicriviroc 150 mg, placebo then

cenicriviroc 150 mg (1 year each), or placebo. Liver biopsies were taken at baseline, Y1, and Y2.
Results: Of 289 adults randomized, 52% were diabetic, and 67% had fibrosis Stage 2/3; 213 subjects had Y2 biopsies available. Although similar proportions of cenicriviroc- and placebo-treated subjects achieved the primary endpoint of $\geq$ 1-stage fibrosis improvement AND no worsening of NASH (Arm A: 15% [15/99]; Arm C: 17% [9/54]) at Y2; proportionally more cenicriviroc-treated subjects achieved $\geq$ 2-stage fibrosis improvement AND no worsening of NASH (Arm A: 11% [7/65]; Arm C: 3% [1/34]). Proportionally more cenicriviroc-treated subjects maintained $\geq$ 1-stage Y1 fibrosis improvement at Y2 (Arm A: 60% [18/30]; Arm C: 30% [3/10]), higher for cenicriviroc-treated subjects with baseline fibrosis Stage 3 (86% [12/14]). Cenicriviroc was associated with reduced high-sensitivity C-reactive protein and fibrinogen, with no effect on liver enzymes. Adverse events were comparable between treatment groups. No deaths occurred.
Conclusion: Cenicriviroc was well tolerated and showed antifibrotic activity in adults with NASH. Most subjects achieving $\geq$ 1-stage fibrosis improvement at Y1 maintained benefit, especially those with advanced fibrosis.
Writing assistance by Complete HealthVizion.

Abstract #373

Effect of Saroglitazar on Non-alcoholic Fatty Liver Disease in patients with diabetic dyslipidemia: a prospective observational study

Omesh Goyal[1], Prerna Goyal[2], Rajoo S. Chinna[3]

[1]D.M.C. and Hospital, [2]R.G. Stone Hospital, [3]D.M.C. and Hospital

Introduction: Saroglitazar is a dual Peroxisome Proliferator-Activated Receptors (PPAR) α and γ agonist approved for diabetic dyslipidemia and hypertriglyceridemia. PPAR-α action of Saroglitazar improves lipid parameters and PPAR-γ action improves insulin sensitivity. Non-alcoholic fatty liver disease (NAFLD) is closely associated with diabetic dyslipidemia and is one of the leading causes of chronic liver disease.
Objectives: We aimed to evaluate the safety and efficacy of saroglitazar in patients with diabetic dyslipidemia associated NAFLD.
Methods: This prospective observational study was conducted in northern India. Inclusion criteria were baseline HbA1c > 6.2% and dyslipidemia (Total cholesterol > 200 mg/dl, triglycerides > 150 mg/dl) and Saroglitazar 4 mg once daily consumption for at least 24 weeks. The laboratory parameters and fibroscan reports at baseline and 24 weeks were compared using t test.
Results: Eighty-four patients with diabetic dyslipidemia were enrolled (age 51.4 $\pm$ 10.3 years; 73.8% males; mean BMI-29.6). Of these 78.5% patients had alanine aminotransferase (ALT) > ULN and evidence of NAFLD on USG/fibroscan. At 24 weeks, serum triglycerides significantly reduced from 334.7 $\pm$ 74 mg/dl to 158.5 $\pm$ 46 mg/dl ($P < 0.0001$), HbA1c from 7.9 $\pm$ 0.54% to 6.4 $\pm$ 0.42% ($P < 0.0001$), ALT from 98 $\pm$ 32 IU/L to 34 $\pm$ 14 IU/L ($P < 0.0001$), and Fibroscan from 11.4 kPa to 9.2 kPa (p = n.s.). Saroglitazar was found to be safe and well tolerated.
Conclusions: Saroglitazar is safe and effective in treatment of diabetic dyslipidemia. In addition, it has favorable effect on liver enzymes and fibroscan. Therefore, saroglitazar can be a potential therapeutic option for the treatment of NAFLD associated with metabolic syndrome.

Abstract #411

Effect of severe hepatic impairment on the pharmacokinetics of cenicriviroc and its metabolites

Surya Ayalasomayajula[1], Li Yao[2], Edward Kaczynski[3], Alexandru Iacob[4], Star Seyedkazemi[5], Eric Lefebvre[6], Ramesh Boinpally[7], Antonia Periclou[8], Eduardo Bruno Martins[9]

[1]NTS-Clinical Pharmacology, Allergan PLC, Madison, NJ, USA, [2]Biostatistics, Allergan PLC, Irvine, CA, USA, [3]Bioanalytical Sciences, Allergan PLC, Madison, NJ, USA, [4]Global Patient Safety and Epidemiology (GPSE), Allergan Inc., Markham, ON, Canada, [5]Clinical Development, Allergan PLC, South San Francisco, CA, USA, [6]Former Employee of Allergan PLC, South San Francisco, CA, USA, [7]NTS-Clinical Pharmacology, Allergan PLC, Madison, NJ, USA, [8]NTS-Clinical Pharmacology, Allergan PLC, Madison, NJ, USA, [9]Clinical Development, Allergan PLC, South San Francisco, CA, USA

Introduction: Cenicriviroc (CVC), a novel, oral, and potent inhibitor of C-C chemokine receptor types 2 and 5, is under clinical development for treatment of liver fibrosis associated with nonalcoholic steatohepatitis.Objective: To evaluate the effect of severe hepatic impairment on the pharmacokinetics (PK) of CVC and its metabolites, M-I and M-II.
Methodology: A single dose of 150 mg CVC was administered orally to 8 patients with severe hepatic impairment and 8 matching healthy participants in this open-label, multicenter study. CVC, M-I, and M-II metabolite concentrations were measured from serial blood samples. PK parameters (maximum concentration [Cmax], area under the curve [AUC] from time 0 to time of last measurable concentration [AUClast], and AUC from time 0 to infinity [AUCinf]) were estimated using Phoenix WinNonlin v8.0.
Results: CVC plasma concentrations in patients with severe hepatic impairment appeared with a median lag time of 1 hour, reaching peak concentrations in a median time of 6 hours (Cmax, 292.4 ng/mL; AUClast, 8089 ng $\times$ h/mL; AUCinf, 10,540 ng $\times$ h/mL). While Cmax decreased by 21.39%, AUClast and AUCinf increased by 39.63% and 77.62%, respectively, in patients with severe hepatic impairment compared to matching healthy participants (Table). Results for M-I and M-II were consistent with observations for CVC. No significant treatment-related adverse events were observed.
Conclusion: Consistent with the elimination pathway, exposure to CVC increased in patients with severe hepatic impairment compared to matching healthy participants. Single-dose administration of 150 mg CVC was safe and well tolerated in patients with severe hepatic impairment.
Writing assistance by Complete HealthVizion.

Abstract #424

The change of skeletal muscle mass is associated with hepatic steatosis in non-alcoholic fatty liver disease

Do Seon Song[1], U. Im Chang[1], Jeong Won Jang[1], Si Hyun Bae[1], Seung Kew Yoon[1], Jin Mo Yang[1], Jong Young Choi[1]

[1]Department of Internal Medicine, The Catholic University of Korea

Background/aim: We aimed to investigate the association between the change of muscle mass and change of fibrosis and steatosis in NAFLD patients.
Method: We analyzed 2893 NAFLD subjects who had health check-up more than twice in St. Vincent's Hospital between November 2009 and December 2017. Sarcopenia index was calculated as ASM

divided by weight (SI %) and ASM divided by body mass index (SI-BMI). Non-invasive markers were used to evaluate the severity of hepatic fibrosis and steatosis; NAFLD fibrosis score (NFS), fibrosis-4 (Fib-4) score, and Forn's index for fibrosis, and hepatic steatosis index (HSI) and fatty liver index (FLI) for steatosis.
Results: The mean age was 47.3 ± 10.4 years, and 1956 subjects (67.6%) were male. Diabetes, hypertension, metabolic syndrome were more prevalent in sarcopenic subjects ($P < 0.01$), and non-invasive fibrosis and steatosis markers were higher in sarcopenic subjects ($P < 0.01$). The mean interval between two health check-up was 39.8 ± 21.9 months. There was no significant association between the change of NFS, Fib-4, and Forn's index and the change of SI % and SI-BMI (all $P > 0.1$). However, the changes of HIS and FLI were significantly associated with the change of SI % and SI-BMI (all $P < 0.01$). Multivariate logistic analysis demonstrated the independent association between the change of skeletal muscle mass and the changes of non-invasive steatosis markers after adjusting for other confounding factors (all $P < 0.001$), but not the changes of non-invasive fibrosis markers (all $P > 0.1$)
Conclusion: The change of muscle mass is strongly associated with the change of hepatic steatosis, but not the change of fibrosis.

Abstract #442

Effect of probiotics for the treatment of fatty liver disease in mice

Na Young Lee[1], Dae Hee Han[1], Haripriya Gupta[1], Gi Soo Youn[1], Ki Tae Suk[2]

[1]Hallym University Medical Center, [2]Hallym University College of Medicine

Background and Aims: Nonalcoholic fatty liver disease (NAFLD) is one of the most common chronic liver diseases. Microbiota modulation by interventions can be used for targeting gut-liver axis in NAFLD. The aim of this study is to find beneficial microbiotas in the treatment of NAFLD.
Method: Six-week male C57BL/6J mice were used in this study. Mice were randomly assigned to normal, Western, and 15 Western diet + microbiota groups (n = 10/group). Used microbiota strains are *Lactobacillus acidophilus*, *L. plantarum*, *L. casei*, *L. paracasei*, *L. fermentum*, *L. helveticus*, *L. bulgaricus*, *Bifidobacterium bifidum*, *Pediococcus pentosaceus* KID7, *L. reuteri*, *L. salivarius*, *L. gasseri*, *Bifidobacterium lactis*, *B. breve*, and *B. longum*. Liver/body weight ratio, liver enzyme, cholesterol, cytokines, and histologic finding were analyzed. Stool microbiome analysis by 16S rRNA-based sequencing was performed.
Results: In liver/body weight ratio, *L. acidophilus* (5.5 ± 0.4), *L. bulgaricus* (5.1 ± 0.5), *P. pentosaceus* KID7 (5.5 ± 0.5), *L. paracasei* (5.7 ± 0.4), *L. helveticus* (5.2 ± 0.4) *L. salivarius* (5.73 ± 0.52), *B. breve* (5.27 ± 0.47), and *B. longum* (4.85 ± 0.57) groups showed significant improvement compared with that of Western group (6.2 ± 0.6, $p < 0.05$). Expression of CD54 in liver, level of cytokines (TNF-a, IL-1b, and IL-6), Frimicutes/Bacteroidetes ratios, and concentration of *Akkermansia muciniphilia* (stool) were significantly improved in *L. bulgaricus, P. pentosaceus* KID7, *L. casei*, and *B. breve* group compared with that of Western group.
Conclusion: Our selected microbiotas have beneficial effects on weight reduction, dyslipidemia, and liver inflammation and steatosis via cytokine signal pathway by modulating gut-miucrobiota. Therefore, microbiota modulation might be effective in the treatment of NAFLD by regulating the gut-liver axis.

Abstract #443

Effect of Korean red ginseng in the treatment of non-alcoholic steatohepatitis

Ki Tae Suk[1], Young Lim Ham[2]

[1]Hallym Univeristy College of Medicine, [2]Daewon University

Background and aims: Korea Red Ginseng (KRG) has been known as a natural product with anti-inflammatory and hepatoprotective effect in liver disease. Gut microbiota plays an important roles in the pathophysiology of nonalcoholic statohepatitis (NASH). We evaluated the effect and mechanism of KRG on patients with NASH.
Method: Between January 2017 and April 2018, a total of 94 patients (KRG: 45 and placebo: 49) were prospectively randomized to receive the 30 days of KRG (2000 mg/day, ginsenoside Rg1 + Rb1 + Rg3 4.5 mg/g) or placebo. Liver function test, fatigue score, pro-inflammatory cytokines, lipopolysaccharide (LPS), and stool microbiome analysis by 16S rRNA-based sequencing were examined and compared after therapy.
Results: In KRG group, the mean levels of alanine aminotransferase (75.6 ± 40.7 → 65.3 ± 41.9 IU/L, $P = 0.040$), gamma glutamyltransferase (95.1 ± 78.0 → 80.2 ± 69.9 IU/L, $P = 0.004$), and fatigue score (34.2 ± 14.2 → 26.0 ± 12.7, $P < 0.001$) were significantly improved after the administration of KRG. The decline of LPS was seen in both groups but it showed a big drop in red ginseng group ($P < 0.05$). Changes in microbiome in the stool were observed in the KRG group. KRG group showed a rise in Firmicutes and Proteobacteria in patients with increased alanine aminotrasferase level. Placebo group revealed contrary results. In patients with improved alanine aminotrasferase, Firmicutes and Proteobacteria in KRG group were decreased and Actinobacteria in placebo group was increased in the stool analysis
Conclusion: KRG might be effective in improving liver enzymes, endotoxin, and fatigue by modulating gut-microbiota in patients with NASH. KRG can be used as a next therapeutic option in patients with NASH.

Abstract #444

Safety and pharmacokinetics of multiple-dose pegbelfermin (BMS-986036) in healthy Japanese and non-Japanese adults

Giridhar Tirucherai[1], Takafumi Ide[1], Diane Shevell[1], Johanna Mora[1], Edgar Charles[1]

[1]Bristol-Myers Squibb

Introduction: Pegbelfermin (BMS-986036), a PEGylated human fibroblast growth factor 21 (FGF21) analog, improved hepatic steatosis, metabolic parameters, and fibrosis biomarkers in patients with non-alcoholic steatohepatitis (NASH) in a phase 2 study.
Objective: Assess safety and pharmacokinetics of multiple-dose pegbelfermin in healthy Japanese and non-Japanese participants.
Methodology: MB130-057 was a phase 1, randomized, placebo-controlled study. Pegbelfermin was administered once-weekly (20 mg or 40 mg [Japanese], 20 mg [non-Japanese]) via subcutaneous abdominal injections on days 1, 8, and 15. The primary objective was safety; secondary objectives included immunogenicity and pharmacokinetics.
Results: Twenty-four participants received pegbelfermin 20 mg (n = 12; 6 Japanese, 6 non-Japanese), pegbelfermin 40 mg (n = 6 Japanese), or placebo (n = 6; 4 Japanese, 2 non-Japanese). Most participants were male (87%); median age was 37 years and mean BMI was 27.5 kg/m^2. Three Japanese (20 mg, n = 1; 40 mg, n = 2)

participants withdrew consent. Thirteen adverse events (AEs; 10 Japanese, 3 non-Japanese) were reported; all were mild or moderate. No serious AEs, discontinuations due to AEs, or deaths occurred. Four participants had detectable anti-pegbelfermin antibodies and five had detectable anti-FGF21 antibodies; none were neutralizing. Pegbelfermin AUCtau, Cmax, and Tmax on day 15 were similar between Japanese and non-Japanese participants at the 20 mg QW dose.
Conclusions: Pegbelfermin was generally well tolerated with no clinically meaningful differences in safety and PK profiles between healthy Japanese and non-Japanese adults, supporting the use of the same dose in both populations. These results warrant further studies to evaluate safety and efficacy of pegbelfermin in Japanese patients with advanced NASH.

Abstract #451

Pharmacokinetics of cenicriviroc and its metabolites (M-I and M-II) in healthy subjects of Japanese ethnicity

Surya Ayalasomayajula[1], Li Yao[2], Edward Kaczynski[3], Danielle Mcgeeney[1], Eduardo Bruno Martins[4], Star Seyedkazemi[4], Ramesh Boinpally[1], Antonia Periclou[1]

[1]NTS-Clinical Pharmacology, Allergan Plc, Madison, NJ, USA, [2]Biostatistics, Allergan Plc, Irvine, CA, USA, [3]Bioanalytical Sciences, Allergan Plc, Madison, NJ, USA, [4]Clinical Development, Allergan Plc, South San Francisco, CA, USA

Introduction: Cenicriviroc (CVC) is a once-daily oral CCR2/CCR5 antagonist under evaluation in adults with nonalcoholic steatohepatitis.
Objective: To evaluate and compare the pharmacokinetics of CVC and its metabolites, M-I and M-II, between healthy subjects of Japanese and Caucasian ethnicity. Biomarker response (MCP-1 and MIP-1β) was also explored.
Methodology: CVC was administered (open-label) to Japanese (150 mg or 300 mg) and Caucasian subjects (150 mg) for 10 days with breakfast (N = 8/dose level). Blood samples were collected on days 1 and 10 to measure CVC, M-I, M-II, MCP-1, and MIP-1β concentrations.
Results: Steady-state levels of CVC, M-I, and M-II were achieved within 7 days, with near-proportional increases in exposures observed in Japanese subjects between 150 and 300 mg doses. Compared to Caucasians, steady-state maximum concentrations of CVC, M-I, and M-II were 1.53-fold, 2.23-fold, and 1.74-fold higher, respectively, and area under the curve over the dosing interval (AUCtau) values were 1.47-fold, 2.00-fold, and 1.56-fold higher, respectively, in Japanese subjects (150 mg). However, observed exposure of CVC in Japanese subjects in this study was similar to historical data in Caucasians. Consistent with the mechanism of action, MCP-1 and MIP-1β serum levels increased significantly on day 1, with no significant further increase on day 10. The extent of change in MCP-1 and MIP-1β serum levels was similar across all 3 groups.
Conclusion: CVC was well tolerated, with no safety concerns. Exposure in Japanese subjects was similar to historical data in Caucasians. Biomarker response appeared similar between doses and ethnic groups.
Writing assistance by Complete HealthVizion.

Abstract #461

The benchmarks Obeticholic Acid and Elafibranor show variable effects on NASH and hepatic fibrosis in diet-induced or chemically-induced animal models

Francois Briand[1], Emmanuel Brousseau[1], Nourdine Faresse[1], Thierry Sulpice[1]

[1]Physiogenex

Introduction: Predictive Non-Alcoholic Steato-Hepatitis (NASH) animal models are required to evaluate efficacy of novel drugs, that have to be compared with benchmarks such as obeticholic acid (OCA, an FXR agonist) and elafibranor (GFT505, a PPARalpha/delta dual agonist).
Objectives: We aimed to evaluate the curative effects of OCA and GFT505 in diet-induced (methionine/choline deficient (MCD) diet fed mouse, diet-induced NASH (DIN) mouse or hamster on a high fat/cholesterol/fructose diet), or chemically-induced (thioacetamide (TAA) injected rat and carbon tetrachloride (CCl4) injected mouse) animal models.
Methodology: Plasma biochemistry, liver histology and NAS scoring were performed in each model to evaluate drugs' efficacy.
Results: In MCD mice, OCA markedly increased plasma ALT/AST levels and only reduced steatosis, while GFT505 significantly reduced ALT/AST and NAS score. In obese/insulin resistant DIN mice, OCA and GFT505 significantly improved ALT/AST levels and NAS scoring. However, OCA better reduced fibrosis, but unlike humans, reduced plasma LDL-cholesterol by 45% ($p < 0.001$ vs. vehicle).
In obese/insulin resistant DIN hamsters, GFT505 significantly reduced ALT by 52%, liver inflammation, hepatocyte ballooning, bridging fibrosis and total NAS score ($p < 0.01$ vs. vehicle). OCA showed limited benefits on NASH, with higher plasma LDL-cholesterol and lower HDL-cholesterol, as observed in humans. OCA and GFT505 showed no effect in TAA rats, but reduced bridging fibrosis in CCl4 mice. However, only GFT505 significantly reduced fibrosis score by 33% in this mouse model.
Conclusion: OCA and GFT505 show variable effects in NASH animal models. These models' characteristics should be carefully considered for better drug evaluation and translation to humans.

Abstract #527

Efficacy of dulaglutide on liver function in type 2 diabetic patientswith fatty liver

Koichi Takaguchi[1], Akemi Tsutsui[1], Tomonori Senoo[1], Takuya Nagano[1]

[1]Kagawa Prefectural Central Hospital

Background: Dulaglutide (once-weekly glucagon-like peptide-1 (GLP-1) receptor agonist) has an appetite suppressing action, so it has also expected therapeutic effect for type 2 diabetes mellitus (T2DM) patients with fatty liver. We evaluated the effect of dulaglutide on liver function test in T2DM patients with fatty liver.
Object: Of 129 patients with T2DM who are recived dulaglutide administration at our hospital, 49 patients (36 males, 13 females, age 62.2 ± 15.3 years old, HbA 1 c 8.2 ± 2.0%, body weight 72.3 ± 16.5 kg, BMI 26.7 ± 4.84 kg/m 2) who has elevated liver function test were evaluated. Duraglutide was administered for 3 months and observed the transition of HbA1c, liver function, triglycelide, LDL-C, HDL-C and uric acid.
Results: Comparing the data at the 3rd month from the start of administration, body weight slightly decreased from 71.4 ± 16.8 kg

to 69.5 ± 29.2 kg after 3 months, HbA1c decreased from 8.19 ± 2.02 to 7.22 ± 1.76%. AST decreased from 54.2 ± 43.3 IU/L to 38.8 ± 12.9 IU/L, ALT decreased from 64.8 ± 38.8 IU/L to 47.3 ± 22.0 IU/L, and the liver function improved. Serum triglyceride increased from 190.0 ± 141 to 194.0 ± 102 mg/dl, HDL-C and LDL-C did not change. Uric acid remained unchanged.
Conclusion: These dates suggested that dulaglutide could improve liver function at T2DM patients with fatty liver.

Abstract #603

GLP-1 receptor agonists reduce liver inflammation in a 3-week Non Alcoholic SteatoHepatitis Mouse Model

Francois Briand[1], Emmanuel Brousseau[1], Nourdine Faresse[1], Thierry Sulpice[1]

[1]Physiogenex

Introduction: Glucagon-like peptide 1 (GLP-1) receptor agonists have anti-inflammatory effects suitable to treat Non-Alcoholic Steato-Hepatitis (NASH).
Objectives: We aim to evaluate GLP-1 receptor agonists in mice fed a 60% high fat, 1.25% cholesterol, 0.5% cholic acid diet with 2% cyclodextrin in drinking water (HFCC/CDX), a diet inducing hepatic cholesterol loading, inflammation and NASH within 3 weeks.
Methodology: C57BL6/J mice were fed the HFCC/CDX diet for 3 weeks, with chow fed mice used as negative control. After 1 week of HFCC/CDX diet, mice were treated i.p. for 2 weeks with vehicle or GLP-1 receptor agonists liraglutide 100 μg/kg QD or exendin-4 10 μg/kg BID.
Results: 3-Week HFCC/CDX diet increased plasma cholesterol, ALT and AST by 47%, 357 and 130% (all $p < 0.001$ vs. chow diet), and significantly increased liver cholesterol, triglycerides and fatty acids by 433, 614 and 270%, respectively. Histology analysis indicated that 3-week HFCC/CDX diet induced liver inflammation (score 3/3) and fibrosis (score 1/4). Importantly, inflammation score was already elevated (score 2/3), after as early as 1 week of HFCC/CDX diet. Liraglutide did not alter ALT/AST, but reduced inflammation score (vehicle: 3/3; liraglutide 2/3), resulting in reduced NAS score ($p < 0.01$ vs. vehicle). In another experiment, exendin-4 and liraglutide significantly reduces plasma cholesterol both by 14%, with an average 30% reduction of hematopoietic cells (CD45+ (FACS) analyses) frequency, including liver lymphocytes and macrophages.
Conclusion: GLP-1 receptor agonists reduce liver inflammation in our 3-week NASH mouse model. This model should be useful to rapidly detect anti-inflammatory effects of drugs targeting NASH.

Abstract #660

Dangfei Liganning Capsules Attenuate the Susceptibility of liver injury in the Rat with Nonalcoholilc Fatty Liver Disease to Toxicity through Regulation of SUV39H2-SIRT1 Signaling Pathway

Qiming Zhou[1], Haiyan Song[2], Dongfei Li[1], Peiyong Zheng[1], Guang Ji[1]

[1]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, [2]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine & CCCRDD

Objective: This study is to investigate the underlying mechanism of the effect of Dangfei Liganning Capsules (DF) on susceptibility of liver injury in nonalcoholilc fatty liver disease (NAFLD) rat to carbon tetrachloride (CCl4) toxicity.
Methods: Male Wistar rats were divided into normal control (N), normal + CCl4 (N-CCl4), NAFLD (HF), NAFLD + CCl4 (HF-CCl4) and DF treatment (DF) group. Rats of N and N-CCl4 were fed with normal diet, other rats with high fat diet. DF were administered for DF grou daily. After 8 weeks, rats of N-CCl4 and HF + CCl4 were intraperitoneal injected with low-dose CCl4. All rats were sacrificed after 48 h and serum and liver tissues were collected. The changes of liver histopathology, serum ALT and AST, hepatic SUV39H2, SIRT1, p65, acetylated p65, IL-1β, MCP-1 were detected.
Results: Low-dose CCl4 did not cause pathological changes in rat liver. Fatty degeneration of hepatic lobules appeared in NAFLD model, and steatosis was more serious in HF + CCl4 group, with hepatocyte balooning and inflammatory infiltration, which were alleviated in DF group. Serum ALT and AST, hepatic pro-inflammatory factors showed no difference in N and N-CCl4 group, but higher in HF + CCl4 than HF group, while down-regulated in DF group. The hepatic SUV39H2, p65 and acetylated p65 showed higher, while SIRT1 lower in HF and HF + CCl4 compared with N group, and more obvious changes were found in HF + CCl4 group, which were restored by DF.
Conclusions: DF could improve the susceptibility NAFLD rat to toxicants. Down-regulating SUV39H2, up-regulating SIRT1 and thereby inhibiting activation of NF-κb signaling partly contributes to the underlying mechanism.

Abstract #661

Inhibition of ceramide de novo synthesis alleviates high-fat diet induced nonalcoholic steatohepatitis in rat and resume impaired autophagy function

Rui-Xu Yang[1], Qin Pan[1], Rui-Nan Zhang[1], Jian-Gao Fan[1]

[1]Department of Gastroenterology, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine

Introduction and Objectives: Ceramide is associating with several pathways involved in insulin resistance, oxidative stress, inflammation, and apoptosis in the pathogenesis of nonalcoholic fatty liver disease (NAFLD). The aim of this study is to investigate the role of ceramide in NAFLD and its effect on the autophagy function.
Methodology: SD rats were randomly divided into three groups (n = 10), which were given standard chow, high-fat diet (HFD) and HFD with oral administration of myriocin (8–16 week). Liver histology and autophagy function were measured. HepG2 cells were cultured with fatty acid, in which lipid accumulation and autophagy markers were analyzed after the myriocin treatment.
Results: The inhibition of ceramide synthesis by myriocin had reversed the elevated body weight, serum transaminases and alleviated dyslipidemia induced by HFD. Liver pathology severities including steatosis, lobular inflammation and ballooning were significantly attenuated by myriocin. The q-PCR analysis revealed the inhibition of ceramide by myriocin resumed the expression of fatty acid metabolism associated genes including the Fabp1, Pparα, Cpt-1α and Acox-2. Impaired autophagy function was observed in the liver of HFD-induced NASH, and the myriocin intervention resumed LC-3 II and p62 to normal levels. In vitro experiment, fatty acid induced marked lipid accumulation and autophagy impairment in HepG2 cells. Myriocin alleviated the lipid accumulation and resumed the LC-3 II and p62 expression induced by the fatty acids.
Conclusion: The inhibition of ceramide synthesis resumed the impaired autophagy function and alleviate NASH, which may reveal the regulation role of autophagy function by ceramide in NASH development.

Abstract #666

Jiangzhi granules improve glucose tolerance of NAFLD mice through regulation of gluconeogenesis by TFF3

Tianbing Cui[1], Haiyan Song[1], Yang Liu[1], Lili Yang[1], Lianjun Xing[1], Guang Ji[1]

[1]Institute of Digestive Diseases, Longhua Hospital, Shanghai University of Traditional Chinese Medicine

Objectives: This study aims to investigate effect of Chinese medicine, Jiangzhi granules (JZG), on glucose tolerance of NAFLD mice and explore the possible mechanism.
Methods: C57BL/6 mice were fed with high-fat-diet to induce NAFLD, with mice fed with chow diet as control. 18 weeks later, some NAFLD mice were administrated orally by JZG for another 4 weeks. Oral gucose tolerance test (OGTT) and insulin tolerance test were carried out. Fasting blood glucose (FBG) and insulin were detected. Pathological changes of liver tissue were observed. RNA sequencing (RNA Seq) was used to detect the differentially expressed genes between groups. Then the function of the selected gene was studied in vitro and in vivo.
Results: JZG treatment lowered the weight and reduced hepatosteatosis appeared in NAFLD mice. The level of FBG, insulin and area under OGTT curve in the model increased, which were decreased by JZG. RNA Seq showed TFF3 was significantly higher in mice liver with JZG administration than NAFLD mice, which were verified by RT-PCR and Western blot. TFF3 was also found expressed less in liver of NAFLD mice. In vitro experiments indicated TFF3 overexpression in hepatocyte could reduce glucose content in culture supernatant, which was induced by oleic acid. TFF3 could downregulate expression of PGC-1α, G6PC, PEPCK. And the expression of these gluconeogenesis related genes, was found up-regulated in NAFLD mice, while decreased by JZG.
Conclusions: JZG can ameliorate the glucose tolerance of NAFLD mice, which might in part through increasing TFF3 expression to inhibit gluconeogenesis.

Abstract #667

Effect of INT-747 on hepatic and adipose tissue diacylglycerol acyltransferase gene isoforms and concomitant triglyceride synthesis in an experimental non-alcoholic steatohepatitis

Balasubramaniyan Vairappan[1], Anjana Chandrasekhar[1]

[1]Jawaharlal Institute of Postgraduate Medical Education and Research

Background: Triglycerides (TG) are the predominant energy storage molecules in eukaryotes, and the DGAT enzymes catalyse its synthesis. We aimed to investigate whether superimposed inflammation increases DGAT (1&2) overexpression and associated hepatic and adipose tissue TG synthesis in non-alcoholic fatty liver disease (NAFLD) and also to study the effect of FXR agonist INT-747 on the regulation of hepatic DGAT-TG pathway in NAFLD. Methods: 90 days after feeding HFD and chow, mice were orally administered INT-747 (5 mg/kg b.w. daily by gastric lavage) in the vehicle (corn oil) for 7 days or vehicle alone. In order to determine the effect of superimposed inflammation on the background of fatty liver, the treatment groups were given either lipopolysaccharide (LPS; 1 mg/kg in 1 ml of saline, IP) or vehicle (saline). Results: When compared to naïve mice, NAFLD mice showed markedly elevated hepatic and adipose tissue DGAT (1&2) protein expressions. LPS challenge to NAFLD mice showed further significant ($p < 0.05$) increase of hepatic DGAT 2 whereas adipose tissue DGAT (1&2) were not altered significantly. INT-747 treatment to NAFLD mice and that received LPS showed significantly ($p < 0.05$) reduced both DGAT 1&2 and hepatic TG synthesis. INT-747 treatment also reduces significantly hepatic inflammatory markers and cytokine concentration in NASH mice. Conclusion: Our study is the first indication of evidence for an association between increased hepatic but not adipose tissue DGAT 2 and associated TG synthesis in NAFLD mice with superimposed inflammation. INT-747 treatment attenuated hepatic TG accumulation by downregulating DGAT 2 overexpression, thereby improving the progression of NAFLD.

Abstract #675

Tofogliflozin improves hepatic disorder of nonalcoholic fatty liver disease in diabetes mellitus

Tomoya Emori[1], Yoshiyuki Ida[2], Shuya Maeshima[2], Ryo Shimizu[3], Izumi Nishikawa[3], Takeshi Hara[1], Hideyuki Tamai[4]

[1]Department of Gastroenterology, Wakayama Rosai Hospital, [2]Second Department of Internal Medicine, Wakayama Medical University, [3]First Department of Internal Medicine, Hidaka General Hospital, [4]Department of Hepatology, Wakayama Rosai Hospital

Background: The effectiveness of weight reduction on patients with nonalcoholic fatty liver disease (NAFLD) has been proven. As sodium-glucose co-transporter 2 (SGLT2) inhibitor is one of the antidiabetic drugs that have an effect of weight reduction, it is expected that SGLT2 inhibitor improves the hepatic disorder of NAFLD patients.
Aim: The aim of this study was to evaluate the effect of tofogliflozin on the hepatic disorder of NAFLD patients with diabetes.
Methods: Between May 2015 and August 2016, 24 NAFLD patients with diabetes who were administered tofogliflozin 20 mg for 6 months were retrospectively analyzed. The primary endpoint was the reduction of ALT value. Complete response was defined as the normal ALT value (less than 33 IU/L in male, 25 IU/L in female; Am J Gastroenterol 2017; 112:18–35.) at 6 months after the start of therapy, and partial response was defined as more than 30% reduction of ALT value from baseline.
Results: Complete response was 33% (8/24), and partial response was 50% (12/24). A significant reduction was observed in body weight, HbA1c, ALT, γ-GTP, uric acid and ferritin values. In comparison of the background factors between the effective and non-effective groups, baseline ALT and HbA1c reduction rate were significantly higher in the effective group. However, no significant difference was seen in weight reduction rate between the two ($p = 0.242$).
Conclusions: Tofogliflozin could improve the hepatic disorder of NAFLD patients with diabetes but also the disease state. HbA1c reduction was more significantly associated with ALT reduction than weight reduction.

Abstract #698

S-Adenosylmethionine alleviates hepatic steatosis by a different pathway of *N*1-methylnicotinamide

Makoto Nakamuta[1], Kenji Ohe[2], Yusuke Murata[2], Masayoshi Mori[2], Shinichi Kiso[3], Yasushi Mastuzaki[4], Naoki Tanaka[5], Kazuhiro Tanabe[6], Nobuhiro Ookubo[6], Naoyuki Togawa[7], Akira Honda[4], Tadashi Ikegami[8], Munechika Enjoji[2]

[1]National Hospital Organization Kyushu Medical Hospital, [2]Fukuoka University, [3]Osaka University, [4]Okyo Medical University Ibaraki

Medical Center, [5]Shinshu University School of Medicine, [6]Lsi Medience Corporation, [7]Mitsubishi Chemical Corporation, [8]Tokyo Medical University Ibaraki Medical Center

Background and aims: *S*-Adenosylmethionine (SAM) is important as a methyl donor during methylation and is involved in production of *N*1-methynicotinamide (MNAM), polyamine, phosphatidylcholine, and sarcosine. These methylated products have an important role in the development of non-alcoholic fatty liver disease (NAFLD) (Dahlhoff C, et al. Mol Metab. 2014; 3:565–80).
Method: C57BL/6J mice (n = 30) were divided into six groups and fed with normal diet (ND): high-fat diet containing fat of 40% (HFD): ND + SAM (SAM mixed with ND to 0.1% wt/wt): HFD + SAM: ND + MNAM (MNAM mixed with ND to 0.1% wt/wt): HFD + MNAM for 8 weeks. Liver MNAM-related metabolites were checked by LC/MS and the expression of liver lipid metabolism-related genes was analyzed by RT-PCR.
Results: Both SAM and MNAM suppressed body weight gain induced by HFD with histological improvement of steatosis but had no effect on ND mice. HFD mice treated with SAM did not change the levels of MNAM, nicotinamide (NAM), MNM, and NAD; however, HFD mice treated with MNAM significantly increased those of MNAM, NMN and NAD but not NAM. Interestingly, both SAM and MNAM similarly and completely suppressed the upregulated expression of genes involved in fatty acid synthesis. Lastly, the Treatment with SAM as well as MNAM activated Sirtuins.
Conclusion: The improvement of fatty liver by SAM was probably mediated by a different pathway from MNAM, because SAM did not increase the level of MNAM; therefore, the hepatic contents of other SAM derivatives are being measured now and are going to be tested for their possible favorable effects on NAFLD.

Abstract #703

The effectiveness of Pentoxifylline in NAFLD: A Meta-Analysis

John Mark Katindig Torres[1], Carlos Rolando Guevara Cuaño[2], Janus P. Ong[3]

[1]Department of Internal Medicine, Philippine General Hospital, Manila, [2]Section of Gastroenterology, Department of Internal Medicine, Philippine General Hospital, Taft Avenue, Manila, Philippines, [3]Section of Gastroenterology, Department of Internal Medicine, Philippine General Hospital, Taft Avenue, Manila, Philippines & Hepatology Society of The Philippines

Introduction: Non-alcoholic fatty liver disease (NAFLD) is a spectrum of liver pathology with varying clinical prognosis. Rising prevalence of NAFLD suggests its correlation with liver failure worldwide. To date, there is no proven pharmacologic therapy for NAFLD. Pentoxifylline with anti-tumor necrosis factor properties has shown improvement on histological parameters, reductions in transaminase levels and serum cytokines among NAFLD.
Methodology: A comprehensive literature search showed 7 randomized controlled trials (N = 222) comparing pentoxifylline (1200 mg/day) with placebo. Two reviewers independently selected studies, assessed quality, and extracted and pooled outcomes including reductions in aspartate (AST) and alanine transaminase (ALT) levels, serum cytokines and liver histology. Statistical analysis was done using the Review Manager Software 5.3.
Results: Pooled results showed that pentoxifylline significantly reduced the ALT (WMD = − 20.08; 95% CI: − 40.20, 0.05) and AST (WMD = -11.38; 95% CI: − 20.47, − 2.29) in NAFLD patients. Pentoxifylline significantly improved steatosis (WMD = − 0.33; 95% CI: − 0.87, 0.21), lobular inflammation (WMD = − 0.45; 95% CI: − 0.89, − 0.01), and fibrosis (WMD = − 0.39; 95% CI: − 0.83, 0.05). Among serum cytokines, significant reduction was demonstrated in TNF Alpha (WMD = − 20.20; 95% CI: − 50.46, 10.41; p = 0.0009) and IL-6 (WMD = 27.72; 95% CI: − 28.78, 84.22, p 0.03) but not in IL-8 (WMD = 1.63; 95% CI: − 10.34, 13.60, p = 0.21) when compared with placebo.
Conclusion: Pentoxifylline decreases aminotransferase activities and improves histology of NAFLD patients. Demonstrating effects on serum TNF-α which plays a key role in progression to hepatic steatosis, it may be used as adjunct to diet and lifestyle modifications in the treatment of NAFLD.

Abstract #750

Independent Predictors of ALT Improvement in Patients with NAFLD: More Than Weight Loss is Needed

Maria Roselle Evangelista Guzman[1], Jason Morven Yu Lim[1], Ann Margaret C. Navarroza[1], Stephen Ng Wong[1]

[1]University of Santo Tomas Hospital

Background: Changes in alanine aminotransferase (ALT) levels over time has not been characterized in patients with nonalcoholic fatty liver disease (NAFLD) in our population. We aimed to determine the factors that predict improvement in ALT levels in NAFLD patients.
Methodology: This is a cross-sectional study of consecutive adult patients with fatty liver on ultrasound from 2007 to 2017 with at least 1 follow-up. Normal ALT levels were pegged at 24 IU/mL and 19 IU/mL for male and female patients, respectively.
Results: A total of 416 patients were included, with 185 (44.5%) showing an improvement of − 28.15 + 36.44 IU/mL in ALT levels after a median follow-up of 11 months. Compared to normal ALT, patients with elevated baseline levels were more likely to have ALT improvement (50.7% vs. 16.9%; $p < 0.001$). Patients with diabetes (51.8% vs. 38.2%; p = 0.006), hypertension (51.9% vs. 34.6%; $p < 0.001$), dyslipidemia (49.3% vs. 32.5%; p = 0.002), and metabolic syndrome (51.7% vs. 35.2%; p = 0.001), and those with higher albumin (4.46 + 0.42 vs. 4.35 + 0.48; p = 0.013), and uric acid (6.26 + 1.51 vs. 5.83 + 1.85; p = 0.009) were more likely to have improved ALT on follow-up. There was no difference in ALT improvement between patients who lost or maintained/gained weight (47.4% vs. 42.8%; p = 0.413). On multivariate analysis, only hypertension (OR 1.63; 95% CI: 1.041–2.553; p = 0.033), metabolic syndrome (OR 1.570; 95% CI: 1.004–2.455; p = 0.48) and albumin (OR 1.65; 95% CI: 0.388–0.944; p = 0.027) were independent predictors of ALT improvement.
Conclusion: Surprisingly, weight changes did not influence improvement in ALT levels in our population. The presence of baseline metabolic risk factors as a predictor of ALT improvement suggests that improvement of these factors over time may have influenced ALT. Further analysis factoring changes in metabolic factors is required.

Abstract #753

Interplay of the Effects of Vitamin E and Weight Changes on ALT levels in Patients with NAFLD

Jason Morven Yu Lim[1], Stephen Ng Wong[1], Maria Roselle Evangelista Guzman[1], Ann Margaret Caraan Navaroza[1]

[1]University of Santo Tomas Hospital

Background: There is evidence that vitamin E improves nonalcoholic fatty liver disease (NAFLD) activity scores (NAS) and alanine

transaminase (ALT) levels in patients with NAFLD. However, the relationship between vitamin E and weight loss on ALT improvement has not been well characterized.
Methods: Patients diagnosed with NAFLD on ultrasound from February 2007 to January 2017 with at least one follow-up visit were included. Baseline demographic, clinical and biochemical characteristics were recorded. ALT levels and weight at last follow-up were compared to baseline in patients with and without vitamin E.
Results: A total of 416 patients were included, of which 61 (14.7%) were given vitamin E. Significantly more patients given vitamin E had elevated baseline ALT (58/61 [95.1%] vs. 281/355 [79.2%]; p = 0.002). Patients given vitamin E also had higher baseline AST (49.1 + 35.8 vs. 36.8 + 25.9; p = 0.012) and lower HBsAg positivity (9.8% vs. 24.5%; p = 0.012). On follow-up, significantly more patients on vitamin E had improvement in ALT (62.3% vs. 41.4%; p = 0.003). This difference was maintained in patients with elevated (62.1% vs. 48.4%; p = 0.062) and normal (66.7% vs. 14.9%; p = 0.072) baseline ALT, but did not reach statistical difference. More underweight/normal patients improved ALT on vitamin E (72.7% vs. 34%; p = 0.019) compared to overweight/obese patients (60% vs. 44.4%; p = 0.062). The effect of vitamin E on ALT improvement was significant only in patients who lost weight (79.2% vs. 41.4%; p = 0.001) and not in patients who maintained/gained weight (51.4% vs. 41.4%; p = 0.285).
Conclusions: Vitamin E significantly improves ALT levels in patients with NAFLD. However, this effect was only seen in patients who lost weight and was not demonstrated in patients who maintained or gained weight, which emphasizes the need for lifestyle changes and weight loss in patients with NAFLD.

Abstract #773

Effect of L-carnitine Supplementation in Non-alcoholic Fatty Liver Disease and Glucose Metabolism: A Meta-analysis

Carlo Antonio De Guzman Boado[1], Jessa Gilda Pacis Pandy[1], Mabel Angela T. Sarita[2], Ian Homer Yee Cua[2]

[1]Department of Medicine, St. Luke's Medical Center, Quezon City, [2]Institute of Digestive and Liver Diseases, St. Luke's Medical Center, Quezon City

Background: Because of the link of NAFLD to metabolic diseases like diabetes and its noted progression to cirrhosis and hepatocellular carcinoma, studies to search for its treatment is needed. L-Carnitine has been shown to have a role in fatty acid and glucose metabolism and may be beneficial in the treatment of NAFLD. The aim of this meta-analysis is to determine the efficacy of L-carnitine supplementation in lowering ALT and HbA1c in NAFLD.
Methodology: Pubmed, Embase, Cochrane and clinical trials databases was utilized to identify RCTs investigating the use of L-carnitine in patients with NAFLD and DM Type 2. Mean differences with 95% CI and OR were pooled using a random-effects model. The outcomes were the level of HbA1c and level of ALT after treatment.
Results: Four RCTs were included in this study (N = 264). Two studies (N = 102) showed significant effect in the HbA1c (P = 0.38) among patients supplemented with L-carnitine (mean difference − 0.15, 95% CI, − 0.49, 0.189). Three studies (N = 176) showed a significant effect towards reduction in the ALT (P < 0000.1) among patients treated with L-carnitine (mean difference − 29.75, 95% CI, − 36.24, − 23.26). A subgroup analysis was done to remove the heterogeneity with the inclusion of patients with NASH. Analysis of two RCTs (N = 102) showed a significant effect towards lowering ALT (P < 0000.1) among patients supplemented with L-carnitine.
Conclusion: L-Carnitine supplementation is effective in lowering down ALT especially in patients with fatty liver. Subgroup analysis show that ALT lowering effect is greater in patients with isolated fatty liver. There was no effect in glycemic control.

Abstract #797

Non Alcoholic Fatty Liver Disease (NAFLD) Fibrosis Score as an Alternative to Fibroscan in patients with NAFLD

Atul Hareendran[1], Krishnadas Devadas[1], Sandeep Narayanan[1], Simna Lubina[1]

[1]Department of Medical Gastroenterology, Government Medical College, Trivandrum, Kerala, India

Introduction: Fibroscan, even though non invasive, is a costly and not routinely available modality in assessing fibrosis.
Objectives: To determine the efficacy of NAFLD Fibrosis Score (NFS), Aspartate Transaminase to Platelet Ratio Index (APRI) and Fibrosis-4 (FIB4) versus Fibroscan in assessing fibrosis in NAFLD.
Materials and methods: Study carried out among NAFLD patients who were diagnosed using ultra sound abdomen showing fatty liver. Liver Function test, blood routine, anthropometry and Fibroscan were carried out. APRI, FIB 4, NFS were calculated for these patients and Area Under the Cure (AUC) was plotted.
Results: Of the 689 patients who were screened, the cut off of significant fibrosis with Fibroscan was taken as 9.9 kPa. AUC was plotted and Cut off were selected which gives the best possible sensitivity, specificity and positive predictive value and negative predictive values for significant fibrosis for APRI, FIB4, and NFS.
Discussion: The findings of high specificity and negative predictive value of NFS score correlates well with the findings in Petta et al. for identifying significant fibrosis.
Conclusion: In a resource limited setting APRI and NFS score can be used as a cheaper alternative for fibroscan for ruling out significant fibrosis.

Abstract #939

Exercise training prevents progression of nonalcoholic steatohepatitis and liver cancer in mice

Kenichi Tanaka[1], Hirokazu Takahashi[1], Keizo Anzai[1], Yuichiro Eguchi[1]

[1]Saga University

Introduction, objectives: Exercise is a robust treatment of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH); however, exercise effects on liver carcinogenesis is unclear. We investigated the effect of exercise training on NASH related hepatocarcinogenesis model in mice.
Methods: 2-Day-old male C57BL/6J wild-type mice were injected with streptozotocin (200 μg per mouse), and fed a high-fat diet (HFD) from 4 to 14 weeks. 6-Week-old mice were divided into 2 groups housed in normal cage (sedentary as a control group (control)) or wheel cage (training group (WCR)). Body weight, glucose level, liver weight, NAFLD activity score (NAS), liver fibrosis stage, and total tumor volume in liver.
Results: There was no difference in body weight between control and WCR mice (23.4 ± 1.1 g vs 23.6 ± 1.5 g, p = 0.94), and in glucose level (571 ± 17.7 mg/dL vs 598 ± 1.5 mg/dL, p = 0.207). Liver weight in WCR group were lower than control group (1.56 ± 0.21 g vs 1.37 ± 0.12 g, p = 0.48). Average NAS and liver fibrosis stage

were improved in WCR group (NAS: 5.3 ± 0.7 vs 3.3 ± 0.9, stage: 1.7 ± 0.3 vs 0.7 ± 0.3). Total tumor volume in liver tended to be lower in WCR group (202 ± 107 cm^3 vs 88.3 ± 35.1 cm^3, p = 0.37). **Conclusion:** Exercise training has preventive effects on progression of NASH and NASH related liver carcinoma in mice.

Abstract #1027

Reprogramig of Fat Metabolism in Hepatic Stelate Cells during steatosis: invitro study

Sumati Rohilla[1], Preety Rawal[1], Rekha Puria[1], Savneet Kaur[2]

[1]Gautam Buddha University, [2]Institute of Liver and Billary Sciences

Fat metabolism is well studied in Hepatic stellate cells (HSCs) during liver fibrosis, however not during early liver injury. In the current study, we comprehensively investigated fatty acid metabolism in correlation with HSC activation in the in vitro models of steatosis.

In vitro models of steatosis were established by culturing Lx2 cells with conditioned media of Huh7 cells treated with BSA (control), or treated with Palmitic acid (PA) at different time points. The expression of fatty acid metabolic genes were studied by real time PCR. Lipid droplets and activation of HSCs were evaluated by Nile red and αSMA staining respectively.

A significantly decreased expression of LRAT gene (involved in storage of vitamin A) and increased expression of αSMA was observed at 24 and 48 h in comparison to control Lx2 cells suggesting activation of HSCs. In comparison to the controls, we observed significant up-regulation of fatty acid metabolic associated genes at 48 h in Lx2 cells treated with CM of Huh7 treated with PA, but not at 24 h. At 72 h, expression of αSMA was decreased and nile red staining increased was indicating deactivation of HSCs.

Steatosis induced activation of HSCs. To revert activated HSCs back to quiescent state, at 48 h the cells illustrated increased uptake of fat from the CM, synthesizing and storing fat in the form of triglyceride to compensate the loss during activation. At 72 h, activated HSCs seem to revert back to the deactivated state.

Drug-Induced Liver Injury

M01 - Pathogenesis and mechanisms

Abstract #569

OX40-dificiency alleviates acetaminophen induced acute liver injury by regulating intrahepatic CD4+ T cells and monocytes

Chunpan Zhang[1], Guangyong Sun[2], Hua Jin[1], Yaning, Wang[1], Tingting Lv[3], Tianqi Wang[1], Shuxiang Li[3], Dong Zhang[1]

[1]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [2]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & Beijing Clinical Research Institute, Beijing, China & Beijing Key Laboratory of Tolerance Induction and Organ Protection Transplantation, Beijing, China, [3]National Clinical Research Center for Digestive Diseases, Beijing, China

Introduction: Overdosage of acetaminophen (APAP) can lead to massive hepatocellular necrosis and is a main cause of acute liver injury (ALI) in humans. Both innate and adaptive immunity are implicated in the progression of APAP-induced ALI. However, the cross talk between innate and adaptive immunity in APAP-induced ALI is largely unknown.
Objectives: To explore the critical role of OX40 in the crosstalk between innate and adaptive immunity in APAP induced ALI mouse model.
Methodology: Wild type (WT) and OX40−/− mice received APAP (300 mg/kg) by intraperitoneal injection. ALI was monitored and the activation, differentiation and proinflammatory cytokine secretion of liver infiltrated immune cells were compared in each group.
Results: WT mice showed significantly increased OX40 expression on CD4+ T cells and elevated plasma OX40 concentrations 24 h after APAP treatment. OX40 deficient mice displayed significantly ameliorated liver injury, accompanied with reduced liver infiltration of Th1, Th17 cells and monocytes compared with those in WT mice. Adoptive transfer of OX40 deficient CD4+ T cells but not WT CD4+ T cells into Rag1−/− mice resulted in alleviated liver injury with decreased infiltration of monocytes and proinflammatory cytokines secretion. Mechanistically, OX40/Fc in vitro stimulations showed that the soluble OX40 up-regulated genes associated with inflammation and tissue infiltration, chemokine receptors, the antigen processing and presentation molecules.
Conclusion: These results demonstrated that OX40 deficiency could improve APAP induced liver injury by regulating both of innate immune cells and adaptive immune cells via binding to its cognate ligand OX40L.

Abstract #585

Protective effects of Capparis Spinosa on triptolide induced mitochondria injury in vitro and in vivo

Ya-Lei Zhang[1], Lu Xing[2], Ting-Ting Zhu[2], Yan-Yan Tao[2], Cheng-Hai Liu[3]

[1]Institute of Liver Diseases, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine & Institute of Cardiovascular Disease, Department of Cardiology, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, [2]Institute of Liver Diseases, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, [3]Institute of Liver Diseases, Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine & Shanghai Key Laboratory of Traditional Chinese Clinical Medicine

Introduction: Triptolide (TP), a diterpenoid triepoxide, has a more severe hepatotoxity from the medicinal plant *Tripterygium wilfordii* Hook. F. (TWF). *Capparis spinosa* L. (CS) is a plant originating from dry regions in west or central Asia and spread particularly across the Mediterranean basin, and its fruits were found to possess significant anti-hepatic injury.
Objectives: To investigate the protective effect and mechanism of CSE on TP induced hepatocytic mitochondria damage in vitro and in vivo.
Methodology: The changes mitochondria and apoptosis of hepatocytes was detected to investigated liver injury induced by TP and the protective effects of the total extract of CS (CSE).
Results: The levels of serum ALT, AST and AKP in acute and chronic injury liver group were significantly increased ($P < 0.01$). However, there was no significant pathology injury in chronic model (Fig. 1). Furthermore, TP caused mitochondrial injury, and promoted the release of cytochrome C in vitro, which leads to liver cell apoptosis. CSE an effectively inhibited the increase of ALT, AST, AKP in serum, MDA and SOD in liver tissue ($P < 0.01$) caused by TP (Fig. 2). CSE could increase the viability of AML-12 cells induced by triptolide ($P < 0.01$), and reduce the apoptosis of AML-12 cells

(Fig. 3). Pathological results showed that CSE can effectively reduce hepatic cell vesicular steatosis and necrosis of liver cells and reduce apoptosis of liver cells in vivo.
Conclusion: TP caused liver cell mitochondrial injury and apoptosis. The CSE has a good protective effect on triptolide induced acute liver injury.

Abstract #795

Genetic variations of ABC transporters and drug-induced hyperbilirubinemia

Yi-Shin Huang[1], Tien-En Chang[1], Chin-Lin Perng[1], Yi-Shiang Huang[1], Ming-Chih Hou[1]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taiwan & National Yang-Ming University School of Medicine, Taipei, Taiwan

Introduction: Hyperbilirubinemia is the ominous sign of drug-induced liver injury (DILI). Hepato-biliary ATP-binding cassette (ABC) transporters play an important role in the transportation of many drugs and bilirubin. Little is known about these transporters and the risk of DILI.
Objectives: To explore the association between genetic variations of the important transporters and the susceptibility to DILI, with special reference to hyperbilirubinemia.
Methodology: A total of 100 patients with anti-tuberculosis drug-induced liver injury (ATDILI), 100 patients without ATDILI, 100 patients with DILI induced by drugs other than anti-tuberculosis agents, and 100 drug-matched patients without DILI were recruited. They were genotyped for the ABCB11 c.1331T>C (rs2287622), ABCB1 c.1236T>C (rs1128503), c.3435T>C (rs1045642), ABCB4 c.1954A>G (rs2230028), ABCC2 c.-1549A>G (rs1885301), c.-24C>T (rs717620), c.1249G>A (rs2273697), c.3972C>T (rs3740066) and c.4544G>A (rs8187710).
Results: There was no statistical difference of all the 9 SNPs of ABC transporters among the four groups. However, in the ATDILI group, the patients with hyperbilirubinemia had higher frequency of ABCC2 rs717620 C/T or T/T genotypes than those without hyperbilirubinemia (55.9% vs. 28.3%, $p = 0.006$). After adjustment with age and gender, the ABCC2 T variant has still shown to increase the risk of hyperbilirubinemia and mortality (OR: 3.52, 95% CI: 1.62–7.64, $p < 0.001$ and OR: 3.95, 95% CI: 1.21–12.82, $p = 0.022$, respectively).
Conclusion: Carriage of ABCC2 rs717620 T variant may have a higher risk of hyperbilirubinemia and mortality in patients with ATDILI. Screening of this variant may help to prevent and mitigate drug-induced hyperbilirubinemia.

M02 - Clinical

Abstract #97

Endoscopic submucosal tunnel dissection of large superficial esophageal cancers in patients with cirrhosis: a propensity score analysis

Linlin Zhu[1], Junchao Wu[1], Yiping Wang[1], Tao Gan[1], Jinlin Yang[1]

[1]West China Hospital of Sichuan University

Background and aims: Based on propensity score analysis (PSM), this study reports the outcomes of endoscopic submucosal tunnel dissection (ESTD) for the treatment of esophageal cancer in patients with liver cirrhosis.
Methods: The study identified 63 patients with 65 lesions who underwent ESTD between October 2014 and April 2018. We used the PSM method to minimize the effect of selection bias. Dissection speed, R0 resection rate, incidence rate of muscular injury, bleeding and perforation were compared between patients with and without cirrhosis.
Results: Eleven patients (13 lesions) were included in the cirrhotic group, and 52 patients (52 lesions) were included in the noncirrhotic group after PSM. Although the average size of the lesions and the mean dissection speed in the cirrhotic group were higher than those of the noncirrhotic groups (14.3 ± 7.9 cm^2 versus 13.5 ± 8.4 cm^2, 25.9 ± 15.8 mm^2/min versus 19.4 ± 12.5 mm^2/min, respectively), there were no significant differences between the two types of lesions ($p = 0.751$, $p = 0.117$, respectively). En bloc dissection was achieved for all lesions, and the R0 resection rate was 84.6% versus 82.7% for the cirrhotic and noncirrhotic group, respectively. Muscular injury occurred in 2 (15.4%) patients, but no bleeding, perforation or esophageal strictures were observed in the cirrhotic group. No significant differences in the R0 resection rate or in muscular injury were observed between the two groups after PSM ($p > 0.05$).
Conclusions: Esophageal ESTD provided similar dissection speed for large superficial esophageal cancers in patients with cirrhosis without increasing operation-related bleeding. It can be considered safe and effective when performed in cirrhotic patients.

Abstract #144

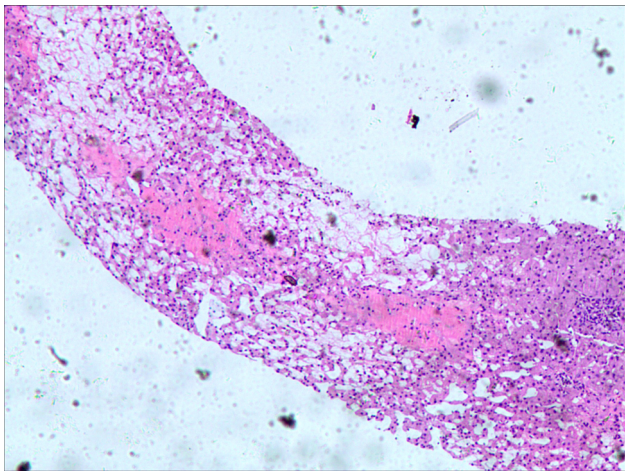
Gynura Segetum Induced Hepatic Sinusoidal Obstruction Syndrome: a High Mortality and Misdiagnosis Rate Liver Disease

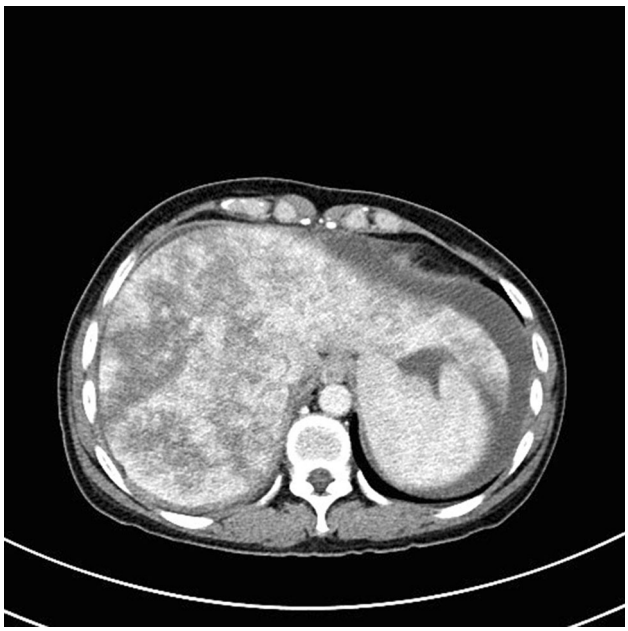
Jun Chen[1], Yi Li[2], Shangzhen Zhou[2], Pengcheng Ou[3], Zhixiong Fang[4], Chuming Chen[5]

[1]The Third Hospital of Shenzhen & The Second Xiangya Hospital, [2]The Second Xiangya Hospital, [3]The First Hospital of Shenzhen, [4]The Central Hospital of Xiangtan, [5]The Third Hsopital of Shenzhen

Background and aims: Gynura segetum (Chinese named Tusanqi or Jusanqi) was widely used in China and often caused hepatic sinusoidal obstruction syndrome (HSOS), but its extent of hepatotoxicity is not sufficiently clear. To describe out the clinical profiles, we performed this study.
Methods: Totally 64 patients whose diagnosis was HSOS induced by Gynura segetum from 8 Chinese tertiary care hospitals between January, 2010 and June, 2018 were enrolled. The general information, diagnosis, disease history, suspected drugs, symptoms and signs, biochemical index, imaging, liver histological, treatment methods, severity and prognosis were collected and statistical analyzed.
Results: The mean age was 58.07 ± 11.44 years. Male patients were predominant in HSOS patients (64.1%). The median of latency period was 75 days. The patients number of definite diagnosis were established in other hospitals was 5 (7.81%), misdiagnosis rate was 92.18%. Hepatomegaly, splenomegaly, ascites and lower limbs edema was presented in 89.1, 76.6, 81.3 and 43.8% patients, respectively. The percentage of characteristic changes of B-ultrasound and CT/MRI was respectively 75.49% and 100%. All liver biopsy presented characteristic pathologic changes. Except for ALT and D-dimer, the liver function and coagulation index at the admission and last time before discharge had not significant difference ($p > 0.05$). The general 6-month mortality was 77.55%, upper-gastrointestinal bleeding was the first cause of death (42.11%), the second cause was liver failure with secondary infection (36.84%), the third cause was liver failure with hepatorenal syndrome (21.05%).

Conclusion: Gynura segetum related HSOS often presented as progressive hepatic congestion and portal hypertension with high mortality and misdiagnosis rate.





Abstract #361

Can Regular Monitoring Liver Function Ameliorate Anti-tuberculosis Drug-induced Liver Injury?

Tien-En Chang[1], Yi-Shin Huang[1], Wei-Juin Su[2], Chin-Lin Perng[1], Yi-Hsiang Huang[1], Ming-Chih Hou[1]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taiwan, [2]Department of Chest Medicine, Taipei Veterans General Hospital, Taiwan

Introduction: Anti-tuberculosis drug-induced liver injury (ATLI) is a common adverse effect of anti-tuberculosis drugs. Whether monitoring liver function regularly can ameliorate ATLI is debatable.
Objectives: To investigate the features of ATLI in Taiwan, and the impact of scheduled monitoring liver function on the ATLI.
Methodology: Patients received anti-tuberculosis treatment at our hospital from 2009 to 2017 were enrolled. The physician's adherence to liver function monitoring and the role of monitoring strategy in the susceptibility of ATLI were evaluated.
Results: A total of 1062 patients were included, of them 469 (44.2%) were monitored liver functions regularly (good monitoring group). ATLI was recognized in 100 (9.4%) patients. Twenty-one of 100 ATLI patients had severe hepatotoxicity and 5 patients died from ATLI. The good monitoring group could early detect more ATLI cases (21.4 vs. 61.6 days, and 14.7% vs. 5.2%) with less peak serum alanine aminotransferase (276.1 vs. 507.1 IU/L) than the poor monitoring group. The good monitoring strategy for all patients could detect more total or severe cases of ATLI than only monitoring in high-risk patients (odds ratio [OR]: 3.00, 95% confidence intervals [CI] 1.92–4.70, and OR: 2.93, 95% CI 1.11–7.83, respectively).
Conclusion: Nearly half patients receiving anti-tuberculosis treatment were monitored liver function regularly in Taiwan. Regular monitoring liver function for all patients could early detect more ATLI cases with less liver injury than only monitoring in high-risk patients. Scheduled surveillance of liver function plays a crucial role in the detection and prevention of ATLI.

Abstract #382

Herbal Medicines Induces Severe Liver Injury than Western Medications: A nationwide multicenter retrospective research

Jun Chen[1], Xinyu Liu[2], Chuming Chen[1], Yingxia Liu[1]

[1]The Third Hospital of Shenzhen, [2]The Third Xiangya Hospital

Background: Herbal medicines (HM) are widely used, however, the clinical features of HM-induced liver injury are not yet clarified.
Objective: To intensive investigate the differences between HM DILI and western medications (WM) DILI.
Design: A nationwide multicenter retrospective research among hospitalized patients.
Setting: 308 medical centers in major cities of China.
Participants: 29,478 DILI patients, who were hospitalized from January 1, 2012 to December 31, 2014.
Measurements: Patients whose RUCAM scores are more than 6 just took either only HM or only WM as causative agent of DILI were analysed. The data on demographics, clinical characteristics, suspicious drugs, and outcome assessments of eligible cases were collected and systematically evaluated.
Results: A total of 3711 HM and 8859 WM cases were enrolled in the study. The mean age of the HM group was 48.24 $\pm$ 14.64 years, and that of the WM group was 44.70 $\pm$ 17.19 years ($p < 0.0001$). Females (59.3%) were predominant in the HM group. The average serum level of ALT, AST, ALP, TBIL and DBIL at baseline and peak value was significantly higher in the HM group ($p < 0.0001$). Although the general mortality of the two groups did not differ significantly ($p = 0.1491$), the liver-related death varied significantly between HM group and WM group (0.35% vs 0.12%, $p = 0.0369$). The incidence of Hy's cases, acute liver failure, and chronic DILI was more frequent in the HM than the WM group (45.03% vs. 14.13%, 1.59% vs. 0.82%, 14.4% vs. 8.78%, respectively).
Conclusion: Depending on clinical characteristics and outcomes, HM might cause severe liver injury and liver-related mortality than WM.

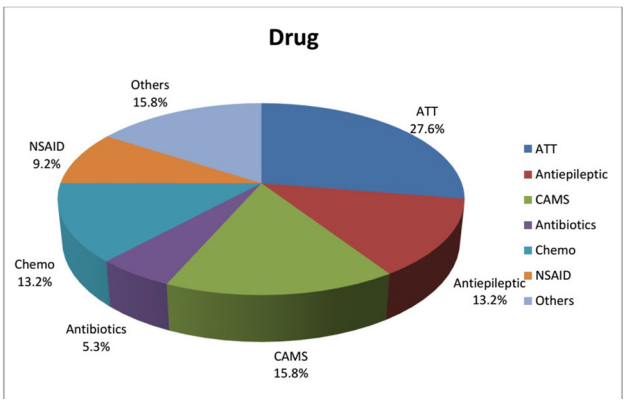
Abstract #390

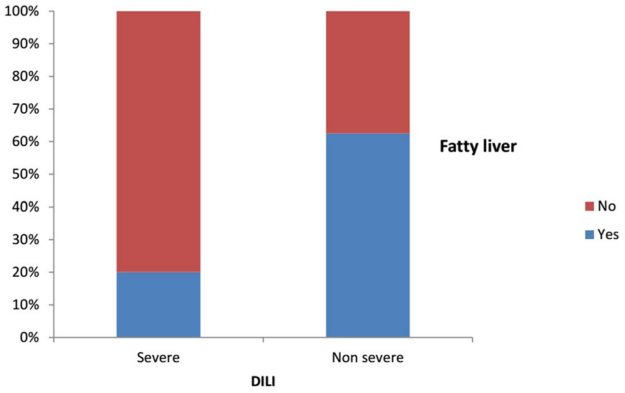
Fatty liver does not predict severity of Drug induced Liver Injury
Fatty liver does not predict severity of Drug induced Liver Injury

Sandeep Narayanan[1], Krishnadas Devdas[1], Rathan Cyriac[1], Ponni Krishnan[2]

[1]Govt Medical College, Trivandrum, [2]General Hospital, Trivandrum

Introduction: Drug hepatotoxicity accounts for 15% of causes among cases of acute liver failure requiring liver transplantation. The factors predicting outcome in DILI has not been well understood. Of late several studies has linked DILI severity with underlying NASH as both the disorders has been thought to be due to mitochondrial dysfunction.
Aims and objectives: Objective of the study was to determine whether fatty liver is an independent predictive factor for severity of drug induces liver injury.
Study design: Observational study.
Methods: All cases with suspected DILI with RUCAM more than 6 were enrolled. Severe DILI was defined as either INR > 1.5 or Ascites or hepatic encephalopathy or other organ failure.
Results: A total of 76 patients were included in the study, out of which 28 had severe DILI. There was 7 cases of fatal DILI, out of which 3 had underlying cirrhosis. Females formed 59.2% of the cohort. The most common cause of DILI was ATT (27.6%), followed by CAMS (15.8%), Chemotherapeutic drugs (13.2%) and antiepileptics (13.2%). Most of the severe DILI cases were due to ATT (46.4% of all severe DILI cases). 67% of the total study population had a baseline ultrasound before exposure to the drug in question. The ultrasound features in those who had a baseline ultrasound was similar in fresh ultrasound. Fatty liver was seen in 39.5% of the patients which is high compared to the population prevalence of around 30% based on previous studies. Only 14.3% of severe DILI patients had fatty liver compared to 56.3% of non severe DILI patients.





Abstract #430

Case of Immune-mediated Drug-induced Liver Injury Induced by Rabeprazole and Mosapride

Mei-Mei Lin[1], *Hong Shi*[1,2,*], Yuan Ji[3], Xi-Zhong Shen[2]

[1]Department of Gastroenterology and Hepatology, Xiamen Branch, Zhongshan Hospital, Fudan University, Xiamen 361000, Fujian, China, [2]Department of Gastroenterology and Hepatology, Zhongshan Hospital, Fudan University, Shanghai 200032, China, [3]Department of Pathology, Zhongshan Hospital, Fudan University, Shanghai 200032, China

Abstract

Immune-mediated drug-induced liver injury (IM-DILI) is a special type of DILI. Differentiation between IM-DILI and AIH is challenging because they share similar clinical and histological patterns. Here we report a Chinese 43-year-old female patient with abnormal liver function. The initial diagnosis was drug-induced liver injury due to the patient's 4 month exposure to rabeprazole and mosapride prior to her presentation. A liver biopsy was performed with pathology suggestive of AIH despite the negative autoimmune antibody panel. The patient was treated with acetate prednisolone at an initial dosage of 60 mg. Her liver function tests showed marked improvement and reached normal limits within a month of treatment with subsequent tapered doses of acetate prednisolone. The patient is currently following up at our outpatient clinic and has shown no signs of deteriorating liver function for 4 years. We eventually diagnosed the patient as IM-DILI due to the sustained remission. Our findings suggest that physicians should always bear in mind the differential diagnosis between IM-DILI and AIH to avoid unnecessary treatment of long-term acetate prednisolone.

Abstract #487

Characteristics and Outcomes of Unintentional and Intentional Acetaminophen (APAP) overdose in Thailand

Natthiya Pholmoo[1], Chalermrat Bunchorntavakul[2]

[1]Rajavithi Hospital & Chulabhorn Research Institute, [2]Rajavithi Hospital

Background/aims: Acetaminophen (APAP) is the leading cause of drug overdose and hepatotoxicity worldwide. Intentional APAP overdose (ITOD) ingestion typically follows suicidal attempt. However, some APAP hepatotoxicity cases may result from unintentional

overdose (UNOD). This study was aimed to compare the clinical characteristics and outcomes of UNOD and ITOD in Thailand.
Method: In this retrospective analytic study, medical records of adults hospitalized with a diagnosis of APAP overdose at Rajavithi Hospital, Bangkok, between January 2013 and December 2017 were reviewed.
Results: A total of 184 patients with APAP overdose were included (17 UNOD and 167 ITOD). The median age was 22 (15–76) years and 79.9% were female. Clinical characteristics and outcomes are summarized in the Table. Overall, 14.7% developed mild hepatotoxicity (AST or ALT $>$ 3xULN), 6% developed severe hepatotoxicity (AST or ALT $>$ 10 xULN and INR $>$ 2.0) and 3 patients developed acute liver failure (1 spontaneously resolved and 2 deaths without liver transplant). When compared to ITOD, patients with UNOD were more likely to have older age, history of alcohol abuse, underlying cirrhosis, jaundice at presentation, and longer ingestion-to-hospital duration. Thus, patients with UNOD were more likely to develop renal injury, hepatotoxicity and liver failure.
Conclusion: UNOD accounts for about 10% of APAP overdose in Thailand. Patients with UNOD are associated with poorer outcomes which may partly explain by underlying chronic liver disease and late presentation to the hospital.

Abstract #689

Histologic Pattern Is Better Correlated with Clinical Outcomes than Biochemical Classification in Patients with Drug-induced Liver Injury

Qiuju Tian[1], Xinyan Zhao[1], Yan Wang[1], Ruiyuan Yang[1], Lan Wang[1], Hong You[1], Jidong Jia[1], Yuanyuan Kong[1], Min Li[1]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, National Clinical Research Center for Digestive Diseases, Beijing, China, [2]Clinical Epidemiology and Evidence-Based Medicine Unit, National Clinical Research Center for Digestive Diseases, Beijing Friendship Hospital, Capital Medical University, Beijing, China

Aims: To compare the association between biochemical classification versus histologic injury pattern and clinical outcomes in patients with drug-induced liver injury (DILI).
Methods: This is a retrospective cohort of DILI patients from 2009 to 2013 in Beijing Friendship Hospital. Biochemical classification was determined by R values. Histologic injury pattern was determined by morphological features. Clinical outcomes were defined as biochemical normalization, persistent abnormal liver biochemistry or death at designated time points. Predictive ability of clinical outcomes by these two classifications was assessed using ROCs. Logistic regression was performed to identify histologic factors associated with outcomes.
Results: 88 out of 214 DILI cases were included for final analysis. Fifty (56.8%) cases had concordant biochemical and histologic classification. Fifty-three (60.2%) cases showed clinical resolution within 6 months, and a further 11, 16 and 6 cases within 1, 2 and 3 year/s, respectively. Compare to biochemical classification, histologic injury pattern was significantly better correlated with abnormal biochemistry at 6 months (AUROCs 0.92 versus 0.60, $P < 0.001$) and 1 year (AUROCs 0.94 versus 0.69, $P < 0.001$), but not for 2 years (AUROCs 0.95 versus 0.79, $P = 0.14$). Interlobular bile duct loss in $>$ 25% portal areas was independently associated with abnormal biochemistry at 6 months, 1 year and 2 years.
Conclusions: Histologic injury pattern is significantly better correlated with clinical outcome at 6 months and 1 year than biochemical classification. Moderate bile duct loss is an important histologic feature associated with persistent biochemical abnormality at 6 months, 1 year, and 2 years.

Abstract #702

Thiamazole-induced Concomitant Acute Cholestatic Hepatitis and Agranulocytosis

Andree Kurniawan[1], Nata Pratama Hardjo Lugito[2], Ignatius Bima Prasetya[3], Regina Stefani Roren[4]

[1]Internal Medicine, Faculty of Medicine, Pelita Harapan University, Karawaci, Tangerang, Banten, Indonesia, [2]Internal Medicine, Faculty of Medicine, Pelita Harapan University, [3]Internal Medicine, Faculty of Medicine, Pelita Harapan University, [4]Faculty of Medicine, Pelita Harapan University

Introduction: Antithyroid drugs have commonly been used for the treatment of hyperthyroidism. Most patients tolerate it well but several cases may develop life-threatening side effects such as agranulocytosis and cholestatic hepatitis. Estimates regarding the frequency of this condition are imprecise, but it probably ranges from 0.1 to 0.2%.
Objective: Present a rare side effect of Thiamazole-induced concomitant acute cholestatic hepatitis and agranulocytosis.
Case report: A 62-year-old female was diagnosed with Graves' disease manifested as severe hyperthyroidism. Treatment with thiamazole 20 mg daily was initiated. Within 8 weeks after starting the therapy, she came with fever, fatigue, jaundice, myalgia and severe weight loss. The laboratory results showed marked leucopenia (640/μL) with neutrophil 8% in differential count. The abdominal ultrasound revealed intra hepatic cholestatic. She was diagnosed having acute cholestatic hepatitis and agranulocytosis because side effect of thiamazole. Others differential diagnoses such viral hepatitis and other tropical infections have been excluded. Patient's symptoms and laboratory abnormalities resolved within 2 weeks following withdrawal of those drug. She also got anti-inflammatory dose of prednisone, granulocyte colony stimulating factor (G-CSF) and other supportive treatment.
Conclusion: Agranulocytosis and cholestatic hepatitis togethers are an extremely rare idiosyncratic side effect of anti-thyroid treatment and considered to be dose and age-related. Antithyroid agents are known rarely to cause liver dysfunction, which is among the small number of their idiosyncratic toxic effects. All practitioner who prescribe the anti-thyroid drugs should aware about their complex pharmacology mechanism and drugs interaction.

Abstract #706

Survey on knowledge of medical workers towards the hepatitis virus screening in tuberculosis patients in Yunnan province: a cross sectional study

Shu Hua Zhan[1], Shi Wu Ma[1]

[1]The 920th Hospital, Joint Logistic Support Force, Pla, Kunming, 650223, China,

Background: The endemic areas of tuberculosis and hepatitis virus are often overlapped in developing countries. The risks of liver injury (DILI and virus-reactivation) are significantly increased in tuberculosis patients co-infected with hepatitis virus, and most easily neglected due to no guideline highlighting these screening before anti-tuberculosis.

Objective: This study was conducted to investigate the knowledge of medical workers towards the hepatitis virus screening in tuberculosis patients.
Methods: This cross-sectional study was conducted in medical workers of tertiary and secondary comprehensive hospitals in Yunnan province during October and December in 2018. The candidates should engage in the diagnosis and treatment of tuberculosis, and their decisions on screening serum biomarkers of HBV and HCV before anti-tuberculosis and glucocorticoid treatment were collected by questionnaire survey.
Results: In candidates responded to questionnaires, the valid questionnaire rate was 92% (493/535). The screening decisions were made by 43.8% of medical workers for anti-HCV and 65.9% for HBsAg before anti-tuberculosis, and by 73.0% for anti-HCV and 75.5% for HBsAg before glucocorticoid treatment in Tuberculosis patients. Before anti-tuberculosis and glucocorticoid treatment, the screening decisions on anti-HCV and HBsAg made by medical workers of tertiary hospitals were more than by those of secondary hospitals. The screening decisions on anti-HCV and HBsAg made by medical workers in department of infectious disease were more than those in other departments.
Conclusion: This is the first survey in China to show the knowledge of medial workers on screening hepatitis virus in tuberculosis. The hepatitis virus screening should be improved in tuberculosis patients.

Abstract #719

Clinicopathological features of Bu-Gu-Zhi induced liver injury, a long term follow up cohort study

Lan Wang[1], Yan Wang[1], Qiuju Tian[1], Ruiyuan Yang[1], Liwei Liu[1], Hong Ma[1], Xinyan Zhao[1]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China,

Background: Bu-Gu-Zhi, one of the most popular Chinese herbs, has been widely used for the treatment of osteoporosis. Till know large size cohort of Bu-Gu-Zhi induced liver injury with thorough follow-up data is lacking.
Objectives: We aims to describe clinicopathologic features of Bu-Gu-Zhi induced liver injury along with prognostic information after de-challenge. Methods: Forty out of 547 DILI patients from 2005 to 2017 were caused by Bu-Gu-Zhi in Beijing Friendship Hospital, which were indentified. Kruskal–Wallis and Chi square tests were performed for continuous and categorical variables statistical analysis.
Results: Treatment of osteoporosis was the main purpose of Bu-Gu-Zhi intake (79.5%). Patients commonly presented with loss of appetite (56.4%), dark color urine (56.4%) and fatigue (53.8%). Median alanine aminotransferase and aspartate aminotransferase at onset were 664 U/L and 414 U/L, respectively. Median alkaline phosphatase and gamma-glutamyl transferase slightly elevated (165 U/L and 187 U/L, respectively). Median total bilirubin (TBIL) and direct bilirubin (DBIL) moderately elevated 49 mmol/L and 36 mmol/L. These patients were divided into three groups—mild (N = 23, 59.0%), moderate (N = 6, 15.4%) and severe injury (N = 11, 25.6%). 9/40 patients had a liver biopsy. Eight biopsies presented with acute cholestatic hepatitic and the remaining one was acute cholestatic injury pattern.
Conclusions: 3/4 Bu-Gu-Zhi induced liver injury was mild to moderate liver injury whereas 1/4 patients had severe liver injury. No patient had liver related death in this cohort. Patients with severe liver injury had significantly more complaints, higher onset serum liver tests, slower course of bilirubin normalization and longer stay in hospital.

Abstract #829

Drug Induced Liver Injury (Dili), A Potential Killer In Hospitalized Patients: A Study From A Tertiary Care Hospital In Pakistan

Farhana Kayani[1], Shahab Abid[1], Faryal Subhani[1], Safia Awan[1], Adeel Abid[1]

[1]Aga Khan Unversity Hospital

Aim: In light of paucity of data on DILI especially from South East Asia, this study aims to evaluate clinical spectrum and predictors of mortality and morbidity of hospitalized patients with suspected DILI.
Methods: 462 cases were identified and categorized on basis of COIMS/RUCAM score and exclusion of other liver diseases. Ratio (R value) between ALT (alanine transferase) and AP (alkaline phosphatase) expressed as $R > 5$; hepatocellular, $R < 2$; cholestatic, and $R > 2 < 5$; mixed. Clinical and laboratory parameters were analyzed to identify predictors of hospital mortality and morbidity in terms of prolonged hospital stay (> 5 days).
Results: Out of 462 patients, 264 (57.6%) were males with mean age being 50.8 years (range, 20–94 years). DILI was classified as definite/highly probable in 31.1%, probable in 62.5%, and possible in 7.4% of cases. Pattern of liver injury was hepatocellular in 25.1%, cholestatic in 56.1% and mixed in 18.7% of patients. Mean total bilirubin levels, ALT and AP levels were 5.37 mg/dl, 358.6 IU/L and 168.6 IU/L, respectively. Antituberculous (ATT) drugs were found to be most common cause (63.9%) followed by homeopathic/herbal meds and others. Altered mental status was present in 98 (21.6%) of patients while rest presented with abdominal pain, vomiting, jaundice and pruritus. In-hospital mortality was 26.5% and prolonged hospital stay was observed in 35.93% of patients. On multivariate analysis mortality was significantly greater in patients with altered mental status, male gender, hepatocellular pattern of DILI, increased INR (> 1.5) and use of ventilator support. Likewise, prolonged hospital stay was associated with female gender, increased ALT, AST aspartate aminotransferase levels, use of ventilator support and mixed pattern of DILI. 92 (25%) patients received *N*-acetylcystiene (NAC); subgroup analysis was conducted to compare with patients who received supportive care. These patients had high INR values (p 0.001), majority had altered mental status (34.8 vs 17.9; $p < 0.001$) and required ventilator support (29.4 vs 10.9; $p < 0.001$). A higher mortality rate was observed in NAC group 38 (41.3%) with prolonged hospital stay in 50 (54.3%).
Conclusion: Most frequent cause of DILI was ATT in hospitalized patients with cholestatic pattern. More than a quarter of patients died during hospital stay. Hence, awareness among physicians is required while prescribing potentially hepatotoxic agents.

Abstract #973

Clinical efficacy of Glycyrrhizin and Corticosteroid for drug-induced liver injury (DILI)

Shin Yasui[1], Shingo Nakamoto[1], Masato Nakamura[1], Susumu Maruta[1], Kengo Kanayama[1], Hiroaki Kanzaki[1], Takahiro Maeda[1], Yuko Kusakabe[1], Kazufumi Kobayashi[1], Kiyono Souichiro[1], Sadahisa Ogasawara[1], Eichiro Suzuki[1], Yoshihiko Ooka[1], Ryosuke Muroyama[1], Tetsuhiro Chiba[1], Hitoshi Maruyama[1], Naoya Kato[1]

[1]Gastroenterology, Chiba University

Introduction: Various factors are involved in the onset of drug-induced liver injury (DILI), and various disease states are present. There are cases in which it can not cope with acute hepatic failure (ALF) and only with withdrawal, but there are few reports on active treatment. Therefore, we examined the effectiveness of glycyrrhizin (GL) and corticosteroid (CS) on DILI.
Method: We examined the effect of GL and CS in 19 patients with high risk of DrILTox ALF score at onset. The primary endpoint was the rate of decrease of AST and ALT after treatment (day 4, day 7).
Result: The median age was 49 years, eight women, 4 cases of ALF. As initial treatment, GL was administered in all cases, and CS was used in 5 cases. In overall cases, the reduction rate of AST and ALT on day 4 were 84%, 61%, and on day 7 were 91%, 80%. In the comparison by treatment, the reduction rate of AST and ALT on day 4 was 76%, 53% in the GL group, 93%, 80% in the combination group, and it was significantly higher in the combination group (P = 0.001, P = 0.002). The reduction rate of AST on day 7 was also 83% in the GL group and 99% in the combination group, and it was significantly higher in the combination group (P = 0.015).
Conclusions: In DILI, CS is an effective treatment which shows hepatocyte suppression effect in combination with GL.

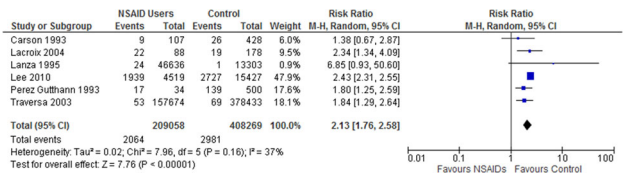
Abstract #1007

Non-steroidal anti-inflammatory drugs: What is the actual risk of liver damage?: A Systematic Review and Meta-Analysis

Sakkarin Chirapongsathorn[1], Chayakrit Krittanawong[2], Ann M. farrell[3]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Phramongkutklao Hospital, College of Medicine, [2]Department of Medicine, Icahn School of Medicine At Mount Sinai, [3]Mayo Clinic Libraries, Mayo Clinic, Rochester, Minnesota, USA

Backgrounds: We performed a systematic review and meta-analysis to evaluate the risk of serious hepatotoxicity in patients taking NSAIDs.
Methods: We conducted a comprehensive search of MEDLINE, Embase, Web of Science, Scopus databases and Cochrane Databased of Systemic Reviews through November 2018 and manually reviewed the literature. Attempts were made to contact the corresponding authors of the relevant studies for additional information when needed. Trial-specific risk ratios (RRs) were estimated and pooled using random-effect model meta-analysis. Between-study heterogeneity was assessed using the I^2 statistic. The quality assessment of included studies and publication bias were assessed.
Result: We included 6 observational studies (4 for case–control studies and two for cohort studies) at moderate risk of bias in which 5045 events of serious hepatotoxicity were reported. NSAIDs users had a significantly higher risk of serious hepatotoxicity (RR, 2.13; 95% CI, 1.76–2.58, I^2 = 37%) compared to any other population that did not involve NSAIDs. Among included medications, flurbiprofen had the highest risk (RR, 5.54; 95% CI, 1.04–29.69) followed by sulindac (RR, 5.05; 95% CI, 2.14–11.94), ibuprofen (RR, 3.02; 95% CI, 2.6–3.53), and diclofenac (RR, 2.48; 95% CI, 2.25–2.74). There was no statistically significant increase risk for piroxicam (RR, 1.46; 95% CI, 0.78–2.73) and naproxen (RR, 1.19; 95% CI, 0.54–2.6).
Conclusions: The use of NSAIDs may be increased risk of serious hepatotoxicity. The caution should be advised when using NSAIDs, especially flurbiprofen, sulindac, ibuprofen and diclofenac.



Complications of Liver Cirrhosis

N01 - Portal hypertension

Abstract #84

Emergency Transjugular Intrahepatic Portosystemic Shunt: an Effective and Safe Treatment for Uncontrolled Variceal Bleeding

Yongjun Zhu[1], Xiaoze Wang[1], Xiaotan Xi[1], Xiao Li[2], Xuefeng Luo[1], Li Yang[1]

[1]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, [2]Department of Interventional Therapy, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College

Introduction: Uncontrolled variceal bleeding (VB) remains a great challenge for clinical treatment. Emergency transjugular intrahepatic portosystemic shunt (TIPS) is a salvage procedure, but unsatisfactory clinical outcomes and a high incidence of complications have been reported.
Objectives: This study aimed to investigate the effect and safety of emergency TIPS performed in our institution during recent years.
Methodology: Fifty-eight consecutive cirrhotic patients with uncontrolled VB who underwent emergency TIPS from March 2009 to November 2017 in our hospital were followed until the last clinical evaluation, liver transplantation (LT), or death.
Results: Overall, 5, 36 and 17 patients belonged to Child–Pugh classes A, B and C, respectively. TIPS was successfully performed in 57/58 (98.3%) patients at 89.5 h (mean) after initial bleeding. After TIPS, bleeding ceased in 52/57 (91.2%) patients, and 51/57 (89.5%) patients had a portal pressure gradient below 12 mmHg. Only one (1.8%) major procedure-related complication occurred without any clinical consequences, and no procedure-related deaths occurred. During follow-up, 55 hepatic encephalopathy (HE) episodes occurred in 19 (33.3%) patients, and the median time of the first HE episode was 3.1 months. Seven (12.3%) patients experienced shunt dysfunction after 8.7 months (median). The 6-week, 1-year and 2-year variceal rebleeding rates were 10.5, 17.1 and 20.0%, respectively. The LT-free survival rates at 6 weeks, 1 year and 2 years were 87.7, 81.8 and 73.6%, respectively.
Conclusion: Our study highlights the fact that emergency TIPS could be effective for patients with liver cirrhosis and uncontrolled VB with few potential complications.

Abstract #85

Effect of Shunt Geometric Parameters on Transjugular Intrahepatic Portosystemic Shunt Patency

Xiaoze Wang[1], Xuefeng Luo[2], Li Yang[3]

[1]West China Hospital, Sichuan University, [2]West China Hospital, [3]West China Hospital

Purpose: To assess the effect of shunt geometric parameters on transjugular intrahepatic portosystemic shunt (TIPS) patency and to quantitatively analyzed change of stent configuration.
Methods: A database of patients who had TIPS preformed from November 2011 to June 2015 was generated. Stent-to-inferior venous cava distance (SIVCD), hepatic vein to stent angle (HVSA) and portal vein to stent angle (PVSA) was measured in two orthogonal planes. The patients meet the standard that SIVCD < 15 mm, HVSA $< 45°$ and PVSA $< 45°$ were classified into the optimal position (OP) group, others classified into non-optimal position (NOP) group. The angle between vertical line and tangent of proximal end of stent (AVTP), distal end (AVTD) and stent bending angle (SBA) were measured in portographic images during TIPS creation and follow-up, respectively.
Result: Among all 495 patients, 327 patients were enrolled in OP group. During the follow-up of mean 698 days, the TIPS dysfunction rate among the patients in OP group was 6.1%, compared with 30.0% among the patients in NOP group ($P < 0.001$). AVTP was significantly decreased by $5.1 \pm 8.7°$ ($P = 0.001$) and SBA was significantly increased by $9.2 \pm 8.5°$ ($P < 0.001$). A Cox multivariate analysis revealed that optimal position of stent ($P < 0.001$) and splenectomy ($P = 0.004$) was associated with TIPS dysfunction.
Conclusion: Initial stent position is predictive of TIPS patency, with stent extending to the hepatocaval junction and reducing the angle with vessels. The stent-graft will gradually straighten after TIPS, thereby impacting the shunt patency.

Abstract #92

Clinical outcome comparison between TIPS and BRTO in patients with Type 2 gastroesophageal varices

Xiaotan Xi[1], Xiaoze Wang[1], Yongjun Zhu[1], Xuefeng Luo[1], Li Yang[1]

[1]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, 37 Guoxue Lane, Chengdu 610041, Sichuan, People's Republic of China

Objective: The aim of this study is to compare the clinical outcome of transjugular intrahepatic portosystemic shunt (TIPS) with balloon-occluded retrograde transvenous obliteration (BRTO) in cirrhotic patients with type 2 gastroesophageal varices (GOV-2).
Method: We retrospectively reviewed cirrhotic patients from January 2012 to December 2017 who received variceal rebleeding prophylaxis measure. In total, 75 patients with GOV-2 were retrospectively analyzed, of whom, 54 patients treated with TIPS and 21 patients treated with BRTO. The rebleeding rate, incidence of hepatic encephalopathy and overall survival rate of the two groups were compared.
Result: In our study, no gastric variceal rebleeding was found in BRTO group. The variceal rebleeding rate in two groups was 16.7% and 19%, respectively, and there was no significant difference between two groups ($P = 0.296$). In the mortality, there is no significant difference between two groups, as well (27.78% vs 9.52%, TIPS vs BRTO, $P = 0.537$); in the incidence of hepatic encephalopathy, the TIPS group was significantly higher than the BRTO group (35.19% vs 0%, $P = 0.004$).
Conclusion: BRTO and TIPS are both effective treatment of variceal rebleeding prophylaxis in cirrhotic patients with type 2 gastroesophageal varices, for the same rebleeding rate and survival; given the lower rates of hepatic encephalopathy in BRTO group compared with TIPS group, we believe that BRTO might be a better alternative.

Abstract #149

Cardiac Profile of Patients with Liver Cirrhosis: A Ten-Year Study

Emily Mae Lim Yap[1], Ira Inductivo Yu[1], Myla Salazar Supe[1]

[1]Philippine Heart Center

Background: Cardiac complications among patients with liver cirrhosis have not yet been reported among filipinos. This study aims to be the first study to describe the electrocardiographic and echocardiographic findings of patients with liver cirrhosis.
Methodology: A retrospective study of 148 patients diagnosed with liver cirrhosis from 2007 to 2016 at the Philippine Heart Center was done.
Results: The mean age was $72.4 + 14$ years with a female:male ratio of 1.1:1. The most common etiology of cirrhosis was viral hepatitis infection (30%, 20). The Child–Pugh classification (CPC) and Model for End-Stage Liver Disease (MELD) were used to determine the severity of liver cirrhosis. There were 31 patients with CPC-A, 84 patients with CPC-B and 15 patients with CPC-C. Fifty-five percent had a MELD score of < 16. QTc prolongation was only seen among those with CPC A (median QTc = 470 ms) and a MELD score of < 9 (median QTc = 485 ms). The mean left ventricular ejection fraction was 54.4%. The mean cardiac output (6.04 L/min) and cardiac index (2.92 L/min/m^2) were normal. Forty-four patients had evidence of diastolic dysfunction ($E/A < 1$), prolonged isovolumic relaxation time (> 80 ms) and prolonged deceleration time (> 200 ms).
Conclusion: A higher mean age of Filipinos with liver cirrhosis was reported in our study. Prolongation of QTc interval was seen among those with early and late stage of cirrhosis. Most of these patients had normal left ventricular systolic function precluding the presence of cirrhotic cardiomyopathy.

Table 1. General characteristics of patients admitted with liver cirrhosis, 2007-2016

Demographics	Frequency (%) Mean +/- SD
No. of patients	148
Age	72.4 ± 14 years
Female	78 (53)
Mean duration of hospitalization (days)	7.5 ± 6
Etiology of cirrhosis	
Hepatitis	30 (20)
a. Hepatitis B infection	24 (16)
b. Hepatitis C infection	6 (4)
Cryptogenic	29 (20)
Non-alcoholic steatohepatitis	27 (18)
Alcohol-related	23 (15)
Schistosomiasis	4 (3)
Hemosiderosis/Hemochromatosis	2 (1)
Autoimmune Hepatitis	1 (0.7)
Portal vein thrombosis	1 (0.7)
Wilson's disease	1 (0.7)
Outcome	
Discharged improved	122 (82)
Expired	26 (18)

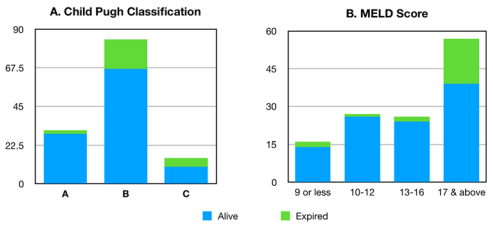


Figure 1. Distribution of patients based on Child Pugh Classification (CPC) and the Model for End Stage Liver Disease (MELD) score (n=130)

Abstract #232

Long-term patency and clinical outcome of the transjugular intrahepatic portosystemic shunt using the expanded polytetrafluoroethylene stent-graft

Xuefeng Luo[1], Jinlin Yang[2], Li Yang[3]

[1]West China Hospital, [2]West China Hospital, [3]West China Hospital

Background: Transjugular intrahepatic portosystemic shunt (TIPS) creation is an established treatment option to management the complications of portal hypertension. Recent data on the long-term outcomes of TIPS are scarce.
Materials and Methods: In this single-institution retrospective study, 495 patients underwent TIPS with the Fluency stent-grafts between December 2011 and June 2015 were evaluated. The cumulative rates of TIPS dysfunction, hepatic encephalopathy (HE), survival, and variceal rebleeding were determined using the Kaplan–Meier method. Cox regression analysis was used to assess the parameters on TIPS patency, occurrence of HE and all-cause mortality.
Results: Technical success was 98.2%. TIPS-related complications occurred in 67 patients (13.5%) during the index hospital stay. TIPS creation resulted in an immediate decrease in mean portosystemic pressure gradient from 23.4 ± 7.1 to 7.6 ± 3.5 mmHg. The median follow-up period was 649 days. Primary TIPS patency rates were 93%, and 73% at 1 and 4 years, respectively, with TIPS establishment via the left portal branch being an independent predicting factor. HE occurred in 151 out of 495 patients (30.5%), and age > 65 was a significant predictor. The cumulative survival rates were 93.4% and 72.6% at 1 and 4 years, respectively. The 1- and 4-year probability of remaining free of variceal bleeding rates were 94.2% and 77.1%, respectively.
Conclusions: This retrospective single-center experience with TIPS using the fluency stent-grafts demonstrates good long-term patency and favorable good clinical results. TIPS establishment via left portal branch strongly predicts shunt dysfunction.

Abstract #233

Randomised Trial of Balloon-Occluded Retrograde Transvenous Obliteration Versus Cyanoacrylate Injection for Prevention of Gastric Variceal Rebleeding

Xuefeng Luo[1], Li Yang[2]

[1]West China Hospital, [2]West China Hospital

Background and Purpose: Gastric variceal bleeding is less common than esophageal variceal bleeding; however, it is associated with a higher morbidity and mortality rate. The aim of our study was to compare the balloon-occluded retrograde transvenous obliteration (BRTO) with cyanoacrylate injection for the prophylaxis of recurrent gastric variceal bleeding.
Methods: Between June 2015 and Feb 2018, 64 patients with variceal bleeding were randomly assigned either balloon-occluded retrograde transvenous obliteration (n = 32) or cyanoacrylate injection (n = 32). The mean duration of follow-up period was 20.9 months in the BRTO group and 22.6 months in the cyanoacrylate group. Foam sclerotherapy using lauromacrogol by BRTO was performed.
Results: The technical success rate was 100% (32/32 patients) in the BRTO group. The amount of lauromacrogol used was 12.5 ± 4.5 ml (range, 3–20 ml). Significant rebleeding occurred in 1 patient (3.1%) of the BRTO group, and 10 patients (31.3%) of cyanoacrylate injection group. The cumulative probability of remaining free of all-cause rebleeding was significantly higher in the BRTO group than in the cyanoacrylate group; the probability at 2 years was 94.7% in the BRTO group and 66.9% in the cyanoacrylate group (p = 0.005). There was no difference in survival with estimated 1-year survival rates for BRTO and cyanoacrylate injection treated patients of 93.3% and 90.6%, and 2-year survival rates of 82.3% and 86.5%, respectively.
Conclusion: These results suggest that the BRTO is more effective than cyanoacrylate injection in prevention of gastric variceal rebleeding. Survival is similar in the two groups.

Abstract #280

Comparison of Effect of Early Versus Delayed Feeding on Rebleeding Following Endoscopic Variceal Band Ligation

Omesh Goyal[1], Sandeep S Sidhu[1], Saurabh Singh[1], Harsh Kishore[1], Rajoo S Chinna[1], Samarth Sidhu[1]

[1]D.M.C. and Hospital, Ludhiana

Background and Aims: Oral feeding following endoscopic variceal ligation (EVL) in cirrhotics is usually delayed due to fear of rebleed. Solid diet is usually further delayed (till 48 h) despite lack of evidence. We aimed to compare the impact of early versus late feeding on rebleeding following EVL.
Methods: This was a prospective randomized controlled trial. In early-feeding group, liquid diet was administered after 1 h following EVL and a regular solid diet was resumed after 4 h. In the delayed-feeding group, patients fasted for first 4 h after EVL, liquid diet was given till 24 h, soft diet for next 48 h and a regular solid diet after 72 h.
Results: Of the 283 cirrhotics screened, 199 were randomized into 2 groups: 98 patients in the early-feeding group and 101 in the delayed-feeding group. Patients with grade 1 esophageal varices, gastric variceal bleed or hepatic encephalopathy were excluded. There were no significant differences in baseline characteristics of the two groups. Very early rebleed rates [1 (1.02%) vs. 1 (0.99%); p = > 0.99] and delayed rebleed rates [2 (2.04%) vs. 4 (3.96%); p = 0.34] were similar in both groups. The protein and calories intake of patients in the early-feeding group was significantly better compared to delayed-feeding group. One month mortality was similar in both groups [3 (3.06%) versus 4 (3.96%); p = 0.49].
Conclusion: This study demonstrates that early feeding with regular solid diet in conscious patients after successful EVL for esophageal varices is safe and provides better nutrition as compared to delayed feeding.

Abstract #299

Upper gastrointestinal bleeding in Egyptian patients with cirrhosis: Post-therapeutic outcome and prognostic indicators

Tamer R. Fouad[1], Eman M. Abdelsameea[1], Wael M. Abdel-Razek[1], Ahmed M. Attia[1], Anwar A. Mohamed[1], Khaled M. Metwally[1], Mary A. Naguib[1], Imam A. Waked[1]

[1]National Liver Institute - Menofia University

Background: Upper gastrointestinal bleeding (UGIB) is a serious complication of portal hypertension in cirrhotic patients. Objective: to identify the risk factors for morbidity and mortality occurring after an UGIB attack.
Methods: A total of 1097 UGIB attacks in 690 patients with liver cirrhosis were studied. Their clinical, laboratory and endoscopic data were reviewed.
Results: Mean age 53.2 ± 10.6 (20–90) years, 78% males and the main cause of liver disease was hepatitis C (94.9%). Complications occurred after 467 attacks (42.6%): hepatic encephalopathy 31.4%, spontaneous bacterial peritonitis 18%, renal impairment 13.2% and re-bleeding in 7.8%, while 199 patients (18.1%) died. Complications followed 78.4% of bleeding from gastric varices, 75% of post-interventional ulcers, 10.8% of peptic ulcers and 5.9% of telangiectasias. By univariate analysis: packed red blood cells (PRBC) units transfused, transaminases, Child–Pugh (CP), Model of End-Stage Liver Disease (MELD) and Albumin-Bilirubin (ALBI) scores, beside the presence of hepatocellular carcinoma (HCC), previous hemorrhage in the previous 6 months and the source of bleeding were associated with occurrence of complications. By multivariate analysis, independent predictors of complications were CP, MELD and ALBI scores (odds ratio; 95% confidence interval: 5.63; 3.55–8.93, 1.15; 1.11–1.19 and 2.11; 1.4–3.19, respectively) beside the presence of HCC (4.89; 2.48–9.64). Mortality predictors were PRBC units transfused (1.11; 1.01–1.24), CP (5.1; 1.42–18.25) MELD (1.27; 1.21–1.32) scores, and presence of HCC (6.62; 2.93–14.95).
Conclusion: High CP, MELD and ALBI scores beside the presence of HCC could predict poor outcome of UGIB. In the absence of these risk factors, early discharge could be considered if the source of bleeding is peptic ulcer or telangiectasia.

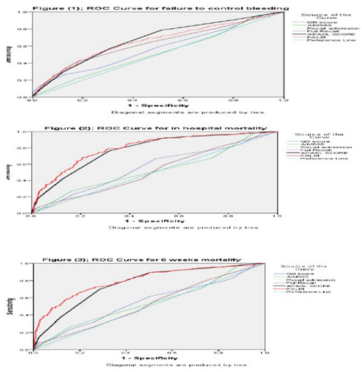
Abstract #307

Validation of APASL severity score in prediction outcome of acute variceal bleeding in Egyptian patients

Marwa Shahat El Fayoumy[1], Mohammed Ahmed El Tabbakh [2], Gamal Abdelkhalak Badra[3], Eman Ahmed Rewisha[4], Imam Abdel Latif Waked[5]

[1]Hepatology and Gastroenterology, National Liver Institute, Menoufia University, [2]Hepatology and Gastroenterology, National Liver Institute, Menoufia University, [3]Hepatology and Gastroenterology, National Liver Institute, Menoufia University, [4]Hepatology and Gastroenterology, National Liver Institute, Menoufia University, [5]Hepatology and Gastroenterology, National Liver Institute, Menoufia University

Background: Asia–Pacific Association for Study of the Liver (APASL) severity score was proposed to predict outcome of variceal bleeding.
Aim: To validate APASL severity score for predicting re-bleeding and mortality in patients with acute variceal bleeding and to compare it to other bleeding scores.
Methods: Patients presenting with acute variceal bleeding were prospectively evaluated, resuscitated, given intravenous antibiotics, and received blood and vaso-active drugs as needed. Endoscopy was performed as early as feasible. The following scores were calculated: AIMS65, Glasgow Blatchford, the Rockall and full Rockall score, the platelet-albumin-bilirubin (P-ALBI), and APASL severity scores. Scores were correlated to treatment failure, in hospital mortality, and 6 weeks mortality.
Results: Esophageal and/or gastric varices was the cause of acute bleeding in 703 cirrhotic patients (71.4% males, mean age 58.1 ± 10.3 years, 18.2% with spurtering blood from varices on endoscopy, 14.1% Child–Turcotte–Pugh (CTP) A, 47.2% CTP B, 38.7% CTP C). Bleeding was controlled in 422 patients (59.9%) and 210 patients died (29.8%), 122 patients (20.5%) during hospitalization, 281 patients (39.9%) had re-bleeding after the first week. The area under the ROC curve (AUROC) for failure to control bleeding, mortality in hospitalization and at 6 weeks for each score are shown in the figures, with APASL score of > 3 offering the best prediction of bleeding control and P-ALBI and APASL offering the best prediction of mortality during hospitalization and at 6 weeks.
Conclusion: APASL severity score predicts re –bleeding, but P-ALBI and APASL severity scores predict mortality in hospital and at 6 weeks.



Test Result Variable(s) For failure to control bleeding	Area
GB score	.571
AIMS65	.520
Recall admission	.633
Full Recall	.629
APASL SCORE	.672
PALBI	.653

Test Result Variable(s) For in hospital mortality	Area
GB score	.559
AIMS65	.526
Recall admission	.520
Full Recall	.518
APASL SCORE	.774
PALBI	.799

Test Result Variable(s) For 6 weeks mortality	Area
GB score	.550
AIMS65	.545
Recall admission	.526
Full Recall	.524
APASL SCORE	.761
PALBI	.799

Abstract #378

The involvement of loop diuretics for the loss of skeletal muscle and prognosis in patients with liver cirrhosis

Naruyasu Kakita[1], Takaaki Tokuda[1], Toru Okahara[1], Kenji Aoi[1], Yukinori Yamada[1]

[1]Kaizuka City Hospital & Gastroenterology and Hepatology

Introduction: Sarcopenia is the major component of malnutrition and a frequent complication in patients with liver cirrhosis that adversely affects clinical outcomes. This study evaluated the effect of loop diuretics on skeletal muscle depletion and prognosis in patients with liver cirrhosis.
Subjects and Methods: A total of 140 patients (82 males, median age of 59) with liver cirrhosis who underwent CT scan 2 times from April 2012 to April 2016 were enrolled. Patients were divided into two groups consisting of the low dose group with 84 patients (20 mg or less/day) and the high dose group with 56 patients (more than 20 mg/day), and the two groups were compared. All patients were administered more than 25 mg of Spironolactone and the BCAA supplementation more than 3 months. Measurement of skeletal muscle mass index (SMI) on CT images at L3 vertebra determined the degree of sarcopenia.
Results: Clinical backgrounds of two groups were similar excluding serum creatinine and eGFR. The rate of change in skeletal muscle mass (ΔSMI/year) was significantly higher in the high dose group ($P = 0.03$) and the dose of furosemide was extracted as an independent factor for skeletal muscle mass reduction. Prognosis was significantly poorer in the high dose group ($P = 0.001$).
Conclusion: The use of high-dose furosemide affects skeletal muscle depletion and prognosis in patients with liver cirrhosis; therefore, the dose of furosemide should not be increased aimlessly, but use of other diuretics like tolvaptan should be considered in the treatment with intractable ascites.

Abstract #384

Oxidative stress contributes to progression of splenic fibrosis in cirrhotic patients with portal hypertension

Yuji Iimuro[1], Toshihiro Okada[2], Jiro Fujimoto[3]

[1]Dept of Surgery, Yamanashi Central Hospital, Kofu, Japan, Dept of Surgery, Hyogo College of Medicine, Nishinomiya, Japan, [2]Dept of Surgery, Hyogo College of Medicine, Nishinomiya, Japan, [3]Dept of Surgery, Hyogo College of Medicine, Nishinomiya, Japan

Background and Aim: Among several non-invasive evaluation of portal hypertension (PH), measurement of spleen stiffness is a reliable method to predict esophageal variceal bleeding, while underlying mechanisms for the increased spleen stiffness remain unclear. We tried to elucidate the pathological changes of spleen and the underlying mechanisms in HCV-positive patients with PH.
Methods: Histological examination was performed using splenic tissues from 42 patients with PH who underwent laparoscopic splenectomy, in comparison with those from non-PH patients.
Results: In addition to splenic sinus congestion, diffuse fibrosis was detected in the splenic cords in the red pulp of PH patients. The degree of the fibrosis well correlated with severity in thrombocytopenia ($p = 0.011$) and splenomegaly ($p < 0.001$). Cells expressing alpha-smooth muscle actin (SMA) dramatically increased in the cord of PH patients, and its expression was network-patterned. Morphological analysis showed that reticular cells in the splenic cord possibly expressed alpha-SMA, suggesting transformation of reticular cells to myofibroblastic cells. Expressions of nicotinamide adenine dinucleotide phosphate oxidases (NOXs) 2 and 4, oxidative stress markers such as nitrotyrosine, and transforming growth factor (TGF)-beta were markedly upregulated in the red pulp of PH patients, implying significant role of oxidative stress in the mechanism for splenic fibrosis.
Conclusion: Splenic fibrosis progresses along with advancement of portal hypertension. This phenomenon possibly contributes to the increased spleen stiffness in patients with PH. Reticular cells in the splenic cord possibly participate in this process through the mechanism including oxidative stress.

Abstract #385

Effect of conventional diuretics versus conventional diuretics plus mannitol on electrolytes for the treatment of cirrhotic ascites

Md. Jamshed Alam[1], Jemima Khan[2]

[1]Department of Hepatology, Shaheed Suhrawardi Medical College, Dhaka, [2]Department of Medicine, Holy Family Red Crescent Medical College, Dhaka

Introduction: Ascites is the most frequent finding of decompensated liver cirrhosis. Response of ascites by conventional diuretics with mannitol is better than conventional diuretics alone without any electrolyte imbalance.
Methods: It was a case control study. 50 patients were taken as cases and 50 were controls. Infusion of 20%, mannitol was given to cases and infusion of 5% D/A to controls. Patients on conventional diuretics for at least 5 days were included in the study.
Results: 75 patients were HBV related decompensated cirrhosis, 15 cases were HCV related decompensated cirrhosis and 10 were NBNC related decompensated cirrhosis. Baseline ALT (90 ± 62) U/L, serum creatinine (1.3 ± 0.7) mg/dl, Serum albumin (24 ± 10) gm/l, serum sodium (126 ± 8) mmol/l, serum potassium (4.5 ± 1) mmol/l, urinary sodium (80 ± 50) mmol/l, urinary volume (1675 ± 1175) ml/day and weight were (68 ± 27) kg. There were significant difference of urinary volume before and after 20% mannitol infusion. Urinary volume were (1300 ± 470) ml/day and (1800 ± 490) ml/day before and after 20% mannitol infusion. Serum Sodium were (129 ± 5.82) mmol/l and ($130\ 0.5 \pm 6.11$) mmol/l before and after mannitol infusion. Serum potassium were (4.2 ± 0.50) mmol/l and (4.3 ± 0.70) mmol/l before and after infusion.
Conclusion: Use of mannitol as an additive to conventional diuretics for the treatment of cirrhotic ascites was safe, available, well tolerated

and cost effective. Mannitol increased the urinary output in cirrhotic patients with ascites without electrolytes imbalance

Abstract #425

Normative values of Sarcopenia in the Indian population

Sandeep S. Sidhu[1], Kavita Saggar[1], Omesh Goyal[1], Harsh Kishore[1], Samarth S. Sidhu[1]

[1]D.M.C. and Hospital

Introduction: Sarcopenia is characterized by the loss of skeletal muscle mass, strength and performance. It is of great prognostic importance in patients with liver cirrhosis (LC).
Objective: The study was design to provide normal values (Computerized Tomography Skeletal muscle index (SMI), Handgrip Strength (HGS), Gait velocity, Chair Stand) for measuring Sarcopenia in Indian Population.
Methods: SMI (cm^2/m^2), HGS (kg), gait velocity (m/min), chair stand, of 3087 non cirrhotic patients who underwent abdominal computed tomography (CT) for acute abdomen were analyzed in this study. The cross-sectional area of skeletal muscles was measured at the level of the third lumbar vertebra on CT (using Tomovision slice Omatic 5.0 software).
Results: 3087 number of patients, 1003 (32%) females and 2084 (67%) males who underwent abdominal CT were enrolled in this study. Mean CTSI in female was 41.25 ± 4.42 vs 44.33 ± 6.56 in Male ($P < 0.0001$). Mean of HGS in female was 25.19 ± 7.57 vs 35.14 ± 8.56 in Male ($P < 0.0001$), mean of Gait velocity in female was 1.76 ± 2.38 vs 1.86 ± 2.22 in male ($P = 0.2524$) and mean of chair stand in female was 10.38 ± 4.42 vs 13.86 ± 2.56 in male ($P < 0.0001$).
Conclusions: This is the largest global data provide normative values of all sarcopenia parameters for adults based on gender. This shall enable future studies on sarcopenia in cirrhotic patients.

Abstract #458

Efficacy and Tolerance of Maximally Tolerable Dose of Propranolol in the Prevention of Esophageal Variceal Rebleeding

Jeong Eun Song[1], Byung Seok Kim[2], Chang Hyeong Lee[3]

[1]Department of Internal Medicine, Daegu Catholic University School of Medicine, [2]Department of Internal Medicine, Daegu Catholic University School of Medicine, [3]Department of Internal Medicine, Daegu Catholic University School of Medicine

Background and Aims: Although the efficacy of propranolol for the prevention of esophageal variceal (EV) rebleeding has been well documented, there is a paucity of clinical data regarding the tolerance of maximal dose of propranolol.
Method: A total of 122 patients, who were treated with emergent EV ligation for acute EV bleeding and have since then taken propranolol for more than 1 month, were enrolled. We retrospectively investigated the clinical course of propranolol treatment, particularly maximally tolerable dose (MTD) of propranolol in these patients.
Results: And 54 patients took low dose (LD) of propranolol (38.2 ± 5.9 mg/day). During the follow-up period (median duration 58 months, range 2–175 months), rebleeding occurred in 29 (53.7%) and 23 (33.8%), LD and MTD of propranolol, respectively ($p = 0.027$). Median duration of maximally tolerable doe of propranolol was 45.5 months (range 1–89 months). Among patients with MTD of propranolol, 18 patients experienced dose reduction, but 12 patients maintained high dose of propranolol ($\geq$ 80 mg/day) after dose reduction. The most common cause of dose reduction was bradycardia (33.3%). A total of 15 patients stopped taking propranolol, 4 patient with LD of propranolol and 11 patients with MTD of propranolol.
Conclusion: MTD of propranolol was well tolerated and showed good efficacy for preventing esophageal variceal rebleeding.

Abstract #483

Severity changes of cirrhotic patients during 10 years period in South Korea: A single center study

Jeong Han Kim[1]

[1]Konkuk University School of Medicine

Background and Aims: Clinical implications including disease severity of cirrhotic patients have been changed since oral antiviral agents for hepatitis B were introduced. On the other hands, alcoholic cirrhosis is still not well controlled and direct acting antiviral agents for hepatitis C are recently introduced. Therefore, we can expect improvement of severity will be observed more prominently in hepatitis B endemic area.
Methods: Medical records of cirrhotic patients visited Konkuk University medical center were retrospectively reviewed. Study period was from year 2008 to year 2017. Clinical status of cirrhotic patients in each year was analyzed according to Child–Pugh score, decompensation, MELD score and mortality.
Results: During 10 years, mean 802 patients were visited in each year. Most common etiology was hepatitis B (56.9% in 2008 and 58.0% in 2017) and alcohol was second (28.5% in 2008 and 26.4% in 2017). Prevalence of decompensated cirrhosis was decreased from 37.3% in 2008 to 15.6% in 2017. Mean Child–Pugh score and MELD score were reduced from 6.4 and 1.0 in 2008 to 5.5 and 9.1 in 2017. Overall mortality was also decreased from 4.5% in 2008 to 1.6% in 2017.
Conclusions: Although major etiology of liver cirrhosis was not changed during 10 years, clinical status was improved. We can expect more improvement if treatment of hepatitis C and alcohol abstinence are successfully introduced.

Abstract #526

Carvedilol versus esophageal variceal ligation (EVL) for primary and secondary prevention of variceal bleeding: systematic review and meta-analysis

Michael Dwinata[1], David Dwi Putera[2], Muhamad Fajri Adda'i[3], Putra Nur Hidayat[4], Irsan Hasan[5]

[1]Department of Internal Medicine, Depati Hamzah General Hospital, Pangkalpinang, Indonesia, [2]Faculty of Medicine and Health, University of Sydney, Sydney, Australia, [3]Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia, [4]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia, [5]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Variceal haemorrhage has high mortality that accounts for 20–30% case among cirrhosis patients. Either NSBBs (Non-

Selective Beta Blocker) or EVL is recommended for primary prevention of variceal bleeding in patients with medium to large varices. Carvedilol was reported to have better results than other NSBBs by additionally decreasing intrahepatic resistance.
Objective: To compare the efficacy of carvedilol with EVL for primary and secondary prevention of variceal bleeding in patients with liver cirrhosis and portal hypertension.
Methodology: Relevant literature was searched in major journal databases (CENTRAL, MEDLINE, EMBASE, Clinicatrials.gov, and WHOICTRP) through March 2018. Only RCTs were included in this meta-analysis.
Results: Seven RCTs were included in this study. In four trials assessing the primary prevention, no significant difference had been found on the events of variceal bleeding (RR 0.74, 95% CI 0.37–1.49), all-cause mortality (RR 1.10, 95% CI 0.76–1.58), and bleeding-related mortality (RR 1.02, 95% CI 0.34–3.10) in patients who were treated with carvedilol compared to EVL. In three trials assessing secondary prevention, there was no difference between two interventions for the incidence of rebleeding (RR 1.10, 95% CI 0.75–1.61). The fixed-effect model showed that compared to EVL, carvedilol decreased all-cause mortality by 49% (RR 0.51, 95% CI 0.33–0.79) with little or no evidence of heterogeneity.
Conclusion: Carvedilol has similar efficacy with EVL for primary prevention of first variceal bleeding in cirrhosis patient with esophageal varices. For secondary prevention, it seems that carvedilol has benefit in reducing all-cause mortality.

Abstract #545

Survival outcome of patients in acute variceal bleeding with acute coronary syndrome discharged on anti-platelet agents

Rajesh Kumar[1], Om Parkash[2]

[1]The Aga Khan University Hospital, [2]The Aga Khan University Hospital

Background: Acute variceal bleeding is one of major and killing complication of advanced liver disease. Data regarding outcome of patients with acute variceal bleeding with acute coronary syndrome is scarce. The aim of this study was to look for survival outcome of those patient who were discharged on anti-platelet agents.
Methods: All the patients included based on inclusion criteria presented at The Aga Khan University Hospital, from February 2002 to February 2017. The medical records were reviewed to evaluate the survival outcome for 1 year.
Results: Out of 27/39 files coded (ICD-9) with acute variceal bleeding and acute coronary syndrome could be retrieved, 4/27 patients excluded from study. The mean age of patient 59. 22 ± 11 years. 10 (44%) patients had CTP C disease, followed by 8 (35%) with CTP B disease. 12 (52%) patient had underlying ischemic heart disease. 7/23 (30%) patients died during same admission but among them only one patient was on dual antiplatelet agents. 16/23 (70%) patients, 4 (18%) patients lost to follow up after discharge. Only 12 patients followed for 1-year survival but only 3 patients were started on single antiplatelet agents (2 patients discharged on asprin and one patient on clopidogrel). 9/12 patients survived over 1 year and patients on antiplatelet agent didn't developed re-bleeding.
Conclusions: Comparing risks versus benefit, single antiplatelet agent looks relatively safer option, which can be offered cautiously in such dilemmas, after achieving hemostasis. For validation, large scale prospective studies should be considered.

Abstract #547

A Correlational Study on Spleen Stiffness and the Presence and Severity of Esophageal Varices in Cirrhotic Patients

Adrian Patrick Patawaran Calimag[1], Ira Inductivo Yu[2]

[1]National Kidney and Transplant Institute, [2]National Kidney and Transplant Institute

Introduction: Bleeding esophageal varices is a complication of liver cirrhosis resulting from portal hypertension that carries significant morbidity, mortality and healthcare costs. There is a need for a safe, reproducible and non-invasive surrogate marker to accurately screen for esophageal varices. Spleen Stiffness can predict the presence and severity of varices in cirrhotic patients with high diagnostic accuracy. However, local data establishing the usefulness of splenic stiffness in predicting the severity of esophageal varices is lacking.
Objectives: To determine the correlation of splenic stiffness measured by transient elastography to presence and severity of esophageal varices.
Materials and Methods: An Ambispective analytic cohort study. A total of 29 patients underwent Spleen stiffness determination by point shear wave elastography and upper-gastrointestinal endoscopy to evaluate for esophageal varices. Relationships between the parameters were characterized using Spearman's correlation coefficients. One-way ANOVA and Fisher's exact test was used to determine the difference between four different grades of esophageal varices.
Results: 19 patients (65.5%) had varices with grade 1 (n = 5, 17.24%), grade 2 (n = 7, 24.14%), and grade 3 (n = 7, 24.14%) respectively. There was a significant difference among four groups in terms of spleen diameter ($p = 0.048$) and spleen stiffness ($p = < 0.001$). A strong positive correlation of spleen stiffness and severity of esophageal varices ($r = 0.821$) was noted. Spleen diameter and severity of esophageal varices were directly correlated but to a lesser degree ($r = 0.446$).
Conclusion: Spleen elastography appears to be a reliable, non-invasive and cost-effective method of variceal screening and should be considered in cirrhotic patients.

Abstract #556

Preliminary Study on Endoscopic Characteristics and Portal Vein Pressure Level in Patients with Repeated Esophageal and Gastric Variceal Bleeding

Qing Ye[1], Huiling Xiang[1], Tinghong Li[1], Fengmei Wang[1]

[1]Department of Gastroenterology and Hepatology, Tianjin Third Central Hospital & The Third Central Clinical College of Tianjin Medical University

Objective: To analyze the endoscopic characteristics and portal pressure in patients with recurrent esophagogastric variceal bleeding.
Methods: 105 patients with recurrent esophagogastric variceal bleeding were treated with TIPS. Sarin classification was used to analyze the types of esophagogastric varices under endoscopy, and the portal vein pressure was measured by puncturing the entrance vein through TIPS approach.
Results: Among all the subjects, 41 patients with portal hypertensive gastropathy, 38 patients with portal vein thrombosis and 77 patients with ascites were involved. Classification of esophagogastric varices under gastroscopy showed 23 cases of GOV1, 18 cases of GOV2, 62 cases of GOV3 and 2 cases of IGV1. The mean portal pressure of 105 patients was 33.8 ± 6.109 mmHg. The portal pressure of GOV1, GOV2, GOV3 and IGV1 patients with different gastroscopic types was 32.78 ± 6.809 mmHg, 32.39 ± 7.277 mmHg,

34.52 ± 5.530 mmHg and 36.00 ± 5.657 mmHg, respectively. There was no significant difference between the patients with different gastroscopic types. There was no significant difference in portal vein pressure between the two groups. The portal vein pressure in the group with portal vein thrombosis was significantly higher than that in the group without portal vein thrombosis ($P < 0.001$); the portal vein pressure in the group with ascites was significantly higher than that in the group without ascites ($P = 0.029$).
Conclusion: Repeated esophagogastric variceal bleeding is associated with a significant increase in portal pressure, especially for patients with portal thrombosis and ascites, early TIPS treatment may be an effective means to reduce re-bleeding.

Abstract #561

Concordance of 24 and 48 h diagnostic follow up ascitic fluid polymorphonuclear leukocytes count in the guidance of the antibiotic therapy

Hanaa Mostafa Badran[1], Maha Mohammad Elsabaawy[1], Warda Othman[1], Mohamed Azazy Mahmoud[1], Heba Samy Ghanem[1], Ayman Alsebaey[1]

[1]Department of Hepatology and Gastroenterology, National Liver Institute, Menoufia University, Shebeen El-Koom, Egypt

Introduction: Spontaneous bacterial peritonitis (SBP) is ascitic fluid infection in patients with liver cirrhosis in the absence of surgical causes. The drop of the ascitic fluid polymorphonuclear leukocytes count (AFPC) ≥ 25% of baseline 48 h post-start of antibiotics is a predictor of antibiotic response.
Aim: To compare diagnostic AFPC 24 h after staring antibiotic to the standard time after 48 h. METHODS: 399 patients with SBP were classified into 2 groups. Group I (31.1%) are patients that lacked ≥ 25% drop and group II (68.9%) the opposite.
Results: The average age was 51.99 ± 11.21 years. Most patients were males (70.9%), normotensive (75.8%), non-diabetics (50.8%), without recent intake history of proton pump inhibitors (75.8%) and B-blockers (77%). Group II patients had statistically significant ($p < 0.05$) serum sodium; 129 (7) vs. 128 (8) and history of diabetes mellitus; 60.3% vs. 39.7%. The baseline AFPC did not differ statistically between group I and II ($p > 0.05$). Group II patients compared to group I had statistically ($p = 0.001$) lower AFPC 24 h [800 (970) vs. 1100 (1700) cell/mm^3], higher percent drop of the AFPC 24 h [28.09 (24) vs. − 10.17 (35)] and ≥ 25% drop [154 (90.6%) vs. 16 (9.4%)]. The 24 h AFPC > 980 cell/mm^3 was associated with AFPC 48 h nonresponse (AUROC = 0.634, $p = 0.001$, 58.87% sensitivity, 64.36% specificity). The 24 h AFPC percent drop > 8% was associated with AFPC 48 h response (AUROC = 0.849, $p = 0.001$, 85.82% sensitivity, 80.49% specificity).
Conclusion: concordance of 24 and 48 h diagnostic follow up ascitic fluid polymorphonuclear leukocytes count in the guidance of the antibiotic therapy.

Abstract #605

Antifibrotic Traditional Chinese Patent Medicines Reduce the Risk of Esophageal Variceal Rebleeding in Patients with Liver Cirrhosis

Qun Zhang[1], Yao Liu[1], Yuxin Li[1], Shuaishuai Niu[1], Bingbing Zhu[1], Yunyi Huang[1], Yuyong Jiang[1], Xianbo Wang[1]

[1]Center of Integrative Medicine, Beijing Ditan Hospital, Capital Medical University

Introduction: The clinical efficacy of antifibrotic traditional Chinese patent medicines (TCPMs) for the treatment of recurrent esophagogastric variceal bleeding (EGVB) remains unclear.
Objective: This study investigated the effect of endoscopy concomitant with antifibrotic TCPM treatment on the incidence of recurrent EGVB in patients with liver cirrhosis.
Methodology: This retrospective study included 555 consecutive patients with EGVB who were treated at the Beijing Ditan Hospital between August 2008 and October 2016. Propensity score matching was performed (ratio 1:2), and 139 patients not using antifibrotic TCPMs (defined as < 28 cumulative defined daily dose [cDDD]) were matched with 278 inception point-matched patients (defined in terms of dose as ≥ 28 cDDD).
Results: Multivariate analysis showed that TCPM treatment was independently associated with recurrent EGVB (adjusted hazard ratio = 0.659, 95% confidence interval = 0.497–0.873, $P = 0.004$). After propensity score matching using a 1:2 ratio, the incidence of rebleeding in the TCPM cohort was significantly lower than that in the non-TCPM cohort (44.6% vs. 58.3%, modified log-rank test, $P = 0.002$). Furthermore, this protective effect only was observed in patients with Child–Pugh grade B (45.6% vs. 56.9%, modified log-rank test, $P = 0.013$). The median rebleeding interval in the TCPM cohort was significantly longer than that in the non-TCPM cohort (113.5 vs. 84 days, $P = 0.002$).
Conclusion: Compared with endoscopy alone, endoscopy concomitant with antifibrotic TCPM treatment can significantly reduce the incidence of rebleeding within 1 year and delay the time until rebleeding in patients with EGVB.

Abstract #610

Risk Factors of Recurrent Variceal Hemorrhage after Esophageal Varices Ligation in Liver Cirrhosis Patients

Juferdy Kurniawan[1], Rino Alvani Gani[1], Irsan Hasan[1], Andri Sanityoso Sulaiman[1], Cosmas Rinaldi A. Lesmana[1], Chyntia Olivia Maurine Jasirwan[1], Kemal Fariz Kalista[1], Saut Horas Hatoguan Nababan[1], Steven Zulkifly[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Background: Variceal hemorrhage (VH) is one of the most common complication in liver cirrhosis, with increasing mortality rate if recurrent VH occurred. The combination of non-selective beta blocker (NSBB) and endoscopic variceal ligation (EVL) is the first line therapy for secondary prophylaxis of VH. However, the incidence of recurrent VH in Indonesia remains high.
Aim: To determine the risk factors of recurrent VH after EVL in liver cirrhosis patients.
Method: We conducted a retrospective study design from patients with upper gastrointestinal (GI) bleeding due to variceal esophageal rupture, who underwent EVL procedure, in Cipto Mangunkusumo National General Hospital during January–December 2016 period. Patients' data and associated risk factors are collected from medical record. The primary outcome is recurrent VH in 1 year after EVL procedure and its associated risk factors.
Results: One hundred and seventy-four patients were enrolled in this study, with mean age of 53 ± 12.02 years. Most of the patients were male (79.3%). In univariate analysis, CP Class B/C, MELD score ≥ 14, platelet count < 100 × 103/μL at the presentation, large varices and red color sign in endoscopy were significantly associated with recurrent VH in 1 year after EVL procedure ($p < 0.05$). Only CP

class B/C and platelet count were found significantly associated with recurrent bleeding episode in multivariate analysis.
Conclusion: CP class B/C and low platelet count can be used as risk predictors of recurrent VH in liver cirrhosis patients.

Abstract #617

The Use of Hemospray Endotherapy in Patients with Portal Hypertensive Bleeding: A Case Series

Enrik John Torres Aguila[1], Juliet Lingat Gopez-Cervantes[1]

[1]St. Luke's Medical Center Global City

Introduction: Hemospray (TC-325) is a novel hemostatic agent recently licensed for endoscopic hemostasis of non-variceal upper gastrointestinal (GI) bleeding in the Europe and America. It acts by creating a mechanical barrier and effecting hemostasis on actively bleeding lesions via endoscopy. It has not been licensed for use in portal hypertensive bleeding and only few case reports worldwide have shown its potential for such.
Methodology: This case series presents two patients with acute hemorrhage secondary to non-variceal portal hypertensive bleeding. The first case is a 67-year-old male known to have hepatocellular carcinoma and portal vein thrombosis diagnosed to have gastric antral vascular ectasia and portal hypertensive gastropathy on gastroscopy. Lesion was initially treated with argon plasma coagulation (APC) which failed to achieve hemostasis; hence, hemospray was applied which resulted cessation of bleeding. The second case is a 42-year-old male who presented with lower GI bleeding secondary to portal hypertensive colopathy. Due to the large area of bleeding mucosa in the ascending, transverse and descending colon, hemospray was applied.
Results: Both patients had no adverse events or recurrence of bleeding within 30 days post-hemospray. For the first case, hemospray was used as salvage therapy because the APC failed to achieve hemostasis. For the second case, it was used as monotherapy.
Conclusion: Hemospray is a novel endoscopic technique that has advantages of being non-traumatic, noncontact and can cover large areas of mucosa. This report demonstrates that hemospray can be used for portal hypertensive bleeding although further data are needed to support its use.

Abstract #645

Evaluation of treatment response after endoscopic variceal obturation with abdominal computed tomography

Yeon Seok Seo[1], Han Ah Lee[1], Hyun Gil Goh[1], Tae Hyung Kim[1], Young-Sun Lee[1], Sang Jun Suh[1], Young Kul Jung[1], Ji Hoon Kim[1], Hyung Joon Yim[1], Jong Eun Yeon[1], Kwan Soo Byun[1], Soon Ho Um[1]

[1]Korea University College of Medicine

Introduction: Current guidelines recommend EVO as a treatment choice for the management of bleeding from gastric varices (GVs). However, high incidence of rebleeding from GVs after EVO remains a problem.
Objectives: This study was performed to evaluate the usefulness of computed tomography (CT) for the prediction of rebleeding after EVO GV bleeding.
Methodology: Patients who were treated with EVO for GV bleeding and performed CT before and after EVO were included. Patients who did not performed CT before and after EVO, those with a previous history of endoscopic treatment for bleeding from GVs, and those with accompanying portal vein invasion by hepatocellular carcinoma (HCC) or other malignancy were excluded.
Results: Fifty-three patients were included. Age was 60.6 ± 11.6 years and 40 patients (75.5%) were men. Alcoholic liver disease was the most frequent underlying liver disease (45.3%). Complete impaction of cyanoacrylate in GVs and feeding vessels were achieved in 40 (75.5%) and 24 (45.3%) of patients, respectively. During the follow-up, GV rebleeding occurred in 9 patients and the cumulative incidences of GV rebleeding at 1, 6, and 12 months were 1.9, 18.9, and 18.9%, respectively. GV rebleeding rate did not differ significantly according to the complete cyanoacrylate impaction in GV, while it differed significantly according to the complete cyanoacrylate impaction in feeding vessels ($P = 0.002$).
Conclusion: Abdominal CT is useful in evaluation of treatment response after EVO. Because incomplete cyanoacrylate impaction in feeding vessels is the risk factor of GV rebleeding, detailed evaluation of feeding vessels on CT after EVO is needed.

Abstract #650

The Correlation of Malnutrition with Child–Pugh Score and MELD-Na Score as a Prognostic Indicator of Mortality and Hepatic Decompensation Among Cirrhotic Patients

Enrik John Torres Aguila[1], Juliet Lingat Gopez-Cervantes[1], Ian Homer Y. Cua[1]

[1]St. Luke's Medical Center Global City

Introduction: Given the strong correlation of nutrition to various clinical outcomes, it is necessary to accurately assess nutritional status of patients with liver cirrhosis. In our knowing, there is no published material regarding cirrhosis and malnutrition locally. Hence, it would be beneficial to establish these associations in the local setting.
Methodology: This was a retrospective cohort study on patients admitted at the St. Luke's Medical Center Global City. All patients were assessed using the Subjective Global Assessment (SGA) tool, Child–Pugh Score, and MELD-Na score and were correlated with clinical outcomes namely in-hospital mortality, length of hospitalization, and decompensation of cirrhosis.
Results: Eighty-two (82) patients were studied and 68% (56) were classified as having high risk of malnutrition. There was significantly higher proportion of decompensated cirrhosis, admission to ICU and mortality rates in the high risk group. Ascites (53.57%), infection (26.79%) and hepatic encephalopathy (15%) were the most common clinical outcomes. If we correlate this with the Child–Pugh Score and MELD-Na score, the pattern remains consistent that the higher the score, the more patients who develop poor outcomes. These begin with a Child–Pugh score of C and a MELD-Na score of > 21. Statistically, higher SGA, Child–Pugh and MELD scores were correlated positively with mortality and longer hospital stay ($p = 0.111$, 0.012, 0.035).
Conclusion: The SGA, Child–Pugh and MELD-Na scores are predictive of mortality and poor clinical outcomes. High scores for these indices are associated with higher probability of admission to ICU and longer hospital stay.

Abstract #716

Budd-Chiari Syndrome Profile in Kariadi General Hospital, Semarang: A Preliminary Research

Gunady Wibowo Rencong[1], Hery Djagat Purnomo[1]

[1]Gastroenterohepatology Division, Internal Medicine Department, Faculty of Medicine Diponegoro University, Kariadi General Hospital, Semarang, Indonesia

Wibowo, Gunady[1] (gun_ady@yahoo.co.id); Hirlan[1] (gastro_semarang@yahoo.com); Prasetyo, Agung[1] (agung_pra@yahoo.com); Indiarso, Didik[1] (doc.indiarso@gmail.com); Purnomo, Hery Djagat[1] (herydjagat@yahoo.co.id).

Introduction: Budd–Chiari syndrome (BCS) is a rare disease which is caused by hepatic vein outflow obstruction that can occur at any point of hepatic vein flow regardless of the cause. BCS has various demography characteristics regarding age, sex, and clinical presentation in the world.
Objectives: This research aimed to describe the BCS' clinical and risk factors characteristic in patients admitted to the Internal Medicine Ward, Kariadi General Hospital.
Methodology: This research used prospective observational methods, enrolling 1366 patients in 2017 periods. The diagnosis of BCS was established using four-phase MSCT imaging.
Results: A total of 18 patients (1.32%) were diagnosed with BCS, 10 of them (55.6%) were male and 8 (44.4%) were female. The mean age in the male group was 51.0 ± 10.9 years, while in the female group it was 40.1 ± 8.3 years. The detection of transudative ascites and intrahepatic collateral vein had a high diagnostic value (94.4%). Among the four patients (22.2%) with protein C or S deficiency, half of them had JAK2 V617F mutation and antithrombin III deficiency. Cirrhosis as an etiological factor was found in 2 patients (11.1%) Subacute clinical presentation was more prevalent than chronic clinical presentation (88.9% vs 11.1%).
Conclusion: This preliminary research showed that secondary BCS was more prevalent.

Abstract #724

Acute Mesenteric Ischemia (AMI) as initial presentation of Noncirrhotic Portal Hypertension (NCPH): A Case Series

Margaret Bilaoen Alba[1], Rafael Ching Chan[1], Felix Misolas Zaño[1]

[1]Section of Gastroenterology, Manila Doctors Hospital

Introduction: Worldwide, only less than 10% of patients with portal hypertension have noncirrhotic liver and the most common initial presentation is variceal bleeding. NCPH with portal vein thrombosis (PVT) may develop acute mesenteric ischemia (AMI) but AMI as initial presentation is uncommon.
Case presentation: Two patients (30-year old female and 24-year old male), presented with progressive abdominal pain secondary to AMI and underwent small intestinal segmental resection. Work up showed mesenteric vein thrombosis, splenomegaly and noncirrhotic liver. Both were discharged and given oral anticoagulation but later discontinued because they were asymptomatic. They were lost to follow up and returned for consult for ascites and melena. Further evaluation of both patients showed gastroesophageal varices, PVT, and noncirrhotic liver. Rubber band ligation of esophageal varices done. Both Protein C and Protein S were deficient. They were discharged and advised maintenance of propranolol and rivaroxaban with regular follow up.
Discussion: Splenomegaly is present in about 95% of NCPH patients and initial presentation can be as serious as AMI. Diagnosis may be delayed because of nonspecific symptoms in an otherwise healthy adult. High-quality controlled trials on management options are also lacking. At present, management of NCPH is based on studies and guidelines drafted for cirrhotic patients.
Conclusion: Early recognition of NCPH to avoid morbid initial presentation of AMI can be difficult. Perhaps, investigation on incidental finding of splenomegaly is one way to identify these patients. Due to poorly defined natural history of NCPH, regular follow up on the status of portal hypertension is recommended.

Abstract #763

Prognosis of portal vein thrombosis after treatment with antithrombin III

Shunhei Yamashina[1], Masahiro Tada[1], Kei Ishizuka[1], Hiroo Fukada[1], Akira Uchiyama[1], Kazuyoshi Kon[1], Kenichi Ikejima[1]

[1]Dept of Gastroenterology, Juntendo University School of Medicine

Background and Aim: Portal vein thrombosis (PVT) is one of the serious disorders in patients with liver diseases. Recently, it was reported that administration with AT-III is a safe and effective therapy for PVT in the patients with lower concentration levels of AT-III. We evaluated that the prognosis of portal vein thrombosis after treatment with AT-III.
Methods: Forty-one patients diagnosed as PVT with less serum level of AT-III than 70% were administrated with AT-III. Efficacy of ATIII therapy on thrombolysis was classified into 2 groups for response (partial to complete response and no response). The data was analyzed to identify the factors associated with efficacy of AT-III and prognosis after treatment.
Results: AT-III treatment was effective in 87.8% of patients (complete response 56.1%, partial response 21.7%). Incidence of accident was 4.8%. The efficacy of AT-III treatment was not correlated with complication with ascites or esophageal varices, liver cancer, however; repeating recurrence of liver cancer was suppressed the efficacy of AT-III treatment significantly ($p < 0.05$). Prognosis after AT-III treatment was significantly related with complications with liver cancer ($P < 0.05$). Increasing serum albumin and renal function (eGFR) significantly improved prognosis after AT-III therapy ($P < 0.05$). Conversely, increasing ALT and CRP significantly worsened prognosis ($P < 0.05$).
Conclusion: These data indicated that AT-III treatment was effective in patients with PVT, however, liver and renal dysfunction tended to worsen prognosis even if AT-III treatment was successful. Taken together, it is suggested that liver and renal function should be taken into account in considering PVT treatment indication.

Abstract #767

Handgrip Strength Versus L3 Level Psoas Muscle Thickness in Assessing Sarcopenia and Prognostication in Cirrhosis

Venugopal Radhika[1], Krishnasamy Narayanasamy[1]

[1]Institute of Hepato Biliary Sciences, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai, Tamilnadu, India 600003

Introduction: Sarcopenia in cirrhosis is a most common but often overlooked complication of cirrhosis which increased the risk of complications and adversely affects the transplant outcome.

Objectives: To Compare the Hand grip Strength (HGS) of Cirrhotic patients against their L3 level Psoas muscle thickness (PMTH) to ascertain whether HGS measurement will be an efficient screening tool for assessing sarcopenia.
Materials and Methods: Consecutive stable and not critically ill cirrhotics of any aetiology were recruited, and PMTH was measured at L3 level using computed tomography (CT), HGS, 6 min walking distance and other nutritional assessment parameters recorded. Prognostic indices for cirrhosis were calculated.
Results: 114 patients were included in the study. Mean age was 46.77 + 9.38 years.78% were males. The common causes for cirrhosis being alcohol related.43.9, 37.7 and 18.4%were in categories A, B, and C of Child–Pugh score respectively. Out of 114, 77.8% were found to have sarcopenia. The mean handgrip strength was found to be 20.8 + 8.39. HGS was less in Child–Pugh C (18.16 + 6.6) than Child–Pugh score A (20.11 + 8.54) and B (21.00 + 9.00) (P = < 0.001). There was significant correlation between HGS and L3 level psoas muscle thickness (P < 0.05). Multivariate logistic regression analysis to assess the tools for sarcopenia showed handgrip strength to be in in the suggestive significance range (P = 0.05). The sensitivity of HGS was 66.7% in predicting sarcopenia.
Conclusion: HGS has significant correlation with L3 PMTH in assessing sarcopenia and can be used as a reliable, inexpensive and sensitive tool for screening.

Abstract #866

The Prevalence and Predictive Factors of Esophageal Varices in Liver Cirrhosis Patients in Indonesia

Andri Sanityoso Sulaiman[1], Rino Alvani Gani[1], Irsan Hasan[1], Cosmas Rinaldi A. Lesmana[1], Juferdy Kurniawan[1], Chyntia Olivia Maurine Jasirwan[1], Kemal Fariz Kalista[1], Saut Horas Hatoguan Nababan[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Esophageal varices (EV) is one of the most serious complications in liver cirrhosis. It is associated with variceal bleeding which significantly increase the mortality rate. Therefore, identify the factors that predict the presence of esophageal varices is important in liver cirrhosis management.
Objectives: To identify the prevalence and predictive factors of EV in Indonesian patients diagnosed with liver cirrhosis.
Methods: We performed a retrospective study comprising of 148 liver cirrhosis patients who performed esophagogastroduodenoscopy (EGD) in Cipto Mangunkusumo National General Hospital of Indonesia from January 2016 to December 2017. Patients demographic and baseline data were collected from medical records. Multivariate analysis was performed to identify to predictive factors of EV and receiver operating characteristic (ROC) curve was used for assessing the specificity and sensitivity of corresponding predictive factors.
Results: 57.4% of patients had EV with predominantly male patients (73%) and mean age of 53 years old. Hepatitis B is the most common etiology of liver cirrhosis (52%). platelets, Child–Pugh Score, Meld Score, and APRI score were the predictive factors of EV in cirrhosis patients with the ROC of 0.717, 0.734, 0.662, and 0.691 respectively ($p < 0.05$). Child–Pugh score higher than 5 was the highest predictive factors of EV with sensitivity and specificity of 77.65 and 61.90, respectively.
Conclusion: Platelets, Child Pugh Score, Meld Score, and APRI score were the predictive factors of EV in liver cirrhosis patients.

Abstract #890

Meta-Analysis: Albumin Infusion in Patients Undergoing Large Volume Paracentesis

Mark Lester Agbing Barsaga[1], Diana Alcantara Payawal[2], Marilyn Talingdan Te[3]

[1]FUMC, [2]FUMC, [3]FUMC

Introduction: Albumin infusion reduces the incidence of post large volume paracentesis circulatory instability among patients with cirrhosis and tense ascites, as compared with no treatment. As stated in the present guideline larger volumes of fluid have been safely removed with the administration of intravenous albumin (8 g/L of fluid removed) in patients with tense ascites whether it was diuretic-resistant or not. However, large-volume paracentesis does nothing to correct the underlying problem but just to correct some of its complications which is ascites.
Objective: To determine whether albumin infusion prevents or reduce the occurrence of circulatory instability in patients undergoing large volume paracentesis in comparison to other treatment modalities.
Methods: The meta-analysis included randomized trials evaluating albumin infusion in patients with tense ascites undergoing large volume paracentesis. We use circulatory instability as our parameter to determine the efficacy of albumin infusion in preventing circulatory instability. Randomized controlled trials were search using PubMed and Cochrane.
Results: Albumin infusion reduced the incidence of large volume post paracentesis circulatory instability. Therefore, mortality was lower in patients receiving albumin than to no treatment and alternative treatments.
Conclusion: This metanalysis provides evidence that albumin reduces morbidity and mortality among patients with tense ascites undergoing large-volume paracentesis, as compared with alternative treatments investigated.

Abstract #893

Meta-analysis on the Use of Sucralfate on Esophageal Ulcers After Endoscopic Therapy of Esophageal Varices

Karlo Ivan Miguel andal Fontanilla[1], Angela Domingo Salvaña[1], Ray Anthony Igloria Bartolome[1], Ray Anthony Igloria Bartolome[1], Gizelle Mica Makiputin Silla[1]

[1]Philippine General Hospital

Background and Objectives: Ulcer formation is a necessary step after endoscipic therapy of esophageal varices. These ulcers may bleed and cause fibrosis and strictures. Sucralfate, an almuminum salt of sulphated glucose, is used as an adjunct in the treatment of gastric and duodenal ulcers. The effect of sucralfate on the healing of esophageal ulcers after endoscopic therapy of esophageal varices is conflicting. This meta-analysis is done to determine the true benefits.
Methods: A comprehensive literature search was done for trials investigating the use of sucralfate in esophageal ulcers. The investigators extracted the relevant data and performed a meta-analysis to determine the effects of sucralfate in healing of ulcers. Cochrane risk of bias tool was used to determine the quality of the studies used.
Results: Eight randomized placebo controlled studies were included in the analysis. Five studies analysed healing, three studies analysed rebleeding and two studies analysed mortality. Ulcer prevalence was similar in both groups at day 7 (RR = 0.89 [0.67, 1.18]); day 14 (RR = 0.64 [0.33, 1.22]); and day 21 (RR = 0.39 [0.09, 1.80]); there

was lower ulcer prevalence at sucralfate group at day 28 (RR = 0.17 [0.05, 0.65]). Rebleeding rate (RR = 0.66 [0.49, 0.90]) and mortality rate (RR = 0.61 [0.39, 0.96]) in the sucralfate group.
Conclusion: The use of sucralfate does not improve ulcer healing rate but decreases rebleeding rate and mortality from ulcers after endosopic therapy of esophageal varices.
Keywords: Meta-analysis, Sucralfate, Esophageal ulcers, Portal hypertension

Abstract #909

Platelet Count/Spleen Diameter Ratio as a Predictive Value for Esophageal Varices Among Patients with Upper Gastrointestinal Bleeding

Maria Aloiza Joven Hadloc[1], Jose A. Tan[1], Stephen Ng Wong[1]

[1]Section of Gastroenterology Chinese General Hospital

Introduction: Upper gastrointestinal bleeding (UGIB) results in substantial morbidity and mortality. Peptic ulcer disease is the most common cause while gastroesophageal varices place second. Vasoactive drugs are first-line treatment for acute variceal hemorrhage, with prophylactic antibiotics recommended. PUD however focuses on acid suppression. Due to significant differences on management between the two, and higher mortality in variceal hemorrhage, identifying esophageal varices (EV) among patients with risk factors or diagnosis of Cirrhosis is important at the outset of UGIB. If EV be identified from easily obtainable clinical variables, a prompter and more appropriate management be given to patients presenting with UGIB.
Objective: This study aims to evaluate capacity of platelet count/spleen diameter ratio in predicting EV in patients presenting with UGIB and underwent gastroscopy in Chinese General Hospital (CGH).
Methodology: This cross-sectional study included 147 patients who presented with UGIB and underwent gastroscopy at CGHMC between January 2012–December 2015. Platelet count/spleen diameter ratio ((N/mm^3)/mm) was assessed in all, and its diagnostic accuracy was calculated.
Results: EV were detected in 77 (52.38%). Mann–Whitney U-test showed that patients with EV have lower platelet count/spleen diameter ratio, and it can be used in predicting EV. Using ROC Curve, cut-off was noted at 1176 with 80.5% probability that platelet count/spleen diameter ratio is < 1176 when patient has EV. Furthermore, positive likelihood ratio of 9.3 and negative likelihood ratio of 0.21 further proves/strengthens result that there is greater likelihood that patients with platelet count/spleen diameter ratio < 1176 has EV and those > 1176 has lesser likelihood.
Conclusion: Platelet count/spleen diameter ratio can predict occurrence of EV in patients presenting with UGIB.

Abstract #926

Non Cirrhotic Portal Cavernoma in a young female: A Case Report

Millette Dela Cruz Castro[1]

[1]University of The East Ramon Magsaysay Memorial Medical Center

Introduction: Cavernous transformation of the portal vein is a rare entity and usually is a sequela of extra-hepatic portal vein thrombosis. We report a case of a 21-year old female presented with a history of intermittent hematemesis which started when she was 1 year old. Prenatal and birth history was unremarkable.
Clinical Presentation: A 21-year old Filipina came in with massive upper GI bleeding with a background history of recurrent bleeding esophageal varices since she was 1 year old. Interval history of her birth and prenatal course of the mother were all unremarkable. Family history was also unremarkable.
Diagnosis: Work ups for viral hepatitis all negative. Portal hypertension is seen on Doppler ultrasound of the spleen and liver. Portal cavernoma is evident on triphasic whole abdominal ct scan. Gastroscopy revealed 4 columns of medium to large sized varices. Patient was maintained on Propanolol 10 mg/tab TID. She was advised for vaccination and is being counselled for contemplated splenectomy. Surveillance gastroscopy was done every 3 months.
Conclusion: NCPH is the most common cause of portal hypertension next to cirrhosis. Two disease entities in NCPH, namely NCPF/IPH and EHPVO are distinct diseases. The diagnosis needs exclusion of cirrhosis in NCPF/IPH and presence of portal cavernoma in EHPVO. Effective management of portal hypertension and its complications results in excellent 5 and 10 years survival.

Abstract #928

Role of CT scan findings as a predictor of gastro-esophageal varices on endoscopy in patients with liver cirrhosis at the National Kidney and Transplant Institute

Lea Aina Alvero Abrazaldo[1], Rene Dimayuga Bautista[1]

[1]Department of Medical Imaging and Therapeutic Radiology, National Kidney and Transplant Institute

Introduction: Esophageal varix is responsible for the massive upper GI bleeding and leading cause of mortality in patients with cirrhosis of the liver. Early detection of varices is imperative to reduce significant complication.
Objective/s: Aims to determine if CT scan findings, such as portal vein diameter, splenic index and presence of esophageal varices, be used as an alternative evaluation tool in predicting and datection of esophageal varices in cirrhotic patients at National Kidney and Transplant Institute.
Methodology: Hospital-based descriptive study (retrospective) that included all patients with liver cirrhosis who underwent Upper GI endoscopy and Whole abdomen CT scan from 2014 to 2017. Endoscopy results and Whole abdomen CT scan images of qualified patients was reviewed for the presence and grading of varices, portal vein diameter and splenic index.
Results: Cirrhotic patients has portal vein diameters of 0.7 cm to 1.9 cm measured in CT scan. Patients with no varices has a mean portal vein diameter of 1.20 cm while the patient with varices has a portal vein diameter of 1.39 cm. Splenic index of liver cirrhotic patients are within the range of 138–2681 cm^3. The mean splenic index of the patients without varices is 659.97 cm^3 while those with varices has a splenic index of 935.88 cm^3.
Conclusion: In patients with liver cirrhosis, portal vein diameter, splenic index and presence of oesophageal varices in CT scan can be used as non-invasive predictors of gastroesophageal varices.
Keywords: Portal vein, Gastric varix, Cirrhosis, Hypertension, portal

Abstract #944

A comparison of splenic pathological changes and immune function in HBV-related portal hypertension and Budd-Chiari syndrome patients with hypersplenism

Suxin Li [1], Na Huang[1], Xiaowei Dang [1], Liang Li [1], Zhenzhen Li [1], Chen Zhang[1], An Jiang[1], Guangyao Kong[1], Fanpu Ji[1], Jun Yang[1], Zongfang Li[1]

[1]National & Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital, Xi'an Jiaotong University & Department of Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital, Zhengzhou University & Shaanxi Provincial Clinical Research Center for Hepatic and Splenic Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University

Object: To compare clinical data, splenic pathological changes and immune function in hypersplenic patients with HBV-related portal hypertension (PH) and Budd–Chiari syndrome (B-CS).
Methods: Totally, 93 patients with Budd-Chiari syndrome (B-CS group), 105 with HBV-related cirrhosis (HBV/PHT group) and 31 healthy Controls were retrospectively enrolled from 2012 to 2017. Flow cytometry was used to measure CD3+ CD4+ T cells, CD3+ CD8+ T cells, myeloid-derived suppressive cells (MDSCs) and Tregs in peripheral blood. Paraffin sections of the spleen were analyzed by H&E and immunohistochemistry. Lipopolysaccharide (LPS) in the plasma was measured by ELISA.
Results: Hypersplenism and PH were more serious in the HBV/PHT group than in the B-CS group ($P < 0.01$). The platelet count was positively correlated with the spleen size in the B-CS group ($P = 0.007$) but not in the HBV/PHT group ($P = 0.171$). In the peripheral blood, Tregs and MDSCs were higher ($P < 0.01$) in the HBV/PHT group than in the B-CS and Control groups. In both the peripheral blood and spleen, CD4+ and CD8+ T cells were lower ($P < 0.01$) in the HBV/PHT group than in the B-CS and Control groups. Substantially more hyperplasia of splenic nodules and more germinal centers were found in the HBV/PHT group than in the B-CS and Control groups. Moreover, iNOS and TLR4 expression in the spleen and the plasma LPS level were significantly higher in the HBV/PHT group than in the B-CS group.
Conclusions: The HBV/PHT group showed more severe immunosuppression and immune dysfunction than the B-CS group. The HBV/PHT group also had more substantial hypersplenism and splenic phagocytosis than the B-CS group.

Abstract #946

Improvement of human platelet aggregation post-splenectomy in hepatitis B virus-related cirrhosis with portal hypertension

Hui Zhang [1], Jian Zhang[2], Song Reng[3], Rui Zhou[4], Xi Liu[5], Guangyao Kong[6], Fanpu Ji[7], Yongzhan Nie[8], Zongfang Li[9]

[1]National and Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University & Shaanxi Provincial Clinical Research Center for Hepatic and Splenic Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, [2]Department of Surgery, The Second Affiliated Hospital of Xi'an Jiaotong University, [3]Department of Surgery, The Second Affiliated Hospital of Xi'an Jiaotong University, [4]Department of Surgery, The Second Affiliated Hospital of Xi'an Jiaotong University, [5]National and Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University, [6]National and Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University, [7]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University & National and Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University, [8]State Key Laboratory of Cancer Biology, National Clinical Research Center for Digestive Disease & Xijing Hospital of Digestive Diseases, Fourth Military Medical University, [9]National and Local Joint Engineering Research Center of Biodiagnosis and Biotherapy, The Second Affiliated Hospital of Xi'an Jiaotong University & Shaanxi Provincial Clinical Research Center for Hepatic and Splenic Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University

Background and Objectives: Hypersplenism is a progressive complication of cirrhosis and is closely associated with anemia, leukopenia, thrombocytopenia, bleeding tendency as well as portal hypertension (PH). Splenectomy plus pericardial devascularization (SPD) is a conventional surgical procedure for cirrhotic hypersplenism, which can reverse pancytopenia, reduce portal pressure and the risk of variceal hemorrhage. However, the changes of platelet aggregation function in chronic hepatitis B (CHB) cirrhotic patients with hypersplenism and the effect of SPD on platelet aggregation have not been reported yet.
Methods: A total of 40 CHB cirrhotic patients with hypersplenism and 17 healthy controls were included in this study, among which 10 CHB patients underwent SPD. Platelet aggregation was induced by adenosine diphosphate (ADP), epinephrine, arachidonic acid, collagen and detected by Aggregation Remote Analyzer Module (AggRAM). The maximum platelet aggregation, primary slope, area under curve of platelet aggregation and the platelet aggregation of different time points in three groups were compared.
Results: The maximum platelet aggregation, primary slope, area under curve of platelet aggregation decreased in cirrhotic patients and restored to normal level after SPD. The mean platelet aggregation value of cirrhotic patients significantly decreased over time (100 s, 120 s, 140 s, 160 s, 180 s, 200 s) and restored to normal level after SPD.
Conclusions: The platelet aggregation function decrease in cirrhotic patients with PH and restore to normal level after SPD. SPD is beneficial to patients with bleeding tendencies by improving the counts and aggregation of platelets.

Abstract #947

Prognostic Factors Associated With Mortality of Acute Variceal Hemorrhage In Cirrhotic Patients: Multicenter Study Results

Kuntapon Akkarachinores[1], Sakkarin Chirapongsathorn[1], Pawinee Saybungkla[1]

[1]Phramongkutklao Hospital

Method: Retrospective study of acute variceal hemorrhage patients who underwent early vasoactive drugs with endoscopic treatment was collected since 1 October 2012–30 September 2018 in Phramongkutklao hospital and Maharat Nakhon Sri Thummarat hospital. Demographic information, medical histories, and laboratory test results were collected. Survival analysis was estimated using the Kaplan–Meier method and compared with log-rank test. Multivariate analysis was performed using the Cox proportional hazard model to identify independent risk factors for mortality and rebleeding at 5-day and 6-week.
Results: 5-Day mortality was 110 (9.6%) and 6-week mortality was 141 (12.33%) out of total 1144 cases which associated risk factors through multivariate analysis composed of MAP < 50 (HR = 2.01, 95% CI: 1.18–3.44, P = 0.011), and high risk stigmata EV on

endoscopic finding (HR = 4.01, 95% CI: 2.50–6.44, P < 0.001). And one additional risk factor that found only in 6-week mortality was Glasgow Blatchford score ≥ 6 (HR = 34.66, 95% CI: 13.88–86.52, P < 0.001). 5-day rebleeding was 155 cases (13.6%) and 6-week rebleeding was 244 cases (21.3%) which associated with risk factors through multivariate analysis composed of MELD score ≥ 18 (HR = 2.46, 95% CI: 1.76–3.45, P < 0.001), Glasgow Blatchford Score ≥ 6 (HR = 2.20, 95% CI: 1.19–4.05, P = 0.012), high risk stigmata EV on endoscopic finding (HR = 2.02, 95% CI: 1.39–2.93, P < 0.001), weekend visit (H = 1.33, 95% CI: 1.00–1.75, P = 0.048), duration of cirrhosis ≥ 2 years (HR1.59, 95% CI: 1.06–2.39, P = 0.025), antiplatelet (HR = 1.83, 95% CI: 1.06–3.17, P = 0.031) and NSAIDS use (HR = 3.39, 95% CI: 2.06–5.60, P < 0.001).
Conclusion: In this study, strong risk factors of 5-day and 6-week mortality in acute variceal hemorrhage were high risk stigmata on endoscopic finding, MAP < 50, and high MELD score. Additional risk factor in 6-week mortality was Glasgow Blatchford Score ≥ 6. 5-day and 6-week rebleeding risk factors also similar with mortality risk factors included Glasgow Blatchford Score ≥ 6, antiplatelet and NSAIDS, duration of cirrhosis and weekend visit.

Abstract #969

Close linkage of portal hypertension and insulin resistance in patients with cirrhosis

Soichiro Kiyono[1], Hitoshi Maruyama[1], Kazufumi Kobayashi[1], Susumu Maruta[1], Hiroaki Kanzaki[1], Takahiro Maeda[1], Masato Nakamura[1], Shingo Nakamoto[1], Shin Yasui[1], Tomoko Saito[1], Kengo Kanayama[1], Yuko Kusakabe[1], Sadahisa Ogasawara[1], Eiichiro Suzuki[1], Yoshihiko Ooka[1], Akinobu Tawada[1], Tetsuhiro Chiba[1], Naoya Kato[1]

[1]Department of Gastroenterology, Chiba University School of Medicine

Introduction: Although portal haemodynamics has a potential role to the insulin resistance (IR), limited data are available regarding the linkage between impaired portal hypertension and glucose metabolism. The study prospectively examined the interrelationships in cirrhosis between the IR and portal haemodynamic abnormality.
Objectives and Methodology: There were 53 cirrhosis patients (61.6 ± 13.0 years), all presenting gastroesophageal varices. Portal haemodynamics were examined by both hepatic venous catheterization and Doppler ultrasound with respect to the homeostasis model assessment (HOMA)-IR and HOMA2-IR. The IR was defined by HOMA-IR > 3.0 or HOMA2-IR > 2.0.
Results: Forty-two patients (79.2%) had collateral vessels; 38 with left gastric vein, 12 with short/posterior gastric vein, 9 with splenorenal shunt. Multivariate analysis provided significant factors; wedged hepatic venous pressure (hazard ratio (HR) 1.183, p = 0.035) for HOMA-IR > 3.0, Body Mass Index for HOMA2-IR > 2.0 (HR 1.490, p = 0.001), and collateral flow volume for both HOMA-IR > 3.0 (HR 1.007, p = 0.015) and HOMA2-IR > 2.0 (HR 1.007, p = 0.009). The best cut-off value of collateral flow volume was 165 mL/min for detecting the HOMA-IR > 3.0 showing area under the receiver operating characteristic curve (AUROC) 0.688 (odds ratio 5.33) with sensitivity 70% and specificity 69.6%, and was also 165 mL/min for detecting of HOMA2-IR > 2.0 showing AUROC 0.698 (odds ratio 5.70) with sensitivity 75% and specificity 65.5%.
Conclusion: This study suggested a close linkage between the IR and impaired portal haemodynamics presented by collateral development reflecting the underlying pathogenesis of portal hypertension in cirrhosis patients.

Abstract #984

Different vascular responses in splenic and mesenteric arteries in experimental cirrhosis

Saadet Turkseven[1], Alessandra Brocca[2], Marco Di Pascoli[3]

[1]Department of Medicine, Unit of Internal Medicine and Hepatology (Uimh), University of Padova, Padova, Italy & Department of Pharmacology, Faculty of Pharmacy, Ege University, Izmir, Turkey, [2]Department of Medicine, Unit of Internal Medicine and Hepatology (Uimh), University of Padova, Padova, Italy, [3]Department of Medicine, Unit of Internal Medicine and Hepatology (Uimh), University of Padova, Padova, Italy

Introduction: In liver cirrhosis, portal hypertension is a consequence of enhanced intrahepatic resistance and portal blood flow, which is secondary to a marked vasodilation in the splanchnic vascular district. If the distinct components of the splanchnic circulation exert different vascular reactivity in cirrhosis has not been elucidated.
Objective: The aim of this study is to evaluate if, in experimental cirrhosis, differences in vascular response between splenic and mesenteric arteries exist.
Methodology: Liver cirrhosis was induced in Spraque–Dawley rats by common bile duct ligation. Sections of superior mesenteric and splenic arteries were dissected and mounted on wire myograph system to obtain cumulative dose–response curves.
Results: In cirrhotic rats, compared to controls, mesenteric arteries but not splenic arteries showed a significant increase in endothelium-dependent relaxation to acetylcholine (ACh). In both groups, COX-inhibitor indomethacin did not change the response of mesenteric arteries to ACh; after adding the NOS-inhibitor Nω-nitro-L-arginine methyl ester (L-NAME), the relaxation was completely abolished in control rats but only partially decreased in cirrhotic rats, suggesting the contribution of other factors in the enhanced vasodilator response. With indomethacin and L-NAME, the relaxation to ACh was similarly decreased in splenic arteries from control and cirrhotic animals. The contraction of mesenteric and splenic arteries induced by phenylephrine were not significantly different in cirrhotic and control rats. Moreover, in cirrhotic rats, iNOS mRNA expression was increased in mesenteric but not in splenic arteries.
Conclusion: In experimental cirrhosis, an increased vasodilator response in mesenteric but not in splenic arteries may contribute to splanchnic overflow.

Abstract #991

Endoscopic cyanoacrylate injection for gastric varices: What is the actual risk or effective therapy? - A systematic review and meta-analysis

Sakkarin Chirapongsathorn[1], Wuttiporn Manatsathit[2], Chayakrit Krittanawong[3], Ann M. Farrell[4]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Phramongkutklao Hospital, College of Medicine, [2]Division of Gastroenterology, University of Nebraska Medical Center, [3]Department of Medicine, Icahn School of Medicine At Mount Sinai, [4]Mayo Clinic Libraries, Mayo Clinic, Rochester, Minnesota, Usa

Backgrounds: We performed a systematic review and meta-analysis to evaluate the effect of endoscopic cyanoacrylate injection in the management of gastric varices.
Methods: We conducted a comprehensive search of MEDLINE, Embase, Web of Science, Scopus databases and Cochrane Databased of Systemic Reviews through November 2018 and manually reviewed

the literature. Attempts were made to contact the corresponding authors of the relevant studies for additional information when needed. Trial-specific risk ratios (RRs) were estimated and pooled using random-effect model meta-analysis. Between-study heterogeneity was assessed using the I^2 statistic. The quality assessment of included studies and publication bias were assessed.

Result: We included 7 randomized controlled trials (6 for secondary prophylaxis and one for primary prophylaxis) at low risk of bias in which 126 deaths were reported in 583 patients with gastric varices. Cyanoacrylate use was associated with significantly lower all-cause mortality (RR, 0.59; 95% CI, 0.36–0.98; $I^2 = 41\%$) and re-bleeding rate after hemostasis (RR, 0.55; 95% CI, 0.32–0.93, $I^2 = 59\%$) compared to any other treatment approach that did not involve cyanoacrylate. When cyanoacrylate was compared to each individual treatment approach, data were sparse limiting comparative conclusions. Use of cyanoacrylate injection was not associated with an increase in serious adverse events. The quality of evidence is moderate, graded down due to the small number of events and wide confidence intervals.

Conclusions: The use of endoscopic cyanoacrylate injection therapy for gastric varices may be associated with lower all-cause mortality and better hemostasis compared to other therapies.

Abstract #1042

Doppler Ultrasound Hepatic Vein Waveform as a Non-invasive Tool in the Assessment of Severity of Portal Hypertension (DPH Trial)

Hasnain Ali Shah[1], Memoona Parveen[2], Zahid Azam[3], Nazish Butt[4], Raza Sayani[5], Tanveer Haq[6], Tanveer Haq[7], Aamir Hameed[8], Aamir Hameed[9], Safia Awan[10]

[1]Section of Gastroenterology, Department of Medicine, Aga Khan University, [2]National Institute of Liver & Gi Diseases, Dow University of Health Sciences, [3]National Institute of Liver & Gi Diseases, Dow University of Health Sciences, [4]Section of Gastroenterology, Department of Medicine, Aga Khan University, [5]Section of Vascular Interventional Radiology, Department of Radiology, Aga Khan University, [6]Section of Vascular Interventional Radiology, Department of Radiology, Aga Khan University, [7]Section of Vascular Interventional Radiology, Department of Radiology, Aga Khan University, [8]Section of Cardiology, Department of Medicine, Aga Khan University, [9]Section of Cardiology, Department of Medicine, Aga Khan University, [10]Section of Gastroenterology, Department of Medicine, Aga Khan University

Background: Portal hypertension is a common and serious complication of cirrhosis. It is important to measure portal pressure to predict complications. Catheterization of hepatic veins to measure HVPG is invasive and no available easily. Radiology literature showed hepaticvein Doppler ultrasound waveform (DUWF) as alternate modality of evaluation of portal pressure. It is noninvasive, cheap and readily available.

Aims: To correlate HVPG with Hepatic Vein DUWF as non-invasive tool and to assess DUWF use after Carvedilol administration to document dynamic changes that can be correlated.

Methods: 46patients baseline investigations done. Hepatic vein DUWF was studied and HVPG done and procedures repeated after oral Carvedilol to lower the HR 25% of baseline.

Results: 46 patients, 33 (75%) males, with mean age 49.1 ± 9.5 were studied. Triphasic, biphasic and monophasic waveforms were observed in 3 (6.8%), 17 (38.6%) and 24 (54.5%) respectively. Post carvedilol administration, waveform changed from monophasic to biphasic in 6 (25%) while heart rate dropped from 81.0 ± 7.0/min to 65.3 ± 19.3 ($p < 0.001$) and HVPG dropped from 14.1 ± 2.7 to 10.6 ± 2.6 mmHg ($p < 0.03$). Waveform changed from monophasic to triphasic with a decrease of HVPG from 17.7 ± 2.2 to 14.2 ± 3.3 mmHg ($p < 0.03$) and HR decreased from 97.0 ± 11.9 to 72.2 ± 10.2/min ($p<0.01$). However, waveform remained unchanged in 14 pts whose waveform was monophasic pre and post Carvedilol, although HVPG dropped from 13.1 ± 2.5 to 10.1 ± 2.9 mmHg and HR dropped from 81.6 ± 10.4 to 69.3 ± 6.3/min ($p < 0.01$).

Conclusion: The results were inconsistent to use Hepatic vein DUWF as a non-invasive tool to replace HVPG as baseline and after Carvedilol intervention to drop HR and portal pressure.

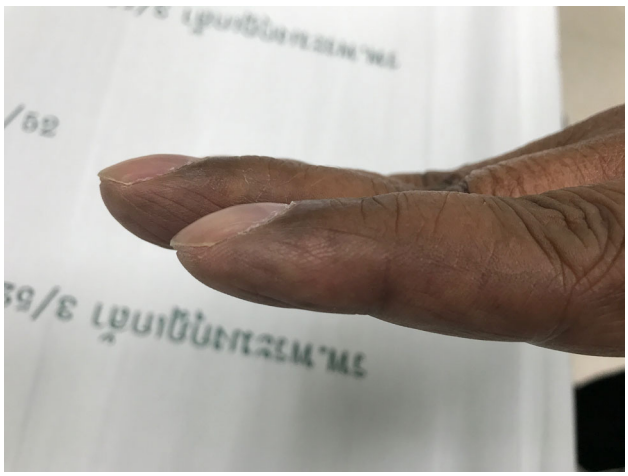
Abstract #1043

A Classic Case of Hepatopulmonary Syndrome

Sakkarin Chirapongsathorn[1], Kanit Bunnag[2], Chayakrit Krittanawong[3]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Phramongkutklao Hospital, College of Medicine, [2]Division of Gastroenterology and Hepatology, Department of Medicine, Phramongkutklao Hospital, College of Medicine, [3]Department of Medicine, Icahn School of Medicine At Mount Sinai

We report the case of a 52-year-old male, a known case of Chronic Liver Disease from chronic hepatitis C with portal hypertension. He presented with dyspnoea, platypnoea, cyanosis, clubbing (Figure 1) and orthodeoxia. He had oesophageal varices and splenomegaly indicating portal hypertension. His arterial blood gas revealed hypoxaemia and orthodeoxia as in Table 2. Chest X-ray showing reticulonodular pattern in the basal zones bilaterally. Contrast echocardiography with agitated saline showed bubble appearance in left atrium and left ventricle after 3rd cardiac cycle suggestive of right to left intrapulmonary shunting. From this clinical background and investigation, a diagnosis of hepatopulmonary syndrome was made. Patient was managed for liver transplantation and hepatitis C treatment.



This Arterial Blood Gas analysis shows characteristic decrease in po2 more than 5 mmHg from supine to upright posture indicating opening of intrapulmonary shunting during upright posture resulting in arterial hypoxaemia

Blood gas analysis	Lying posture (37 deg C)	upright posture after 3 mins (37 deg C)	Normal range
PH	↑ 7.49	7.44	7.35-7.45
pCO_2	↓ 22.mmHg	↓ 24.7 mmHg	32-48
pO_2	↓ 60 mmHg	↓ 55 mmHg	96-108
$cHCO_3$	↓ 16.6 mmol/L	↓ 16.7 mmol/L	24-28
Anion Gap	18.6 mmol/L	16.8 mmol/L	10-12
pO_2 (A)	122 mmHg	119 mmHg	
pO_2 (A-a)	62 mmHg	63 mmHg	

Abstract #1064

A nationwide study of non-selective beta-blockers in cirrhotic patients with refractory ascites

Yu-Chen Chang[1], Jin-Shiang Cheng[2], Wei-Chun Huang[3], Ping-I Hsu[4], Sung-Shuo Kao[5], Wen-Chi Chen[6]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, [2]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, [3]Division of Cardiology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan & Department of Critical Care Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, [4]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan & School of Medicine, National Yang-Ming University, Taipei, Taiwan, [5]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan & School of Medicine, National Yang-Ming University, Taipei, Taiwan, [6]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan & School of Medicine, National Yang-Ming University, Taipei, Taiwan

Background and Aims: The impact of non-selective beta-blockers (NSBBs) on the prognosis of cirrhotic patients with refractory ascites remains controversial. This study is aimed to compare the survival between the patients with refractory ascites using and without using NSBBs.
Methods: Cirrhotic patients with refractory ascites using NSBBs and controls matched by age and gender in a 1:1 ratio were extracted from The National Health Insurance Research Database of Taiwan. The baseline characteristics including the etiology of liver cirrhosis, comorbidities, and treatment of esophageal varices were compared. Cox regression analysis was used to examine the risk of mortality.
Results: 2224 subjects were enrolled in each group. The demographic data were similar except that more NSBBs group patients had a history of alcoholic cirrhosis, hypertension, peptic ulcer disease, and endoscopic therapy for gastroesophageal varices and more non-NSBBs group patients had a history of chronic kidney disease. The mean survival was 35.0 ± 32.0 months in NSBBs group and 20.4 ± 26.7 months in non-NSBBs group ($P < 0.0001$). NSBBs (RR: 0.58, 95% CI: 0.54–0.62, $P < 0.0001$), diabetes (RR: 1.18, 95% CI: 1.10–1.27, $P < 0.0001$), chronic kidney disease (RR: 1.17, 95% CI: 1.06–1.29, $P = 0.003$) and cerebrovascular accident (RR: 1.25, 95% CI: 1.10–1.42, $P = 0.001$) were the independent predictors of the mortality.
Conclusions: The use of NSBBs was associated with improved survival in a nationwide cohort of cirrhotic patients with refractory ascites. A history of diabetes, chronic kidney disease, and cerebrovascular accident was the predictors of mortality.

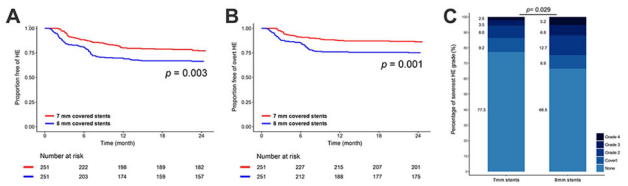
Abstract #1071

Transjugular intrahepatic portosystemic shunt with 7 mm covered stent reduces hepatic encephalopathy without losing shunt function for prevention of portal hypertension rebleeding

Yifan Wu[1], Chuan Liu[2], Zhendong Yue[3], Hongwei Zhao[4], Lei Wang[5], Xiaoxue Du[6], Fuliang He[7], Fuquan Liu[8], Xiaolong Qi[9]

[1]Chess Group, Department of Interventional Therapy, Beijing Shijitan Hospital, Capital Medical University, Beijing, China, [2]Chess Group, Hepatic Hemodynamic Lab, Institute of Hepatology, Nanfang Hospital, Southern Medical University, Guangzhou, China, [3]Chess Group, Department of Interventional Therapy, Beijing Shijitan Hospital, Capital Medical University, Beijing, China, [4]Chess Group, Department of Interventional Therapy, Beijing Shijitan Hospital, Capital Medical University, Beijing, China, [5]Chess Group, Department of Interventional Therapy, Beijing Shijitan Hospital, Capital Medical University, Beijing, Chian, [6]Chess Group, Hepatic Hemodynamic Lab, Institute of Hepatology, Nanfang Hospital, Southern Medical University, Guangzhou, China, [7]Chess Group, Department of Interventional Therapy, Beijing Shijitan Hospital, Capital Medical University, Beijing, Chian, [8]Chess Group, Department of Interventional Therapy, Beijing Shijitan Hospital, Capital Medical University, [9]Chess Group, Department of Interventional Therapy, Beijing Shijitan Hospital, Capital Medical University & Chess Group, Hepatic Hemodynamic Lab, Institute of Hepatology, Nanfang Hospital, Southern Medical University

Introduction: Transjugular intrahepatic portosystemic shunt (TIPS) has been recommended for portal hypertensive bleeding in cirrhosis. However, there is no international consensus yet regarding the priority diameter selection of the covered stents.
Objectives: The study aims to explore whether the 7 mm covered stents would equip with more advantages than 8 mm covered stents for the prevention of portal hypertensive bleeding in cirrhosis. Methodology: In this retrospective study, cirrhotic patients receiving TIPS procedure with a 7 mm or 8 mm covered stent for the treatment of variceal rebleeding between January 2011 and September 2015 in our center were analyzed.
Results: A total of 502 eligible patients were enrolled. During a 24-month follow-up, there was no significant difference between the 7 mm and 8 mm stents groups considering the free of shunt dysfunction rates, free of rebleeding rates, survival rates, free of all-cause rebleeding and death rates with p value of 0.915, 0.840, 0.735, 0.237, respectively. Notably, the group with patients receiving 7 mm covered stent had a higher free of HE rate (77.1% vs 66.4%, $p = 0.003$, Figure 1A) and overt HE rate (86.3% vs 75.2%, $p = 0.001$, Figure 1B) over the group with patients receiving 8 mm covered stent. Moreover, the percentages of severest grade of HE episodes were significantly different between the groups ($p = 0.029$, Figure 1C).
Conclusion: Our study suggested a favorable overall outcome with 7 mm covered stents compared with 8 mm covered stents in TIPS procedure for portal hypertension rebleeding prevention in cirrhosis.



Abstract #1072

Portal Pressure Gradient Measured Immediately After Transjugular Intrahepatic Portosystemic Shunt Placement: Poor in Predicting Rebleeding in Patients with Portal Hypertension

Fangze Huang[1], Chuan Liu[2], Fuquan Liu[3], Xinlong Lin[4], Xiangbo Zeng[5], Yanna Liu[6], Fuquan Liu[7], Xiaolong Qi[8]

[1]Hepatic Hemodynamic Lab, Institute of Hepatology, Nanfang Hospital, Southern Medical University, Guangzhou, China, [2]Hepatic Hemodynamic Lab, Institute of Hepatology, Nanfang Hospital, Southern Medical University, Guangzhou, China & Chess Frontier Center, Lanzhou University, Lanzhou, China, [3]Chess Group; Department of Interventional Therapy, Beijing Shijitan Hospital, Capital Medical University, Beijing, China, [4]Hepatic Hemodynamic Lab, Institute of Hepatology, Nanfang Hospital, Southern Medical University, Guangzhou, China, [5]Hepatic Hemodynamic Lab, Institute of Hepatology, Nanfang Hospital, Southern Medical University, Guangzhou, China, [6]Hepatic Hemodynamic Lab, Institute of Hepatology, Nanfang Hospital, Southern Medical University, Guangzhou, China & Chess Frontier Center, Lanzhou University, Lanzhou, China, [7]Department of Interventional Therapy, Beijing Shijitan Hospital, Capital Medical University, [8]Chess Group, Hepatic Hemodynamic Lab, Institute of Hepatology, Nanfang Hospital, Southern Medical University

Introduction: A portal pressure gradient (PPG) above 12 mmHg after transjugular intrahepatic portosystemic shunt (TIPS) can indicate a postoperative rebleeding in patients with variceal bleeding caused by portal hypertension. A recent study has verified that measure timing influenced the accuracy of PPG.
Objectives: This study aimed to analyze the direct relationship between immediate PPG measured under local anesthesia and postoperative rebleeding to investigate whether immediate PPG could predict a rebleeding after TIPS in portal hypertension.
Methodology: This retrospective study included eligible patients receiving TIPS between January 2011 and September 2015 in China. Immediate PPG was measured after TIPS placement under local anesthesia. A propensity score matching analysis was performed in 159 cases to match bleeding patients with non-bleeding patients in at a ratio of 1:2 to reduce the confounding factors. Relationship between immediate PPG with a threshold of 12 mmHg and a postoperative rebleeding was analyzed.
Results: A total of 502 consecutive patients were enrolled. No significant difference was observed in occurrence of rebleeding between patients with immediate PPG $\geq$ 12 mmHg and $<$ 12 mmHg neither before nor after (8.7% vs. 12.8%, p = 0.09; 31.2% vs. 35.3%, p = 0.4) matching (Figure 1). Predictive performance of PPG for rebleeding was poor with the area under survival receiver operating characteristic curve of 0.415 (95% CI: 0.332–0.514).
Conclusion: Our study found that a threshold of 12 mmHg for PPG measured immediately after TIPS under local anesthesia could not predict rebleeding in portal hypertension.

Abstract #1078

A Simplified Prognostic Model to Predict Mortality in Patients with Acute Variceal Bleeding: Multicenter Study Results

Kuntapon Akkarachinores[1], Amnart Chaipresert[2], Pawinee Saybungkla[3], Sakkarin Chirapongsathorn[4]

[1]Division of Gastroenterology and Hepatology, Department of Medicine Phramongkutklao Hospital, [2]Division of Nephrology, Department of Medicine Phramongkutklao Hospital, College of Medicine, [3]office Research Development, Phramongkutklao College of Medicine, [4]Division of Gastroenterology and Hepatology, Department of Medicine, Phramongkutklao Hospital, College of Medicine

Background and Aims: Acute variceal bleeding (AVB) is a serious complication associated with high mortality. The aim of our study was to investigate mortality predictors and develop a new simple prognostic model using easily verified factors at admission in AVB patient.
Method: Between October 2012 and September 2018, 1144 consecutive patients with AVB from Phramongkutklao hospital in Bangkok and Maharat Nakhon Sri Thummarat hospital in Nakhon Sri Thummarat were included. A simplified prognostic model was developed using multiple logistic regression after indentifying significant predictors of 6-week mortality. Mortality prediction accuracy was assessed with area under the receiver operating characteristic (AUROC) curve. We compared the new model to existing models of model for end-stage liver disease (MELD), Child–Pugh scores and Glasgow Blatchford Score.
Results: The 6-week overall mortality rate was 12.3%. Multivariate analysis showed that mean arterial pressure (MAP), model for end-stage liver disease (MELD), high-risk stigmata of esophageal varices or peptic ulcer on endoscopic finding and the Glasgow Blatchford Score were independent predictors of mortality. A new logistic model using these variables was developed. This model's AUROC was 0.972, which was significantly higher than that of MELD (0.787), Child–Pugh scores (0.701), and Glasgow Blatchford Score (0.916). Two external validation studies showed that the AUROC of our model was consistently higher than 0.8.
Conclusion: Our new simplified model accurately and consistently predicted 6-week mortality in patients with acute variceal bleeding using objective variables measured at admission. Our system can be used to identify high risk acute variceal bleeding patients.

Figure 1: Receiver operating characteristic (ROC) curves of a simplified prognostic models used to predict 6-week mortality in patients with acute variceal bleeding

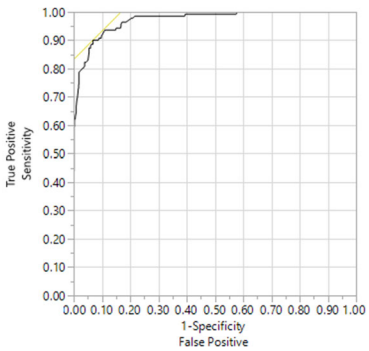


Table 1: Factor predicting in acute variceal bleeding

Factor	Likelihood ratio	P-value
MELD score	24.1458	<.0001*
MAP (mmHg)	6.9849	0.0082*
High-risk stigmata of esophageal varices	89.8794	<.0001*
Glasglow Blatchford score	31.9755	<.0001*
Peptic ulcer	17.8277	<.0001*

Abstract #1083

The therapeutic effect of davigtran in the liver cirrhosis patients with portal vein thrombosis

Hee Bok Chae[1]

[1]Chungbuk National University Hospital

Background: Portal vein thrombosis (PVT) is a uncommon complication of liver cirrhosis patients. PVT can aggravate the portal hypertension, in turn the complication of liver cirrhosis such as ascites, esophageal varix, and hepatic encephalopathy. Thrombolytic therapy can resolve the PVT and reverse the disease progression. The aim of this study is to find out the thrombolytic effect in portal vein thrombosis in the LC patients. The study design was a prospective randomized comparative study of the two drugs, dabigatran and warfarin.
Subjects/methods: The LC patients with main portal vein thrombosis who they were diagnosed 2 years ago from the starting the one dose of the drug. We enrolled the other group of patients were administered with warfarin.
Results: Total 5 patients were enrolled (Dabigatran group: control group 3:2), M (5). AST/ALT 35.2./16 U/L, Total bilirubin 1.6 mg/dL. Any patients couldn't achieve the goal. The study will go on until total number of subjects is 50 patients. Authors guessed that the negative result may be because the LC patients already had an organic thrombi and the change of cavernous transformation. In that case, PVT can not be revolved easily. It needs a further large scale, and the more strict enrollment indication of the study.

N02 - Encephalopathy

Abstract #83

Sarcopenia helps predict the risk of hepatic encephalopathy and transplantation-free survival after transjugular intrahepatic portosystemic shunt in cirrhosis

Yongjun Zhu[1], **Xiaoze Wang**[2], **Xiaotan Xi**[3], **Xiao Li**[4], **Xuefeng Luo**[5], **Li Yang**[6]

[1]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, [2]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, [3]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, [4]Department of Interventional Therapy, National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, [5]Department of Gastroenterology and Hepatology, West China Hospital, Sichuan University, [6]department of Gastroenterology and Hepatology, West China Hospital, Sichuan University

Background: Hepatic encephalopathy (HE) remains one of the most common challenges after transjugular intrahepatic portosystemic shunt (TIPS). Sarcopenia was associated with clinical outcomes of patients with cirrhosis. This study was aimed to evaluate the association between preoperative sarcopenia and the incidence of HE and liver transplantation (LT)-free survival after TIPS with covered stents.
Methods: Preoperative CT images taken at the 3rd lumbar vertebra from 189 patients were quantified for definition of sarcopenia. Incidence of sarcopenia and post-TIPS HE, LT-free survival and the association between them were analyzed.
Results: Sarcopenia was present in 74 (39.2%) patients. HE occurred in 64 patients (33.9%) after a median time of 17.7 (IQR 4.5–28.8) months follow-up. Patients with sarcopenia had a significantly higher incidence of HE ($p = 0.009$) and tended toward lower LT-free survival ($p = 0.082$) than nonsarcopenic patients. The SSA score including sarcopenia (OR = 1.776, $p = 0.024$), sodium (OR = 1.112, $p = 0.003$) and age (OR = 1.032, $p = 0.006$) yielded a concordance statistic (C-statistic) of 0.714 for predicting overall HE. The BSA score including bilirubin (OR = 1.025, $p = 0.014$), sarcopenia (OR = 2.495, $p = 0.025$) and albumin (OR = 1.186, $p < 0.001$) generated a higher C-statistic (0.770, 95% CI 0.689–0.850) than MELD (0.639, 95% CI 0.539–0.739), MELDNa (0.685, 95% CI 0.583–0.787), MELD-sarcopenia (0.681, 95% CI 0.565–0.797) and MELD-L3SMI (0.644, 95% CI 0.538–0.750) for overall LT-free survival. Both scores gave excellent C-statistics at 3-, 6- and 12-month for corresponding outcomes.
Conclusion: Preoperative sarcopenia independently increased incidence of HE and decreased LT-free survival after TIPS. Clinical scores including sarcopenia provided excellent discriminative performances for predicting the risk of post-TIPS HE and LT-free survival.

Abstract #94

Nutritional Therapy Improves Quality of Life in Liver Cirrhosis with Minimal Hepatic Encephalopathy- Randomized Controlled Trial

Sudhir Maharshi[1], **Barjesh Chander Sharma**[2]

[1]Department of Gastroenterology, Sms Medical College and Hospitals, Jaipur, [2]Professor, Department of Gastroenterology, G B Pant Hospital, New Delhi

Introduction: Minimal hepatic encephalopathy (MHE) impairs health related quality of life (HRQOL), predicts development of overt hepatic encephalopathy (HE) and associated with poor prognosis. There are limited data on nutritional therapy for HRQOL in patients with MHE.
Objectives: To assesse the effects of nutritional therapy on cognitive functions and HRQOL in patients of cirrhosis with MHE.
Methodology: A randomized controlled trial conducted in a tertiary care setting on patients of cirrhosis with MHE who were randomized to nutritional therapy (group A: 30–35 kcal/kg/day and 1.0–1.5 g of vegetable protein/kg/day) and no nutritional therapy (group B: diet as patients were taking before) for 6 months. MHE was diagnosed based on psychometry hepatic encephalopathy score (PHES). HRQOL was assessed by sickness impact profile (SIP) questionnaire. Primary endpoints were improvement in HRQOL and improvement or worsening in MHE.
Results and Conclusions: 120 patients were randomized to group-A (n = 60, age 42.1 ± 10.3 year, 48 men) and group-B (n = 60, age

42.4 ± 9.6 year, 47 men). There was no significant difference in baseline characteristics between the two groups. Baseline PHES (− 8.12 ± 1.32 vs − 8.53 ± 1.38; p = 0.08) and SIP score (14.25 ± 5.8 vs 15.44 ± 5.03; p = 0.85) were comparable in both the groups. Improvement in PHES (ΔPHES 3.86 ± 3.58 vs 0.52 ± 4.09; p = 0.001) and HRQOL (Δ SIP 3.24 ± 3.63 vs 0.54 ± 3.58; p = 0.001) were higher in group A compared to group B. Reversal of MHE was also higher in group A (71.1% vs 22.8%; p = 0.001). In conclusion nutritional therapy is associated with improvement in HRQOL and effective in treatment of MHE.

Abstract #200

Levocarnitine for Treatment of Hyperammonemia in Patients with Liver Cirrhosis

Soichiro Mashima[1], Akio Moriya[2], Yoshiaki Iwasaki[3], Masaharu ando[4]

[1]Mitoyo General Hospital, [2]Mitoyo General Hospital, [3]Okayama University, [4]mitoyo General Hospital

Introduction: Hyperammonemia in patients with liver cirrhosis is associated with hepatic encephalopathy. Levocarnitine activates the urea cycle and promotes ammonia metabolism. However, the optimum dosage of levocarnitine in patients with liver cirrhosis has not been well established.
Objectives: To analyze the hyperammonemia alleviating effect of levocarnitine by dosage.
Methodology: We obtained clinical data of 41 patients with liver cirrhosis prescribed with levocarnitine. The initial dosage of levocarnitine was stratified into low-dosage (750–1000 mg/day, 33 cases) and high-dosage (1500–2000 mg/day, 8 cases). According to propensity score, we conducted a 1:2 matching and compared 8 cases in the high-dosage group with 16 cases in the low-dosage group.
Results: In the high-dosage group, the median of serum ammonia levels at the initiation of levocarnitine administration and after 1 week, 1 month, 2 months, 3 months, and 6 months were 134 μg/dl, 80 μg/dl, 59 μg/dl, 60 μg/dl, 111 μg, and 79 μg/dl, respectively. In the low-dosage group, those were 105 μg/dl, 93 μg/dl, 83 μg/dl, 87 μg/dl, 46 μg/dl, and 100 μg/dl, respectively. The alleviation of hyperammonemia to < 70 μg/dl in 6 months after the initiation was achieved in 88% of the high-dosage group, whose proportion tended to be higher than that of 44% of the low-dosage group (P = 0.079).
Conclusion: To alleviate hyperammonemia, administration of levocarnitine 1500–2000 mg/day is possibly more effective than that of 750–1000 mg/day, suggesting high-dosage administration of levocarnitine may fill the body carnitine pool promptly and shorten the time to affect the serum ammonia.

Abstract #253

Difference in Sleep pattern as assessed by Polysomnography in patients with Liver Cirrhosis With and Without Minimal Hepatic Encephalopathy

Jatinder Pal Singh[1], Vinod Puri[1], Sudhir Maharshi[1], Barjesh Chander Sharma[1]

[1]GB Pant Institute of Postgraduate Medical Education and Research

Background: Minimal hepatic encephalopathy (MHE) is the mildest form of hepatic encephalopathy without cognitive impairment, but patients have abnormal neuropsychological and/or neurophysiologic findings. Sleep disturbances have been reported in patients with cirrhosis of liver. In this study we compared Polysomnography (PSG) parameters in patients of liver cirrhosis with and without MHE.
Methods: 100 patients of cirrhosis (50 with MHE and 50 without MHE) enrolled. Assessment of MHE was done by psychometric hepatic encephalopathy score (PHES) and critical flicker frequency (CFF). All patients underwent basic laboratory investigations along with arterial ammonia estimation. Overnight PSG was done in both the groups. Severity of liver disease was assessed by child turcotte pugh score (CTP) and model for end stage liver disease (MELD). Statistical tests used as appropriate.
Results: Basic characters were similar in all 100 patients including Child and MELD score. Mean PHES score in patients with MHE was − 7.64 as compared to − 1.22 in patients without MHE. CFF score was significantly lower (34.8 ± 3.54 vs. 42.4 ± 5.4 Hz) and arterial ammonia was significantly higher (93.74 + 14.83 vs. 60.92 + 18.47) in MHE group as compared to no-MHE group. PSG parameters such as total sleeping time (231.5 ± 72.6 vs. 294.6 ± 76.3 min), sleep efficiency (59.5 ± 1.6 vs. 73.7 ± 1.28%) and REM sleep (13.4 vs. 22.5%) were significantly lower whereas sleep latency (47.9 ± 27.2 vs. 35.1 ± 11.8 min) was significantly higher in patients with MHE.
Conclusions: MHE impairs quality and quantity of sleep and disturbs sleep pattern in patients with cirrhosis.

Table 1. Baseline characters of both the groups

Parameters	MHE (n=50)	No-MHE (N=50)	p value
Age(years) Mean ± SD	45.3 ± 11.2	46.3 ± 10.4	0.69
Sex Male %	90	88	0.79
CTP score (Mean±SD)	7.96 + 1.25	7.38 + 1.18	0.08
MELD (Mean±SD)	12.31 + 4.49	11.52 + 4.05	0.36
Hb (gm%)	9.36 + 1.58	10.18 + 1.86	0.06
INR	1.58 + 0.51	1.43 + 0.44	0.12
Bilirubin	2.55 + 2.46	2.13 + 1.17	0.28
Total Protein	6.62 + 0.91	6.92 + 0.64	0.06
Albumin	3.10 + 0.43	3.17 + 0.50	0.50
Creatinine (mg%)	0.92 + 0.18	0.94 + 0.12	0.405
Serum sodium (meq/lit)	130.42 + 6.07	131.88 + 7.34	0.28
Serum potassium (meq/lit)	4.15 + 0.51	4.06 + 0.46	0.39
Ammonia μmol/L (Mean ±SD)	93.74 + 14.83	60.92 + 18.47	0.001

MHE- Minimal Hepatic encephalopathy, CTP Child Pugh Turcotte, MELD -Model of End stage Liver Disease, INR- International Normalised Ratio

Table 2: Sleep parameters in both the groups as recorded by PSG

Sleep parameters	MHE (n=50) (Mean ± SD)	No-MHE (n=50) (Mean ± SD)	P value
Total Recording time(TRT) min	391.78 + 65.94	398.86 + 70.28	0.605
Total Sleeping time(TST) min	231.52 + 72.61	294.62 + 76.28	0.001
Sleep Efficiency (TST/TRT) %	59.49 + 1.65	73.70 + 1.28	0.001
Sleep latency (min)	47.94 + 27.21	35.06 + 11.80	0.003
Awake Time (Min)	160.26 + 73.70	104.24 + 55.79	0.001
LatencyREM (min)	71.06 + 27.99	57.90 + 12.59	0.003
N1	10.26 + 6.76	14.28 + 8.74	0.12
N2	40.88 + 13.99	34.8 + 12.21	0.23
N3	35.46 + 16.51	28.44 + 12.99	0.20
REM	13.40 + 3.09	22.48 + 8.81	0.001
Periodic limb movement index (Periodic limb movements/ hour)	19.8 + 10.11	10.04 + 5.46	0.001
Arousals/ hour	5.84 + 2.66	2.29 + 1.09	0.001
Mean SPo_2	93.62 + 3.85	93.8 + 3.23	0.801

MHE- Minimal Hepatic encephalopathy, N - Non rapid eye movement sleep, REM -Rapid eye Movement

Abstract #260

Optimal selection of sedative drug during gastroduodenoscopy in cirrhotic patients to avoid minimal encephalopathy

Young Seok Kim[1], Jeong-Ju Yoo[1], Sang Gyune Kim[1]

[1]Soonchunhyang University School of Medicine

Background: The indiscriminate use of sedative drug during endoscopy can pose a risk of minimal hepatic encephalopathy (MHE) in cirrhotic patients. However, it has not been studied yet which drugs are safest. The aim of this study is to evaluate which one among midazolam, propofol, or combination therapy, was the least likely to cause MHE by using Stroop test.
Methods: This randomized prospective study included consecutive 60 patients who underwent upper GI endoscopy at tertiary hospitals in Korea. Patients were randomly assigned to one of three groups, midazolam, propofol, or combination group, and underwent Stroop test before endoscopy, and 2 h after the completion of endoscopy.
Results: Fifteen patients (46.9%) were Child–Pugh class A, and 17 (53.1%) were Child–Pugh class B or C. Alcohol was the most common etiology (21, 65.6%). Patients did not show significant changes in Ontime, offtime on Stroop test before and after drug administration, and there was no significant difference between the three treatment groups. Also, there was no significant vital sign changes after drug use in all groups. However, with respect to subjective indicators, the satisfaction scores of patient and nursing staff was higher in the combined group than in the other two groups, and time to recovery was shorter in propofol than other groups.
Conclusion: In patients with cirrhosis, sedative endoscopy using midazolam, propofol, or combination therapy is relatively safe, and was not associated with increased risk of MHE.

Abstract #426

Rifaximin treatment for cirrhosis with hepatic encephalopathy

Shuichi Tange[1], Hideo Yoshida[1], Hiroyoshi Taniguchi[1], Koshiro Fukuda[1], Rintaro Fukuda[1], Rintaro Fukuda[1], Tatsuya Matsuno[1], Kensaku Noguchi[1], Hirobumi Suzuki[1], Shinzo Yamamoto[1], Yukiko Ito[1], Akiko Saito[1], Ryo Nakata[1]

[1]Japanese Red Cross Medical Center

Introduction and Objectives: In September 2016, rifaximin, minimally absorbed antibiotic, was approved for the treatment of hepatic encephalopathy in Japan. The aim of this study is to evaluate the safety and the efficacy of rifaximin for cirrhotic patients.
Methods: Patients to whom rifaximin was administered between May 2017 and September 2018 was enrolled. Rifaximin was orally administered 1200 mg daily. We evaluated the improvement of hepatic encephalopathy. The change of serum NH3 concentration at pre-treatment, 2, 4, and 12 weeks after administration was reviewed.
Results: Rifaximin was administered for 19 patients. Eight were male and eleven were female. Median age was 74 years (range 43–85). Eight patients had alcoholic liver disease, 4 had HCV, 1 had HBV, and 6 had other liver disease (AIH, metastatic liver tumor, cryptogenic). One patient was Child A, 8 were Child B, and 6 were Child C. Among nine patients who were prescribed due to encephalopathy, six patients were improved, 2 showed no change, and 1 was unknown. Serum NH3 level was 180 ± 71/166 ± 101/157 ± 91/154 ± 51 at pre-treatment/2/4/12 weeks after prescription. Five out of 15 patients who received rifaximin for more than 2 weeks died during follow-up period. Mean survival time was 46 days (range 16–495 days). Rifaximin was terminated in four patients because of adverse effect. The complication were general malaise, dizziness, oral ulcer, and indefinite complaints.
Conclusions: Rifaximin was administered safely for the treatment of cirrhotic patients. In many cases, hepatic encephalopathy was improved by rifaximin.

Abstract #456

Validation of Korean stroop test in the screening of minimal hepatic encephalopathy

Eileen L. Yoon[1], Dae Won Jun[2], Jae Yoon Jeong[3], Tae Yeob Kim[4], Do Seon Song[5], Sang Bong Ahn[6], Hee Yeon Kim[7], Young Kul Jung[8], Myeong Jun Song[9], Sung Eun Kim[10], Hyoung Su Kim[11], Soung Won Jeong[12], Sang Gyune Kim[13], Tae Hee Lee[14], Yong Kyun Cho[15]

[1]Sanggye Paik Hospital, Inje University, [2]Hanyang University Hospital, Hanyang University College of Medicine, [3]Hanyang University Guri Hospital, Hanyang University College of Medicine, [4]Leeheart Medical Clinic, [5]St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, [6]Nowon Eulji Medical Center, Eulji University College of Medicine, [7]Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, [8]Korea University Medical Center, [9]Daejeon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, [10]Hallym

University Sacred Heart Hospital, Hallym University College of Medicine, [11]Kangdong Sacred Heart Hospital, Hallym University College of Medicine, [12]College of Medicine, Soonchunhyang University, [13]Soonchunhyang University College of Medicine, Soonchunhyang University Bucheon Hospital, [14]Konyang University College of Medicine, [15]Sunkyunkwan University School of Medicine

Background/Aims: Minimal hepatic encephalopathy (mHE) has poor prognosis but hardly drawn attention when patients have no symptoms. We aimed to validate Korean stroop test in the screening of mHE

Methods: Chronic hepatitis B related liver cirrhosis (LC) patients without history of overt hepatic encephalopathy were recruited prospectively from 13 centers for 2 years. All participants completed Portosystemic encephalopathy syndrome test (PHES) and Korean stroop test. Korean stroop test is consisted of 2 on-states (color, word) and 2 off-states (inhibition, switching). Correct response rates and response times were measured. Four types of "OnTime + offTime" have been analyzed (color + inhibition, color + switching, word + inhibition, and word + switching). mHE was diagnosed when PHES scores less than − 4. Healthy controls (HC) were also recruited (n = 376).

Results: Among 223 LC patients, 67.3% was male. Mean age was 53 years. Prevalence of mHE was 20.6%. Response times for each states showed negative correlation with PHES scores ($p < 0.001$). Also color + inhibition, color + switching, word + inhibition, and word + switching showed negative correlation with PHES scores, − 0.361, − 0.310, − 0.442, and − 0.336, respectively (all $p < 0.001$). The highest AUC in the discrimination of mHE among various "OnTime + offTime" was word + inhibition (AUC 0.75, 95% C.I. 0.67–0.84, $p < 0.001$). Mean values of word + inhibition were significantly different among the three groups, which were 54.6 ± 13.2 s, 63.4 ± 18.2 s, and 83.4 ± 27.8 s in HC, LC without mHE, and LC with mHE, respectively (all $p < 0.001$). Among various factors, time for word + inhibition was the only significant factor (OR 1.04, 95% C.I. 1.02–1.06, $p < 0.001$) in multivariate analysis for diagnosis of mHE.

Conclusions: Korean stroop test is simple and valid method for screening of mHE.

Abstract #481

Proposal and Assessment of Diagnostic Accuracy of a New Scoring System (NSS) for Hepatic Encephalopathy (HE) for Predicting 30-day Mortality

Jose Mathew[1], Krishnadas Devadas[1], Sandesh K.[1], Manoj Yadav[1], Neeraj V.[1], Nibin Nahas[1], Simna L.[1], Jijo Jairus[1], Atul Hareendran[1], Tharun Tom[1]

[1]Government Medical College Thiruvananthapuram

Background: West Haven Criteria (WHC), Glasgow Coma Scale (GCS) and HESA (Hepatic Encephalopathy Scoring Algorithm) are used to assess HE.

Objectives: Primary objective: Propose and assess the diagnostic accuracy of NSS for HE for predicting 30-day mortality. Secondary objectives: Compare the NSS with WHC and to study whether the change that occur in NSS at 12-h after admission is a good predictor of 30-day mortality.

Method: NSS was developed by incorporating parameters of WH, GCS and HESA with lower inter-observer variability and higher reproducibility and by arranging them in the ascending order of neurocognitive impairment. To differentiate lower grades of HE from patients without HE, DACT (digit span test, altered sleep rhythm, calculations, and Tremor) was taken, as they were statistically different between Grade 1 and Garde 0. The total list of parameters was grouped into 4. Eye opening-verbal response-motor response-DACT (Digit Span, Altered sleep, Calculations, Tremor) Figure 1. 640 patients admitted with cirrhosis and its complications were evaluated with WHC. 425 patients had HE by WHC − 33.9, 27.8, 22.4 and 16% had GradeI, II, III and IV (WHC) respectively. NSS was applied to that 425 patients. Total score = E+V + M + D. Change in total score at 12-h was also found.

Results: Change in Grade in WHC Vs Change in score in NSS at 12 h-11.8% Vs 70.1%. Diagnostic accuracy—Figure: 2. Change-in-score based on 30-day mortality—Figure: 2

Conclusion: NSS had a better diagnostic accuracy compared with WHC. It represented the subtle changes in neurocognitive changes. The change in NSS score at 12-h in NSS was useful in predicting 30-day mortality.

Abstract #804

Validity, Reliability and Diagnostic Value of Encephalapp Stroop Test in Diagnosing Covert Hepatic Encephalopathy

Stefanus Satrio Ranty[1], andri Sanityoso Sulaiman[2], Juferdy Kurniawan[3]

[1]Department of Internal Medicine - Fakultas Kedokteran Universitas Indonesia - Rumah Sakit Cipto Mangunkusumo, [2]Division of Hepatobiliary - Department of Internal Medicine - Fakultas Kedokteran Universitas Indonesia - Rumah Sakit Cipto Mangunkusumo, [3]Division of Hepatobiliary - Department of Internal Medicine - Fakultas Kedokteran Universitas Indonesia - Rumah Sakit Cipto Mangunkusumo

Background: Covert hepatic encephalopathy (CHE) is the lightest HE spectrum difficult to detect, associated with significant decrease in quality of life. No gold standard to detect CEH. EncephalApp Stroop Test as a newer diagnostic tool is easier, faster and its availability in various health institutions is expected to be applied in Indonesia for CEH detection.

Objective: To validate and test the reliability and diagnostic ability of EncephalApp Stroop Test to diagnose CHE, compared to the Psychometric Hepatic Encephalopathy Score (PHES) and Critical Flicker Frequency (CFF).

Methods: This study is a cross-sectional test, targeted at patient with liver cirrhosis in Jakarta, to obtain area under the curve (AUC), cut-off point, likelihood ratio, positive predictive value (NPV), positive likelihood ratio (LK+), sensitivity and specificity of the Indonesian version of EncephalApp Stroop Test, compared to PHES and CFF. Validity and reliability tests were first carried out. All patients first underwent a Mini Mental State Examination to rule out the possibility of overt EH or other cognitive impairments and Ishihara Test to rule out color blindness.

Results: Thirty subjects participated in validity and reliability tests, and eighty in diagnostic tests. The application showed excellent internal consistency (Chronbach's alpha 0.942 test) and correlation coefficient 0.78. OnTime + offTime was the best parameter (AUC: 0.897; (95% CI: 82.9%–96.5%); sensitivity 88.6%; specificity 80%; PPV: 0.77; NPV: 0.9; LK+: 4.4; LK−: 1.4; and cut-off point ≥ 188.8 s).

Conclusion: The EncephalApp Stroop Test is valid and reliable, and proven to be a good diagnostic modalities in diagnosing CHE.

Abstract #806

The Efficacy of Rifaximin Plus Lactulose versus Lactulose Alone in the Treatment of Hepatic Encephalopathy Among Patients with Decompensated Chronic Liver Disease: A Meta-Analysis

Karlo Pan Fidel[1], Diana Alcantara Payawal[2]

[1]Cardinal Santos Medical Center, [2]Cardinal Santos Medical Center

Introduction: Hepatic encephalopathy (HE) is associated with high mortality. Clinical trials have shown that Rifaximin is as effective as lactulose in management of HE. Recently, multiple studies have been done comparing Rifaximin plus lactulose versus lactulose alone for the treatment of HE, however they have conflicting findings. These conflicting results together with limited literature available on this subject encouraged us to conduct this study.
Objective: Determine the efficacy of Rifaximin plus Lactulose as compared to Lactulose alone in the reversal of hepatic encephalopathy and in decreasing mortality among patients with decompensated chronic liver disease.
Methodology: We performed electronic searches of articles from PUBMED and Cochrane. The primary endpoint were reversal of HE and decrease in overall mortality. Meta-analysis was performed and results were presented as odds ratios (OR) with 95% confidence intervals (CI). Analyses were performed to evaluate the risk of publication bias and heterogeneity.
Results: We included 6 RCTs with 893 patients. Overall, there was a significant difference between Rifaximin plus lactulose and lactulose alone in terms of reversal of HE (OR: 3.07; 95% CI: 2.28–4.14) and reducing mortality (OR: 0.36; 95% CI: 0.24–0.54). We excluded one RCT because it was observed to be an outlier to both endpoints.
Conclusion: Rifaximin plus lactulose is more effective than lactulose alone in both the reversal of HE and the reduction of mortality in patients with decompensated chronic liver disease.

Abstract #819

L-Carnitine suppresses loss of skeletal muscle mass in patients with liver cirrhosis

Masatsugu Ohara[1], Goki Suda[1], Taku Shigesawa[1], Kazuharu Suzuki[1], Akihisa Nakamura[1], Naoki Kawagishi[1], Masato Nakai[1], Takuya Sho[1], Kenichi Morikawa[1], Koji Ogawa[1], Naoya Sakamoto[1]

[1]Department of Gastroenterology and Hepatology, Hokkaido University Graduate School of Medicine

Introduction: Novel therapeutic options for sarcopenia in patients with liver cirrhosis (LC) are urgently required. It remains unclear whether carnitine supplementation affects sarcopenia and loss of skeletal muscle mass in patients with LC. Therefore, in this retrospective, propensity-matched study, we aimed to investigate the effects of carnitine supplementation on the loss of skeletal muscle mass in patients with LC.
Methods: In this retrospective study, 158 patients with LC were screened. Of those, 35 patients who were treated with L-carnitine for more than 6 months and for whom skeletal muscle mass changes could be evaluated by computer tomography were enrolled. Of those 158 patients, 79 patients who did not receive L-carnitine supplementation, served as controls. Cases and controls were matched for age, sex, presence of hepatocellular carcinoma (HCC), and branched chain amino acid (BCAA) administration using propensity score matching.
Results: 35 patients who received L-carnitine supplementation and 35 propensity score-matched patients who did not receive carnitine supplementation were enrolled. Compared with control patients, patients who received L-carnitine had significantly worse liver function. However, loss of skeletal muscle mass was significantly suppressed in patients receiving L-carnitine, and a significant effect was observed in patient subgroups stratified by age, sex, presence of HCC, and BCAA administration. Ammonia levels were significantly less in those receiving L-carnitine. However, even in L-carnitine patients without ammonia decrease, loss of skeletal muscle was significantly suppressed.
Conclusion: L-Carnitine suppresses loss of skeletal muscle mass, so L-carnitine may be novel therapeutic option for sarcopenia in patients with LC.

Abstract #854

Large Spontaneous Portovenous-Hepatic Shunt Complicated by Hepatic Encephalopathy in a Non- cirrhotic Adult Treated with Direct Closure: A Case Report

Fatimin Leila B. Sawadjaan[1], Edhel Tripon[1], Ryan De Gracia[1]

[1]The Medical City

Introduction: Intrahepatic shunts are rare malformations of the vessels supplying the liver. They are usually congenital and seen in young males. The disproportionate shunting of the blood from the portal vein can lead to development of hepatic encephalopathy (HE). Non-traumatic spontaneous development of these shunts in an adult are rare and the etiopathogenesis has not been known. Previous case reports were treated with interventional radiologic occlusion or liver resection.
Case: We report the case of a 56 year-old woman who presented with new onset HE with a non- cirrhotic liver and no known liver disease. CT showed a dilated and tortuous right main portal vein showing communication with a dilated middle hepatic vein measuring 1.7 cm in caliber consistent with a portosystemic shunt. Due to the size of the shunt, endovascular embolization was not viable. Patient underwent hepatotomy with dissection and closure of the portovenous-hepatic vein shunt. A doppler ultrasound done 2 months postoperatively showed reduction in the size of the main portal vein with normal velocity and good flow to the liver.
Conclusion: Spontaneous intrahepatic shunts should be considered in the diagnosis of new onset hepatic encephalopathy in an adult with no identifiable liver etiology. Symptomatic large caliber spontaneous intrahepatic shunts may be successfully treated with modest dissection and closure.

Abstract #995

Polyethylene Glycol versus Lactulose for the Treatment of Overt Hepatic Encephalopathy: A Meta-Analysis

Enrik John Torres Aguila[1], Carlos Paolo Dimatatac Francisco[1], Ian Homer Yee Cua[1]

[1]St. Luke's Medical Center Global City

Introduction: Hepatic encephalopathy (HE) is one of the most common causes of hospitalization in patients with cirrhosis. It poses an increasingly recognized burden on the health care system and the patient's quality of life. Lactulose has been the standard pharmacologic treatment for overt HE for a long time. Recently, polyethylene

glycol (PEG) electrolyte solution has been studied as an alternative but only a limited research has shown positive effects.
Methodology: A comprehensive literature search from the PubMed Central, Embase, Cochrane Library, and Ovid was performed with the following search terms: polyethylene glycol, lactulose, and hepatic encephalopathy. Two studies were selected and validation was done using the Jadad scale. Trial results were combined under a fixed-effects model. The Cochrane Review Manager Software version 5.0 was used for all analyses. The primary outcome of study was improvement of HE scoring algorithm (HESA).
Results: Two trials comprising of 148 patients met the inclusion criteria. In the fixed-effect model, it showed statistically significant increase in the rates of improvement in the HESA ($p < 0.0001$) among patients given PEG compared to those given lactulose (93.15% vs. 65.33%; RR 1.42, 95% CI: 1.19–1.69). The two trials showed moderate heterogeneity (I2 = 47%). This can be due to differences in the population of the 2 studies specifically their Child–Turcotte–Pugh scores.
Conclusion: PEG is an effective treatment for rapid resolution of HE. It significantly increased the rate of improvement in the HESA suggesting it may be a good alternative to the standard lactulose therapy given its rapid action.

Abstract #1051

Validating the asterixis score

Piyush Kumar Thakur[1]

[1]Dept of Gastroenterology, IMS, Bhu

Introduction: Asterixis has been included in West Haven grading system. However, number of flaps doesnt change the grade of hepatic encephalopathy (HE). Asterixis has been graded according to number of flaps as Rare, Occasional, Frequent and Continuous. However, this has not been validated in any study.
Objective: To correlate the number of flaps in asterixis with CTP and MELD scoring systems and with risk of hospitalisation.
Methodology: CTP, MELD score and number of flaps at admission were evaluated in 63 patients with HE admitted in the wards. These patients were subsequently followed for a period of 12 months. Pearson correlation coefficient and Chi square tests were used.
Results: There was a weak correlation between number of flaps and CTP and MELD scores ($R = -0.1092$ and -0.1132). However, number of flaps were significantly associated with the risk of subsequent hospital admissions.
Conclusion: Apart from CTP and MELD score, patients should be assessed with the number of flaps, if feasible, as it is associated with future risk of hospitalisation.

Abstract #1076

Frequency of Minimal Hepatic Encephalopathy In Cirrhotic Patients With Normal Neurological Examination

Talal Khurshid Bhatthi[1]

[1]PIMS

Introduction: Hepatic encephalopathy is a chronic neuropsychiatric syndrome which is secondary to cirrhosis of liver and carries prognostic implications.
Objectives: To detect the frequency of minimal hepatic encephalopathy in patients with cirrhosis who have normal neurological examination presenting in tertiary care setting.
Study Design: Cross-sectional survey.
Methods: A total of 150 cases were included in this study. Bispectral index of the patients was calculated by the researcher by applying bispectral index monitor pad on the forehead and graded from 0 to 100.
Results: 22 patients (14.7%) were 20–40 years old, 98 patients (65.3%) were 41–60 years of age while 30 patients (20.0%) were between 61 and 70 years of age, mean age of the patients was observed 51.25 ± 11.32. out of 150 patients, 90 patients (60.0%) were male and remaining 60 patients (40.0%) were female, minimal hepatic encephalopathy was noted in 91 patients (60.7%).

N03 - Infections and acute-on-chronic liver failure

Abstract #147

Prognostic Value of Urinary Neutrophil Gelatinase-Associated Lipocalin For Diagnosis of Spontaneous Bacterial Peritonitis

Tamer Refaat Fouad[1], Eman M. Abdelsameea[1], Maha A. Elsabaawy[1], M. Ashraf M. Eljaky[1], Soha Zaki El-Shenawy[1], Nabil M. Omar[1]

[1]National Liver Institute - Menofia University

Background: Cirrhotic patients with ascites are at high risk to develop spontaneous bacterial peritonitis (SBP) which increases morbidity and mortality. Neutrophil gelatinase- associated lipocalin (NGAL) is known to be elevated with bacterial infection and its urinary level could be a promising biomarker for SBP diagnosis. Objective: To test urinary NGAL as a marker for SBP diagnosis.
Methodology: Urinary NGAL level was compared between two matched groups of Egyptian cirrhotic patients with ascites, mostly secondary to hepatitis C infection (98%). Group 1 with SBP (n = 41) and group 2 without SBP (n = 45), after exclusion of acute kidney injury and other common infections like urinary, chest, skin and gastrointestinal infections.
Results: By univariate analysis urinary-NGAL, high total bilirubin, serum creatinine, international normalized ratio, ascetic neutrophil count (ANC) and Model of End-Stage Liver Disease, beside low platelet count, all were significantly correlated with the presence of SBP. By multivariate analysis only ANC and urinary-NGAL, could independently predict SBP development. Urinary-NGAL at a cut-off value of 1225 pg/mL showed a sensitivity of 95% and specificity of 76% in prediction of SBP.
Conclusion: Urinary-NGAL independently predicts SBP, if acute kidney injury and other infections were excluded. SBP could be suspected if its level is above 1225 pg/mL. Further work is needed to test if it could be used as a non-invasive bedside screening test at the outpatient clinic for suspected SBP or as a part of routine examination for asymptomatic patients with cirrhotic ascites.

Abstract #165

Vitamin D as a predictor of severity in patients with cirrhosis of liver

Zubin Pradeep Sharma[1], Ravindra Sharma[1], Divya Sharma[1]

[1]Department of Gastroenterology, Aditya Gastro Centre

Introduction: In patients with chronic liver diseases, the prevelance of vitamin D deficiency is much higher and is practically universal. Its deficiency is associated with raised mortality, bacterial infections

portal hypertension complications and fibrosis severity. This study was conducted to assess the relationship of vitamin D deficiency to the severity in patients with liver cirrhosis as evident by CTP and MELD scores.
Methods: Our Study included 60 patients with chronic liver disease of various etiologies, vitamin D levels measured in all patients.
Results: Vitamin D deficiency was observed in all 60 patients, insufficiency (10–30) in 39 patients, deficiency (< 10) in 21 patients. 4 patients with CTP class A had insufficiency, 15 patients with CTP class B had insufficiency, 41 patients in CTP had severe deficiency respectively. 15 patients.
Conclusion: This study was conducted to study the relation of Vitamin D deficiency to the severity in patients with liver cirrhosis as evidenced by CTP and MELD scores. Vitamin D deficiency was severe in cirrhotic patients in Child–Pugh class-C and MELD score more than 25.

Abstract #166

Bacteraemia in SBP as a Predictor of Prognosis

Zubin Pradeep Sharma[1], Ravindra Sharma[2]

[1]Department of Gastroenterology, Aditya Gastro Centre, [2]Aditya Gastro Centre

Aim: Prevalence of spontaneous bacterial peritonitis (SBP) in hospitalized decompensated cirrhotic patients is 20–30%. Blood culture is resultant of bacteraemia. Morbidity and mortality with SBP is very high. Our aim is to study the survival of bacteraemia patients with SBP.
Methods: Admitted cirrhotic patients in our hospital who underwent paracentesis were included in the study. Patients with neutrocytic ascites (PMN > 250 cells/mm^3), blood culture was sent before initiating antibiotics. Two groups were compared for analysis as culture positive and culture negative. The demography, clinic al profile and laboratory parameters including survival was studied for 90 days.
Results: 106 patients had SBP. Blood culture was positive in 28 patients. There was no age, gender and etiological difference between two groups. Significant predictors of bacteraemia was raised creatinine, CTP Class C, MELD > 15 and cirrhosis related complications ($p < 0.05$). 75% bacteraemia patients expired as compared to 31%.
Conclusions: Blood culture positive is associated with high rates of mortality and it is a poor prognostic factor in patients with SBP.

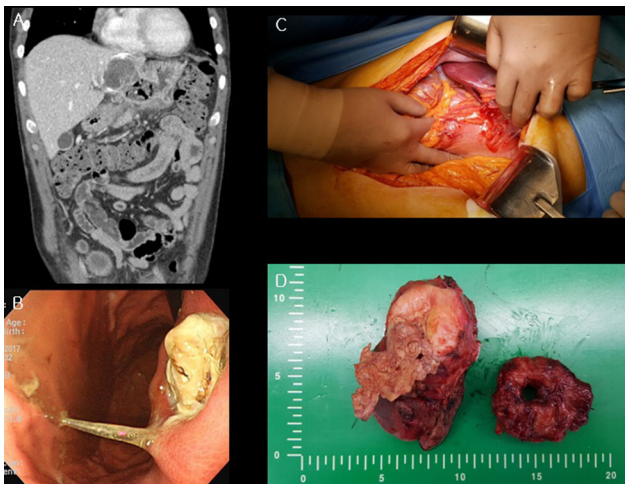
Abstract #266

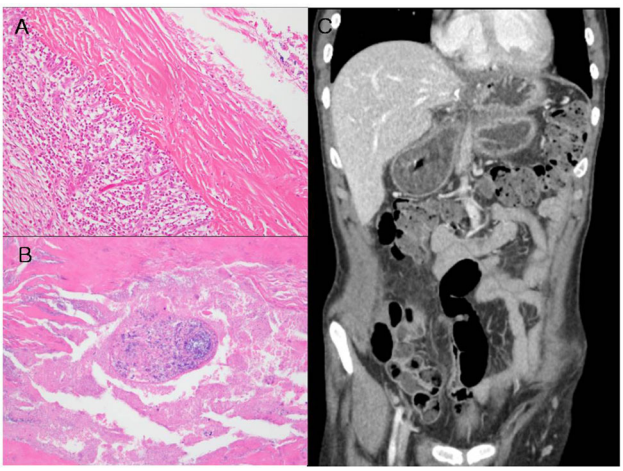
An Unusual Case of Hepatic Hydatid Cysts Complicated with Phlegmonous Gastritis

Chung Hwan Jun[1], Sung Bum Cho[1], Sung Kyu Choi[1]

[1]Chonnam National University Hospital

Echinococcosis is a well-known disease caused by infection with the tapeworm Echinococcus. However, South Korea is not an endemic area, and this disease has been rarely reported. The liver is the most commonly involved organ, and the cysts are mostly asymptomatic; however, fatal secondary bacterial infections or rupture can occur. We report a rare case of a hepatic echinococcal cyst complicated with phlegmonous gastritis. A 49-year-old Uzbekistan man presented with a fever and epigastric pain. Computed tomography of the abdomen showed a calcified mass in the epigastric area and an abscess in the gastric wall communicating with the gastric lumen. Two calcified masses were also observed in the pelvis. Endoscopy revealed a huge gastric ulcer with pus leaking from the base. A culture sample obtained using endoscopic ultrasonography-guided fine needle aspiration of the abscess was positive for *Streptococcus constellatus* and *Prevotella heparinolytica*. Enzyme-linked immunosorbent assay results for echinococcus were positive. The patient was treated with parenteral antibiotics and albendazole. Surgical removal of the mass and gastric wedge resection were performed. Deoxyribonucleic acid sequencing from the tissue revealed Echinococcus granulosus. After 6 months, he is alive with no recurrence.





Abstract #423

Influence of previous acute decompensation and organ failure on the long-term prognosis in cirrhotic patients with decompensation

Do Seon Song[1], Tae Yeob Kim[2], Eileen L. Yoon[3], Jin Mo Yang[1], Hee Yeon Kim[1], Chang Wook Kim[1], Young Kul Jung[4], Hyung

Joon Yim[4], Soung Won Jeong[5], Sang Gyune Kim[5], Jae Young Jang[5], Moon Young Kim[6], Dong Hyun Sinn[7], Ki Tae Suk[8], Dong Joon Kim[8]

[1]Department of Internal Medicine, The Catholic University of Korea, [2]Department of Internal Medicine, Leeheart Medical Clinic, [3]Department of Internal Medicine, Inje University, [4]Department of Internal Medicine, Korea University, [5]Department of Internal Medicine, Soonchunhyang University, [6]Department of Internal Medicine, Wonju College of Medicine, Yonsei University, [7]Department of Internal Medicine, Samsung Medical Center, [8]Department of Internal Medicine, Hallym University College of Medicine

Background/Aims: To investigate long-term mortality depending on the experience and time of previous acute decompensation (AD) and severity of organ failure (OF) in cirrhotic patients with AD.
Methods: A total of 1252 cirrhotic patients with AD were prospectively followed up. OF was defined according to the chronic liver failure-sequential organ failure assessment (CLIF-SOFA). The severity of OF was divided into high CLIF-SOFA (≥ 7) and low CLIF-SOFA (< 7). We then classified 3 groups according to the experience and time of previous AD as follows: G1, no previous AD; G2, AD one or more years before, G3, AD within a year.
Results: During follow-up duration (14.9 ± 10.6 months), the presence of previous AD negatively affected long-term survival in low CLIF-SOFA (82.6% vs 73.0%, $P < 0.001$) and high CLIF-SOFA (54.6% vs 40.4%, $P = 0.041$). Also, in 1009 patients who survived for more than 3 months following AD (i.e. "long-term survivors"), the presence of previous AD showed similar pattern (low CLIF-SOFA, 85.1% vs 75.1%, $P < 0.001$; high CLIF-SOFA, 80.5% vs 64.0%, $P = 0.004$). In total, G3 patients showed a significantly lower survival rates than G1 and G2 patients, although no significant difference was seen between G1 and G2 patients in low CLIF-SOFA ($P < 0.001$) and high CLIF-SOFA ($P = 0.003$). However, in terms of long-term survivors with high CLIF-SOFA, G2 and G3 patients showed a significantly lower survival rates than G1 (80.5% vs 67.3% and 60.0%, $P = 0.021$ vs $P = 0.004$, respectively).
Conclusions: Long-term prognosis was related to the severity of OF and the time of previous AD. Especially, for long-term survivors, previous AD was associated with high mortality regardless of the point of experience.

Abstract #427

Microbiological Characteristics and Clinical Outcomes of Spontaneous Bacterial Peritonitis in Acute Decompensated Cirrhosis Patients: A Multicenter Retrospective Study

Jing Liu[1], Xin Zheng[1], Hang Yan Gao[2], Bo Xian Wang[3], Ping Zhi Qian[4], Jun Jin Chen[5], Yan Huang[6], Ji Zhong Meng[7], Bo Xiao Lu[8], Hong Guo Deng[9], Feng Liu[10], Hai Li[11]

[1]Department of Infectious Diseases, Institute of Infection and Immunology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, [2]Department of Hepatology, First Hospital of Jilin University, Jilin, China, [3]Center of Integrative Medicine, Beijing Ditan Hospital, Capital Medical University, Beijing, China, [4]Department of Liver Intensive Care Unit, Shanghai Public Health Clinical Centre, Fudan University, Shanghai, China, [5]Hepatology Unit, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, China, [6]Department of Infectious Disease, Hunan Key Laboratory of Viral Hepatitis, Xiangya Hospital, Central South University, Hunan, China, [7]Department of Infectious Disease, Taihe Hospital, Hubei University of Medicine, Hubei, China, [8]Liver Disease Center, First Affiliated Hospital of Xinjiang Medical University, Xinjiang, China, [9]Department of Infectious Diseases, Southwest Hospital, Third Military Medical University, China, [10]Department of Infectious Diseases and Hepatology, Second Hospital of Shandong University, Shandong, China, [11]Department of Gastroenterology, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

Introduction: Objectives: To investigate microbiological characteristics and clinical outcomes in acute decompensated cirrhotic patients with spontaneous bacterial peritonitis (SBP).
Methodology: We retrospectively analyzed 432 acute decompensated cirrhotic patients with SBP from 11 teaching hospitals in China (January 2012–May 2018). Cox-proportional hazard regression analyzed the impact of disease and related variables on 28-day mortality.
Results: Total 455 strains were isolated from ascites culture samples. Gram-negative bacteria (GNB), gram-positive bacteria, and fungi caused 51.2, 44.2, and 1.6% episodes of SBP, respectively. Gram-positive bacteria, the major pathogens in the HBV-related cirrhotic patients with SBP, showed an increase (34.5–54.5%) between 2012 and 2015 and 2016–2018. The episodes were classified as nosocomially-acquired (NA) (41.2%), healthcare-related (HCA) (34.7%), and community-acquired (CA) (24.1%). *Escherichia coli* (51.3%) and *Klebsiella pneumoniae* (32.4%) were the extended-spectrum β-lactamase (ESBL)-producing isolates. The prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) was 38.5%. Ceftazidime, cefepime, aztreonam, and amikacin were recommended for non-multidrug-resistant (MDR) GNB infections, piperacillin/tazobactam and carbapenem for MDR GNB infections in CA SBP and HCA or NA SBP, respectively, and vancomycin or linezolid for gram-positive infections, regardless of drug-resistance status. Mortality curves analysis demonstrated significantly higher mortality on the 7th day for GNB infections than for gram-positive bacterial infections (63.6% vs. 28.6%, $p = 0.012$). Multivariate analysis disclosed urinary tract infections, upper gastrointestinal bleeding, and hepatic encephalopathy as key independent predictors of 28-day mortality.
Conclusion: The microorganism spectrum and independent risk factors were identified in acute decompensated cirrhotic patients with SBP. These results might contribute to optimize therapy and improve clinical outcomes.

Abstract #521

Incidence, predictors and prognosis of liver failure in patients wieh hepatitis E as an acute insult

Yijin Wang[1], Hongyang Liu[1], Jingmin Zhao[1]

[1]The 5th Medical Center, Chinese Pla General Hospital

Introduction: Hepatitis E virus (HEV) infection has been recently recognized as an important insult of acute or acute-on-chronic liver failure (A(C)LF).
Objectives: This study aimed to identify incidence, predictors and outcomes of HEV infection related liver failure (HEV-LF).
Methods: All patients with symptoms of suspected acute viral hepatitis were screened for HEV infection in a tertiary hospital. Patients with hepatitis E who developed or not developed A(C)LF between 2011 and 2017 were recruited to compare their basal clinical features and prognosis.
Results: 737 patients were diagnosed with hepatitis E during the study period, among which 62 (8.41%) developed liver failure with HEV infection as an acute event. At multivariate analysis, ascites, spontaneous peritonitis, intestines injury, lactate dehydrogenase, alpha fetoprotein and carbohydrate antigen 125 were found to be independent predictors of A(C)LF during hospitalization. Of the 62 HEV-LF patients, 40 (64.52%) became recovered/improved, 20 (32.25%) were

failed to treatment and 2 (3.23%) died. Presenting hepatic encephalopathy, higher glucose and higher international normalized ratio were independent predictors of poor prognosis of HEV-LF. In addition, we found cirrhosis is the predominant chronic liver disease (CLD) that associated with development and poor prognosis of A(C)LF, compared to alcoholic liver disease and chronic hepatitis B.
Conclusions: Patients with hepatitis E are at high risk to develop A(C)LF, especially in patients with CLD. Different CLDs impacted the incidence and prognosis of HEV-LF distinctively. The identified variables shall help to identify HEV patients with high risk for developing liver failure and the risk population with poor outcomes.

Abstract #551

Clinical characteristics and 28-day outcomes of first bacterial infections in patients with HBV related acute-on-chronic liver failure

Chen Li[1], Haibin Su[1], Jinhua Hu[1], Xiaoyan Liu[1]

[1]Liver Failure Treatment and Research Center, The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China

Introduction and Objectives: Bacterial infections (BIs) was a trigger of acute-on-chronic liver failure (ACLF) and play pivotal roles in the deterioration of clinical course. Our aims was to investigate the clinical characteristics and 28-day outcomes of first BIs in patients with HBV-ACLF as defined by COSSH (Chinese Group on the Study of Severe Hepatitis B).
Methodology: 159 patients with HBV-ACLF combined with first BIs were selected for a retrospective analysis.
Results: 194 cases BIs were occurred, 71.7% ACLF patients had nosocomial BIs and 18.9% ACLF patients developed multiple site BIs. Pneumonia (49.7%), spontaneous bacterial peritonitis (42.1%), and bacteremia (16.4%) were most prevalent. As the ACLF grade increased, the incidence of pneumonia showed an upward trend ($P = 0.020$). 61 strains of bacteria was cultivated from 50 patients, 83.6% were gram-negative bacteria and 18 strains of bacteria were multi-drug resistance. *Escherichia coli* (44.3%), *Klebsiella pneumoniae* (23.0%) were most common bacteria. As the ACLF grade increased, the 28-day transplant-free survival rates showed an downward trend (ACLF-1, 55.7%; ACLF-2, 29.3%; ACLF-3, 5.4%; $P < 0.001$). Independent predictors of 28-day outcomes of patients were age (HR: 1.023), acute kidney injury (AKI) (HR: 2.691), bacteremia (HR: 1.896), INR (HR: 1.756) and invasive catheter (HR: 2.151). The COSSH-ACLF scores (AUC = 0.810) for 28-day outcomes was superior to MELD scores (AUC = 0.714) and Child–Pugh scores (AUC = 0.703).
Conclusion: For HBV-ACLF combined with first BIs patients, pneumonia was the most common site, and the incidence was ascended with increasing ACLF grade. Age, AKI, bacteremia, INR and invasive catheter were independent predictors of 28-day outcomes. COSSH-ACLF scores showed a good predictive value for 28-day outcomes.

Abstract #626

Cirrhosis patients with severe periodontitis have higher risk of malnutrition and re-admission due to infection

Xianghui Sun[1], Jing Liang[1], Tao Han[1]

[1]Tianjin Third Central Hospital

Objectives: Periodontal disease, a source of subclinical and persistent infection, was reported to be prevalent in patients with cirrhosis, but the clinical characteristics and significance are largely unknown. The aim of this study was to examine the characteristics of periodontal disease and the relationship between severe periodontitis and risk of malnutrition and infection in liver cirrhosis patients.
Methods: A total of 163 cirrhosis patients and 158 health control people were included and underwent oral examinations. Meanwhile, liver function, cirrhosis glasses, personal habits, NRS2002 nutritional risk score and the frequencies of re-admission due to infection within 2 years were recorded in all patients with cirrhosis.
Results: The prevalence of periodontitis and edentulous in cirrhosis patients were 85.3% and 10.4%, which were significantly higher than those in the control group (74.1% and 1.3%, $P < 0.05$). Clinical probing depths (PD) of the gingival pockets and clinical attachment level (CAL) of the gingiva were higher than those in the control group (5.1 mm vs 3.2 mm, $P < 0.01$ and 4.3 mm vs 2.6 mm, $P < 0.01$). Severe periodontitis was more common in cirrhosis patients than in the control group (28.8% vs 7.6%, $P < 0.01$), but not related to Child–Pugh glasses. Severe periodontitis in cirrhosis patients is not correlated to cirrhosis etiology and severity, while those patients with severe periodontitis have higher risk of malnutrition and re-admission due to infection ($P < 0.01$).
Conclusion: Our study suggests a high prevalence and severity of periodontal disease in patients with liver cirrhosis. Cirrhosis patients with severe periodontitis have higher risk of malnutrition and re-admission due to infection.

Abstract #629

Characterization of the Circulating Microbiome in Acute-on-chronic Liver Failure Associated with Hepatitis B

Wei Wu[1], Ruihong Zhao[1], Yu Shi[1], Jifang Sheng[1]

[1]The First Affiliated Hospital of Zhejiang University

Background: Patients with hepatitis B-related acute-on-chronic liver failure (HB-ACLF) may have an increased circulating microbial burden. This study aimed to assess circulating microbial load and composition and to explore the association between the circulating microbiome and both systemic inflammation and clinical outcome in HB-ACLF.
Methods: Plasma from 49 HB-ACLF patients, 15 healthy controls (HCs) and 18 patients with compensated liver cirrhosis (C-LC) was analyzed for chemokines/cytokines and bacterial DNA and further analysed by 16S rDNA pyrosequencing. Linear discriminant analysis effect size (LEfSe) and inferred metagenomics analyses were performed.
Results: The circulating bacterial DNA was significantly increased in HB-ACLF patients compared to that in the control groups. The overall microbial diversity was significantly decreased in HB-ACLF patients. HB-ACLF patients were enriched with Moraxellaceae, Sulfurovum, Comamonas, and Burkholderiaceae but were depleted in Actinobacteria, Deinococcus-Thermus, Alphaproteobacteria, Xanthomonadaceae and Enterobacteriaceae compared to controls. Network analysis revealed a direct positive correlation between Burkholderiaceae and chemokine IP-10 in HB-ACLF patients. The relative abundance of Prevotellaceae independently predicted 28-day mortality. Inferred functional metagenomics predicted an enrichment of bacteria with genes related to methane, alanine, aspartate, glutamate, pyrimidine, purine and energy metabolism.
Conclusions: HB-ACLF patients display increased circulating microbial burden, altered microbiome composition and a shift in microbiome functionality. The dysbiosis in circulating microbiota is associated with systemic inflammation (SI) and clinical outcome in HB-ACLF.

Abstract #668

Utility of STRIATIN as a novel prognostic marker in decompensated cirrhosis

Balasubramaniyan Vairappan[1], Vignesh Venkat[2], Pazhanivel Mohan[3], Palanivel Chinnakali[4]

[1]Department of Biochemistry, Jawaharlal Institute of Postgraduate Medical Education and Research & Dhanvantari Nagar & Pondicherry, [2]Department of Biochemistry, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), [3]Department of Medical Gastroenterology, Jawaharlal Institute of Postgraduate Medical Education and Research, [4]Department of Preventive and Social Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research

Background/Aim: Striatin is a 110 kDa caveolin-1/Ca^{2+}-calmodulin binding protein and could activate endothelial nitric oxide synthase (eNOS); however it's role in liver disease remains obscure. We aimed to investigate the role of striatin and its association with hepatic nitric oxide (NO) bioavailability in the development of end-stage liver disease.
Methods: 40 cirrhotic patients (both compensated and decompensated) and 40 healthy individuals were enrolled in the study. Blood striatin and cGMP levels were measured by ELISA and biochemical parameters by Beckman Coulter autoanalyser. Hepatic tissue striatin and peNOS proteins expression were analysed by Western blotting and immunohistochemistry.
Results: The serum ALT, AST, bilirubin, gamma GT, creatinine and ALP were significantly ($P < 0.0001$) elevated whilst serum albumin concentration was decreased in cirrhotic patients when compared to healthy individuals. The systemic striatin level was significantly decreased in cirrhotic patients compared to normal healthy volunteers [7.54 ± 0.6 vs. 10.9 ± 0.3 ng/ml, respectively; $P < 0.0001$] and was further significantly decreased in decompensated cirrhotic patients when compared to compensated cirrhosis [6.98 ± 0.5 vs. 7.54 ± 0.6 ng/ml, respectively; $P < 0.01$]. Furthermore, hepatic striatin protein expression was significantly decreased in decompensated and compensated cirrhosis in a stepwise manner and was positively correlated with decreased hepatic peNOS protein expression.
Conclusion: Our results suggested that hepatic stritin expression was decreased in cirrhosis and was associated with poor survival times in patients with decompensated cirrhosis and may serve as an independent marker for better outcomes. Thus, our study provides a promising biomarker for the prognostic prediction of end-stage liver disease and a potential therapeutic target for cirrhotic patients.

Abstract #712

Association Between Intra-Abdominal Infection and Portal Vein Thrombosis Manifestations in Liver Cirrhosis

Andree Kurniawan[1], Nata Pratama Hardjo Lugito[2], Ignatius Bima Prasetya[2]

[1]Internal Medicine, Faculty of Medicine, Pelita Harapan University, Karawaci, Tangerang, Banten, Indonesia, [2]Internal Medicine, Faculty of Medicine, Pelita Harapan University

Introduction: Portal vein thrombosis (PVT) is considered to be a common complication of liver cirrhosis especially in Hepatocellular Carcinoma (HCC). However, the understanding of PVT in cirrhosis is incomplete. Previous study found that *C. difficile* infections increases risk for venous thromboembolism in HCC patients. There is limited study evaluating relation between intra-abdominal infection and PVT especially in liver cirrhosis population.
Objective: To know association between intra-abdominal Infection and PVT in liver cirrhosis.
Methods: This was a cohort retrospective study using liver cirrhosis database 2014–2018 in our general hospital. Patients with heart failure, chronic kidney disease, and cancer other than HCC were excluded. Liver cirrhosis was diagnosed at least using abdominal ultrasound. Intra-abdominal infection comprises from complicated which extends into peritoneal space associated with abscess formation and peritonitis to uncomplicated intramural inflammation of the gastrointestinal tract. PVT evaluation were using either Doppler US or abdominal CT scan. Association between them was evaluated using relative risk and confidence interval.
Results: Eighty-two subjects fulfilled criteria for liver cirrhosis. Eleven of 82 (13.4%) intraabdominal infections were noticed. All infections were related to *C. difficile* infection, 3 were related to cholecystitis, and 2 subjects with *Entamoeba histolytica*. Nineteen of 82 (11%) subject were also comorbid with HCC. Seven subjects were developed PVT. Only 3 of 11 intra-abdominal infections related to PVT with relative risk 4.84 confident interval (0.97–7.41).
Conclusions: Intra-abdominal (*C. difficile*) infections did not associate with manifestation of PVT in liver cirrhosis. Further study with bigger sample size was needed to confirm this result.

Abstract #738

Association Between Use of Proton Pump Inhibitor and Spontaneous Bacterial Peritonitis – A Systemic Review and Meta-analysis

Marianne Linley Loo Sy[1], Jose Isagani Belen Janairo[2], Juliet Lingat Gopez-Cervantes[1], Ian Homer Yee Cua[1]

[1]Institute of Digestive and Liver Diseases, St. Luke's Medical Center - Global City, [2]Biology Department, College of Science, De La Salle University

Introduction: The use of proton pump inhibitors (PPI) among patients with ascites has been associated with higher incidence of spontaneous bacterial peritonitis (SBP). Previous studies showed conflicting results. The latest meta-analysis in 2015 has also not establish its association. Recently, larger and better quality studies were done to re-evaluate the causality of PPI use and development of SBP.
Objective: We aim to re-assess the association between PPI use and SBP incidence with larger and better quality data.
Methods: We searched Medline, Embase, Cochrane, and Google scholar for relevant articles published up to November 2018. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using a random-effects model. Sub group analysis were done to decrease heterogeneity.
Results: A total of ten case–control, nine cohort, and two randomized controlled trial studies were analyzed. The over- all analysis indicated that PPI use was associated with SBP (OR = 2.02 [1.51, 2.69]). The association was seen across all study designs: case–control studies (OR = 2.98 [2.07, 4.27]), cohort studies (OR = 1.26 [1.08, 1.48]), and RCT (OR = 2.29 [1.17, 4.47]).
Conclusion: There is increasing and stronger evidence in terms of association of PPI use and SBP. Addition of more cohort studies and randomized control trials has supported this association. However, the quality of evidence is still low to moderate based on the GRADE framework since there are only 2 randomized controlled trials and with the highest association seen among case control studies.

Abstract #778

The occurrence of Systemic inflammatory response syndrome and sepsis in Acute-on chronic liver failure do not have any impact on viscoelastic (Sonoclot) parameters

Sadaf Khan[1], Radhika Kapil[1], Priyanka Jain[2], Ashok Choudhury[3], Chhagan Bihari[1]

[1]Department of Hematology, Institute of Liver and Biliary Sciences, New Delhi, India, [2]Department of Clinical Research, Institute of Liver and Biliary Sciences, New Delhi, India, [3]Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Hemostatic status in ACLF patients with the setting of systemic inflammatory response syndrome (SIRS) and sepsis has not been studied widely by global coagulation methods.
Objective: To assess the coagulation profile by viscoelastic technique in ACLF patients and with the onset of SIRS and sepsis.
Patients and Methods: This study included cirrhosis and ACLF patients (n = 124 each). Sonoclot variables, activated clotting time (ACT), clot rate (CR), and platelet function (PF) were assessed. These parameters were assessed in ACLF patients with and without SIRS and sepsis within one week of admission and their association with day 30 mortality.
Results: ACLF occurred at a younger age than cirrhosis (43.5 ± 11 vs 52.0 ± 10yrs, $p < 0.001$). INR was significantly higher in ACLF ($p < 0.001$) as compared to cirrhosis. ACLF patients had prolonged ACT (211.4 ± 111.6 v/s 176.3 ± 48.3, p = 0.001), decreased CR (29.0 ± 15.4 v/s 31.8 ± 13, p = 0.045), but comparable PF (2.1 ± 1.2 v/s 1.8 ± 1.2, p = 0.145) than cirrhotics. Patients who developed SIRS (n = 20) and without SIRS (n = 43), did not show any difference in ACT (p = 0.712), CR (p = 0.294) and PF (p = 0.796) but PT was raised (p = 0.001). Likewise, who had sepsis (n = 16) and without sepsis (n = 21) had no difference in ACT (p = 0.617), CR (p = 0.294), PF (p = 0.267) and PT (p = 0.077). Also no significant difference was noted between SIRS and sepsis cases. Those who died (n = 41) had higher ACT and INR ($p < 0.001$ each).
Conclusions: Patients with ACLF had a hypocoagulable state as compared to cirrhosis. No significant change in coagulation parameters with development of sepsis and SIRS was noted in ACLF patients.

Abstract #805

Lactate-free AARC ACLF score is the best prognostic marker for patients with alcohol induced ACLF treated with pentoxifylline

Shamshersingh Gajendra Chauhan[1], Alisha Raje Chaubal[1], Kailash M. Kolhe[1], Vikas A. Pandey[1], Meghraj R. Ingle[1], Akash P. Shukla[1]

[1]Department of Gastroenterology, Lokmanya Tilak Municipal General Hospital & Medical College

Introduction: Acute-on-chronic liver failure (ACLF) is a disease with a distinct spectrum of liver injury, with a rapid downhill course Here we describe three new scores – Albumin Bilirubin Index (ALBI), platelet albumin bilirubin index (PALBI) and lactate-free AARC ACLF score (LFAA), in predicting short-term mortality in patients with alcohol-induced ACLF when compared to standard validated scores.
Methods: Consecutive patients diagnosed as alcohol-induced ACLF as per the APASL 2014 definition were included in the study. Standard scores – MELD, MELD-Na, Maddreys' discriminant function, CLIF-OF &CLIF-C ACLF scores, APACHE II, ALBI, PALBI, and LFAA were calculated. The endpoints of the study were to predict short-term mortality in alcohol-induced ACLF patients using ALBI, PALBI and LFAA and finding the cut-offs of these new scores and comparing it with standard validated scores.
Results: 67 patients were studied with 97% being male. Mean age was 45.78 + 8.15 years.44 patients died. The cut-offs, area under the ROC curve; sensitivity and specificity, positive and negative predictive values of the new prognostication scores were, respectively: ALBI (− 0.57; 0.948; 90.9% and 82.6%; 77.69% and 93.15%), LFAA (7; 0.968; 95.5% and 96.7%; 95.075 and 96.99%), PALBI (− 0.28; 0.59; 61.4% and 52.2%; 46.13% and 66.98%). LFAA and ALBI outnumbered the valid prognostic scores in predicting short-term mortality. PALBI underperformed when compared to all other scores.
Conclusion: Thus incorporating albumin and bilirubin in a mathematical equation (for ALBI) or combining it with creatinine and grade of hepatic encephalopathy (for LFAA) would help in prognosticating the patients with ACLF on admission.

Abstract #852

Prognostic performance of AARC Score and CLIF C ACLF Score in a cohort of patients with Acute On Chronic Liver Failure (ACLF)

Jijo Varghese[1], Krishnadas Devadas[2], Biji Benny[3], Neehar Shanavas[1], Atul Hareendran[1], Nibin Nahaz[1], Tharun Tom[1], Rathan Cyriac[1]

[1]Senior Resident Medical Gastroenterology Medical College Trivandrum, [2]Professor and Head of the Department Medical Gastroenterology Medical College Trivandrum, [3]Senior Resident, Medical Gastroenterology Medical College Trivandrum

Introduction: Development of ACLF carries a high mortality. Early prognostication will help in better management and survival.
Objectives: To compare prognostic performance of AARC score, CLIF C ACLF score and other indices
Methodology: Prospective analysis of 30 patients who have ACLF by APASL criteria and followed up for 6 months. AUROC (SPSS version 23) was derived for each prognosis score and compared.
Results: Out of the 30 patients evaluated 28 males (93.33%) and 2 females (6.66%). Commonest precipitating factor was alcoholic hepatitis (53.33%) followed by hepatitis B (40%), hepatitis A (3.33%) and autoimmune Hepatitis (3.33%). Table 1 shows the discriminative statistics of various prognostic indices studied. AUROC of AARC Score, CLIF C SOFA, MELD, MELD Na, ALBI score and UKELD score were 0.991, 0.87, 0.885, 0.83, 0.7, 0.63, respectively for 4 weeks mortality. AUROC of AARC Score, CLIF C SOFA, MELD, MELD Na, ALBI score and UKELD score were 0.98, 0.91, 0.9, 0., 0.75, 0.645, respectively for 24 weeks mortality.
Conclusion: According to our study AARC score (cut off of > 10) was the best predictor of mortality at 4 weeks (AUROC 0.991, sensitivity of 100%, specificity of 88%, PPV 86% and NPV 100%) and 24 weeks (AUROC 0.98, sensitivity of 93%, specificity of 88%, PPV 87% and NPV 93%).

Abstract #896 Scoring System for Predicting The 90-Days Mortality Among Hospitalized Cirrhotic Patients: A Lesson Learnt from National Referral Hospital

Background: Previous study reported the 2-years mortality rate of hospitalized liver cirrhotic patients in Cipto Mangunkusumo National General Hospital was 75.3%. Kaplan–Meier analysis showed the largest increase of mortality rate was during the first 90-days after admission.
Aim: To find the scoring system for predicting of 90-days mortality among hospitalized cirrhotic patients.
Method: Retrospective study design was conducted from patients with liver cirrhosis who hospitalized in Citpo Mangunkusumo Hospital during 2017 period. All hospitalized cirrhotic patients registered with a completely filled medical record were included in this study. The cirrhotic patients who admitted to hospital ward for elective procedure (biopsy, variceal ligation, endoscopy) were excluded.
Results: Of 124 patients, 74.2% of cirrhotic patients were male and 47.6% had Child–Pugh (CP) class C. The most common etiology of hospital admission was variceal hemorrhage (34%), followed by hepatic encephalopathy (22%) and massive ascites (16%). The 90-days mortality rate in cirrhotic patients was 54.8%. In multivariate analysis, age $\geq$ 60 years old, CP score $\geq$ 8 and leukocytosis ($\geq$ 12,000/μL) were significantly associated with 90-days mortality. The scoring system and the mortality risk are shown in Table 1 and Table 2, respectively, with AUC value 0.89.
Conclusion: Age $\geq$ 60 years old, CP score $\geq$ 8 and leukocyte $\geq$ 12,000 μL at the admission can be used as scoring system for predicting 90-days mortality in hospitalized cirrhotic patients.

Abstract #927

Scoring System for Predicting The 90-Days Mortality Among Hospitalized Cirrhotic Patients: A Lesson Learnt from National Referral Hospital

Rino Alvani Gani[1], Irsan Hasan[1], Andri Sanityoso Sulaiman[1], Cosmas Rinaldi A. Lesmana[1], Juferdy Kurniawan[1], Steven Zulkifly[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

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Conclusion: Age $\geq$ 60 years old, CP score $\geq$ 8 and leukocyte $\geq$ 12,000 μL at the admission can be used as scoring system for predicting 90-days mortality in hospitalized cirrhotic patients.

Abstract #953

Histone deacetylase 2 is closely related with mitochondrial apoptosis pathway through regulating acetylated histone H3 in acute liver failure

Yao Wang[1], Zuojiong Gong[1]

[1]Department of Infectious Diseases, Renmin Hospital of Wuhan University, Wuhan, China

The purpose of this study was to investigate the modulation of HDAC2 on mitochondrial apoptosis in ALF. The cellular model was established with LO2 cells stimulated by TNF-α/D-galactosamine (D-gal). Rats were administrated by LPS/D-gal as animal model. The cell and animal model were then treated by HDAC2 inhibitor CAY10683. HDAC2 was regulated up or down by lentiviral vector transfection in LO2 cells. The levels of HDAC2, mitochondrial apoptosis molecules, acetylated histone H3 (AH3) and histone H3 (H3) were assayed. The serum ALT, AST, TBIL, openness degree of MPTP and liver tissue pathology was detected. Compared with cell and rat model group, the mRNA and protein levels of HDAC2, bax, cyt c, apaf1, cleaved-caspase3, cleaved-caspase9, as well as apoptosis rate were decreased, whereas the level of bcl2 was elevated after being treated with CAY10683. In the HDAC2 down- or up-regulated LO2 cells, the mitochondrial apoptosis pathway was inhibited or activated respectively. After treated with LPS for HDAC2 down- or up-regulated LO2 cells, the mitochondrial apoptosis pathway was furtherly suppressed or activated. The MPTP value was elevated in CAY10683-treated groups compared with rat model group. Liver tissue pathological damage and apoptotic index in CAY10683-treated group was significantly reduced. In addition, down-regulated or over-expressed HDAC2 could accordingly increase or decrease AH3 level, and TNF-α/D-gal could enhance the acetylation effect. HDAC2 is closely related with mitochondrial apoptosis pathway through regulating AH3 in ALF. Inhibiting HDAC2 could be a therapeutic agent for treating acute liver failure.

Abstract #981

Prognostic Factors Associated With Morbidity and Short-term Mortality In Patients With First Episode of Spontaneous Bacterial Peritonitis: An Experience of A Single Tertiary Center

Abdel-Naser Elzouki[1], Ibrahim Y. Abubeker[2], Ahmed Salem[2], Aamir Waheed[2], Abdelrahman Al-Zubier[2], Abazar Saeed[2]

[1]Hamad General Hospital, Hamad Medical Corporation & Weill Cornell Medical College, [2]Hamad General Hospital, Hamad Medical Corporation

Objective: To identify the risk factors associated with morbidity and short-term mortality in cirrhotic patients with SBP.
Methodology: In a retrospective study, 333 cirrhotics admitted to Hamad General Hospital-Qatar from 2007 to 2012 were reviewed. All data were analyzed with respect to demographic parameters, clinical and laboratory features and radiological characteristics on day one of admission. Diagnosis of cirrhosis was based on the combination of clinical, laboratory and imaging findings. SBP was diagnosed by

abdominal paracentesis in the presence of polymorph-neutrophil cell $\geq$ 250 cells/mm^3 in the ascetic fluid. Multivariate logistic regression was used to analyze significant variables. The proportional hazards Cox regression model was used to analyze the hazard rates of the predictors adjusted by age and gender.
Results: A total of 63 cirrhotics with SBP were identified. 61 (96.8%) patients were diagnosed with SBP for the first time. The overall 30-day in-hospital mortality rate was 19% (n = 12). Median survival duration for those who died was 8 days. The mortality rate was higher in patients with multiple-antibiotic resistant bacteria than in those with other bacteria. Multivariate Cox proportional regression analysis showed Child–Pugh score (HR = 1.23, 95% CI: 1.05 to 1.82, p = 0.027), MELD-Na score (HR = 1.29, 95% CI: 1.10 to 1.92, p = 0.023), and acute kidney injury (HR = 2.09, 95% CI: 1.41 to 3.47, p = 0.01) were associated with 30-day in-hospital mortality.
Conclusion: SBP has a predictable impact on short-term mortality in patients with cirrhosis and ascites. In addition to the multiple-antibiotic resistance to the bacteria, severities of both hepatic and renal dysfunction were the independent predictors of outcome.

Abstract #988

Intracranial Invasive Mycosis Mimicking Hepatic Encephalopathy in Patient with Cirrhosis: A Case Report

Nipun Verma[1], Akash Roy[1], Chirag Ahuja[2], Sunil Taneja[1], Madhumita Premkumar[1], Ajay Kumar Duseja[1], Virendra Singh[1], Radha Krishna Dhiman[1]

[1]Department of Hepatology Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, [2]Department of Neuroradiology Post Graduate Institute of Medical Education and Research

Background: Invasive mycosis (IM) is often poorly recognized and leads to high mortality in patients with cirrhosis. We describe a case of intracranial IM mimicking hepatic encephalopathy (HE) in a patient with decompensated cirrhosis (DC).
Case Summary: A 45-year-old male with alcohol related DC, abstinent for 6 months, presented with jaundice, altered sensorium, fever and generalized headache for 3 days. At admission, he had a fall that was attributed to generalized seizure, following which he was intubated for airway protection. Examination revealed fever (temperature: 38.1 °C), tachycardia (rate: 119/minute), grade-III HE, bilateral up-going plantars, with normal power, tone and deep tendon reflexes. Investigations showed anemia (hemoglobin: 10.2 g/dl), thrombocytopenia (platelet: 50,000/mm3), leukocytosis (leucocytes: 12,200/mm3), hyperbilirubinemia (total/conjugated bilirubin: 3.3/1.4 mg/dL), elevated aminotransferases (AST/ALT: 172/100 U/L), hypoalbuminemia (albumin: 3.1 mg/dL), sterile blood/urine cultures and cirrhosis with ascites on abdominal ultrasound. He was managed with anti hepatic coma measures, broad-spectrum IV antibiotics, antiepileptics and supportive measures. However, sensorium worsened and patient developed hypotension over next 4 days. Careful examination showed unilateral (right) pro-optosis, chemosis and pupilaryanisocoria. Serum Galactomannan was high (1.7). CE-MRI brain (Figure 1) showed multifocal infarcts (right medial temporal, cerebellar and brainstem), extensive inflammatory changes (right orbit and infratemporal fossa) with right internal carotid thrombosis: characteristic of IM. Patient was started on liposomal amphotericin-B, however he succumbed to the illness on day 7 of admission.
Conclusions: Intracranial IM can mimic HE and is associated with high mortality in patients with cirrhosis. High index of suspicion, positive serological biomarkers and characteristic radiology may provide key to the diagnosis of IM in patients with cirrhosis.

Abstract #1018

Assessment of prognosis based on various prognostic models and predictors of mortality for 91 patients with hepatitis B virus-related acute-on-chronic liver failure

Xueyun Zhang[1], Yue Ying[1], Yuxian Huang[1]

[1]Department of Infectious Diseases, Huashan Hospital, Fudan University

Introduction: Hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF) presents a high short-term mortality which necessitates accurate initial clinical decision making.
Objectives: Nine prognostic models were used to assess prognosis and prognostic indicators which influenced the mortality of HBV-ACLF patients were analyzed.
Methodology: 91 HBV-ACLF patients were retrospectively selected in Huashan Hospital from July 2014 to July 2018. The predictive value of nine prognostic models was assessed by areas under the receiver-operating characteristic curves (AUROCs), and prognostic indicators about mortality of HBV-ACLF patients were selected by logistic regression model.
Results: Within all the 91 patients enrolled, 46 died in 90 follow-up days. Chinese Group on the Study of Severe Hepatitis B-ACLF (COSSH-ACLFs) model presented best predictive value than other models (AUROC of total patients: 28-day mortality was 0.946, 90-day 0.920; AUROC of patients graded by number of organ failures, grade 0–1: 28-day mortality was 0.900, 90-day 0.846; grade 2–3: 28-day mortality was 0.957, 90-day 0.917). Independent predictors of mortality were age, total bilirubin, coagulation failure, hepatic encephalopathy and platelet count. Platelet count showed significant difference between HBV-ACLF patients according to the 90-day survival status ($P < 0.001$), and was negatively associated with COSSH-ACLFs scores. The low-platelet count group ($\leq 63 \times 109$/L) showed lower survival probability compared to high-platelet count group ($> 63 \times 109$/L, 31.0% vs. 67.0%, P = 0.0001).
Conclusion: This study confirmed COSSH-ACLFs predict prognosis of HBV-ACLF patients more accurately than other prognostic models and platelet count was associated with the severity and prognosis of HBV-ACLF patients.

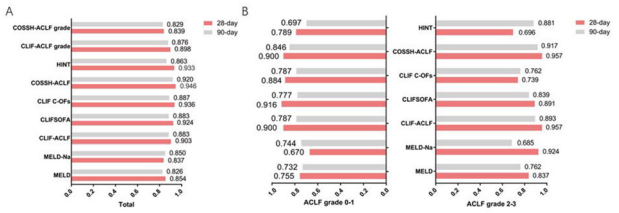


Figure 1 AUROCs of 9 prognostic score to predict the 28-day and 90-day mortality of patients with hepatitis B virus-related acute-on-chronic liver failure in total (A), grade 0-1 and grade 2-3 (B).

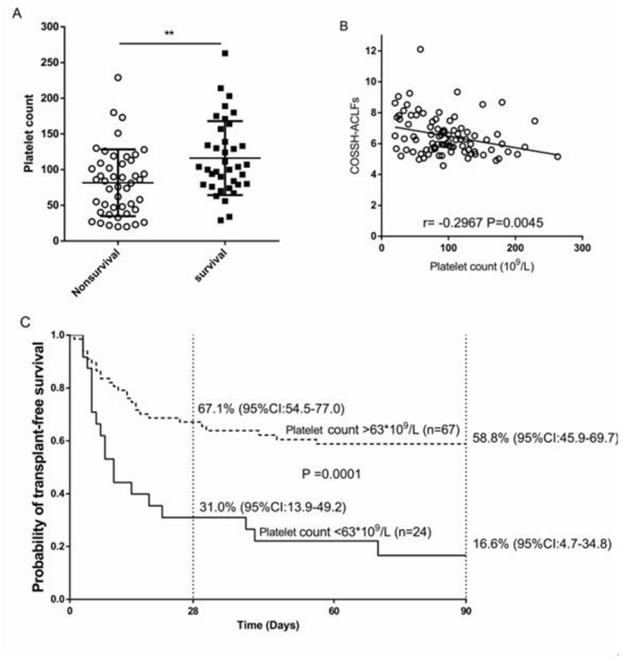


Figure 2 Platelet counts showed significant difference between patients with hepatitis B virus-related acute-on-chronic liver failure according to the 90-day survival status($P < 0.001$) (A).The platelet count level was negatively associated with COSSH-ACLFs (B); The low-platelet count group (≤63×10^9/L) showed lower survival probability compared to high-platelet count group (>63×10^9/L) (P =0.0001) (C)

N04 - Hepatorenal and hepatopulmonary syndromes

Abstract #148

Incidence, predictors and prognosis of renal impairment after upper gastrointestinal bleeding in Egyptian patients with cirrhosis

Tamer Refaat Fouad[1], Wael M. Abdel-Razek[1], Mary A. Naguib[1], Mohamed M. Abbasy[1]

[1]National Liver Institute, Menofia University

Background: Renal impairment is a serious complication of liver cirrhosis.
Objective: To assess the relationship between UGIB and renal impairment.
Methodology: Consecutive UGIB patients with liver cirrhosis were reviewed. Renal impairment defined if serum creatinine > 1.5 mg/dL or ≥ 50% above baseline; patients with baseline renal impairment were excluded (n = 7). Thirty-six clinical and laboratory variables were examined at admission.
Results: Ninety UGIB episodes in 87 patients were included and variceal bleeding was the main cause (81.1%). Mean age 59.5 ± 11.4, 73% males, 26% diabetes, 33.3% had hepatic malignancy and 62.2% had a previous bleeding attack. Renal impairment occurred in 15 (16.6%) patients and was reversible in 9 (60%). Mortality among renal impairment patients was 20% (all had irreversible renal impairment), while it was 6.7% among those without (p = 0.126). Factors associated with the development of renal impairment were low hemoglobin and hematocrit, high creatinine, model for end-stage liver disease (MELD) and MELD-Na beside history of previous bleeding. Low MELD-Na was the only variable associated with the renal improvement. By multivariate analysis, the independent predictors of renal impairment were high MELD (odds ratio: 0.644, 95% confidence interval: 1.296, 1.139–1.475, p < 0.0001); area under the curve (AUC) 0.842 (p < 0.0001) and low baseline hemoglobin (0.644, 0.454–0.912, p = 0.013); AUC 0.732 (p = 0.005). Conclusions: Renal impairment is common after UGIB in Egyptian patients with cirrhosis. It could be predicted with the baseline assessment of severity of bleeding by hemoglobin and liver function by MELD score. Irreversibility of renal function, although less frequent, is associated with higher mortality.

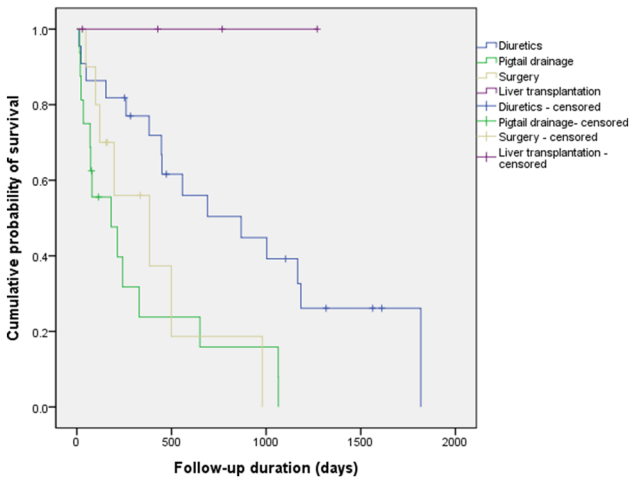
Abstract #276

Various Treatment Modalities in Hepatic Hydrothorax: What is Safe and Effective?

Yoon Jae Hyun[1], Sung Kyu Choi[1], Sung Bum Cho[1], Chung Hwan Jun[1]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Chonnam National University Hospital

Background/aims: Hepatic hydrothorax is a complication of decompensated liver cirrhosis that is difficult and complex to manage. There are limited data concerning which treatment is optimal after liver transplantation. We compared the clinical features and outcomes of patients treated with various modalities, with a particular focus on surgical management.
Methods: From January 2013 to December 2017, 52 patients diagnosed with hepatic hydrothorax were enrolled.
Results: Mean Child–Turcotte–Pugh and Model for End Stage Liver Disease scores were 10.1 and 19, respectively. Patients underwent four modalities: serial thoracentesis (n = 22, 42.3%), pigtail drainage (n = 16, 30.8%), surgery (n = 10, 19.2%), and liver transplantation (n = 4, 7.7%); mortality rate and mean survival duration were 68%/712 days, 88%/265 days, 60%/297 days, and 0%/623 days, respectively. Regarding the management of refractory hepatic hydrothorax, surgery was associated with less frequent needle puncture (23.5 times in the pigtail group vs. 9.3 times in the surgery group), lower occurrence of hepatorenal syndrome (50% vs. 30%), and non-inferior cumulative overall survival (402 days vs. 221 days) compared with the pigtail group. In multivariate analysis for poor survival, Body Mass Index < 19, refractory hepatic hydrothorax not managed with liver transplantation, Child–Turcotte–Pugh score > 10, and history of severe encephalopathy (grade > 2) were associated with poor survival rate.
Conclusions: Liver transplantation is the optimal method for managing refractory hepatic hydrothorax. In patients who are ineligible for liver transplantation, surgery is an option considering that it provides better quality of life and a non-inferior survival duration compared with pigtail drainage.



Abstract #480

Validation of New International Club of Ascites-Acute Kidney Injury (ICA-AKI) criteria in patients with Cirrhosis and evaluation of Delta creatinine

Jose Mathew[1], Krishnadas Devadas[1], Neeraj V.[1], Sandesh K.[1], Manoj Yadav[1], Simna L.[1], Jijo Jairus[1], Nibin Nahas[1]

[1]Government Medical College Thiruvananthapuram

Background: AKI is an important prognostic indicator in cirrhosis. New criteria (NC) was proposed by ICA for patients with Cirrhosis by the modification of KDIGO (Kidney Disease Improving Global outcome) criteria.
Methods: We performed a prospective study to validate, the NC by ICA in patients with cirrhosis. The primary outcome was 90-day survival. Secondary outcomes were progression and resolution of AKI and evaluation of Delta creatinine (difference of baseline creatinine and peak creatinine) in predicting the 90-day survival. We collected data from 492 consecutive patients admitted with cirrhosis and its complications in a tertiary hospital in India.166 patients had AKI.4 of the 166 patients underwent liver transplantation in the 90 days follow up. Remaining 162 patient's data was analysed.
Results: Most common aetiology of AKI in stage 1A was pre-renal causes, while in stage 1B, 2 and 3 it was HRS 90-day survival Figure 1A. Progression of AKI Figure 1B. Resolution of AKI Figure 2A. Delta creatinine Figure 2B
Conclusion: In patients with cirrhosis, we validated the NC by showing the association between AKI stages with 90-day survival. Higher the stage of AKI, poorer was the survival. Progression of AKI was associated with poorer prognosis and resolution was associated with better prognosis, in all stages of AKI. Within each stage of AKI, Delta creatinine was useful to differentiate survivors from non-survivors. Delta creatinine concept may help to identify those with higher risk of mortality in each stage of AKI and may help to suggest a more dynamic prediction model.

Abstract #725

Urinary Neutrophil Gelatinase Associated Lipocalin, Is Superior than Serum Creatinine As a Diagnostic Marker for Early Identification of Acute Kidney Injury in Cirrhotic Patients

Md Rofiqul Islam[1]

[1]Rajshahi Medical College Hospital

Background: Acute kidney injury (AKI) is known to increase mortality in cirrhotic patients, therefore early identification is utmost significance. The AKI diagnosis in the early possible period in the hospitalized cirrhotic patients can save many lives.
Objective: The main aim of this study was to determine the accuracy of uNGAL as a diagnostic marker for early identification of AKI in cirrhotic patients.
Materials and Methods: This cross sectional study was carried out at Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka. A total 70 patients of decompensated cirrhosis and decompensated cirrhosis with AKI prone conditions were included for the study. Serum creatinine (sCr) level 03 months before the admission was collected wherever available and used as baseline sCr. In patients without a previous sCr value, the sCr on admission was used as baseline. Where the baseline sCr was normal then the patients were included for the study. Patients were then monitored with sCr at 24 h and 48 h. Urine sample for NGAL was collected within 24 h after admission.
Results: Mean serum creatinine were 1.02 ± 0.24 in Group A and 2.27 ± 1.01 in Group B. Comparison of mean uNGAL between Patients of decompensated cirrhosis with AKI and without AKI, uNGAL was significantly higher in AKI group and it detects the development of AKI early than serum creatinine. The optimal cutoff value was $\geq$ 50 ng/mL providing 91.4% sensitivity, 94.3% specificity, 92.8% accuracy.
Conclusion: uNGAL is a valid marker than serum creatinine for the early diagnosis of AKI in cirrhotic patients.

Abstract #1009

The Prognostic Value of 24-hour Urine Sodium (24-hr UNa) in Cirrhotic Patients With Ascites on Diuretics

Sukanta Chandra Das[1], Naymul Hasan[2], Birendra Nath Saha[3], Chanchal Kumar Ghosh[4]

[1]Gastroenterology Division of Internal Medicine, General Hospital, Narayanganj, Bangladesh, [2]Department of Gastroenterology, Bogra Shaihid Zia Medical College, [3]Department of Gastroenterology, Gazipur Medical College, [4]Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University

Introduction: Ascites due to cirrhosis can be mobilized with sodium restriction (88 mEq/day) and diuretics. Patients with non-responder to diuretics may have pre-hepatorenal syndrome and a poor prognosis. Diuretic response can be monitored by measuring 24-h UNa which can also be a prognostic marker.
Objective: The aim of this study was to evaluate the value of 24-h UNa as a prognostic marker in cirrhotic patient with ascites on diuretics.
Methods: This cross-sectional study included 100 patients of cirrhosis on diuretics irrespective of dosage. 24-h urine was collected after proper instruction and tested accordingly for 24-h UNa. At the same time liver and renal function tests including electrolyte were done to calculate MELD and CTP score.

Results: Out of 100, 48 (48%) subjects had excreted ≥ 78 mmol/day of sodium and 52 (52%) subjects excreted < 78 mmol/d.64 subjects belong to CTPS "B" and 36 in CTPS "C"group. Majority of the cases (81.3%) of CTPS "B" group had excreted ≥ 78 mmol sodium/day and 51.9% patients of the CTPS "C" group had 24 h urinary sodium < 78 mmol/day. In patients who excreted < 78 mmol/day MELD score was 17.71 ± 4.51 and it was 14.60 ± 2.98 in patients who excreted ≥ 78 mmol/day of urinary sodium. These differences were statistically significant ($p < 0.001$).
Conclusion: This study showed that advanced cirrhosis have relatively lower natriuresis in response to diuretics. So, 24-h UNa can be considered as a prognostic indicator. But multicentered studies are needed for further recommendation.

Table :Distribution of different variables of the study population according to the 24-hr urine sodium excretion.

	24 hr Urine (mmol/day)		p value
	≥ 78 (Mean ± SD)	< 78 (Mean ± SD)	
TPC (/cumm)	139187 ± 47631	126711 ± 52478	0.217
S. Creatinine (mg/dl)	1.18 ± 0.15	1.28 ± 0.12	<0.001
S. Na(mmol/L)	130.48 ± 4.41	129.63 ± 4.13	0.319
S. K (mmol/L)	4.43 ± 0.59	4.13 ± 0.67	0.023
Bilirubin (mg/dl)	2.23 ± 1.11	3.82 ± 2.80	<0.001
Albumin (gm/L)	26.27 ± 3.40	23.64 ± 4.28	0.001
Prothombin time (INR)	1.46 ± 0.29	1.58 ± 0.29	0.021
CTPS B	39 (81.3%)	25 (48.1%)	0.001
CTPS C	9 (18.8%)	27 (51.9%)	0.001
MELD	14.60 ± 2.98	17.71 ± 4.51	<0.001
Spot urine sodium(mmol/L)	88.32 ± 42.86	36.83 ± 23.98	<0.001
Spot urine potassium (mmol/L)	34.33 ± 11.67	27.50 ± 10.86	0.003

Mann-Whitney U test was done to measure the level of significance
P value <0.05 is significant.

TPC, Total platelet count; Na, sodium; K, potassium; ALT, alanine aminotransferase ;AST, aspartate aminotransferase; MELD, model for end stage liver disease; CTPS, Child Turcotte Pugh Score.

Abstract #1031

Liver biopsy is still needed in liver transplantation recipients; single center experience

Eman Abdelsameea[1], Ayman Alsebaey[1], Maha Mohammad Elsabaawy[1], Khalid Gameel[1], Nermin Ehsan[2], Khalid Aboelela[3]

[1]Department of Hepatology and Gastroenterology, National Liver Institute, Menoufia University, [2]Department of Pathology, National Liver Institute, Menoufia University, [3]Department of Hepatobiliary Surgery, National Liver Institute, Menoufia University

Background: Liver transplantation is a final treatment for decompensated liver disease.
Aim: Description of post-liver transplant histopathology.
Methods: We enrolled 89 patients divided into two groups according to if they underwent on demand liver biopsy (n = 34; 38.2%) or not (n = 55; 61.8%). Albumin-bilirubin (ALBI) score and Model for End-Stage Liver Disease (MELD) assessed the degree of liver dysfunction.
Results: Patient underwent liver biopsy (LB) were 44.65 ± 8.46 years old, mainly males (88.2%) with average MELD of 8.74 ± 4.71. Most patients were positive pretransplant for HCV (91.2%) and 29.4% had hepatocellular carcinoma on top of hepatitis C. Patients underwent LB had worse liver dysfunction by ALBI score (− 2.62 ± 0.6 vs. − 2.96 ± 0.5; $p = 0.014$) but comparable MELD. The time till first biopsy was 19.88 ± 11.22 (4–44) months. It was not different statistically with various histopathology ($p > 0.05$). Histopathology of first biopsy was viral chronic hepatitis (50%), acute rejection (20.6%), steatohepatitis (11.8%), chronic rejection (5.9%), chronic hepatitis (5.9%), biliary obstruction (2.9%) and cytomegalovirus hepatitis (2.9%). Most patients were F1 (38.2%) and A1 (35.3%). The immunosuppressive drug regimen had no impact on the histopathology ($p > 0.05$). Patients with hepatitis C pretransplant had in a descending manner the following histological diagnosis ($p = 0.001$): viral chronic hepatitis 16 (51.6%), acute rejection 7 (22.6%), steatohepatitis 4 (12.9%), chronic rejection 2 (6.5%), biliary obstruction 1 (3.2%) and CMV hepatitis 1 (3.2%). Some patients required on demand second (n = 9) and third biopsied (n = 5) that were the same as the first biopsy or completely different.
Conclusion: Liver biopsy is a useful tool for diagnosis of liver transplantation complications.

Pediatric Hepatology

O01 - Biliary atresia and cholestasis

Abstract #230

Liver Transplantation on a Patient with Biliary Atresia Post-Kasai Procedure Presenting with Recurrent Pyogenic Cholangitis

Enrik John Torres Aguila[1], Ian Homer Y. Cua[1]

[1]St. Luke's Medical Center Global City

Introduction: Biliary atresia is a childhood disease of the liver in which one or more bile ducts are abnormally narrow, blocked or absent and Kasai hepatoportoenterostomy is one of its treatment option. Among the long-term complications however is recurrent abscesses which could significantly affect a patient's quality of life and survival. In some clinical settings, liver transplantation may be an option.
Methodology: This is a case of a 21-year-old female, Filipino, diagnosed to have biliary atresia, who underwent Kasai procedure. She was apparently well until 1 year prior when she had repeated hospitalizations presenting with high grade fever, epigastric pain, and jaundice. A liver CT scan showed cirrhotic changes and clusters of multifocal abscesses with necrotic areas. She was treated for recurrent pyogenic cholangitis as guided by cultures and given multiple antibiotics. Due to her poor quality of life, she eventually underwent living donor liver transplantation.
Results: Our patient had recurrent biliary infection likely because of her previous surgery being a primary risk factor of infection and bacterial translocation. This can be addressed with prompt administration of antibiotics but is only a temporizing measure most of the time. Our patient eventually underwent living donor liver transplantation due to the recurrent infection which afforded improvement of her quality of life.
Conclusion: Patients with biliary atresia are predisposed to develop liver cirrhosis hence prompt surgical management is needed to improve survival. Nevertheless, some patients may experience variable degrees of liver dysfunction even after successful surgery where liver transplantation may ultimately become necessary.

Abstract #249

Emodin can Repair Gallbladder Interstitial Cajal-like Cells in Acute Cholecystitis

Zhenpeng Huang[1], Hu Qiu[2], Baoping Yu[2]

[1]Xi'an Medical University, [2]Renmin Hospital of Wuhan University & Key Laboratory of Hubei Province for Digestive System Diseases

Introduction: Interstitial Cajal-like cells (ICLCs) are known as one of the players in affecting gallbladder motility, and will be injured in acute cholecystitis (AC). Emodim can enhance the contractibility of gallbladder.
Objectives: This study explored emodim morphological and molecular mechanisms underlying gallbladder ICLCs changes in AC.
Methodology: 50 adult guinea pigs were randomly divided into 5 groups, a sham-administered group (control group), 2 groups of guinea pigs intraperitoneally administered emodin 6 h before common bile duct ligation (CBDL), and 2 groups of guinea pigs that were not administered the emodin, but were subjected to CBDL. Guinea pigs were held for 24 h or 48 h after surgery. Histological inflammation was detected by hematoxylin–eosin staining, the morphology of gallbladder ICLCs was examined by immunohistochemistry, TUNEL assay was used to detect apoptosis, and western blot and real-time PCR were performed to detect SCF and c-kit protein and mRNA expression.
Results: Inflammation in emodin groups were slighter than those in common groups ($P < 0.05$). There were no differences in ICLCs morphology between groups. During AC, ICLCs were lost, densities of ICCs in emodin groups were all higher common groups ($P < 0.05$). SCF and c-kit protein and mRNA expression levels decreased during AC, emodin groups expression levels were all higher common groups (all $P < 0.05$). Further, ICLCs apoptosis increased in AC, emodin groups ICLCs apoptosis were all higher common groups ($P < 0.05$).
Conclusion: Emodin can repair gallbladder ICLCs injury in AC and associated with gallbladder motility disorder.

Abstract #783

Hepatorenal syndrome in children: Low prevalence but high mortality!

Priti Vijay[1], Snehavardhan P. Pandey[2], Bikrant Bihari Lal[2], Rajeev Khanna[2], Vikrant Sood[2], Seema Alam[2]

[1]Pediatric Hepatology, Institute of Liver and Biliary Sciences, New Delhi, [2]ILBS, New Delhi

Background and Aims: Hepatorenal syndrome (HRS) has been poorly described in pediatric literature. Our objective was to describe the profile, management and outcome of children with HRS.
Methods: HRS and response to treatment were defined as per latest (2017) HRS-AKI criteria by ICA (International Club of Ascites). Poor outcome was defined as death or need for liver transplant within 3 months of development of HRS.
Results: Sixteen children satisfying the definition of HRS were included; 7 presented as ACLF (n = 92) and 9 presented as decompensated chronic liver disease (n = 323). Mean age of these children were 11.1 ± 5 years with albumin of 2.2 ± o.4 g/dl and INR of 2.75 ± 1.2. Fifteen had grade 3 AKI and one had grade 2 AKI. All of them were type 1 HRS with oliguria in 13 (81.2%). Twelve children were treated with albumin plus terlipressin, 2 infants with albumin plus noradrenaline and 2 children did not receive either. Five out of 12 (42.3%) and one of the 2 (50%) children in the terlipressin and noradrenaline group showed response to treatment. Terlipressin was infused for a median of 7 days (range 5–16 days) and was discontinued in 2 children due to peripheral ischemia. Five children received hemodialysis with no improvement. Resolution of AKI on medical therapy was 37.5% in HRS group. There was 69% mortality within 3 months in children presenting with HRS-AKI.
Conclusion: HRS is not uncommon in pediatric liver disease. The response to terlipressin/noradrenaline and albumin is seen in only about 1/3rd of children.

Abstract #824

Randomised controlled trial to compare the efficacy and safety of sodium benzoate versus standard medical therapy in children with chronic liver disease

Snehavardhan Radheyshyam Pandey[1], Priti Vijay[1], Rajeev Khanna[1], Bikrant Biharilal Raghuvanshi[1], Vikrant Sood[1], Seema Alam[1]

[1]Institute of Liver and Biliary Sciences, New Delhi, India

Background: The aim of this study was to compare the safety and efficacy of adding SB to standard medical therapy (SMT) in the management of hyperammonia in children with CLD.
Methods: This double blind randomised controlled trial was done in < 18 years of age with hyperammonemia (> 150 μg/dl in infants, > 100 μg/dl in older children). Those with SB received in the prior week, baseline sodium > 155 mEq/L, Grade III ascites or ammonia > 400 μg/dl were excluded. The children were randomised to receive either SB (Group A) or placebo (Group B) along with SMT (Lactulose and Rifaximin) for a period of 5 days. The primary outcome measures were change in ammonia and resolution of hepatic encephalopathy (HE) on day 5.
Results: Of the 88 patients included: 44 each were randomised to Group A and B. The baseline characteristics including ammonia were comparable between the two groups. Ammonia was significantly lower on day 1 and 2 in group A but comparable on day 3–5 (Table 1). There was significant decline in ammonia between day 0 and 5 in both the groups. Resolution of overt HE was comparable in both groups (Group A 57.1% vs Group B 53.8% (OR 0.87, 95% CI 0.34–2.2, p = 0.816). Although not significantly but more children developed ascites in the SB group (Table 2).
Conclusion: SB with SMT versus SMT alone lowers ammonia transiently without significant difference in resolution of HE.

Abstract #834

Acute Kidney injury in Pediatric Liver disease- Spectrum, presentation, management and outcome

Priti Vijay[1], Snehavardhan P. Pandey[1], Bikrant Bihari Lal[1], Rajeev Khanna[1], Vikrant Sood[1], Seema Alam[1]

[1]ILBS, New Delhi

Background and Aims: There is limited data on acute kidney injury (AKI) in pediatric liver disease. This is a descriptive study of AKI among pediatric liver diseases.
Methods: Data of children younger than 18 years of age admitted in pediatric hepatology ward in last 8 years was retrieved. Children satisfying the KDIGO definition of AKI were identified. Poor outcome was defined as death or need for liver transplant within 3 months of development of AKI. Results: of the 4243 children with liver diseases, 150 (3.5%) children fulfilled the definition of AKI. AKI was present in 23/92 (25%) ACLF, 51/212 (23.7%) ALF and

55/323 (17%) decompensated chronic liver disease. One-hundred one (67.3%) had oliguria. Grade 3 AKI was seen in 97 (64.5%), grade 2 in 28 (18.6%) and grade 1 in 25 (16.7%). Mean age of presentation was 10.5 ± 5.4 years and PELD score of 26 ± 11. The most common etiology of AKI was pre-renal (56%) followed by renal (44%) [Figure 1]. Eighty-four children (56%) showed response to medical therapy; of whom 73 (87%) survived with native liver. Among 66 non-responders, only 1 patient survived with native liver beyond 3 months. Dialysis was indicated in 53 but only 33 received it. Overall, only 50% of children with AKI survived beyond 3 months with their native liver.

Conclusion: AKI develops in 3.5% of pediatric liver disease and 17–25% children with advanced liver disease. The most common cause of AKI was pre-renal. Response to medical therapy is seen in about 50%; with 50% mortality at 3 months.

Abstract #863

Natural history of hepatopulmonary syndrome (HPS) in Biliary Atresia (BA) versus Other chronic liver diseases (CLD)

Snehavardhan Radheyshyam Pandey[1], Priti Vijay[1], Vikrant Sood[1], Rajeev Khanna[1], Bikrant Biharilal Raghuvanshi[1], Seema Alam[1]

[1]Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: Prevalence of HPS in children 9–40%. Aims and objectives: To study the prevalence, natural history and risk factors of HPS in BA versus other CLD.

Methodology: All children (BA and CLD) older than 6 months of age, except those with pre-existing respiratory and cardiac diseases, were included in the study and were followed up every 3–6 monthly. Patients were diagnosed as HPS on the basis of 2D echo and P (A-a) O2 > 15 mmHg (criteria 1) or elevated age appropriate upper limit of normal value for P (A-a) O2 (Criteria 2).

Results: During the study period of 18 months, there were 42 children of BA (Successful 26 and Unsuccessful 16) and 62 of CLD. Criteria 2 diagnosed 6 additional patients compared to Criteria 1. HPS was present in 53.8% of successful versus 87.5% of unsuccessful BA and 38.7% of CLD during the study period. Median duration of developing HPS was 29.8 months (95% CI 7.6–51.9) for BA vs 110 months (95% CI 36.7–119.2) for CLD. In the BA group, the prevalence of HPS increased by 0.7–1% per month. Fig. 1 and 2 shows the outcome and follow up in BA (Successful and Unsuccessful) and CLD groups. Among the risk factors, low serum albumin in BA whereas higher splenic Zscores in CLD were found to be significant risk factors for HPS.

Conclusions: The prevalence of HPS in BA is higher compared to other CLD. Lower serum albumin in BA and higher splenic Z scores in other CLD are independent risk factors for HPS.

Abstract #906

Effect of special fortified indigenous diet on growth and outcome in children with infantile cholestasis - Prospective Interventional Randomized Controlled Trial

Arti Pawaria[1], Seema Alam[1], Rajeev Khanna[1], Dinesh Rawat[1]

[1]Department of Pediatric Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India & MBBS & DM Fellow, Department of Pediatric Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: This study was conducted to effect of special fortified indigenous diet on growth, hepatic morbidity and outcome in children with infantile cholestasis.

Methods: Out of 65 malnourished children (as per WHO 2006 classification) with infantile cholestasis syndrome, 40 (0.5–3 years) randomized to 2 groups: Group 1 (nutritional intervention) received nutritional supplement in addition to standard nutritional counseling by trained dietician and control group (Group2) received standard nutritional counseling. Nutritional status was assessed by weight, height, body mass index, mid upper arm circumference (MUAC), mid arm muscle circumference (MAMC), triceps and subscapular skin fold thicknesses (TSF, SSF), mid arm muscle area (MAMA). Clinical, anthropometry and outcome were collected at follow up visits at 1, 3, 6, 9, 12 months.

Results: There were 20 children in each group. Nutritional intervention group showed significantly higher increase in all anthropometric measurements as compared to control group (table 1). Patients who survived with native liver had significantly higher increase in weight ($p = 0.002$), height ($p < 0.001$), SSF ($p = 0.024$), MUAC ($p = 0.002$), MAMC ($p = 0.004$), MAMA ($p = 0.004$), MUAA ($p = 0.002$) (table 2). Increase in height and MUAC were found to be significant independent predictors of outcome. On multivariate analysis, increase in height [10.93 ± 0.69 vs. 3.45 ± 1.25, HR 0.64 (95% CI 0.52–0.79), $p < 0.001$] and MUAC [1.38 ± 0.25 vs. 0.34 ± 0.33, HR 0.433 (95% CI 0.22 – 0.87), $p = 0.019$] were significantly associated with decreased risk of death/liver transplant.

Conclusions: Nutritional intervention using indigenously prepared oral nutritional supplements in malnourished children with infantile cholestasis showed significant improvement in anthropometric measurements.

O02 - Viral and autoimmune hepatitis

Abstract #222

Predictive value of intrahepatic hepatitis B virus covalently closed DNA and serum HBsAg in children with chronic hepatitis B treated with interferon

Yanwei Zhong[1], Yanmin Shi[1], Fang Chu[1], Liang Yan[1], Ce Shi[1], Liyan Hao[1], Xiuchang Zhang[2], Min Zhang[1]

[1]Pediatric Liver Disease Therapy and Research Center, [2]Hebei North University

Objectives: To evaluate the predictive value of intrahepatic cccDNA and serum HBsAg levels in children with HBeAg-positive chronic hepatitis B (CHB) treated with interferon (IFN).

Methods: A total of 63 children with HBeAg-positive CHB were enrolled. Baseline intrahepatic cccDNA,serum HBsAg, HBV DNA levels and other biochemical parameters were measured. Age, sex, HBV DNA, ALT, HBV cccDNA and HBsAg were introduced into logistic regression analysis; the area under the receiver operating characteristic curve was used to explore the predictive value of intrahepatic cccDNA and serum HBsAg in children with CHB receiving 48 weeks IFN.

Results: 13 patients achieved HBsAg seroconversion. Age, baseline intrahepatic HBV cccDNA level and serum HBsAg titer had a significant association with HBsAg seroconversion after 48 weeks of antiviral treatment. Baseline intrahepatic cccDNA level was positively correlated with serum HBsAg titer ($r = 0.464$, $p = 0.000$); log10 0.08 copies/cell and log10 3.68 IU/mL were taken as cccDNA and HBsAg cutoff value, the sensitivity, specificity, positive and negative predictive values of predicting the likelihood of achieving HBsAg seroconversion were 92.0, 46.2, 86.8, 60.0 and 86.0%, 69.2,

91.2 and 56.3%, respectively; there was no significant statistical difference between the serum HBsAg titer and intrahepatic cccDNA level in predicting the likelihood of achieving HBsAg seroconversion ($p = 0.146$).
Conclusions: Age, baseline intrahepatic cccDNA and serum HBsAg levels were the main factors affecting antiviral efficacy. Using log10 0.08 copies/cell and log10 3.68 IU/mL equivalent as cutoff of HBV cccDNA and HBsAg may predict therapeutic efficacy in children with HBeAg-positive CHB treated with IFN at 48 weeks.

Abstract #368

Predictive utility of HBsAg level on the virological response (VR) in children with HBeAg positive CHB

Yanwei Zhong[1], Min Zhang[1], Fang Chu[1], Liyan Hao[1], Ce Shi[1]

[1]302 Hospital Pediatric Liver Disease Therapy and Research Center, Institute of Infectious Diseases

Background/Aim: To explore the predictive factors of interferon (IFN) therapy in children with HBeAg positive chronic hepatitis B (CHB).
Methods: 220 HBeAg positive children patients with CHB treated with IFN were enrolled. These patients were divided into two groups according to the baseline levels of HBsAg, ALT and HBV DNA, respectively. Their correlation with VR and SR at weeks 48 of treatment were analyzed.
Results: There was significant difference in the loss rate of HBeAg and HBsAg between the group with baseline levels of HBsAg $\leq$ 1500 IU/ml and HBsAg $>$ 1500 IU/ml. The former showed that the loss rate of HBeAg (64.3% vs 37.2%, $p = 0.007$), the loss rate of HBsAg (50.0% vs 24.4%, $p = 0.005$), but compared with HBsAg $>$ 1500 IU/ml group, there was no difference in HBeAg seroconversion rate (39.3% vs 32.6%, $p = 0.484$). Comparison between the group with baseline levels of ALT $>$ 2ULN and ALT $\leq$ 2ULN, there was no statistical difference in the loss rate of HBeAg and HBeAg seroconversion rate. The former demonstrated the loss rate of HBeAg (44.6% vs 38.8%, $p = 0.186$), the HBeAg seroconversion rate (39.2% vs 24.5%, $p = 0.059$). Comparison between the group with baseline levels of HBV DNA $\leq$ 108 IU/ml and the group with HBV DNA$>$108 IU/ml, there was significant difference in the loss rates of HBeAg (50.4% vs 28.7%, $p = 0.002$), but there was no statistical difference in the seroconversion rate of HBeAg (38.9% vs 26.4%, $p = 0.063$).
Conclusions: Baseline HBsAg level $\leq$ 1500 IU/ml and HBV DNA $\leq$ 108 IU/ml has high predictive value of loss rates of HBeAg in the HBeAg positive pediatric patients treated with IFN.

Abstract #513

Pharmacokinetics of Once Daily Sofosbuvir or Ledipasvir/Sofosbuvir in HCV-Infected Pediatrics Aged 3 to $<$ 6 Years Old

Rebecca Begley[1], Naoto Fujiyama[1], Chenyu Wang[1], Amy Meng[1], Benedetta Massetto[1], Jiang Shao[1], John Ling[1], Anita Mathias[1]

[1]Gilead Sciences

Background: Pharmacokinetic (PK) data indicates that SOF 200 mg and LDV/SOF 45/200 mg are appropriate doses in children 6 to $<$ 12 years old (y). For children 3 to $<$ 6 y, SOF and LDV/SOF oral granules have been developed; the PK of these granules was assessed in children 3 to $<$ 6 y.
Methods: HCV-infected children (3 to $<$ 6 y) received oral granules of SOF or LDV/SOF. Doses were selected to target exposures similar to adults; subjects $\geq$ 17 kg received 200 mg SOF or 45/200 mg LDV/SOF, and subjects $<$ 17 kg received 150 mg SOF or 33.75/150 mg LDV/SOF, once daily. Pediatric exposures (AUCtau and Cmax) from subjects in the Intensive PK sampling were compared via ANOVA to exposures in Phase 2/3 SOF or LDV/SOF adult clinical programs. The primary PK endpoint was AUCtau of GS-331007 and LDV, as applicable, with predefined PK equivalence bounds of 50–200%. Safety was assessed throughout the study.
Results: All but 1subject completed IPK assessments (LDV/SOF; discontinued treatment due to Grade 1 vomiting). At baseline, median (range) age (years) for 11 subjects in the SOF + RBV PK lead-in was 5 (3, 5), weight (kg) was 17 (13, 19). Median (range) age and weight for 14 LDV/SOF subjects were 5 (3, 5) and 20 (12, 28), respectively. The GS-331007 Cmax (SOF + RBV) was modestly higher; these increases are not considered clinically relevant based on established exposure-safety analyses.
Conclusion: SOF or LDV/SOF were well tolerated and provided similar exposures to those observed in adults.

Abstract #514

Ledipasvir/Sofosbuvir for 12 Weeks Is Safe and Effective in Children 3 to $<$ 6 years old with Chronic Hepatitis C Virus Infection

Kathleen Schwarz[1], Philip Rosenthal[2], Karen F. Murray[3], Jonathan R. Honegger[4], Benedetta Massetto[5], Naoto Fujiyama[5], Chenyu Wang[5], Diana M. Brainard[5], Rebecca Begley[5], Jiang Shao[5], Bandita Parhy[5], Sanjiay Bansal[6], William Balistreri[7]

[1]Johns Hopkins Hospital, [2]University of California San Francisco, [3]University of Washington School of Medicine and Seattle Children's Hospital, [4]The Ohio State University Medical Center, [5]Gilead Sciences, [6]King's College Hospital, [7]Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine

Background: Sofosbuvir-based regimens have been approved for patients 12 to $<$ 18 years; for younger children the only approved treatment is still pegylated interferon plus ribavirin for up to 48 weeks. The current study evaluated the safety and efficacy of LDV/SOF in HCV- infected children 3 to $<$ 6 years old.
Methods: Patients 3 to $<$ 6 years old with HCV Genotype 1 or 4 were enrolled into this open-label study to receive weight-based doses of LDV/SOF as granules (LDV 33.75 mg/150 mg if weight $<$ 17 kg or LDV 45 mg/SOF 200 mg if weight $\geq$ 17 kg) for 12 or 24 weeks based on cirrhosis status and prior treatment with interferon. The efficacy endpoint was SVR12. Safety was assessed by adverse events (AEs) and clinical/laboratory data.
Results: 34 children, 33 with GT1 and 1 with GT4, were enrolled and treated. All were treatment naïve and vertically infected. No patient was known to be cirrhotic. All patients were assigned to 12 weeks of treatment. Overall, the SVR12 rate was 97% (33/34) with no virologic failures. A 3-year old patient early discontinued treatment on day 5 due to "abnormal drug taste". No patients experienced a Grade 3–4 AE or a serious AEs. The most common AEs reported ($\geq$ 10% of patients) were vomiting, pyrexia, cough, rhinorrhea and pharyngitis streptococcal.
Conclusions: This all-oral, interferon-free regimen was highly efficacious and well tolerated, supporting its use as a treatment option for children 3 to $<$ 6 years old.

O03 - Metabolic and genetic diseases

Abstract #366

Genetic Diagnosis of Patients with Gilbert Syndrome: 4 Novel Mutations Found in the Chinese Population

Leilei Gu[1], Yue Han[2], Donghua Zhang[3], Qiming Gong[4], Xinxin Zhang[2]

[1]Department of Gastroenterology and Hepatology, Ruijin Hospital North, Shanghai Jiao Tong University School of Medicine, Shanghai, China, [2]Research Laboratory of Clinical Virology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China & Department of Infectious Diseases, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, [3]Research Laboratory of Clinical Virology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, [4]Department of Infectious Diseases, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Introduction: Cases with unexplained unconjugated hyperbilirubinemia are often encountered in clinical work, which may be considered as hereditary jaundice. Gilbert Syndrome (GS) is more common and is an autosomal recessive disease.
Objectives: In this study, UGT1A1 gene were tested in patients with elevated indirect bilirubin, which make the definite diagnosis of GS, and to detect novel pathogenic mutations.
Methodology: 208 patients with clinically suspected GS were enrolled between 2015 and 2018. Genomic DNA was extracted from the leucocytes of patients. The promoter, exons, flanking intronic regions of UGT1A1 were amplified by polymerase chain reaction (PCR). PCR products were sequenced on an ABI3730 DNA Analyzer. Sequencing results were analyzed against common mutation databases (HGMD, etc.), and online prediction tools (Mutation Taster, etc.) were applied to determine pathogenicity when novel mutations were found.
Results: Amongst these patients, 117 patients were diagnosed as GS by identifying homozygous or compound heterozygous mutations, and 58 patients were heterozygote carriers for GS. 10 pathogenic mutations were detected, including a promoter mutation, a frameshift mutation, a premature stop codon mutation, and 7 missense mutations. And 4 of them were found to be novel mutations, namely p.L166Afs*16, p.E424*, p.Y67F, and p.S306F.
Conclusion: The mutations A (TA)7TAA in the promotor (30.1%) and p.G71R (28.0%) were frequently found in this study, which is similar to previous reports. The 4 novel mutations found enriched the mutation spectrum of UGT1A1 in the Chinese population and need to be verified by further functional experiments.

Abstract #726

Study for Spectrum of UGT1A1Variations Associated with Inherited Nonhemolytic Unconjugated Hyperbilirubinemia

Xiong Qing Fang[1], Yang Yong Feng[1]

[1]Nanjing Second Hospital, Affiliated to Nanjing University of Chinese Medicine

Objective: To compare and analyze patient's general condition, laboratory testing and the spectrum of UGT1A1 variations of Chinese Gilbert syndrome (GS) and Crigler–Najjar syndrome type II (CNS-II).
Methods: A retrospective study was conducted on inherited unconjugated hyperbilirubinemia patients who attended outpatient and inpatients department of our hospital from January 2015 to July 2018 and their demographic characteristics, 1aboratory testing, and UGT1A1 variations were statistically analyzed.
Results: 51 inherited unconjugated hyperbilirubinemia patients were included, including 44 GS and 7 CNS-II; the ratio of male to female was 2.9:1. The average age of onset was (36.11 ± 13.17) years. Six variants were identified, including c.-40-39insTA, c.-3279T>G, c.211G>A (p.G71R), c.686C>A (p.P229Q), c.1091C>T (p.P364L), c.1456T>G (P.Y486D).most mutations were c.211G>A (58.82%, 30/51); followed by TATAbox c.-40_-39insTA (27.5%, 14/51), exon5 c. 1456T>G (25.5%, 13/51). The medians of total bilirubin (TB) and unconjugated bilirubin (UCB) in CNS-II patients were significantly higher than that in GS patients [155.91 (130–207) vs. 38.25 (29–52.15) μmol/L, $U = 0.00$, $P < 0.01$; 144.13 (120.8–197) vs. 30.00 (21.7–46.75) μmol/L, $U = 0.00$, $P < 0.01$, respectively]. The frequencies of c.1091C>T and c.1456T>G in GS patients were all greater than that CNS-II patients ($P < 0.01$). There were no differences in age, TB, UCB, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) between the c.211G>A homozygous variants and heterozygous variants ($P > 0.05$).
Conclusion: The c.211G>A variant, c.-40_-39insTA variant and c.1456T>G variant are major pathogenic variants; the c.211G>A variant slightly influence the level of total bilirubin, on the contrary, c.1091C>T and c.1456T>G variant varied at GS and CNS-II patients.
Keywords: Inherited unconjugated hyperbilirubinemia, Gilbert syndrome, Crigler–Najjar syndrome, UGT1A1

O04 - Pediatric liver transplantation

Abstract #851

Efficacy and safety of High volume plasma exchange in children with acute liver failure – a prospective pilot study

Arti Pawaria[1], Snehavardhan Pandey[2], Seema Alam[3], Rajeev Khanna[4]

[1]MD & MBBS & DM Fellow, Department of Pediatric Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India, [2]MD & DNB & Department of Pediatric Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India, [3]MD & MBBS & Professor and Head, Department of Pediatric Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India, [4]MD & MBBS & Associate Professor, Department of Pediatric Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India

Introduction: This is the first prospective study in children where efficacy of addition of high volume plasma exchange (HVPE) to standard medical therapy (SMT) is compared with SMT alone in setting of ALF.
Methods: This study was conducted (2016–2018) to analyze the outcome of HVPE in children with ALF (children ≥ 10 kg with INR ≥ 4 or INR ≥ 3 with hepatic encephalopathy) with primary objective to determine transplant free survival at day 4, 7, 14 and 30. Patients were divided into two groups: HVPE group (HVPE + SMT) and SMT alone (SMT group). Outcome was assessed using Kaplan-Meyer survival analysis.
Results: of 60 PALF cases, 48 children, median age 9.5 years, were enrolled: 24 patients underwent 57 sessions of HVPE. Demographic, etiologic and baseline characteristics were comparable in both groups except higher indeterminate etiology in HVPE group (41% vs. 29%). HVPE resulted in significant better improvement in biochemical parameters in HVPE versus SMT group (Table 1). There was no increase in complications in HVPE group. Median length of transplant free survival was significantly longer in HVPE [7.5 versus. 4, HR 0.917, 95% CI 0.84 to 0.98), p = 0.047]. HVPE in ALF resulted

in significantly increased survival at day 4 (83.3% vs. 58.3%, p = 0.048) and 7 (58.3% vs. 33.3%, p = 0.041, Fig 1). Survival at day 14 and day 30 was not significantly different between two groups (p = 0.344 and 0.403).
Conclusions: HVPE increases survival with native liver till day 7 in patients with ALF and provides a window for arranging logistics for LT.

Basic Hepatology Research

P01 - Basic hepatology research

Abstract #89

Mitofusin2, a rising star in acute-on-chronic liver failure, triggers autophagy via PI3 K/Akt/mTOR signaling pathway

Ran Xue[1], Qinghua Meng[1]

[1]Beijing You-An Hospital, Capital Medical University

Aim: Acute-on-chronic liver failure (ACLF) is a life-threatening syndrome with poor prognosis. Burgeoning researches have begun to prove that mitochondria play a crucial role in liver failure. Mitofusin2 (Mfn2) plays an indispensable role in mitochondrial fusion and adjusting function. However, the role and underlying mechanisms of Mfn2 on cell autophagy of ACLF is still unclear. Our aim was to explore the effect of Mfn2 on multiple biological functions involving cell autophagy in ACLF.
Methods: In this research, we constructed ACLF animal model and hepatocyte autophagy model, using virus to deliver Mfn2 to liver cells, so that we can assess the effect of Mfn2 on autophagy and apoptosis in ACLF. Besides, we uncovered the biological mechanism of Mfn2-induced autophagy of ACLF using western blotting, RT-PCR, electron microscopy, and transient transfection of a GFP-LC3-expressing construct.
Results: Mfn2 significantly attenuated ACLF, characterized by ameliorated gross appearance and microscopic histopathology of liver, reduced serum AST, ALT and TBIL level. Mfn2 improved the expression of LC3-II, Atg5 and Bcl-2, and down-regulated the expression of Bax in ACLF. Meanwhile, like rapamycin, Mfn2 also significantly inhibited the expression of p-PI3K, p-Akt and p-mTOR in ACLF.
Conclusions: Our finding suggests that Mfn2 influences multiple biological functions of ACLF via PI3K/Akt/mTOR signaling pathway. This study will provide a reliable theoretical basis for the application of Mfn2 as an effective target for ACLF treatment, reversing or delaying the process of ACLF.

Abstract #170

Assessment of Depression in Patients with Cirrhosis of Liver

Zubin Pradeep Sharma[1], Ravindra Sharma[1], Itee Sidana[2]

[1]Department of Gastroenterology, Aditya Gastro Centre, [2]Department of Psychiatry, Aditya Gastro Centre

Aim: To determine whether patients with cirrhosis and depressive symptoms have a different neuropsychological cognitive profile from patients with cirrhosis without depressive symptoms.
Methods: Adult outpatients with diagnosis of cirrhosis of liver who did not have clinically overt hepatic encephalopathy were included in the study. Patients underwent neuropsychological testing and evaluation for depression using the Beck Depression Inventory-2 (BDI-2).
Results: 60 patients were included in the study. 38 patients were classified as depressed (BDI-2 score > 14), with a mean BDI-2 score of 22. The 38 patients with depression were similar to the 22 non-depressed patients in level of education and age. There was a higher percentage of man in the depressed group than in non-depressed group. No etiology of liver disease was associated with depression. In linear regression analyses, decreases in cognitive function were associated with higher BDI-2 scores.
Conclusions: Depressive symptoms are associated with worsened cognitive function in cirrhosis. Depressive symptoms may worsen cognitive impairment in patients with cirrhosis, therefore treatment of depression should be considered in such patients.

Abstract #198

Autophagy Inhibitor, Chloroquine did not affect tumor development in a transgenic mouse model of HCC

Sunyeong Shin[1], Hyuk Moon[1], Kyungjoo Cho[1], Simon W. Ro[2], Beom Kyung Kim[3], Seung Up Kim[4], Do Young Kim[5], Kwang-Hyub Han[6]

[1]Brain Korea 21 Plus Project for Medical Science College of Medicine & Yonsei Liver Center, Severance Hospital, [2]Yonsei Liver Center, Severance Hospital, [3]Yonsei Liver Center, Severance Hospital & Department of Internal Medicine Yonsei University College of Medicine, Seoul, Korea, [4]Yonsei Liver Center, Severance Hospital & Department of Internal Medicine Yonsei University College of Medicine, Seoul, Korea, [5]Yonsei Liver Center, Severance Hospital & Department of Internal Medicine Yonsei University College of Medicine, Seoul, Korea, [6]Brain Korea 21 Plus Project for Medical Science College of Medicine & Yonsei Liver Center, Severance Hospital & Department of Internal Medicine Yonsei University College of Medicine, Seoul, Korea

Introduction: Liver cancer is the second most common cause of cancer-related deaths worldwide. Autophagy is an intracellular recycling process by which damaged or superfluous proteins are delivered to lysosomes for degradation, and then utilized as energy resources and macromolecular precursors. Autophagy in cancer is a highly debated subject. Research has shown that autophagy can become either tumor-promoting or tumor-suppressive depending on cellular or genetic context.
Aims: In this study, we investigated the role of autophagy in hepatocellular carcinoma (HCC) by applying an autophagy inhibitor, chloroquine to a transgenic mouse model of HCC.
Methods: Transposons were constructed encoding an activated from of RAS (HRASG12 V) and short hairpin suppressing P53 (shp53). Transposons were hydrodynamically delivered to livers of 6-week-old C57BL/6 mice. Mice were administered intraperitoneally with chloroquine at a daily dose of 60 mg/kg for 5 weeks. Control mice were given a phosphate buffered saline (PBS). Mice were monitored at least twice per week.
Conclusion: Our study suggests that autophagy inhibition via chloroquine treatment does not affect HCC development in a transgenic mouse model of HCC.

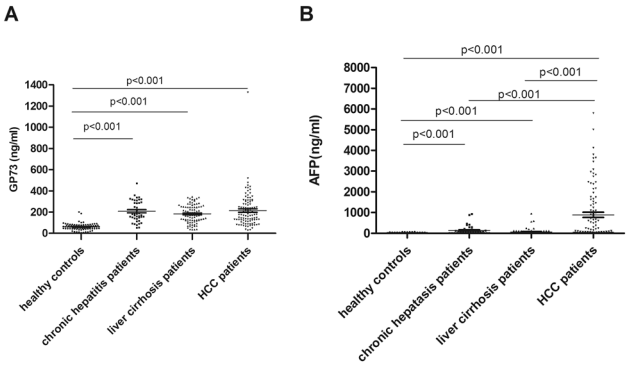
Abstract #204

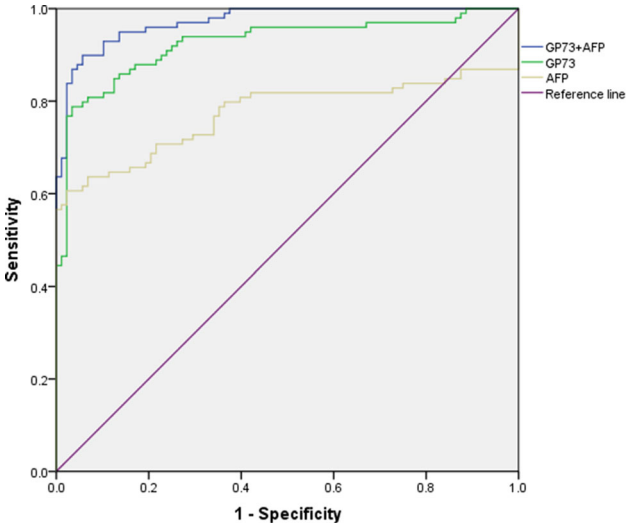
Development and potential application of a simultaneous multiplex assay of Golgi protein 73 and alpha-fetoprotein for hepatocellular carcinoma diagnosis

Jing Xiao[1], Fei Long[1], Longbo Hu[1], Hua Cai[1], Tao Peng[1], Wenli Chen[2]

[1]State Key Laboratory of Respiratory Disease, Sino-French Hoffmann Institute, School of Basic Medical Science, Guangzhou Medical University, Guangzhou, China, [2]Department of Infectious Diseases, Guangdong Academy of Medical Sciences, Guangdong Provincial People's Hospital, Guangzhou, China

Introduction: Detecting a single biomarker may not meet the requirement for the diagnosis of hepatocellular carcinoma (HCC).
Objectives: This study aimed to develop a simultaneous multiplex assay of Golgi protein 73 (GP73) and alpha-fetoprotein (AFP).
Methodology: A multiplex assay of GP73 and AFP was developed using xMAP technology. This assay demonstrated the cross-reactivity, sensitivity, precision, accuracy. Additionally, the utility of this assay was illustrated by detecting serum GP73 and AFP.
Results: The multiplex assay was successfully developed to detect GP73 and AFP, without cross-reactivity. The sensitivity was GP73 0.215 ng/ml and AFP 0.666 ng/ml. The range of detection was 0.98–861.08 ng/ml and 2.01–1848.73 ng/ml, respectively. The intra- and inter-assay coefficients of variation (CVs) were < 10%, with 75–125% of recovery rates. It demonstrated a good correlation with enzyme linked immunosorbent assay (ELISA), with correlation coefficients of GP73 0.818 and AFP 0.982. The levels of GP73 and AFP in healthy controls, patients with chronic hepatitis, liver cirrhosis, HCC were 61.64 ± 30.60 ng/ml, 208.4 ± 99.42 ng/ml, 183.7 ± 82.78 ng/ml, 214.1 ± 160.5 ng/ml, and 24.87 ± 14.52 ng/ml, 134.4 ± 216.5 ng/ml, 66.45 ± 133.4 ng/ml, 891.4 ± 1278 ng/ml, respectively. The area under the ROC curve (AUC) for the combination of GP73 and AFP was 0.972 with sensitivity 90.91% and specificity 98.86% for the diagnosis of HCC.
Conclusions: A simultaneous multiplex assay of GP73 and AFP was successfully developed. It may provide a reliable reference for the early diagnosis of HCC.





Abstract #226

Gut microbial metabolite, deoxycholic acid, induces proliferative inhibition in hepatocyte with steatosis via stimulation of mitochondrial oxidative stress

Jinzhi Wang[1], Fang Sun[1], Jijun Luo[1], Qin Pan[1], Jiangao Fan[2]

[1]Department of Gas-Troenterology, Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, [2]Department of Gas-Troenterology, Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine & Shanghai Key Laboratory of Children's Digestion and Nutrition

Introduction: Dysbiosis of gut microbiota underlies hepatocyte injury of nonalcoholic fatty liver disease (NAFLD). Deoxycholic acid (DCA), microbial metabolite of cholic acid, displays abnormality during the microecological imbalance. However, the association of DCA and NAFLD-related hepatocellular impairment remains uncertain.
Objectives: To investigate the effect of DCA on proliferative characteristics of hepatocytes and underlying mechanisms.
Methodology: HepG2 cells, with (FFA + DCA groups) or without free fatty acid (FFA, oleic acid: palmitic acid = 2:1) administration (DCA groups), were subjected to DCA (0, 300, 400, 500uM) stimulation for 12 h. The hepatocellular steatosis, triglyceride (TG), mitochondrial membrane potential (MMP), reactive oxygen species (ROS), and proliferative property were analyzed by oil red O staining, GPO Trinder method, JC-1 probe, DCFH-DA probe, and CCK-8 assay, respectively.
Results: In contrast to those without DCA exposure (0 μM), both DCA groups and FFA + DCA groups shared the decrease of MMP and upregulation of ROS in a dose-dependent manner. Proliferative attenuation took place on account of the mitochondrial depolarization and resultantly oxidative stress. Moreover, there was statistical deterioration of these intracellular markers in FFA + DCA groups in comparison to DCA groups at the same DCA concentration (Fig 1c, d), $P < 0.01$). Then the significant inhibition of cell proliferation rate characterized these FFA + DCA groups (Fig. 1e), $P < 0.01$). Except for that of DCA groups, FFA + DCA groups treated by different concentrations of DCA demonstrated comparable TG levels (Fig 1b).

Conclusion: DCA inhibits hepatocellular proliferation on a basis of mitochondrial oxidative stress. Steatosis may exacerbate the DCA-induced hepatocyte inviability.

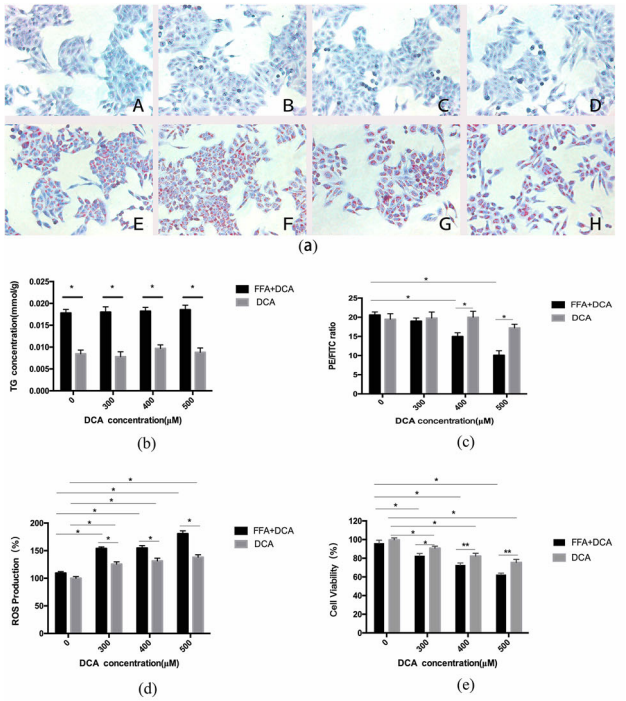


Figure1 (a)Effect of DCA and FFA on hepatic steatosis (×200); (b)TG concentration in HepG2; (c)Induction of mitochondrial depolarization by DCA; (d)ROS production caused by DCA intervention; (e)Effect of different concentrations of DCA on the viability of HepG2 cells. A: DCA group (0 μM DCA); B: DCA group (300 μM DCA); C: DCA group (400 μM DCA); D: DCA group (500 μM DCA); E: FFA + DCA group (500 μM FFA + 0 μM DCA);F: FFA + DCA group (500 μM FFA + 300 μM DCA); G: FFA + DCA group (500 μM FFA + 400 μM DCA); H: FFA + DCA group (500 μM FFA + 500 μM DCA). DCA:deoxycholic acid; FFA:free fatty acid. The presented results are expressed as means ± SD; *,P<0.01;**,P<0.001.

Abstract #238

Molecular insights into the grapeseeds extract's influence against induced-liver cancer both In vivo and in vitro

Amr Amin[1], Alaaeldin Hamza[2], Gehan Heeba[3], Hanan Elwy[4], Chandraprabha Murali[5], Raafat El-Awady[6]

[1]UAE University, [2]National Organization for Drug Control and Research, [3]Minia University, [4]National Organization for Drug Control and Research, [5]UAE University, [6]University of Sharjah

The purpose of this study was to investigate the anti-cancer property of grape seed extract (GSE) during early stages of developing liver cancer using a two-stage carcinogenic model combining diethylnitrosamine (DEN) and 2-Acetyl Aminofluorene (2-AAF). Administration of GSE at doses 25, 50 and 100 mg/kg per day started at the beginning of promotion periods and continued for 14 weeks. GSE dramatically inhibited pre-neoplastic foci formation as well as significantly decreased the number and the area of placental glutathione-S-transferase in livers of DEN-2AAF-treated rats by approximately 4 & tenfold deductions, respectively. GSE's effects were associated with induced apoptosis, reduced cell proliferation, decreased oxidative stress and down regulation of histone deacetylase activity and inflammation makers, such as cyclooxygenase 2, inducible nitric oxide synthase, nuclear factor-kappa B-p65 and p-phosphorylated tumor necrosis factor receptor expressions in liver. GSE treatment also decreased the viability of HepG2 cells and induced early and late apoptosis through activating caspase-3 and Bax. Furthermore, GSE induced G2/M and G1/S cell cycle arrest. The present study provides evidence that the GSE's anticancer effect is mediated through the inhibition of cell proliferation, induction of apoptosis, modulating oxidative damage and suppressing inflammatory response.

Abstract #273

Study of polymorphism of xeroderma pigmentosum complementation group C (XPC) – XPD in chronic liver disease and healthy individuals

Nitin Bhartia[1], Anup Kumar Das[2], Ranjan Bhattacharyya[3]

[1]Department of Medicine, Assam Medical College & Hospital & Dibrugarh, India, [2]Professor & Department of Medicine, Assam Medical College & Hospital & Dibrugarh, India, [3]Senior Resident & Department of Medicine, Assam Medical College & Hospital & Dibrugarh, India

Introduction: Cirrhosis a premalignant condition, xeroderma pigmentosum complementation group C (XPD) gene has polymorphisms Lys751Gln (751) and XPD Asp312Asn (312) that are associated with various malignancies including Hepatocellular carcinoma (HCC). We hypothesized that the gene polymorphisms also have role in cirrhosis.
Objectives: To study polymorphism of xeroderma pigmentosum complementation group C (XPC): XPD in chronic liver disease patients and healthy individuals.
Methodology: Two hundred cases and two hundred age, sex, ethnicity matched healthy controls were included. Inclusion criteria for patients were presence of cirrhosis and age > 13 years. Exclusion criteria were: patients with hepatocellular carcinoma, budd chiari syndrome, isolated portal vein thrombosis and other causes of non cirrhotic portal fibrosis.
Results: Fifty-one patients with chronic liver disease (CLD) i.e. (25.5%) had 751 polymorphism and 20 (10%) had 312 polymorphism. SNP, not detected in the control group. SNP 751 polymorphism was seen in 29 (14.5%) and 312 polymorphism in 13 (6.5%) patients of age group 41–60 years. SNP's are more with increasing age. Incidence of SNP's 751 and 312 was more in females. Smoking strongly associated in CLD patients with 751 polymorphism.
Conclusion: Both the polymorphisms are significantly associated with cirrhosis. How these minor alleles contribute to development of cirrhosis needs to be determined.

AGE	N	Percent	XPDLys751 Gln POLYMOR PHISM (HETERO ZYGOUS)	XPDLys751 Gln POLYMOR PHISM (HOMOZY GOUS)	XPDAsp312 Asn POLYMOR PHISM (HETERO ZYGOUS)	XPDAsp312 Asn POLYMOR PHISM (HOMOZY GOUS)
13-20	0	0	0	0	0	0
21-30	24	12	2	3	1	0
31-40	49	24.5	7	1	3	0
41-50	59	29.5	11	4	5	2
51-60	44	22	4	10	3	3
>60	24	12	6	3	1	2
Total	200	100	30	21	13	7

Table1: AGE Distribution

Observations: From the above table it is observed that maximum no of patients with XPDLys751Gln heterozygous polymorphism is within the age group of 41-50 years (11/30=33.67%) , similarly homozygous polymorphism for XPD Lys751Glu is maximum in the age group of 51-60 years (10/21=47.62%) . Again maximum no of cases with XPDAsp312Asn heterozygous polymorphism is within the age group of 41-50years (5/13=38.46%) and homozygous polymorphism for XPD Asp312Asn is within the age group of 51-60 years(3/7=42.85%).

SMOKING	N	Percentage	XPDLys751Gln POLYMORPHISM (HETEROZYGOUS)+ (HOMOZYGOUS)	XPDAsp312Asn POLYMORPHISM (HETEROZYGOU S)+ (HOMOZYGOUS)
PRESENT	49	24.5	4+17=21	4+1=5
ABSENT	151	75.5	26+4=30	9+6=15
p value			0.0013	0.9563

Table 2: Relation with Smoking

Observation: XPDLys751Gln polymorphism is 42.86% (21/49) among smokers and 19.87% (30/151) among non smokers. Similarly XPDAsp312Asn polymorphism is 10.20% (5/49) among smokers and 9.93% (15/151) among non smokers.

Abstract #354

The immunoregulatory effects of CD8 T cell derived perforin on diet-induced nonalcoholic steatohepatitis

Tian Qi Wang[1], Guang Yong Sun[1], Ya Ning Wang[1], Shu Xiang Li[2], Xin Yan Zhao[3], Hua Jin[1], Chun Pan Zhang[1], Dan Tian[1], Kai Liu[1], Wen Shi[1], Yue Tian[1], Dong Zhang[4]

[1]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China, [2]National Clinical Research Center for Digestive Diseases, Beijing, China, [3]National Clinical Research Center for Digestive Diseases, Beijing, China, [4]Experimental and Translational Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, China & National Clinical Research Center for Digestive Diseases, Beijing, China

Introduction: The liver is a central immunological organ with a high density of immune cells that play important roles in the development of nonalcoholic steatohepatitis (NASH). However, the underlying mechanisms remain obscure.

Objectives: We aimed to determine the role of perforin in the regulation of NASH development.

Methodology: WT and Prf1null mice consumed either a methionine and choline-deficient diet (MCD) for 4 weeks or a high-fat diet (HFD) for 16 weeks. NASH development was monitored and the activation, differentiation and proinflammatory cytokine secretion of liver infiltrated immune cells were compared in each group.

Results: Prf1null mice showed significantly higher plasma ALT levels, with increased liver fat accumulation, lobular inflammation and focal necrosis compared with WT mice fed with MCD or HFD. Perforin deficiency promoted the M1 polarization of infiltrated monocytes and increased accumulation, survival, activation and proinflammatory cytokine production of CD8 T-cells. Adoptive transfer indicated that CD8 T-cell derived perforin played a protective role in the development of NASH. In vitro, perforin deficiency decreased cytotoxicity of CD8 T-cells towards bone marrow-derived monocytes and promoted proinflammatory cytokine production of monocytes. Furthermore, RNA sequencing data indicated that the perforin deficiency inhibited cell apoptosis and enhanced the activation, migration and proinflammatory cytokine production of CD8 T-cells in mice with NASH.

Conclusion: We have elucidated an important role of perforin from CD8 T-cells in restricting hepatic inflammation in mice with NASH and suggest that therapies designed to maximize the function of endogenous perforin in CD8 T-cells might have potential benefits as NASH treatments.

Abstract #357

Fgl2 deficiency resists viral fulminant hepatitis through abrogating inflammatory macrophage activation

Fang Xiao[1], Hongwu Wang[1], Ran Tao[1], Xinxin Weng[1], Peng Wang[1], Di Wu[1], Xiaojing Wang[1], Weimin Yan[1], Dong Xi[1], Xiaoping Luo[1], Xiaoyang Wan[1], Qin Ning[1]

[1]Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology

Background and Aims: Virus-induced acute liver failure (or viral fulminant hepatitis, VFH), is devastating liver disease without specific intervention agents. Understanding the molecular and immune mechanism underlying VFH progression will give implications on therapeutic targets. Fgl2 is a membrane protein expressed on macrophages and promotes fulminant hepatitis progression, however, the detailed mechanism underlying immune alterations and through which Fgl2 modulates immune response during VFH remains unclear.

Design: Hepatic macrophages were analyzed in fgl2−/− mice and wild type littermates infected with murine hepatitis virus strain 3 (MHV-3) which induced VFH in mice. Phagocytosis, polarization, and inflammatory signaling were evaluated in fgl2−/− macrophages in response to Lipopolysaccharide or viral stimulation.

Results: Fgl2 expression is increased on macrophages in patients of HBV-associated liver failure. Kupffer cells (KCs) were replaced of by infiltrating monocyte-derived macrophages (MoMFs) in which Ly6Chigh MoMFs dominated myeloid cell population. Fgl2 was robustly induced on proinflammatory MoMFs and KCs following viral infection. In Fgl2-deficient mice, infiltrating macrophages were significantly reduced with less of Ly6Chigh MoMFs and more Ly6Clow MoMFs during VFH. Mechanistically, Fgl2 depletion impaired macrophage function as manifested by lowered capacity of phagocytosis, antigen-presentation potential, and attenuates proinflammatory polarization by abrogating IRF3 and NF-κB activation in response to viral infection.

Conclusion: Proinflammatory infiltrating macrophages were the major source of inflammation during VFH progression. Fgl2 induction on these cells orchestrates a positive feedback look for macrophages-derived inflammatory expansion leading to VFH progression by directly promoting classical inflammatory signaling.

Abstract #371

Proteomic approaches to identify the regulation of human telomerase reverse transcriptase in hepatocellular carcinoma cells

Sung Hoon Choi[1], Do Young Kim[1], Kwang-Hyub Han[1], Jun Yong Park[1]

[1]Department of Internal Medicine, Yonsei University College of Medicine & Yonsei Liver Center, Severance Hospital

Background/Aim: The human telomere transferase (hTERT) is very tightly regulated in large long-lived species. Telomerase is expressed during early human fetal development, is turned offin most adult tissues, and then becomes reactivated in almost all human cancers such as hepatocellular carcinoma (HCC). However, the exact mechanism regulating these switches in expression are not known. This study evaluated whether Knockdown of hTERT in HCC cell lines inhibited cell cycle and proliferation, and analyzed hTERT regulating proteins by proteomic analysis.
Methods: HCC cell lines were transfected with siTERT and cultured under normal conditions. Following transfection, the expression levels of TERT, StAR (steroidogenic acute regulatory protein), and HKR3 (Human Kruppel-related 3) were further confirmed as the proteomic analysis of hTERT through western blotting, while tumor growth was measured by cell proliferation assay and cell cycle assay (PI staining).
Results: hTERT regulating HCC cell lines showed that the up-regulation of T-StAR expression and down-regulation of HKR3 expression led to the increase of hTERT expression and telomerase activity. The inhibition of hTERT by small RNA interference led to the repression of tumor growth.
Conclusion: Our results suggested that T-STAR has a positive correlation with the telomerase activity while HKR3 may be a negative regulator. This conclusion is important to further explore the regulation pathways of human telomerase activity.

Abstract #392

The Importance of Liver Involvement in Crimean Congo Hemorrhagic Fever Infection

Selcuk Kaya[1], Gurdal Yilmaz[1], Firdevs Aksoy[1], Iftihar Koksal[1]

[1]Karadeniz Technical University, Medical Faculty, Department of Infectious Diseases and Clinical Microbiology, Trabzon, Turkey

Introduction: Crimean Congo Hemorrhagic Fever (CCHF) is a tick-borne disease and also the most prevalant type of infection among viral hemorrhagic fever over the world. It seen in more than 30 countries and may lead to the mortal infections. Virus spreads to lymphoid organs, reticuloendothelial cells via lymph and monocytes.
Objective: Detect the liver involvement and its prognostic significance in our patients.
Methodology: This study conducted at our hospital, between 2010 and 2017. One hundred fifty-two patients diagnosed with CCHF infection were evaluated retrospectively. Patients whose CCHF diagnoses were confirmed through detection of IgM using ELISA and/or the genomic segment of the virus using RT-PCR in the National Reference Virology Laboratory. The patients were divided into 2 groups; G1: ALT levels $\geq$ 150 U/L (n = 39), G2: $<$ 150 U/L (n = 113).
Results: Nineteen (48.7%) and 59 (52.2%) of patients were male in G1 and G2. Mean age of patients were 47.4 $\pm$ 17.1 and 50.0 $\pm$ 16.6 in G1 and G2. Levels of mean serum platelet counts were significantly lower in favor of G1 however aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), activated partial thromboplastin time (aPTT) were higher in G1 than G2. Mortality was seen in 6 (15.3%) and 1 (0.008%) patients in groups, respectively (Table).
Conclusion: Even if not the main target is liver, elevation of liver function tests are being thought that possibility of liver involvement in the course of systemic disease. Increase in liver function tests could be related with mortality therefore it should pay more attention such those patients.

Table: Clinicoepidemiological, laboratory and prognostic properties of patients according to the serum ALT levels.

	CCHF patients ALT≥150 n=39 (%)	CCHF patients ALT<150 n=113 (%)	p
Age	47.4±17.1	50.0±16.6	0.467
Gender (male)	19 (48.7)	59 (52.2)	0.707
Living in endemic area	34 (87.1)	102 (90.2)	0.588
Husbandry	32 (82)	82 (72.5)	0.238
Hospitalization duration	7.9±6.0	7.0±3.4	0.540
Need for thrombocyte	24 (61.5)	56 (49.5)	0.196
Mortality	**6 (15.3)**	**1 (0.008)**	**0.001**
Fever	36 (92.3)	91 (80.5)	0.087
Bleeding	20 (51.2)	39 (34.5)	0.064
PLT	**33410±22641**	**63754±34914**	**<0.0001**
WBC	1807±817	2206±1170	0.062
Hb	13.8±2.2	13.8±2.1	0.924
ALT	**325±180**	**66±34**	**<0.0001**
AST	**806±707**	**152±117**	**<0.0001**
T-bil	0.6±0.5	0.6±0.5	0.547
D-bil	0.3±0.4	0.2±0.4	0.122
LDH	**1459±920**	**799±518**	**<0.0001**
CPK	1165±1918	803±1848	0.373
Mg	567±486	771±911	0.762
PT	13.6±2.4	13.8±2.8	0.617
aPTT	**48.9±15.0**	**36.7±8.3**	**<0.0001**
INR	1.29±0.58	1.01±0.32	0.629
D-dimer	29.1±25.3	19.0±9.8	0.800

Abstract #409

Pegylated Interferon-α Inhibits the Proliferation of Hepatocellular Carci¬noma Cells by Downregulating miR-155

Ying Zhang[1], Ning Cheng[1]

[1]Sixth Department of Liver Diseases, Dalian Sixth People Hospital, Dalian Medical University, Dalian, Liaoning, PR China

Background: Interferon-α (IFN) has shown potential benefits in patients with hepatocellular carcinoma (HCC), and these effects may be mediated by inhibiting cancer cell proliferation. However, the detailed mechanisms underlying the anti-proliferative effects of IFN remain obscure. In this study, we evaluate the role of the novel oncogenic microRNA (miRNA) miR-155 in the anti-proliferative effects of pegylated interferon-α (PEG-IFN) on HCC cells.
Methods: The effects of PEG-IFN on HepG2 cell proliferation, migration and invasion were determined using the MTT assay, flow cytometry analysis and the Transwell assay, respectively. Reverse transcription quantitative polymerase chain reaction was used to analyse miR-155 expression. The levels of proteins involved in Wnt/

β-catenin signal transduction were determined by western blot analysis and immunofluorescence staining. Mimics of miR-155 were transfected into HepG2 cells to assess the role of miR-155 in the PEG-IFN-induced anti-proliferative effect.
Results: PEG-IFN significantly inhibited the proliferation, migration and invasion of HepG2 cells in a dose-dependent manner by inhibiting cell cycle progression. In parallel with reduced cell proliferation, migration and invasion, miR-155 was efficiently downregulated by PEG-IFN in a dose-dependent manner. Moreover, the transfection of miR-155 decreased the inhibitory effect of PEG-IFN on HepG2 cell proliferation, migration and invasion, as well as the downregulation of proteins in the Wnt/β-catenin pathway.
Conclusions: The anti-proliferative effects of PEG-IFN on HCC are at least partially attributable to the downregulation of miR-155.

Abstract #465

Messenger RNA transcriptome profiling reveals a distinct phenotype of human bone marrow mesenchymal stem cell-derived hepatocytes

Dongyan Shi[1], Jiaojiao Xin[1], Wenchao Ding[1], Jing Jiang[1], Qian Zhou[1], Suwan Sun[1], Yinyun Lu[1], Beibei Guo[1], Xingping Zhou[1], Jun Li[1]

[1]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine

Introduction: Human bone marrow mesenchymal stem cell differentiated hepatocytes (hBMSC-Heps) are promising alternatives to primary human hepatocytes (PHHs) for end-stage liver disease treatment. However, the differentiation basis remains unclear.
Objectives: To clarify the transcriptome characteristics of hBMSC-Hep.
Methodology: hBMSCs were isolated from bone marrow of health volunteers, and differentiated into hepatocytes. Messenger RNA sequencing was used to perform transcriptome profiling of hBMSC-Heps. hBMSCs and PHHs were used as controls.
Results: hBMSC-Heps exhibited a polygonal morphology, and expressed hepatocyte-specific genes such as albumin and alpha fetoprotein. hBMSC-Heps had a significantly different gene expression profile compared to hBMSCs. There were 630 up-regulated and 1082 down-regulated genes observed in hBMSC-Heps and PHHs compared with undifferentiated hBMSC. The up-regulated genes mainly involved in hepatic metabolism, lipid transport, inflammatory and immune responses. The down-regulated genes mainly associated with stem cell characteristics (multipotent differentiation, cell cycle regulation, cytoskeleton reorganization, et al.). Confirmatory quantitative RT-PCR of 18 genes (9 up- and 9 down-regulated) with $>$ fivefold changes had the similar results. Furthermore, the in vivo transdifferentiation system in pigs with fulminant hepatic failure confirmed 5 hepatogenic genes (TDO2, HP, SERPINA3, LBP and SAA1) similarly upregulated expression with 150-fold change in liver tissues at day 7 after hBMSC transplantation. Such 5 genes mainly contributed to the liver metabolism and inflammation.
Conclusion: hBMSC-derived hepatocytes possessed a hepatic transcriptome profile and expressed hepatic specific genes in vitro and in vivo, which might be used for future clinical application. The five genes could be potential biomarkers for characterization of hBMSC-derived hepatocyte.

Abstract #519

Study on preventive effect against non-alcoholic fatty liver disease (NAFLD) by propolis

Tomohiro Ogawa[1]

[1]Center for the Advancement of Higher Education, Faculty of Engineering, Kindai University

Introduction: Propolis is a honeybee product and has more than 300 components. We previously have reported the benefit effect of propolis on lipid metabolism and liver injury. However, each effect of propolis components on liver injury has understood poorly. In this study, we examined the effect of propolis components on free fatty acid-treated hepatic cells and fatty liver in mice.
Materials and Methods: Mice which gave high-fat diets or methionine and choline-deficient diets induced fatty liver, inflammation and fibrosis. We examined the effect of propolis on these models with histological analysis, gene expression analysis, and biochemical analysis. A human hepatocellular carcinoma cell line HepG2 cells were induced cell apoptosis by free fatty acid (0–800 μM) and then added propolis (0–0.1 mg/ml) or propolis components (0–0.1 μM). The effect of propolis and its components was analyzed by cell proliferation test, fat staining, and gene expression analysis related to endoplasmic reticulum (ER) stress by real-time PCR.
Results: Propolis suppressed fat accumulation and liver metabolism in fatty liver-induced mice. Additionally, propolis suppressed gene expression related to ER stress such as CHOP, ATF4, IRE1a, and GADD34. Propolis suppressed cytotoxicity in a dose-dependent manner on free fatty acid-treated HepG2 cells. Furthermore, we identified some propolis components which inhibited the cytotoxicity. Additionally, the expression of genes related to ER stress significantly suppressed in propolis-treated HepG2.
Conclusions: Propolis contains many components, and some of components have protective effect against liver damage, suggesting the preventive effect of liver damage by propolis components.

Abstract #538

Interaction between HBx gene and Alcohol; Is there really synergy effect on hepatic steatosis?

Jung Hwan Yu[1], Jin-Woo Lee[1], Eun Young Cho[2], Hong-Seob So[3]

[1]Department of Internal Medicine, Inha University College of Medicine, Korea, [2]Department of Internal Medicine, Wonkwang University College of Medicine, Korea, [3]Department of Microbiology, Wonkwang University College of Medicine, Iksan, Korea

Introduction/objectives: HBx (hepatitis B viral protein) gene is a hepatitis B viral protein and associated with hepatocarcinogenesis. Until now, the association between HBx gene and alcohol-induced hepatic steatosis is not well understood. The aim of this study is to investigate the relationship between HBx gene and alcohol, and the mechanism of hepatic steatosis in HBx transgenic mice.
Methodology: HBx transgenic (TG) and control C57BL/6 mice were used for alcohol-induced hepatic steatosis experiment.
Results: In alcohol fed mouse model, we could find out that HBx TG mice had more triacylglycerol accumulation in liver tissue and more lipid droplet (especially microvesicular steatosis) on the liver tissue slide than wild-type control mice. To investigate the association between HBx gene and hepatic steatosis, we analyzed the gene associated with beta oxidation and lipid accumulation. We could find out that genes associated beta oxidation such as ACOX1, EHHADH,

PEX11a, CTP1A, and MCAD were decreased, and genes associated lipid accumulation were increased PLIN3 and FSP27 in HBx TG mice. In binge drinking mice model, to investigate the effect in a short time period, we could also get the similar result. As a result, we could see that HBx TG mice had more synergy effects in alcohol-induced hepatic steatosis than WT mice by decreasing beta oxidation of lipid.
Conclusion: Although it is not known exactly how hepatitis B affects fatty liver disease, this study seems to be useful in revealing these interrelationships, particularly in confirming the effect of HBx gene and beta oxidation reduction on fatty liver formation.

Abstract #541

Multi-transcriptomes analyses reveal prioritized genes specifically associated with liver fibrosis progression independent of etiology

Wei Chen[1], Xiaoning Wu[1], Xuzhen Yan[1], Aiting Yang[1], Hong You[1]

[1]Liver Research Center, Beijing Friendship Hospital, Capital Medical University

Introduction: Elimination or suppression of causative factors can raise the possibility of liver fibrosis regression. However, different injurious stimuli will give fibrosis from somewhat different etiologies, which, in-turn, may hamper the discovery of liver fibrosis-specific therapeutic drugs.
Objectives: To clarify the common therapeutic targets specific to liver fibrosis regardless of any etiology.
Methodology: Transcriptomic datasets regarding to liver fibrosis with different etiologies were retrieved from public available Gene Expression Omnibus (GEO) database. A series of bioinformatics analyses including differentially expressed genes (DEGs) identification, functional enrichment analysis, gene–gene interaction network establishment and hub gene analysis, correlation analysis, and robustness analysis were carried out. Experimental verification was performed in cultured hepatic stellate cells (HSCs).
Results: A total of 111 up-regulated and 16 down-regulated genes were identified specific to liver fibrosis independent of any etiology. These genes were predominately enriched in some KEGG pathways including "PI3K-AKT signaling pathway", "Focal adhesion" and "ECM-receptor interaction". Subsequently, 5 prioritized liver fibrosis-specific genes including COL4A2, THBS2, ITGAV, LAMB1 and PDGFRA were screened. These genes were positively associated with each other and liver fibrosis progression. They could robustly separate all stages of samples in all datasets with diverse etiologies when they were regarded as observed variables applied to PCA plots. Expressions of all the five genes were confirmed in cultured primary mouse HSCs and TGFβ-induced LX-2 cells.
Conclusion: Our current study highlighted the common cellular and molecular events underlying general liver fibrosis regardless of any etiology. These data may provide potential targets for liver fibrosis therapy.

Abstract #553

Delay in hepatocyte proliferation and prostaglandin D2 synthase expression for cholestasis due to endotoxin during partial hepatectomy in rats

Yusuke Wakasa[1], Norihisa Kimura[1], Toshiyuki Yamada[2], Takeshi Shimizu[1], Kenichi Hakamada[3], Shigeki Tsuchida[1]

[1]Department of Gastroenterolocal Surgery, Hirosaki University Graduate School of Medicine, [2]Department of Biochemistry and Genome Biology, Hirosaki University Graduate School of Medicine, [3]Department of Gastroenterological Surgery, Hirosaki University Graduate School of Medicine

Background/aims: We examined lipopolysaccharide (LPS)-induced effects of cholestasis on hepatocyte proliferation and anion transporter expression after hepatectomy.
Methods: Male Sprague–Dawley rats were subjected to 70% partial hepatectomy (PH) and/or LPS injection, and tissues were harvested at 0, 24, 72, and 168 h. Gene expression was analyzed by microarray analysis and quantitative real-time polymerase chain reaction, and protein levels and localization were analyzed by western blotting and immunohistochemistry, respectively.
Results: Plasma bile acid levels were significantly higher in the LPS + 70% PH group than in the 70% PH group. Ribonucleotide reductase regulatory subunit M2 and proliferating cell nuclear antigen peaked at 24 and 72 h in the 70% PH group and LPS + 70% PH group, respectively. Multidrug resistance-associated protein member 2 and organic-anion-transporting polypeptide 1a1 and 1a2 were significantly reduced in the PH groups at 24 h. Chemokine ligand 9 (Cxcl9) increased after 24 h in the LPS groups. The number and shape of Cxcl9-positive cells in the LPS groups were similar to CD163-positive cells. Hematopoietic prostaglandin D2 synthase (Ptgds2) was only detected in the LPS + 70% PH group.
Conclusions: LPS-induced cholestasis after PH may depend on Ptgds2-induced suppression of hepatocyte proliferation rather than suppression of anion transporter expression.

Abstract #558

A case of sudden loss of vision secondary to bilateral endogenous endophthalmitis as septic complication of pyogenic liver abscess caused by *Klebsiella pneumonia*

Marc Julius Hernandez Navarro[1], Ian Homer Yee Cua[1]

[1]St. Luke's Medical Center - Quezon City

Significance: Endogenous endophthalmitis (EE) is an uncommon intraocular infection with potentially devastating visual consequences. It is initially associated with visual impairment, leading to loss of vision despite aggressive treatment (1, 2). A pyogenic liver abscess (PLA) is a serious life-threatening condition. EE is reported to be the most serious septic complication of pyogenic liver abscess with stated incidence of 0.84% during 1 year of pyogenic liver abscess follow-up (2).
Clinical presentation: Presented with a 61-year-old, female, non-hypertensive, diabetic, who came in because of loss of vision. She presented with two weeks history of eye pain, photophobia, erythema, and sudden blurring of vision that progressed to loss of vision involving both eyes. Pertinent initial physical examination revealed no light perception, severely hyperemic conjunctivae, slightly hazy cornea, lens opacity; the rest of the physical examination was unremarkable.
Management: Managed initially as panuveitis, given topical opthalmic drops, valaciclovir, oral prednisone, and acetazolamide. She underwent pars plana vitrectomy, phacoemulsification, with intravitreal injection of antibiotics, on both eyes. Purulent vitreous aspirate and blood cultures exposed *Klebsiella pneumonia*. To further investigate, ultrasound of the abdomen was done which revealed a hepatic abscess in the right lobe measuring approximately 4.0 × 5.0 × 5.2 cm. Patient was then managed accordingly as a case of pyogenic liver abscess secondary to *Klebsiella pneumonia* complicated with bilateral endogenous endophthalmitis.
Recommendations: Early recognition of the disease is a must because failure to make a timely diagnosis and to intervene at an early

stage poses substantial risks (including permanent loss of vision) to affected patients.

Abstract #567

DLL4 restores damaged liver by protecting hepatocytes and enhancing cholangiocyte differentiation

Suwan Sun[1], Dongyan Shi[1], Jiaojiao Xin[1], Jing Jiang[1], Qian Zhou[1], Jiang Li[1], Li Shao[1], Lingling Yang[1], Hozeifa Mohamed Hassan[1], Yinyun Lu[1], Beibei Guo[1], Xingping Zhou[1], Jun Li[1]

[1]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine

Introduction and objectives: Hepatocyte necrosis and intrahepatic cholangiolar injury are the main pathological mechanisms of fulminant hepatic failure (FHF). Delta-like ligand 4 (DLL4)–mediated Notch activation contributes to reversing hepatic and biliary injury. However, its detailed mechanism is still unclear. This study aimed to clarify the role of DLL4 in restoring damaged liver by protecting hepatocytes and enhancing cholangiocyte differentiation.
Methodology: The efficacy of DLL4 was evaluated in a rat model of FHF by determining the survival rate, observing the liver structure and examining the biochemical index. The human hepatocyte line QSG-7701 was transfected with pcDNA-DLL4 and si-DLL4 to evaluate the protective effects of DLL4. The potency of DLL4 in inducing cholangiocyte differentiation from human bone marrow mesenchymal stem cells (hBMSCs) was assessed by measuring the expression of cholangiocyte-specific genes and proteins.
Results: DLL4 treatment significantly prolonged the survival of rats with FHF ($p < 0.05$). Liver tissue structure and biochemical functions were significantly improved in rats in the DLL4 treatment group. The hepatocyte-specific markers albumin (ALB), alpha fetoprotein (AFP), cytokeratin 18 (CK18), hepatocyte nuclear factor 4 alpha (HNF4 alpha) and cytochrome P-450 (CYP450) were upregulated by DLL4 overexpression and downregulated by DLL4 knockdown in cultured QSG-7701 hepatocytes. Furthermore, hBMSC-derived cholangiocyte-like cells induced by DLL4 showed a specific increase in the expression of cholangiocyte-specific genes (e.g., CK19, Sox9 and CFTR).
Conclusion: DLL4 restores damaged liver by protecting hepatocytes and enhancing cholangiocyte differentiation from hBMSCs, and DLL4 has the potential to be used in future clinical therapeutic applications.

Abstract #607

MicroRNA-221-5p Contributes to Liver Cancer Progression through Upregulation of CD44/TGF-β1 Expression

Na Ri Park[1], Jung Hoon Cha[1], Sung Woo Cho[1], Jeong Won Jang[1], Jong Young Choi[1], Seung Kew Yoon[1], Si Hyun Bae[1]

[1]The Catholic University Liver Research Center, College of Medicine, The Catholic University of Korea, Seoul, Korea

Introduction/Objectives: CD44 have known as important modulators of epithelial-mesenchymal transition (EMT) together with transforming growth factor beta1 (TGF-β1). Moreover, CD44 and TGF-β1 double positive more enhanced cancer stem cell characteristics acquisition, EMT, and metastasis. This study aimed to investigate the function of miRNA-221-5p regulating the EMT with CD44/TGF-β1 in HCC cells.
Methodology: We sorted CD44− and CD44+ liver cancer stem cells by fluorescence-activated cell sorting (FACs) in TGF-β1-positive SNU-368 cells and TGF-β1-negative SNU-354 cells. The miRNA profiles of CD44− and CD44+ HCC cells were analyzed by next-generation sequencing (NGS). miR-221-5p mimic and inhibitors were transfected into HCC cells. The expression of mRNA and protein were detected by quantitative real-time PCR (qRT-PCR) and western blot.
Results: miRNA NGS data were compared among CD44 or TGF-β1 single expression HCC cells and CD44/TGF-β1 double positive HCC cells. The results showed that miR-221-5p expression was up-regulated in CD44+/TGF-β1+ cells than an expression of either one alone. TGF-β1-stimulated SNU-354 cells increased expression of miR-221-5p and induced EMT. Inhibition of TGF-β1 in SNU-368 cells reduced expression of miR-221-5p and suppressed EMT. Overexpression of miR-221-5p induced EMT with up-regulation of CD44/TGF-β1. miR-221-5p overexpression also showed enhanced migration. Inhibition of miR-221-5p showed increased E-cadherin with down-regulation of CD44/TGF-β1. Finally, TGF-β1 stimulation after miR-221-5p inhibition induced neither the mesenchymal phenotype nor cell migration.
Conclusion: Overexpression of miR-221-5p promotes EMT with the high expression of CD44/TGF-β1. By the inhibition of miR-221-5p showed reversed EMT. The results suggest that CD44/TGF-β1-regulated miR-221-5p may serve as specific biomarkers and therapeutic targets for HCC.

Abstract #624

Clinical Profile, Diagnostic Characteristics and Management of Patients with Liver Abscess: A Single Center Experience

Herlyn Cervantes Abasolo[1]

[1]Cebu Doctors' University Hospital

Introduction: As one of the developing country and with the rising incidence of diabetes mellitus, prompt diagnosis and application of ideal management in patients with liver abscess should be implemented to avoid high mortality rate.
Objectives: To describe the clinical profile, diagnostic characteristics and management approach of patients with liver abscess in our locality and recognize diagnostic features that influences management.
Methodology: This is a retrospective descriptive study using the data retrieved from the medical records of patients diagnosed with liver abscess from January 2014 to November 2018. Pertinent data were identified and Chi square testing was used to determine possible diagnostic features that influence choice of management. Level of significance was set at 0.05.
Results: A mean age of 49.88 + 15.713 years with male predominance was noted. Fever and abdominal pain were the most common symptoms and majority of the abscess are located in the right lobe and are solitary. Only the size and volume of the abscess are significant in the factors that influence management (p value of 0.005 and 0.009, respectively) in which abscess measuring < 5 cm with less than 100 cc volume are more likely to be intervened medically.
Conclusion: Consistent with other studies, liver abscess are more common in males and frequently presents with fever and abdominal pain. Most abscesses are solitary and located in the right lobe. Abscesses < 5 cm with volume of < 100 cc, are more likely to be managed conservatively while radiologic invasive procedures are preferred for abscess of more than 10 cm and > 200 cc in volume.

Abstract #663

Pristine C60 fullerenes suppress liver fibrosis and early carcinogenesis on rat hepatocellular carcinoma model

Halyna Kuznietsova[1], Natalia Dziubenko[1], Tetiana Herheliuk[2], Olena Perepelytsina[2], Yuriy Prylutskyy[1], Uwe Ritter[3], Peter Scharff[3], Volodymyr Rybalchenko[1]

[1]Taras Shevchenko National University of Kyiv, [2]Institute for Problems of Cryobiology and Cryomedicine of the National Academy of Sciences of Ukraine, [3]Technische Universität Ilmenau

Introduction: Hepatic cancer in most cases is the consequence of liver fibrosis and cirrhosis and attributed to oxidative stress, therefore antioxidants usage could be promising treatment of those.
Objective: To evaluate the possible protective effects of effective free radical scavengers pristine C60 fullerenes using rat hepatocellular carcinoma (HCC) model and their impact on expression of EGFR and cytokeratin receptors (CKR) as profibrotic markers.
Methods: *N*-Diethylnitrosamine (DEN) + CCl4-induced HCC model was used. Pristine C60 fullerene aqueous colloid solution (C60FAS; 0.15 mg/ml) was injected daily at dose of 0.25 mg/kg starting in 2 weeks from DEN injection. Liver injury was evaluated according to 13-point scale, blood serum biochemical tests were performed. EGFR and CKR expression in HepG2 cells were assessed after 48 h incubation with 10 and 100 μg/ml C60FAS.
Results: HCC-rats at 10-week stage (corresponds to liver fibrosis) demonstrated liver damage score 8.2 points and alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) increase. C60FAS decreased liver injury and normalized ALP and LDH, suggesting inhibition of liver fibrogenesis. In HCC-rats at 15-week stage (corresponds to cirrhosis and neoplasia) liver injury progressed, alanine-(ALT) and aspartate-aminotransferases (AST), conjugated and unconjugated bilirubin, ALP and LDH dramatically increased (by 2–28 times). C60FAS diminished liver injury, depressed ALP and LDH and normalized bilirubin. C60FAS inhibited EGFR and CKR expression in HepG2 cells in a dose-dependent manner (by 22–70%).
Conclusion: C60FAS could inhibit liver fibrogenesis and malignant degeneration and maintain its functional activity. These effects could be realized through inhibition of EGFR and CKR expression in liver cells.

Abstract #686

Ruptured Liver Abscess With Hepatopleural Fistula Formation: A Case Report

Marie Rose Antoniette Sitchon Ajoc[1], Junmay Giltendez Dacal[1], Enjel A. Gabriel[1], Marie Geraldine San Jose Lim[1]

[1]Cebu Doctors' University Hospital

Significance: Pyogenic liver abscess causing thoracic empyema due to rupture of an abscess is rare. The formation of hepatopleural fistula secondary to this condition is even rarer with few cases reported but only involving amoebic liver abscess.
Clinical Presentation: A 53 year old female, Filipino patient with no predisposing medical conditions presented initially with 4 weeks anorexia, body malaise and intermittent right upper quadrant discomfort later developing subcostal pain and dyspnea. Chest imaging revealed right pleural effusion which on thoracentesis showed frankly purulent fluid and a septated liver abscess located at superior aspect of the right hepatic lobe. A fistulous tract to the adjacent right pleural space was confirmed later with CT scan.
Management: Patient initially underwent thoracentesis and drainage of liver abscess with pigtail catheter drain. Negative culture, persistent leukocytosis and delayed resolution of empyema prompted referral for chest tube thoracostomy insertion with deloculation and prolonged IV antibiotics. Serial imaging showed improvement along with decreasing volume of drainage. Meropenem was completed for 2 weeks and patient was sent home on oral ciprofloxacin for total duration of 6 weeks.
Recommendations: Hepatopleural fistula formation from a ruptured liver abscess is a rare condition. However, this should be considered as one of the differential diagnosis in patients with empyema thoracis even in the setting of atypical presentation and absence of risk factors to this condition. Mean time to resolution of abscess and closure of hepatopleural fistula after drainage as well as indications for removal of drains need further studies.

Abstract #747

Early satiety and abdominal discomfort with latent myeloproliferative neoplasm

Kogula Kumaresan Rajoo[1], Olga Ivanovna Tarasova[1], Alexander Vasilivich Pivnik[1], Manana Aleksandrovna Sokolova[2], Nikolai Igorivich Stuklov[1], Pavel Petrovich Ogurtsov[1]

[1]Rudn University, [2]National Research Center for Hematology

Background: Although early satiety and abdominal discomfort are usually attributed to gastrointestinal pathologies, our experience indicates that hematological factors need to be excluded especially myeloproliferative neoplasms regardless of the complete blood count results.
Case: Ten women aged between 20 and 51 years old were referred to our team for further investigation with complaints of early satiety and abdominal discomfort accompanied by generalized weakness and fatigue. They had previously undergone a battery of test (complete blood count, blood biochemistry, liver function test, and esophagogastroduodenoscopy) at their respective care providers. As per their medical records, their results were not indicative of any pathology. Our team repeated the complete blood count and blood biochemistry with results within the normal parameters. On physical examination, an enlarged spleen was palpated in all the women. An abdominal ultrasound confirmed our findings. On suspicion of latent myeloproliferative neoplasm, the women were tested for Jak2V617F mutations. They tested positive for the Jak2V617F mutations although only four of them had positive bone marrow changes in a subsequent bone marrow biopsy.
Conclusion: Jak2V617F mutation testing is a non-traumatic, non-invasive, precise and sensitive method for the diagnosis of myeloproliferative neoplasms especially in cases of latent myeloproliferative neoplasms which do not exhibit changes in the peripheral blood and bone marrow in the initial stages of the disease.

Abstract #765

Human menstrual blood-derived stem cells secretome attenuates liver injury by inhibiting NLRP3 inflammasome through autophagy and promote liver regeneration after partial hepatectomy

Yalei Zhao[1], Linxiao Fan[1], Er'mei Chen[1], Kaizhou Huang[1], Lanjuan Li[1]

[1]State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, Collaborative Innovation Center for Diagnosis and

Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China

Introduction: Recently, many researches focus on the therapeutic role of stem cell derived factors in liver diseases for their paracrine effect. Human menstrual blood-derived stem cells (MenSCs) have been demonstrated in various disease models for their therapeutic potential. While, whether MenSCs derived secretome (MenSC-Secretome) have a role in liver regeneration remains unclear. Thus, we discussed here whether MenSC-Secretome could promote liver regeneration in a rat model and the potential mechanism.
Objectives: To investigate the potential role of MenSC-Secretome in liver regeneration.
Methodology: Partial hepatectomy (PH) was conducted according to the classical 70% liver mass resection. Sprague Dawle rats were randomly assigned to 5 groups: normal control group (NC), sham control group (Sham), partial hepatectomy and vehicle treated group (PH), partial hepatectomy and non-conditoned medium group (NM), partial hapetectomy and MenSC-Secretome group (MenSC-S). Rats were sacrificed at 24 h and 48 h after PH and plasma and liver tissue were harvested.
Results: After PH, TLR4, NLRP3 and cleave-Caspase1 were up-regulated in liver and plasma IL1β was also elevated, which indicated the NLRP3 inflammasome was activated. In MenSC-S group, the liver/body weight was higher and Ki67+ positive hepatocytes were more ($P < 0.05$), with less severe liver injury. Moreover, liver expression of LC3-II was elevated and LC3-I was degraded, thus autophagy was promoted after MenSC-S treatment. And expression of NLRP3 and cleave-Caspase1 was attenuated compared to the PH group and plasma IL1β was also normalized.
Conclusion: MenSC-Secretome might promote autophagy to inhibit NLRP3 inflammasome after liver partial hepatectomy and promote liver regeneration.

Abstract #775

Development of murine model of Acute-on-Chronic Liver Failure

Nidhi Nautiyal[1], Deepanshu Maheshwari[1], Dhananjay Kumar Mathur[1], Rekha Kumari[1], Anupama Parasar[1], Chhagan Bihari[2], Rakhi Maiwall [7], Anupam Kumar[1], Shiv Kumar Sarin[3]

[1]Molecular and Cellular Medicine, Institute of Liver and Biliary Sciences, [2]Department of Pathology, Institute of Liver and Biliary Sciences, [3]Department of Hepatology, Institute of Liver and Biliary Sciences

Introduction: Acute-on-chronic liver failure (ACLF) is characterized by liver failure due to acute hepatic injury on an underlying chronic liver disease, accompanied by acute decompensation, organ failure, and high mortality. Pathophysiology of disease remains unclear, thus necessitating the need for animal model.
Aim and objective: To develop murine model mimicking characteristics of human ACLF.
Methodology: Intraperitoneal dose of CCl4 was given to C57BL6/C mice (n = 25), 5 animals were sacrificed at week 10 to confirm cirrhosis. Remaining animals were injected with LPS and Acetaminophen. Animals were sacrificed on day 2 and day 11 for biochemical and histopathological analysis. Ascitic Fluid (AF) was collected wherever possible.
Results: Cirrhosis was confirmed through histological and biochemical changes post 10 weeks of CCl4 dosage, increase in AST (198 ± 10.75 IU/L); ALT (155 ± 22 IU/L); Total Bilirubin (0.68 ± 0.09 mg/dL); Ammonia (263 ± 19.2 μg/dL); decrease Albumin (1.2 ± 0.24 mg/dL) were observed. Histology showed no evident secondary organ damage. After LPS and Acetaminophen dose, 4 animals died within 24 h. Liver histology of mice at day 2 showed necrosis, fibrosis and inflammation. Animals sacrificed on day 11 showed AF with SAAG 1.27 ± 0.1 g/DL. Histology showed bridging fibrosis, cholestasis, increased inflammation and necrosis with increased Ammonia (623.4 ± 63.9 μg/dL); Total Bilirubin (1.53 ± 0.16 mg/dL); decreased AST (124 ± 29.45 IU/L); ALT (98.75 ± 21.2 IU/L); Albumin (1.2 ± 0.1 g/dL); Creatinine (0.14 ± 0.01 mg/dL) and BUN (15.8 ± 0.86 mg/dL). Out of 14 animals; 4 showed interstitial pneumonia (IP); 3 showed Acute-Tubular-Necrosis (ATN); 1 showed both IP and Exudate Pneumonia and 2 showed the presence of both IP and ATN.
Conclusion: Our model shows close similarity with human ACLF displaying all the characteristics as per APASL guidelines.

Abstract #785

Evaluation of GeneXpert for Detecting HCV Viral Load from Dried Plasma Spots Collected on Filter Paper

Anugrah Dwi Handayu[1], Rino Alvani Gani[1], Irsan Hasan[1], Andri Sanityoso Sulaiman[1], Chyntia Olivia Maurine Jasirwan[1], Juferdy Kurniawan[1]

[1]Hepatobiliary Division, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital, Jakarta, Indonesia

Introduction: Hepatitis C virus (HCV) is one of the leading causes of chronic liver diseases in the world. To detect RNA, dried plasma spots collected on filter paper can be used as an alternative method to collect sample in remote area with limited laboratory facility.
Aim: To compare HCV RNA detection between dried plasma spots collected on filter paper with peripheral blood plasma samples using GeneXpert tools.
Materials and Methods: Eight plasma samples were obtained from chronic hepatitis C patients. HCV RNA is tested using Xpert® HCV Viral Load. Approximately 200 μL of plasma was dropped on 3 × 1 cm Whatman filter paper 90-mm. As the filter paper dry in the plastic clip, it is stored for 1 week at room temperature (27–33 °C). The filter paper is then dissolved in 1 mL of Nuclease Free Water and incubated for an hour at 37 °C. After that, we use Xpert® HCV Viral Load to detect HCV RNA.
Results: In dried plasma spots collected on filter paper group, HCV RNA was detected on 8/8 (100%). However, the level of HCV RNA was decrease about 2 log compared to peripheral blood plasma samples.
Conclusions: HCV RNA detection from dried plasma spots collected on filter paper can be recommended as an alternative methods in limited setting area.
Keywords: HCV RNA, GeneXpert, filter paper.

Abstract #786

Comparison of the Safety and Efficacy of Two Percutaneous Ethanol Injection Techniques for Non-parasitic Hepatic Cysts

Ron Michael Murcia Tan[1], Stephen Ng Wong[2]

[1]Chinese General Hospital, [2]Chinese General Hospital & University of Santo Tomas Hospital

Background: There are no universally accepted techniques for percutaneous ethanol sclerotherapy (PES) of hepatic cysts. Increasing the volume of ethanol may increase efficacy at the expense of increased

complications. We aimed to compare two PES techniques with different ethanol volumes.
Methods: Consecutive patients with evaluable non-parasitic hepatic cysts who underwent PES from May 2007–July 2018 were included. Method1 underwent PES with ethanol (99.9%) not exceeding 100 mL and 10% of the aspirated volume while Method 2 exceeded these parameters. Cyst volume was estimated on ultrasound at 1 and 6 months, and every 6 months thereafter, after PES. PES effectivity was analyzed only in patients with > 1 month follow-up while PES safety was assessed for all patients.
Results: A total of 60 patients were included. The most common indications for PES were pain (83.3%) and early satiety (13.3%). Method 2 patients (n = 38) had significantly larger cysts (13.9 ± 4.4 vs. 9.8 ± 2.7; $p < 0.001$) with larger volumes (1353.6 ± 1100.2 vs. 498.5 ± 457.6; $p < 0.001$) and consequently larger volume of ethanol injected (197 ± 76 vs. 71.4 ± 28; $p < 0.001$). There was no difference in complication rates between the 2 methods (Method 1 = 0% vs. Method 2 = 10.5%; p = 0.286). Although all complications (bleeding/hypotension [n = 3] and intoxication [n = 1]) occurred in Method2, none resulted in significant morbidity. As a percentage of the aspirated volume, cyst volume significantly decreased over time with no difference between the 2 methods at 1 month: Method 1 = 35.2 ± 30.5% vs. Method 2 = 56.2 ± 27.1%; p = 0.103, 6 months: Method 1 = 18.2 ± 23.8% vs. Method 2 = 29.6 ± 34.1%; p = 0.355, and at last follow-up: Method 1 = 31.7 ± 64.3% vs. Method 2 = 22.7 ± 28%; p = 0.637).
Conclusion: PES is an effective treatment option for symptomatic hepatic cysts. Caution is warranted in increasing the volume of injected ethanol because it doesn't increase effectiveness and may lead to more complications.

Abstract #803

Intermittent restraint stress attenuates hepatic steatosis and inflammation in a high fat-diet fed-mouse model

Chang Gue Son[1], Sung Bae Lee[1]

[1]Institute of Traditional Medicine and Bioscience, Daejeon University, South Korea

Nonalcoholic fatty liver disease (NAFLD) is major cause of chronic liver disorders and the NAFLD prevalence has been reported as 9–40% of the general populations in worldwide. Meanwhile, stress is another risk factor in the development and progression of diverse diseases including metabolic syndrome and cardiovascular disease. We have evaluated the effects of intermittent restraint stress, which did not damage the liver, on NAFLD in a high-fat diet (HFD) mouse model. C57/BL6 mice had free access to a 60% HFD for 8 weeks, with or without repeated restraint stress conducted (3 h, 3 times a week). HFD feeding substantially increased fat accumulation overall including liver tissues. The levels of hepatic total cholesterol and triglycerides were significantly ameliorated in HFD with stress group compared to the HFD alone group. These beneficial results were in accordance with liver enzyme levels (AST, ALT) and hepatic levels of TNF-α and oxidative stress parameters (ROS, NO and malondialdehyde). The HFD feeding induced the unbalance between lipogenesis and lipolysis, which were evidenced by alterations of serum insulin level, hepatic protein kinase B (AKT) activity and the gene expressions especially related to lipogenesis. However, the intermittent restraint stress significantly attenuated those alterations and augmented the elevation of serum epinephrine concentration. Energy expenditure markers (UCP1, PGC1α) in brown adipose tissue were reduced by each stress or HFD, while moderately normalized in HFD with stress group. Thus our findings showed the beneficial effects of intermittent restraint stress on high fat intake-associated hepatic steatosis and inflammation.

Abstract #833

In vitro Hepatic Bio-engineering: Bi-directional dual cell repopulation in decellularized liver

Dinesh Mani Tripathi[1], Savneet Kaur[2], Preety Rawal[2], Sumati Rawal[3], Abhishak Gupta[2], Shiv Kumar Sarin[2]

[1]Institute of Liver and Biliary Sciences, Delhi, India, [2]Institute of Liver and Biliary Sciences, New Delhi, India, [3]Institute of Liver and Biliary Sciences (ILBS), [4]Institute of Liver and Biliary Sciences Vasant Kunj, New Delhi

Introduction: Whole-organ decellularization has emerged as a lucrative option for tissue engineering and generation of bioartificial organs. However, inappropriate cell seeding limits the applications of the artificial organ development.
Objectives: The present study aimed at decellularization of whole rat liver followed by repopulation with parenchymal and non-parenchymal cells.
Methodology: Rat livers were decellularized in situ by portal vein perfusion. Ultra-structural characterization of decellularized liver matrix was carried out by tissue histology, DNA quantification assays and scan electron microscopy (SEM). Fluorescently labeled hepatic immortalized cell line Huh7 and human umbilical vein endothelial cells (HUVECs) in appropriate ratios were seeded into decellularized whole-liver scaffolds. In vitro, Huh7 were seeded via the biliary duct and HUVECs through the portal vein, respectively. Post-recellularization, cell adhesion in the livers was quantified by fluorescence microscopy and histology.
Results: Histology and SEM analysis demonstrated acellularity and preservation of three-dimensional micro anatomy of decellularized liver. Connective tissue fibers and intact vascular structures were clearly visible in cell free spaces. DNA content of decellularized liver was less than 50 ng/mg of tissue confirming complete acellularity. After 24 h of recellularization, parenchymal cells seeding through biliary duct led to 40% hepatocyte distribution into parenchymal matrix, and about 65% HUVECs were simultaneously observed on liver sinusoids. Seeded cells maintained significant viability in recellularized liver. Functional assays are underway to assess the functionality of recellularized liver at various time points.
Conclusion: Liver recellularization via bi-catherization using dual cell population is a potential approach for the production of bio-engineered liver grafts for various applications.

Abstract #873

Correlation of FibroScan with CAP and 2 D-Echocardiography Findings on Diabetic patients in Fatima University Medical Centre (FUMC) – A Retrospective Observational Study

Parashu Ram Ghimire[1]

[1]Fatima University Medical Centre

Introduction/background: In this study the status of liver steatosis and fibrosis has been evaluated, correlated with the 2 D Echocardiography results.
Objective: The aim of this study was to co-relate the findings of transient elastography (FibsoScan) and controlled attenuation parameters (CAP) to that of the 2 D echocardiography results.

Methods: The retrospective observational study was performed on the diabetic patient who underwent FibroScan and 2 D echocardiography.
Results: A total of 33 patients were enrolled in the study to evaluate and correlate results of FibroScan with CAP to that of 2D Echocardiography results. Mean age is around 55, mostly female (60.6%) and pre obese (57.6%), mean duration of diabetes is 5.8 years. The results show that 16 (48.5%) of them has probable minimal fibrosis, while 7 (21.2%) are classified as gray zone, 1 (3.0%) for probable advanced while 9 (27.3%) are classified with probable cirrhosis. Fibrosis is not significantly associated with wall motion status, LVH, pulmonary artery pressure, pericardial effusion, EF, inter-ventricular septum, diastolic/systolic dysfunction. The steatosis results against the result of 2D Echo, result show that 13 (39.4%) of them are classified as minimal, while 3 (9.1%) are mild, 6 (18.2%) are moderate and 11 (33.3%) classified as severe. Results show that steatosis is also not significant to 2 D echocardiography.
Conclusion: Although our study shows Diabetes has a role to development on liver fibrosis and steatosis but not significant to the result of 2 D echocardiography to develop cardiac diseases as alone risk factor.

Abstract #899

3-Dimensional in vitro cultures of hepatic cells on decellularised liver scaffolds improve viability and functionality of cultured cells

Abhishak C. Gupta[1], Preety Rawal[1], Dinesh Mani Tripathi[1], Sumati Rohilla[1], Savneet Kaur[1], Shiv K. Sarin[1]

[1]Institute of Liver and Biliary Sciences

Introduction: Liver cells possess diminished functional ability both in the standard 2-dimensional in vitro cultures and also demonstrate limited efficacy after in vivo transplantations, thus limiting their clinical and regenerative applications. In this regard, decellularized tissue matrix has emerged as a natural scaffold that is used to enhance the in-vitro properties of a variety of cell types.
Aim: The primary goal of this study was to create a decellularized liver (DCL) matrix for 3-dimensional (3D) cultures of hepatic cells.
Methods: DCL was developed by portal vein cannulation and perfusion with detergents and characterized by histology. Enzymatically digested DCL matrix was mixed with commercially available matrigel. Hepatocytes cell lines (Huh7) were cultured in 3D conditions with or without DCL-matrigel for 14 days. Phenotypic and functional analysis of cultured cells was done by cell morphology, gene expression, immunostaining and albumin assays at day7 and 14.
Results: Huh7 cells demonstrated significantly increased proliferation in 3D conditions with DCL-matrigel than in cultures with matrigel alone. Gene expression of hepatocyte specific markers, Asialoglycoprotein Receptor 1 (ASGR-1), HNF-4a, and CK19 was increased more than two and fourfold at day 7 and 14 in 3D-DCL-matrigel conditions. Liver-specific (ASGR-1) immunostaining also showed significantly enhanced expression in 3D-DCL-matrigel conditions at day 14. Also, in presence of DCL-matrigel, secretion of hepatocyte marker albumin in Huh7 cells, was significantly increased in the supernatants at day 7 and 14, respectively as compared to matrigel alone.
Conclusion: We conclude that 3D cultures of hepatic cells with DCL-matrigel enhances the viability and functionality of hepatic cells.

Abstract #1011

Association of Hepatic Steatosis and Fibrosis with Cardiovascular Disease Using Fibroscan and 2 D- Echocardiography Among Patients with Type 2 Diabetes Mellitus: Retrospective Observational Study

Parashu Ram Ghimire[1], Diana Alcantara Payawal[1], Marilyn Talingdan Te[1]

[1]Fatima University Medical Centre

Introduction: Type 2 diabetes mellitus (T2DM) is associated with fatty liver andl cardiovascular disease. At present imaging studies, transient elastography (fibroscan) with controlled attenuated parameter (CAP) and 2 D echocardiography (2D echo) can be employed to assess hepatic steatosis and fibrosis and cardiac function.
Objective: The aim of this study was to correlate results of fibroscan with 2 D echo among patients with type 2 diabetes mellitus.
Methods: This is a retrospective observational study. All patients who underwent Fibroscan and with T2DM and 2D echo result were included in the study. Multivariate analysis was done to assess the correlation of fibroscan with 2 D echo results.
Results: A total of 33 patients were included in the study. Mean age is 55, mostly female (60.6%), pre obese (57.6%) with mean duration of diabetes is 5.8 years. Fibroscan results showed that 16 out 33 (48.5%) have probable minimal fibrosis, 7 (21.2%) within the gray zone, 1 (3.0%) has advanced fibrosis and 9 (27.3%) have probable cirrhosis. Hepatic fibrosis is not significantly associated with wall motion status, LVH, pulmonary artery pressure, pericardial effusion, EF interpretation, inter-ventricular septum, diastolic/systolic dysfunction. Likewise, CAP results showed that 13 out of 33 (39.4%) have minimal steatosis, 3 (9.1%) have mild steatosis, 6 (18.2%) have moderate steatosis and 11 (33.3%) have severe steatosis. Results showed that steatosis is also not significantly associated to 2 D echo.
Conclusion: This study showed that among patients with T2DM, hepatic fibrosis and steatosis are not associated with cardiac dysfunction.

Abstract #1036

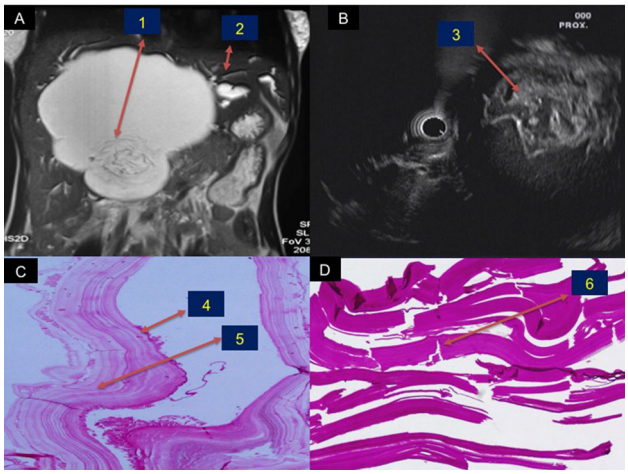
A case of Hydatid Cyst with biliary obstruction: A multi modality approach

Verma Nipun[1], Akash Roy[2], Sunil Taneja[2], Ajay Kumar Duseja[2], Radha Krishna Dhiman[2]

[1]Assistant Professor Department of Hepatology Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, [2]Department of Hepatology Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh

Introduction: Management of hydatid cyst with biliary obstruction requires a multimodality approach. Herein we present a case of hydatid cyst managed with multimodality approach.
Case Report: A 42-year-old female presented with right upper quadrant pain for 30 days with jaundice and vomiting for 6 days. Examination revealed icterus and tender hepatomegaly. Investigations showed elevated bilirubin (total/conjugated: 3.98/2.3 mg/dl) and raised transaminases and alkaline phosphatase (AST/ALT/ALP: 86/145/709 IU/ml). Blood counts, renal function and coagulogram were normal. T2W coronal MRI image of abdomen showed hepatomegaly (24 cm), large exophytic hyperintense cystic lesion in right lobe of liver with hypointense floating membranes seen within it causing biliary obstruction and bilobar IHBRD with non-patent primary confluence. Endoscopic ultrasound showed large cystic lesion with hyperechoic membranes within it suggestive of hydatid cyst, WHO stage C3A. Oral albendazole therapy followed by surgical

excision with deroofing of cyst was done. Histopathology showed fibrocollagenous pericyst and eosinophillic laminated, avascular, refractile ectocyst which was periodic acid stain positive. Post-operative period was uneventful and is doing well on follow-up.
Conclusion: Though common intricacies of hydatid cyst management still remain a challenge. In cases of biliary obstruction multimodality approach leads to optimal outcomes.



Abstract #1047

Arrestin domain-containing protein 3 is associated with NAFLD and NASH development

Tatsuo Kanda[1], Masahiro Ogawa[1], Naoki Mastumoto[1], Shunichi Matsuoka[1], Mitsuhiko Moriyama[1]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Nihon University School of Medicine

Introduction: Prevalence of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) is increasing worldwide. Several effective drugs for these diseases are now in development and under clinical trials. It is important to reveal the mechanism of the development of NAFLD and NASH.
Objectives: We investigated the role of arrestin domain-containing protein 3 (ARRDC3), which is linked to obesity in men and regulates body mass, adiposity and energy expenditure, in the progression of NAFLD and NASH.
Methodology: We performed knockdown of endogenous ARRDC3 in human hepatocytes and examined the inflammasome-associated gene expression by real-time PCR-based array. We also examined the effect of conditioned medium from endogenous ARRDC3-knockdown-hepatocytes on the apoptosis of hepatic stellate cells.
Results: We observed that free acid sen hanced the expression of ARRDC3 in hepatocytes. Knockdown of ARRDC3 could lead to the inhibition of inflammasome-associated gene expression in hepatocytes. We also observed that conditioned medium from endogenous ARRDC3-knockdown-hepatocytes enhances the apoptosis of hepatic stellate cells.
Conclusion: ARRDC3 has a role in the progression of NAFLD and NASH and is one of the targets for the development of the effective treatment of NAFLD and NASH.

Abstract #1062

Autophagy regulates lipid metabolism

Masaaki Komatsu[1]

[1]Asahimachidori Ichiban-Chou Chuo-Ku, Niigata

A growing body of evidence has revealed the importance of selective autophagy in removal of specific soluble proteins, protein aggregates, damaged mitochondria, and invasive bacteria from cells. Dysfunctions of autophagy have been directly linked to human pathogenic conditions including metabolic disorders, neurodegenerative diseases, and cancer. However, metabolic regulation through selective autophagy remains largely uncharacterized. Here, we show that a deficiency in selective autophagy is associated with suppression of lipid oxidation via a transcriptional regulatory mechanism. The production of ketone bodies upon fasting was significantly impaired by loss of Atg7 or Atg5 in the liver. This impairment arose from transcriptional down-regulation of genes that encode enzymes involved in β-oxidation, which occurred due to suppression of transactivation by PPARα, a master regulator of lipid metabolism. In mechanistic terms, NCoR1, a nuclear receptor co-repressor 1, which interacts with PPARα and suppresses its transactivation, bound to the autophagosomal GABARAP family proteins and was ultimately degraded by autophagy. Consequently, loss of autophagy caused marked accumulation of NCoR1 and subsequently suppressed PPARα activity, resulting in impairment of lipid oxidation. These results suggest that autophagy contributes to full activation of PPARα upon fasting by promoting degradation of its repressor, NCoR1 and is involved in β-oxidation and subsequent production of ketone bodies.