Alcoholic steatohepatitis/non-alcoholic steatohepatitis

# 1027 Fyn tyrosine kinase can be especially associated with the development of hepatic steatosis by taking methionine-choline-deficient diet that reflects the starvation state

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Aims: Fyn tyrosine kinase (Fyn) is one of the Src-family protein kinases and has been previously reported to decrease hepatic triglyceride level of ordinary diet-fed Fyn−/− mice, compared with control mice. These reports suggest a possibility that Fyn may affect hepatic function. Here, we provided a methionine-choline-deficient diet (MCD), which increases triglyceride and histologically causes the expression of non-alcoholic steatosis in the liver of rodents, and high-fat diet (HFD) to Fyn−/− mice to investigate the presence or absence of histological changes in their livers. Methods: Mice were divided into three groups; standard diet (SD), HFD, and MCD were given to 8-week-old male Fyn−/− mice (n=5) and C57BL/6J Fyn+/+ (Fyn+/+) mice (n=5) as controls, respectively, for 8 weeks. Results: Standard diet-fed Fyn−/− mice showed the trend of the decrease in hepatic triglyceride compared with SD-fed Fyn+/+ mice. However, there is no significant difference in the histological findings of two groups. HFD-fed mice showed a development of the same degree in hepatic steatosis between the two groups. Interestingly, MCD-fed Fyn−/− mice showed significantly more aggravation of hepatic steatosis, compared with MCD-fed Fyn+/+ mice. MCD-fed Fyn−/− mice showed a significant increase in the expression of sterol regulatory element-binding protein (SREBP)-1c and SCD-1. These mice showed a significant decrease in the expression of PPAR-α and CPT-1a. There is no significant difference in the expressions of hepatic lipogenic-related gene such as ACC1, SREBP-1c, SCD1, PPAR-α, and CPT-1a in the HFD groups. Conclusions: Fyn might be associated with the development of hepatic steatosis by taking MCD that reflects the starvation state.

# 1031 Serum alanine/aspartate aminotransferase and aspartate aminotransferase-to-platelet ratio index in Siberian adolescents with moderately elevated body mass index

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Introduction: Overweight and obesity among the adolescent population are coming to be of a pandemic nature and have been found to be associated with non-alcoholic fatty liver disease (NAFLD). Elevated alanine aminotransferase (ALT) is commonly used as a surrogate marker of NAFLD. Some authors state that aspartate aminotransferase (AST) may be a marker of a more aggressive course of NAFLD. Data regarding the association of body mass index (BMI) and liver enzymes in Siberian population are limited. Methods: Fifty Siberian adolescents with BMI ≥ 25 were paired according to age and sex with 50 subjects with BMI < 25. All adolescents were otherwise healthy without virus hepatitis markers. BMI was calculated by dividing weight (kg) by height squared (m). ALT and AST were measured using an enzymatic rate method. Aspartate aminotransferase-to-platelet ratio index (APRI) was calculated by the following equation: (AST level/AST upper level of normal/platelet count) × 100. Mann–Whitney test and logistic regression were used. Results: The overweight group exhibited a higher ALT and lower AST/APRI ratio levels. The multivariable logistic regression model, after adjusting for age and gender, showed that BMI > 25 was strongly associated with abnormal (above our laboratory upper limit) AST, but not ALT, levels. Adjusted odds ratios were 5.69 (95% confidence interval [CI]: 1.43–22.7) and 1.82 (95% CI: 0.69–4.76) for elevated-above-upper-limits AST and ALT, respectively. APRI did not vary in accordance to BMI, and platelet count was higher in overweight adolescents. Conclusion: Both ALT and AST levels, but not APRI, are associated with moderately elevated BMI in Siberian adolescents. Only AST of abnormal level (according enzymes upper limits) shows a significant relationship with high BMI (> 25). We suggest that, in the Siberian adolescent population, NAFLD should be taken into consideration in patients with not only ALT but also AST that are persistently elevated.

# 1257 Fatty liver disease associated with bladder cancer

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Background: Fatty liver is regarded as a feature of metabolic syndrome in the liver. Metabolic syndrome is associated with a higher risk of bladder cancer. However, the association between fatty liver and bladder cancer is unclear. Aim: The aim is to investigate the association between fatty liver disease and bladder cancer. Material and Methods: The records of all patients (n=79) who were diagnosed with bladder cancer in our hospital between 2009 and 2013 were reviewed. We also randomly collected non-cancer adults (n=120) as the control group. Anthropometric measurements, biochemical tests for liver and metabolic function, and abdominal computed tomography (CT) were assessed. Fatty liver was confirmed by CT if the attenuation of the liver was at least 10 Hounsfield units (HU) less than that of the spleen or if the attenuation of the liver was less than 40 HU. Results and Discussion: The prevalence of fatty liver was 21.5% in the bladder cancer and 6.7% in the control group (P=0.004). The cancer group had older age and was predominantly male. By using multiple logistic regression analysis to adjust these variables, fatty liver was found to be associated with an increased risk of bladder cancer (P=0.016; odds ratio, 3.53; 95% confidence interval, 1.27–9.81). Conclusion: Fatty liver was associated with bladder cancer. Further studies are needed to confirm whether fatty liver is a factor for the development of bladder cancer.
Background and Aims: Non-alcoholic fatty liver disease (NAFLD) is the most common form of chronic liver disease and is associated with metabolic syndrome. Various epidemiological studies have reported prevalence rates between 5% and 30%. Local epidemiological data suggest an increasing prevalence of metabolic syndrome in Singapore. However, data on NAFLD are limited. We investigated the prevalence and local perceptions of NAFLD in Singapore. Methods: Attendees at a gastroenterology public forum were enrolled in a cross-sectional observational study, evaluating demographic, anthropometric, liver ultrasound, and clinical information. The diagnosis of NAFLD was based on sonographic criteria. Metabolic syndrome was defined according to International Diabetes Federation guidelines. Perceptions of NAFLD were explored using a self-administered questionnaire. Results: Two hundred and twenty-seven subjects were recruited with NAFLD diagnosed in 40% of the cohort. Subjects with NAFLD tended to be male (53.9% vs 33.9%, P = 0.007), are older (mean age 57.4 vs 51.9 years old, P = 0.012), had higher mean body mass index (BMI: 24.4 vs 21.6 kg/m², P < 0.001), with larger waist circumferences (P = 0.01) and more often fulfilled criteria for metabolic syndrome (25% vs 11.4%, P = 0.014). Interestingly, subjects with NAFLD had a mean BMI (24.4 kg/m²) that was within the non-obese range. The majority of subjects had heard of NAFLD, but they tended to underestimate their risk of having the disease. Receptiveness towards screening for NAFLD was positive. Conclusion: Our study suggests a significant local prevalence of NAFLD including non-obese individuals. Despite general awareness about NAFLD, they tended to underestimate their risk of having the disease. Better public education is needed to improve understanding.

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# 1399 Usefulness of controlled attenuation parameter for quantifying hepatic fat content in patients with biopsy-proven non-alcoholic fatty liver disease
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Background and Aim: Non-invasive steatosis-quantifying methods are required for non-alcoholic fatty liver disease (NAFLD) patients in order to monitor disease severity and assess therapeutic efficacy. Controlled attenuation parameter (CAP) evaluated with vibration-controlled transient elastography can predict the presence of steatosis, but its application to absolute hepatic fat quantification remains unclear. The aim of this study was to examine whether CAP is correlated to real hepatic fat content in NAFLD patients. Methods: Fifty-nine NAFLD patients underwent percutaneous liver biopsy were enrolled. CAP was measured using FibroScan® just before liver biopsy. The percentage of fat droplet area to hepatocyte area in the biopsied specimen was determined morphometrically using a computerized optical image analyzing system. The correlation between CAP and liver histology was examined. Results: Controlled attenuation parameter showed an excellent correlation to actual liver fat percentage in the NAFLD patients having body mass index (BMI) < 28 kg/m² (r = 0.547, P < 0.001), especially < 25 kg/m² (r = 0.678, P = 0.001), but the meaningful correlation disappeared in patients with BMI > 28 kg/m². In patients with BMI < 28 kg/m², CAP quantitativeness was affected by the presence of fibrosis, but not hepatocyte ballooning and lobular inflammation. Conclusions: Controlled attenuation parameter may be a promising tool for quantifying hepatic fat content in NAFLD patients having no or mild obesity without liver fibrosis. Further improvement of CAP performance is needed for the NAFLD patients having BMI > 28 kg/m² or hepatic fibrosis.

# 1483 Silymarin for the treatment of non-alcoholic steatohepatitis: Interim analysis of a randomized, double-blind, placebo-controlled trial
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Background/Aims: Silymarin, derived from the milk thistle plant, Silybum marianum, has been used as a herbal remedy for diseases of the liver. Methods: This is a randomized, double-blind, placebo-controlled study of silymarin 700 mg t.i.d. for the treatment of non-alcoholic steatohepatitis (NASH). All included patients had biopsy-proven NASH, were given lifestyle advice, and received either silymarin or placebo for 48 weeks. A repeat liver biopsy was performed at the end of the study. Histology was reported using the NASH Clinical Research Network scoring system. Results: A total of 64 patients completed the study at the time of this interim analysis. Mean age was 50.2 ± 11.4 years and consisted of 43.8% men. The baseline characteristics were comparable between the silymarin (n = 30) and placebo (n = 34) groups. Significantly more patients in the silymarin group experienced NASH resolution (defined as NAS < 3) compared with the placebo group (13.3% vs 0%, P = 0.043). There was also a significant decrease in the fibrosis stage in the silymarin group (Δ = −0.367, P = 0.019). This was not observed in the placebo group (Δ = +0.147, P = 0.282). A significantly higher percentage of patients in the silymarin group had improvement in fibrosis stage compared with the placebo group (36.7% vs 14.7%, P = 0.043). In addition, four patients in the
placebo group developed cirrhosis, while none of the patients in the silymarin group did. **Conclusions:** A significantly higher percentage of patients experienced NASH resolution and improvement in fibrosis stage after 48 weeks of treatment with silymarin compared with placebo.

**Aims:** This study aimed to investigate histone deacetylase 1 (HDAC1) expression in liver tissue of mice in the course of non-alcoholic fatty liver disease (NAFLD) and its correlation to sterol regulatory element-binding protein (SREBP) and to further study the possible mechanism. **Materials and Methods:** C57BL/6 mice were fed with chow diet and high-fat diet (HFD) for 1, 5, and 9 weeks. Expressions of HDAC1, HDAC3, and SREBP in liver tissue of mice were detected by western blot and real-time reverse transcription–polymerase chain reaction. HDAC1, HDAC3, and SREBP expressions in HepG2 cells were detected by western blot after the cells were treated with oleic acid for 24 h with or without HDAC1 inhibitor pretreatment. **Results:** The liver of mice had the appearance of obvious steatosis after 9 weeks of HFD. Compared with the liver tissue of mice fed with chow diet, the liver tissue of mice fed with HFD for 9 weeks had statistically increased expressions of HDAC1 and SREBP protein (both P < 0.05), but HDAC3 appeared to have no difference. The protein expression of HDAC1 in mice liver was positively correlated to the duration of HFD (r = 0.941, P < 0.05). The mRNA levels of SREBP in liver tissue of mice fed with HFD for 5 and 9 weeks were statistically higher than those of mice fed with chow diet (both P < 0.05), and no differences were found in expressions of HDAC1 and HDAC3. Accompanied with a large amount of fat granules accumulating in HepG2 cell stained by oil red after being treated with oleic acid for 24 h, the protein expressions of HDAC1 and SREBP in HepG2 cells were dramatically increased compared with those of cells without oleic acid treatment (both P < 0.05), and HDAC3 had no change. After HepG2 cells were pretreated with HDAC1 inhibitor, the elevated of SREBP protein induced by oleic acid was obviously inhibited. **Conclusions:** HDAC1, but not HDAC3, plays an important role in the course of NAFLD, which could at protein level accelerate the formation of NAFLD through inducing the protein and mRNA expression of SREBP. **Keywords:** HDAC1, non-alcoholic fatty liver disease (NAFLD), SREBP.

**# 1509 Fibroblast growth factor 21 expression during the course of mice non-alcoholic fatty liver disease and its correlation to sterol regulatory element-binding protein**

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**Aims:** This study aimed to investigate the fibroblast growth factor 21 (FGF21) expression in liver tissue and serum from different stages of mice non-alcoholic fatty liver disease (NAFLD) and its correlation to sterol regulatory element-binding protein (SREBP). **Materials and Methods:** C57BL/6 mice were fed with chow diet and high-fat diet (HFD) for 1, 9, and 18 weeks. Expressions of FGF21 and SREBP in liver tissue of mice were detected by western blot and real-time reverse transcription–polymerase chain reaction. Serum FGF21 was examined using ELISA. **Results:** The liver of mice exhibited the typical appearance of fatty liver after 9 weeks of HFD with a large amount of fat granule accumulation in hepatocytes. Compared with mice fed with chow diet, FGF21 mRNA level in liver tissue from mice fed with HFD increased a little in the first week (P > 0.05) and began dramatically higher in the 9th and 18th weeks of HFD (both P < 0.05), with a positive correlation to the duration of HFD (r = 0.952, P = 0.000) and the SREBP mRNA level (r = 0.725, P = 0.000). On the other hand, FGF21 protein expression in liver tissue from mice fed with HFD decreased a little in the first week (P > 0.05) and began statistically lower in the 9th and 18th weeks of HFD compared with mice of chow diet (both P < 0.05). Opposite changes were found in the expression of SREBP protein. Furthermore, compared with mice of chow diet, serum FGF21 of HFD mice became higher a little in the first week (P > 0.05) and obviously higher in the 9th and 18th weeks of HFD (both P < 0.05), with a positive correlation to the duration of HFD (r = 0.944, P = 0.000) and the FGF21 mRNA level of liver tissue (r = 0.910, P = 0.000) and a negative correlation to the protein expression of FGF21 in liver tissue (r = –0.704, P = 0.000). **Conclusions:** In the course of mice NAFLD, the FGF21 mRNA level of liver tissue increased, protein expression decreased, and serum level became higher, accompanied by the elevation of SREBP in liver. This suggests a high secretion of FGF21 from liver would appear with a high level of transcription and synthesis of FGF21 in liver under HFD, which is closely correlated to hepatic steatosis. **Keywords:** FGF21, non-alcoholic fatty liver disease (NAFLD), SREBP.

**# 1620 Effects of modulation NF-E2-related factor 2 expression on anti-oxidant ability and potential mechanisms in BRL-3A and HSC-T6 cells**

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**Background:** NF-E2-related factor 2 (Nrf2) is an important transcription factor for cell defense against oxidative stress reaction. Nrf2 may play a clearly protective role in non-alcoholic steatohepatitis (NASH), but the exact mechanism and target cells are still not clear. **Methods:** The stably transfected HSC-T6 and BRL-3A cells with up/down expression of Nrf2 were constructed by lentiviral vectors. Cells were divided into normal group and oxidative stress stimulation group treated with glucose oxidase. Further, reactive oxygen species were detected by flow cytometry. And survival rate of cells and levels of malondialdehyde, lactate dehydrogenase, and superoxide dismutase were detected by ELISA. Last, expression levels of p66Shc and IQGAP1 protein in cells were detected by western blot. **Results and Discussion:** Stably transfected HSC-T6 and BRL-3A with modulation Nrf2 expression were successfully constructed, as confirmed by reverse transcription–polymerase chain reaction and western blot. After oxidative stress stimulation, malondialdehyde, lactate dehydrogenase, and reactive oxygen species levels were decreased, while the survival rate and the level of superoxide dismutase increased under upregulation of Nrf2 (P < 0.05); and we obtained the opposite result under downregulation of Nrf2 (P < 0.05). Then, the p66Shc level was decreased, while the IQGAP1 increased under upregulation of Nrf2 in both groups (P < 0.05); and we obtained the opposite result under downregulation of Nrf2.
# 1717 Protective effect and mechanism of NF-E2-related factor 2/heme oxygenase-1 pathway on the high-fat-diet-induced insulin resistance in rats

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**Background:** Our previous studies have confirmed that curcumin can increase Nrf2 nuclear translocation and has protective effects on oxidative stress in hepatocytes. This study aims to investigate the protective effects on insulin resistance and non-alcoholic steatohepatitis of the activation of the NF-E2-related factor 2 (Nrf2)/heme oxygenase-1 (HO-1) pathway induced by curcumin. **Methods:** The oxidative stress model of human LO2 hepatocytes was prepared with glucose oxidase (GO). LO2 hepatocytes were divided into control group, model group, curcumin-treated group, and inhibitor group. LO2 hepatocytes in the control group were normally cultured, while LO2 hepatocytes in the model group were treated with 100 U/L GO for 2 h. LO2 hepatocytes in curcumin-treated group were treated with 30-μm curcumin for 12 h. And LO2 hepatocytes in the inhibitor group were treated the same as in the curcumin-treated group in the presence of 0.1-μM wortmannin (PI3K inhibitor) for 1 h. Expressions of Nrf2, HO-1, and insulin signaling pathway were detected by western blot. **Results and Discussion:** For expressions of Nrf2 nuclear translocation and HO-1, those in the model group were a little higher than those in the control group, and those in the curcumin-treated group increased significantly compared with those in the model group, but those in the inhibitor group were lower than those in the curcumin-treated group. For the expressions of phosphorylated JNK and IRS-1, those in the model group were higher than those in the control group, and those in the curcumin-treated group were lower than those in the model group, and the figure of the inhibitor group was between those of the model group and the curcumin-treated group. There was also no significant change of total IRS-1 and JNK expressions among different groups. **Conclusion:** Insulin resistance caused by oxidative stress can be reduced by inducing the Nrf2/HO-1 pathway, and its effect may improve the insulin signaling pathway by reducing the phosphorylated JNK level and increasing the phosphorylated IRS-1 one.

# 1729 Clinical application of transient elastography in the prediction of underlying liver disease in a group of patients with chronic kidney disorders

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**Introduction:** Non-alcoholic fatty liver disease is associated with cardiovascular morbidity and mortality. Patients with chronic kidney disease (CKD) are in increased risk of cardiovascular deaths. **Aim:** This study aimed to investigate the presence of possible liver disease detected by functional liver tests and transient liver elastography (TE) in a group of the patients with different stages of chronic kidney disease (CKD). We investigated also whether the type of disorder end length of dialysis treatment in patients with CKD have any effect on steatosis and fibrosis grade, as documented by TE. **Patients and Methods:** Eighty patients with various stages of CKD were divided into subgroups in regard to etiology and duration of hemodialysis treatment. Liver stiffness was used to quantify liver fibrosis. Controlled attenuation parameter (CAP) was used to quantify liver steatosis. The device used was FibroScan (Echosens, Paris). The cut-off value for liver steatosis was 215 dB/m, and for the presence of fibrosis, it was a liver stiffness of >7 kPa. Functional liver tests were measured for all patients. **Results:** No statistically significant correlations were detected between liver enzymes and CAP value. There was a statistically significant correlation detected between the value of liver enzymes and liver stiffness value ($r=0.231$). We did not find statistically significant differences between etiology and duration of hemodialysis in regard to the functional liver test and CAP value. There was a statistically significant frequency of liver stiffness detected ($P<0.05$) in regard to etiology (with a higher frequency in autoimmune kidney disease). **Conclusion:** Transient liver elastography provides the opportunity for non-invasive screening of non-alcoholic fatty liver disease in CKD patients.

**Keywords:** liver steatosis, liver stiffness, transient elastography.

# 1774 Triglyceride regulation by leptin in alcoholic liver disease

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**Introduction:** Alcohol-induced fatty liver disease is the most common and earliest response to the progression of fibrosis, cirrhosis, and/or hepatocellular carcinoma. The mechanism by which ethanol causes fatty liver disease is complex and not fully understood; however, augmented triglyceride (TG) accumulation in the hepatocyte is strongly associated with fatty liver and has been proposed as an important biochemical mechanism. We have previously noted that the potential beneficial effect of leptin on alcohol elicited toxicity in vitro. **Objective:** The purpose of this study was to evaluate the effect of leptin on ethanol-induced elevated hepatic TG synthesis and fatty acid composition in mice. **Material and Methods:** CD-1 mice ($n=10$ group) were studied for 45 days. Four groups were studied: (i) control; (ii) leptin + control (230 μg/kg intraperitoneal every alternate day from day 30); (iii) alcohol (6.32 g/kg daily by gastric lavage, for 45 days); and (iv) alcohol + leptin (as prior dosing). **Results:** Compared with naive mice, mice with ethanol supplementation had significantly ($P<0.05$) increased plasma and hepatic TG concentrations and a key enzyme involved in TG synthesis such as acyl-CoA diacylglycerol acyltransferase (DGAT2). Leptin administration to ethanol-treated mice shows significantly ($P<0.05$) reduced hepatic and plasma TG concentrations and DGAT2 enzyme protein expression. Furthermore, ethanol supplementation significantly ($P<0.05$) increased the percentage of palmitic acid (16:0), stearic acid (18:0), oleic acid (18:1), and docosapentaenoic acid (22:5) levels, whereas...
Background: Controlled attenuation parameter (CAP) was introduced as a fibroscopic probe to estimate hepatic steatosis in patients with non-alcoholic fatty liver disease. The XL probe did not further improve the accuracy of CAP and LSM for the estimation of hepatic steatosis and fibrosis in NAFLD patients and gave higher CAP value and lower LSM value compared with the M probe.

# 2079 Effect of allicin on cecum microbiota in alcoholic fatty liver disease mice

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Introduction: Recently, scientists have found that gut microbiota may play a role in the pathogenesis or progression of certain liver diseases, including alcoholic liver disease. Allicin is a pharmacologically active substance found in fresh aqueous extract of garlic, which has been found to have antimicrobial activity. The objectives of this study are to investigate the impact of allicin on the status of gut microbiota and its relationship with alcoholic fatty liver. Materials and Methods: The alcoholic fatty liver mouse experimental model was developed using male C57BL/6 mice that were fed an alcohol-containing liquid diet (Lieber-DeCarli diet). Allicin was administered orally every day for 4 weeks in the treatment group. Results: The results indicated that allicin significantly reduced relative liver weight, fatty liver score, and also regulates fatty acid composition, warranting further population-based mechanistic studies.

Conclusion: Thus, exogenous leptin administration to ethanol-fed mice significantly reduced hepatic TG synthesis and also regulates fatty acid composition, warranting further population-based mechanistic studies.
level. In addition, the negative correlations were observed in control (36 species) and alcoholic fatty liver disease groups (19 species) with allicin treatment. **Conclusion:** Allicin exhibits a potential hepatoprotective effect against alcoholic fatty liver disease possibly due to pathogenesis-inhibiting changes exerted by allicin in the gut microbiota. Therefore, future work is required to verify the relationship between cecum microbiota and the production of triglycerides in the gut.

**Keywords:** alcoholic fatty liver, allicin, gut microbiota.

# 2080 The role of B lymphocytes in the pathogenesis of non-alcoholic fatty liver disease

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**Aims:** It is demonstrated that B lymphocytes (B cells) play a role in the pathogenesis of obese-related diseases. However, the features of B cells in non-alcoholic fatty liver disease (NAFLD) have not been well illustrated. In this present study, we investigated the roles of intrahepatic B cells in NAFLD mice. **Methods:** An NAFLD mouse model was established by feeding with high-fat diet for 16 weeks. The proportion of B cells was calculated by flow cytometry. mRNA levels of interleukin (IL)-6, IL-10, and tumor necrosis factor (TNF)-α in liver tissue, intrahepatic lymphocytes, and intrahepatic B cells were quantified by real-time polymerase chain reaction. Cytometric Bead Array and Luminex methods were used to detect the cytokines and immunoglobulin (Ig) levels of plasma and culture supernatant or liver homogenate, respectively. **Results and Discussion:** The proportions of B cells were significantly increased in livers (\( P = 0.03 \)) and spleens (\( P = 0.00 \)) of the NAFLD group (Fig. 1). Plasma IL-6 levels were higher in the NAFLD group (\( P = 0.00 \)). Consistently, mRNA expression of IL-6 was upregulated in both liver tissues (\( P = 0.04 \)) and intrahepatic lymphocytes (\( P = 0.03 \)) in NAFLD mice. However, IL-10 mRNA level decreased (\( P = 0.04 \)) while TNF-α mRNA level increased (\( P = 0.04 \)) in NAFLD intrahepatic B cells. The secretion of IL-6 (\( P = 0.00 \)) and TNF-α (\( P = 0.00 \)) was promoted by lipopolysaccharide (LPS) stimulation in the B cells from NAFLD livers. As other studies had shown that the portal vein LPS level increased during the progression of NAFLD, intrahepatic B lymphocytes might promote this disease through secreting pro-inflammatory cytokines. Meanwhile, plasma IgA decreased (\( P = 0.04 \)) while IgG2a increased (\( P = 0.01 \)), and IgG2a (\( P = 0.00 \)) was elevated in the liver homogenate of NAFLD mice. **Conclusions:** The intrahepatic B cells were increased in NAFLD and might promote the disease by secreting IL-6, TNF-α, and IgG2a.

**Keywords:** B lymphocytes, cytokines, immunoglobulin, non-alcoholic fatty liver disease.

**Figure 1** The percentages of B lymphocytes in CD45+ cells from the livers and spleens of control and non-alcoholic fatty liver disease (NAFLD) groups.
Hepatocellular Carcinoma and Liver Tumors

**# 1003 Comparison of the clinical features of hepatocellular carcinoma with cryptogenic, alcohol, and viral hepatitis etiologies**

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**Significance:** In western societies, features of metabolic syndrome (MS) are increasingly seen in hepatocellular carcinoma (HCC) patients with cryptogenic etiology. However, it is unknown if this applies to Asians. We aimed to compare clinical characteristics of HCC patients divided according to etiology.

**Methodology:** Records of HCC patients from May 2006 to October 2013 were analyzed. HCC etiology was divided into viral hepatitis, alcohol, and cryptogenic. Baseline characteristics were compared. Statistical differences were evaluated by univariate analysis using t-test and chi-squared test for continuous and categorical variables.

**Results:** Among 334 patients, viral hepatitis accounted for 61.7%, alcohol 9.9%, and cryptogenic 28.4%. Majority (60.4%) were overweight/obese, and 47% had overt cirrhosis with no differences between the three groups ($P > 0.05$). Cryptogenic patients were significantly older than both viral and alcohol patients ($68.6 + 12.2$ vs $63.7 + 12.6$ vs $62.0 + 9.0$; $P = 0.003$), were more likely to be female (25.3% vs 16% vs 3%; $P = 0.01$), and tend to be diabetic (31.6% vs 20.1% vs 27.3%; $P = 0.124$) and to have a family history of HCC (11.6% vs 8.7% vs 0%; $P = 0.126$). Alcoholic patients, on the other hand, had larger tumors ($P = 0.037$) and were more likely to be heavy smokers ($P < 0.001$).

**Conclusions:** Hepatocellular carcinoma patients with cryptogenic etiology have different demographics than hepatitis and alcoholic patients because of their higher mean age and a greater proportion of them are female. Although components of MS were not more common, there was a trend for a higher proportion of diabetic patients in the cryptogenic group. Other components of MS like body mass index and triglycerides may have been affected by cachexia associated with HCC.

**Keywords:** alcohol, cryptogenic, hepatocellular carcinoma, metabolic syndrome, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis.

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**# 1010 IGFBP1 mediates pregnane X receptor-induced morphological changes and migration of hepatocellular carcinoma cells**

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**Background/Aims:** Pregnan X receptor (PXR), an orphan member of the nuclear receptor superfamily, is activated in response to numerous therapeutics and xenobiotics. The expression of PXR mRNA has increasingly seen in hepatocellular carcinoma (HCC) patients with cryptogenic etiology. However, it is unknown if this applies to Asians. We aimed to compare clinical characteristics of HCC patients divided according to etiology.

**Methodology:** Records of HCC patients from May 2006 to October 2013 were analyzed. HCC etiology was divided into viral hepatitis, alcohol, and cryptogenic. Baseline characteristics were compared. Statistical differences were evaluated by univariate analysis using t-test and chi-squared test for continuous and categorical variables.

**Results:** Among 334 patients, viral hepatitis accounted for 61.7%, alcohol 9.9%, and cryptogenic 28.4%. Majority (60.4%) were overweight/obese, and 47% had overt cirrhosis with no differences between the three groups ($P > 0.05$). Cryptogenic patients were significantly older than both viral and alcohol patients ($68.6 + 12.2$ vs $63.7 + 12.6$ vs $62.0 + 9.0$; $P = 0.003$), were more likely to be female (25.3% vs 16% vs 3%; $P = 0.01$), and tend to be diabetic (31.6% vs 20.1% vs 27.3%; $P = 0.124$) and to have a family history of HCC (11.6% vs 8.7% vs 0%; $P = 0.126$). Alcoholic patients, on the other hand, had larger tumors ($P = 0.037$) and were more likely to be heavy smokers ($P < 0.001$).

**Conclusions:** Hepatocellular carcinoma patients with cryptogenic etiology have different demographics than hepatitis and alcoholic patients because of their higher mean age and a greater proportion of them are female. Although components of MS were not more common, there was a trend for a higher proportion of diabetic patients in the cryptogenic group. Other components of MS like body mass index and triglycerides may have been affected by cachexia associated with HCC.

**Keywords:** alcohol, cryptogenic, hepatocellular carcinoma, metabolic syndrome, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis.

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**# 1018 Hepatic angiosarcoma with dyskeratosis congenita**

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**Introduction:** Dyskeratosis congenita is a disorder of poor telomere maintenance and is known to increase the risk of developing multiple types of malignancy, including epithelial cancers, particularly head and neck squamous cell carcinoma and gastrointestinal cancers. However, there are few reports of liver tumors arising in dyskeratosis congenita patients. We herein report the second case of hepatic angiosarcoma arising from dyskeratosis congenita. Case Description: A 23-year-old man was pointed out to have a liver tumor and subsequently consulted our hospital. He had a history of mental retardation. The patient was diagnosed with dyskeratosis congenita based on the following triad: (i) nail dystrophy; (ii) oral leukoplakia; and (3) abnormal skin pigmentation at 16 years of age. At 19 years of age, hepatosplenomegaly and liver dysfunction were noted. A hepatic tumor measuring 10 cm in diameter was detected on a routine checkup using abdominal ultrasound at 23 years of age. There was no history of alcohol consumption or smoking, and there was no reported exposure to Thorotrast, vinyl chloride, or arsenic. Hepatitis B surface antigens and HCV antibodies were negative, as were anti-nuclear antibodies and anti-mitochondrial antibodies. Abdominal computed tomography (CT) and magnetic resonance imaging revealed multiple hypervascular tumors, mainly in the hepatic right lobe. 18F-Fluorodeoxyglucose positron emission tomography/CT showed increased uptake with a maximum standardized uptake value of 7.8 in the hepatic tumors and vertebral metastases. A needle liver biopsy disclosed atypical cell infiltration with spindle-shaped or oval-shaped nuclei, and immunohistochemistry showed positive results for vimentin, CD31, CD34, and blood coagulation factor VIII. The diagnosis based on the needle biopsy was epithelioid hemangioendothelioma or angiosarcoma. He died 4 months after the first detection of the hepatic tumor as a result of tumor progression and disseminated intravascular...
coagulation. An autopsy revealed a diagnosis of angiosarcoma with metastasis to the lung, left adrenal gland, spleen, and vertebral.

# 1035 Tolvaptan for hepatocellular carcinoma patients with poor liver function

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**Aims:** The aim of this study is to evaluate the efficacy of tolvaptan for hepatocellular carcinoma (HCC) patients with poor liver function. **Patients and Methods:** Between Oct. 2013 and Feb. 2015, we evaluated 19 HCC patients with poor liver function treated using tolvaptan (female/male: 4/15, median age: 69 years old). Treatment dose is 7.5 mg/body in all patients. We evaluate the efficacy (disappearance of ascites/hydrothorax or weight loss over 5%), survivals, and toxicity. **Results:** We evaluated 19 patients. Child–Pugh was A/B/C = 1/14/4 patients. Mean Model for End-stage Liver Disease score was 11.45 (7.49–18.16) points. HCC stage was I/II/III/IVA/IVB = 1/0/2/8/5 patients. Virus infection was HBV/HCV/HBV + HCV/non-HBV, non-HCV = 6/7/3/3. The mean follow-up period was 96.5 days. Tolvaptan was considered effective in 11 patients (57.9%) without major complications. The overall survival is 90 days, and median survival time of tolvaptan effective patient and non-effective patients is 167 and 87 days, respectively (P = 0.0673). Prothrombin time–international normalized ratio and serum K+ were pointed out as predictive factors of effect. **Discussion:** The treatment effect of tolvaptan appeared in 57.9% of patients who had HCC with poor liver function, and the predictive factor is prothrombin time–international normalized ratio and serum K+. However, this study includes only a small number of patients and is retrospective; therefore, a prospective study with a larger sample size is necessary to define the treatment effect and the predictive factor. **Conclusion:** Tolvaptan may be effective as palliative therapy for HCC patient.

# 1057 Safety and effectiveness of sorafenib in elderly patients with hepatocellular carcinoma

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**Aim/Background:** With the progressive aging of society, the number of elderly patients with hepatocellular carcinoma (HCC) is increasing. Here, we investigated the efficacy and safety of sorafenib (SOR) for HCC and compared the results between elderly and non-elderly patients. **Materials/Methods:** Elderly (≥75 years old, n = 15) and non-elderly (< 75, n = 45) HCC patients being treated with SOR in the Ehime Prefectural Central Hospital were enrolled, and their clinical features were retrospectively evaluated. **Results:** There were no significant differences in age (79.4 ± 2.6 vs 65.2 ± 7.0 years, P = 0.026), performance status (0.1:2.3:4) (11:4:0:0 vs 43:1:0:0, P = 0.017), total bilirubin (0.62 ± 0.18 vs 0.85 ± 0.40 mg/dL, P = 0.017), and epidermal growth factor receptor (69.5 ± 5.4 vs 76.6 ± 27.4 mg/L/min/1.73 m², P = 0.009), while gender, body mass index, etiology, Child–Pugh class, tumor markers (α-fetoprotein [AFP], AFP-L3, and des-γ-carboxyprothrombin), maximum intrahepatic tumor size, intrahepatic tumor number, TNM stage, and starting dose of SOR did not show significant differences between elderly and non-elderly groups. There were no differences between the elderly and non-elderly groups for time to progression (median 10.2 vs 5.7 months, P = 0.332), rate of stopping SOR (3 and 6 months: 35.7% and 59.8% vs 46.4% and 65.0%, P = 0.936), and overall survival (6 months and 1 and 2 years: 84.8%, 66.0%, and 28.3% vs 59.8%, 43.0%, and 23.9%, P = 0.983). **Conclusion:** Sorafenib is safe and effective regardless of age.

# 1061 Colonoscopy in the diagnosis of graft-versus-host disease and cytomegalovirus enteritis

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**Introduction:** Graft-versus-host disease (GVHD) and cytomegalovirus (CMV) enteritis are important complications following allogeneic hematopoietic stem cell transplantation (allo-HSCT). We explored the role of colonoscopy in the diagnosis of GVHD and CMV enteritis following allo-HSCT to identify the endoscopic manifestations of GVHD and CMV enteritis. **Aims and Methods:** From 2006 to 2013, 57 patients have undergone allo-HSCT. A retrospective analysis of the colonoscopic manifestations of GVHD, CMV enteritis, and GVHD with concurrent CMV enteritis (GconC) and their related clinical issues. **Results:** Twenty patients underwent colonoscopies with diagnoses of 13 GVHD, 4 CMV enteritis, and 3 GconC. Both GVHD and CMV enteritis had colonic mucosal lesions with various manifestations under colonoscopy. Deep ulcers (0 of 4) were not specific endoscopic manifestations for CMV enteritis, but tortoise shell-like changes of the mucosa (11 of 13) were specific for GVHD, while mucosal edema, erythema, congestion, erosion, and shallow ulcers could not be used to differentiate GVHD from CMV enteritis. GconC patients have no specific endoscopic manifestations but colonic mucosal lesions with various manifestations. All GVHD and CMV enteritis were defined histologically as the presence of gland apoptosis and CMV immunostaining. **Conclusion:** Endoscopy may play a significant role in early diagnosis of GVHD and CMV enteritis in patients following allo-HSCT, and histologic examination of gastrointestinal biopsies is needed to confirm the final diagnosis.

# 1086 Alternative implication of serum vascular endothelial growth factor in living donor liver transplantation for hepatocellular carcinoma

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**Background:** This study aimed to clarify the level of vascular endothelial growth factor (VEGF) on patients with hepatocellular carcinoma (HCC) who underwent living donor liver transplantation (LDLT); it is possibly related to the recurrence of HCC or possibly came from the rapid regeneration of the liver graft after LDLT. **Methods:** Data from 50 recipients who underwent LDLT for HCC were collected in this 2-year study. Three serum VEGF time factors were
analyzed. VEGF_1 was defined as pre-LDLT day 1, and VEGF_2 as post-LDLT day 1. VEGF_3 was divided into VEGF_3N, which is 1 month post-LDLT without HCC recurrence (n = 41), and VEGF_3P, which is the day of HCC recurrence (n = 9). The time to HCC recurrence was 90–1352 days. Wilcoxon signed-rank test and mixed-model repeated-measure analysis were used to investigate. Results: The data profile was presented as Table 1. There was statistical significance only between VEGF_1 and VEGF_3N and between VEGF_1 and VEGF_2 (P = 0.022 and 0.012), but there was no significant difference between VEGF_2 and VEGF_3N, between VEGF_1 and VEGF_3P, between VEGF_2 and VEGF_3P, and between VEGF_3N and VEGF_3P (all were P > 0.05). Discussion: For both HCC recurrence and liver graft regeneration after LDLT, angiogenesis and the VEGF receptor pathways might be activated, possibly resulting in the loosening of intercellular junctions of endothelial cells and promoting angiogenesis. The VEGF receptor pathway plays a physiological role that may not differentiate between HCC recurrence and liver graft regeneration after LDLT. Liver graft regeneration requires significant blood flow and leads to the activation of this pathway. Conclusions: The implication of VEGF in case of LDLT should be that liver graft regeneration may play a major role in the clinical investigation.

### Table 1 Descriptive statistics

|       | N  | Mean   | Standard deviation | Minimum | Maximum |
|-------|----|--------|--------------------|---------|---------|
| VEGF_1| 50 | 249.7374 | 188.3295          | 42.64   | 640.73  |
| VEGF_2| 50 | 356.4900 | 325.4820          | 3.20    | 1150.26 |
| VEGF_3N| 41 | 418.5220 | 378.2367          | –51.98  | 1226.99 |
| VEGF_3P| 9  | 229.7011 | 85.2757           | 174.17  | 378.25  |

### Table 2 Test statistics (Wilcoxon signed-rank test)

|       | VEGF_1 | VEGF_2 | VEGF_3N | VEGF_3P | VEGF_1 | VEGF_1 | VEGF_2 | VEGF_2 | VEGF_1 | VEGF_3N |
|-------|--------|--------|---------|---------|--------|--------|--------|--------|--------|---------|
| Z     | –2.289 | –0.889 | –3.035  | –1.599  | –2.506 | –1.125 |
| Asymptotic significance (two-tailed) | 0.022  | 0.374  | 0.761   | 0.110   | 0.012  | 0.260  |

†Based on negative ranks. †Based on positive ranks.

# 1093 Malignant peripheral nerve sheath tumor of the liver

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Introduction: Malignant peripheral nerve sheath tumor (MPNST) of the liver is rare. Most cases of MPNST are accompanied by neurofibromatosis 1 (von Recklinghausen’s disease). Materials and Methods: We herein report a case of a 72-year-old woman with MPNST without neurofibromatosis 1, which was diagnosed by an autopsy. In addition, we review the pertinent literature of MPNST of the liver. Results: The tumor occupied the entire lobe of the liver and was 18 cm in maximum diameter. The tumor revealed necrosis and cystic changes with hemorrhage and metastasized to the peritoneum. Microscopically, it was composed of pleomorphic spindle cells with hyperchromatic nuclei and mitogenic figures. The spindle cells stained positive for both S-100 and vimentin antibodies, which suggests this is an autopsy case of MPNST of the liver.

# 1126 Novel function of eltrombopag as an antitumor agent for hepatocellular carcinoma

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Introduction: Sorafenib is the only available chemotherapeutic agent for advanced hepatocellular carcinoma (HCC) at present, but it cannot be used in patients with liver cirrhosis (LC) nor thrombocytopenia. In our previous studies, it was revealed that LC can be reduced by an increment of platelets with administration of thrombopoietin (TPO). Eltrombopag (EP), TPO receptor agonists, has antitumor effects on several kinds of cancers in spite of lack of the TPO receptor. It is still unclear whether EP has an antitumor effect on HCC. The aim of this study was to clarify the antitumor effect of EP on HCC in vitro. Materials and Methods: To verify the antitumor effects of EP in vitro with HepG2, Hep3B, and HuH7, the assays were carried out for cell proliferation with WST8, DNA synthesis with BrdU, flow cytometry, and western blot. To clarify the antitumor mechanism of EP, iron preloading into HCC was performed and determined the effect of iron chelator deferoxamine. In addition, the combination effect of EP and sorafenib were investigated. Results: It was revealed that EP had a strong antitumor effect on HCC by suppression of cell cycle-related protein cyclin D1 and resulted in cell cycle arrest in the G0/G1 phase. Iron preloading into HCC cells resulted in an inhibition of the anti-proliferative effects of EP. Antitumor effect of EP did not compete with sorafenib. Conclusion: Our results suggest that EP would be a good candidate for chemotherapy of HCC in patients with LC and thrombocytopenia.

Keywords: cell cycle, cirrhosis, eltrombopag, hepatocellular carcinoma, HuH7, iron chelate, thrombocytopenia, thrombopoietin, liver cancer, liver cirrhosis, sorafenib.

# 1157 Active tumor treatment versus supportive care for patients with Barcelona Clinic Liver Cancer stage D hepatocellular carcinoma

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Background: Patients with Barcelona Clinic Liver Cancer (BCLC) stage D hepatocellular carcinoma (HCC) often have poor clinical outcomes. The purpose of this study was to compare the effect of active tumor treatment and supportive care for patients with BCLC stage D HCC. Methods: We conducted a retrospective study. There were a total of 138 patients who were diagnosed as BCLC stage D HCC at Taipei City Hospital Ren-Ai Branch from 1999 to 2013. The duration
of patients’ survival was calculated from the date of diagnosis to death or the date of last follow-up. Survival analysis was performed by the Kaplan–Meier method, and a comparison was made by log–rank test. Factors associated with survival rate were analyzed by Cox’s regression analysis. Results: There were 46 (33.3%) patients who underwent different kinds of tumor treatment including operation, percutaneous ethanol injection, radiofrequency ablation, and radiotherapy. The remaining 92 (66.7%) patients received supportive care. Patients with active tumor treatment had a significantly higher survival rate of 1–3 years compared with those treated with supportive care (26.1%, 20.9%, and 6.3% vs 3.1%, 1.6%, and 0%, \( P = 0.001 \)). Multivariate Cox regression analysis revealed that male gender (hazard ratio [HR]: 2.059, 95% confidence interval [CI]: 1.315–3.224, \( P = 0.002 \)), tumor number > 3 (HR: 1.511, 95% CI: 1.009–2.263, \( P = 0.045 \)), and supportive care (HR: 2.758, 95% CI: 1.749–4.348, \( P < 0.001 \)) were independent risk factors associated with poor survival. Conclusions: The overall survival of patients with BCLC stage D HCC is quite poor. Active tumor treatment provides superior survival benefit than supportive care for patients with BCLC stage D HCC. Further studies with a large patient number are required to prove these preliminary findings.

# 1163 Evaluation of laparoscopic multipolar radiofrequency ablation for small hepatocellular carcinoma

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Background: Radiofrequency ablation (RFA) has played a key role in the management of small hepatocellular carcinoma (HCC) worldwide. We have performed laparoscopic RFA (LRA) using a multipolar RFA system (CelonPOWER System, Olympus Medical Systems, Japan) for treatment of HCCs since 2014. We assessed the efficacy and safety of multipolar LRA by short-term results. Methods: We performed LRA under general anesthesia in patients with HCCs ≤ 4 cm and ≤ 3 nodules. An RFA needle applicator was inserted under laparoscopic ultrasonography guidance, regardless of tumor location. It aimed at the parallel insertions based on “dosimetry table” and no-touch ablation as much as possible. Results and Discussion: Fifty-nine patients with 100 HCCs were treated by multipolar LRA. The maximum diameter of tumor averaged 22.7 ± 6.3 mm (10–42). Operative time was 145 ± 40 min. The median follow-up time was 6.5 months (0.7–16.6). In all cases, sufficient ablated area as planned was obtained, and there was no procedural complication and local recurrence. The laparoscopic approach offers parallel insertion of multiple applicators without limitation by echo window and/or the ribs. Especially in case of HCC in hepatic surface, it is highly useful to avoid thermal injury to adjacent organs by maintaining the space with pneumoperitoneum and immersion (Fig. 1). There was no local recurrence in the short-term results. To attempt at no-touch ablation may lead to attainment of a sufficient safety margin. Conclusions: Although multipolar LRA required some proper skills, it is efficacious in treatment for localized HCCs by gaining a good ablated area safely.
# 1165 FIB-4 index is a predictor of background liver fibrosis and overall survival after curative resection of hepatocellular carcinoma

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**Background and Objectives:** The FIB-4 index is a simple formula for predicting liver fibrosis. This study aimed to examine the relationship between the preoperative FIB-4 index and background liver fibrosis in non-tumor regions of surgical specimens and investigate whether the FIB-4 index is a useful predictor in hepatocellular carcinoma (HCC) patients after curative resection. **Methods:** A total of 493 HCC patients treated with curative resection were retrospectively analyzed. We assessed the utility of the FIB-4 index as a predictor of advanced liver fibrosis (F4). The cut-off value for the FIB-4 index was determined using a receiver operating characteristic curve analysis, and the impact of the FIB-4 index on overall survival after surgery was evaluated. **Results:** F4 was found in 236 patients (47.9%). The FIB-4 index was significantly higher in the patients with F4 than in those with F0–F3 (P < 0.001). An FIB-4 index of 2.87 was the best cut-off point for predicting F4. In the multivariate analysis, the FIB-4 index was found to be an independent prognostic factor for overall survival after curative resection (hazard ratio: 1.71, 95% confidence interval: 1.18–2.47, P = 0.004). Additionally, elevated des-y-carboxyprothrombin (P = 0.011) and α-fetoprotein (P = 0.011) levels, the presence of microsatellite lesions (P = 0.014), and a serum albumin level lower than 40 g/L (P = 0.016) were also significant predictors of overall survival. **Conclusions:** The present study showed the FIB-4 index to be a predictor of background liver fibrosis and overall survival in patients treated with hepatectomy for HCC with curative intent.

# 1181 Transcatheter arterial chemoembolization combined with sorafenib versus sorafenib for hepatocellular carcinoma: A retrospective study

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**Background/Aims:** Sorafenib, which is an orally administered targeted therapy, inhibits multiple protein kinases. At present, sorafenib is the only approved systemic therapy for patients with advanced disease (BCLC-C) HCC. Sorafenib combined with transarterial chemoembolization (TACE) is now more widely applied to treat unresectable HCC. The purpose of our study is to compare the overall survival of patients with HCC who were treated with sorafenib combined with TACE compared with sorafenib monotherapy. **Methods:** We collected baseline characteristics of HCC patients who ever received sorafenib treatment and were recruited from Ren-Ai Branch, Taipei City Hospital, during April 2010 to March 2014. Survival analysis was performed by the Kaplan–Meier method, and a comparison was made by log–rank test. Factors associated with survival rate were analyzed by Cox’s regression analysis. **Results:** There were 106 patients (84 men and 22 women) who had ever received sorafenib treatment. The mean age was 65±11.8 years (range, 38–90 years). Among them, 54 patients (50.9%) received sorafenib monotherapy, and 21 patients (19.8%) received combination therapy of sorafenib with TACE. There were no significant differences in terms of sex, age, tumor size, number of tumor, prevalence of HBV/HCV infection, child classification, and BCLC stage between patients treated with sorafenib alone and sorafenib + TACE. However, patients receiving sorafenib alone had a significantly higher ratio of α-fetoprotein (AFP) > 400 ng/mL (60% vs 30%, P = 0.034) and shorter sorafenib treatment period (< 2 months sorafenib treatment, 70% vs 38%, P = 0.009). Patients receiving combination therapy of sorafenib with TACE had a significantly longer mean and median survival period compared with those receiving sorafenib alone (15.0 ± 3.4 and 10.9 ± 2.9 vs 5.2 ± 1.1 and 2.6 ± 0.6, respectively, P < 0.001). Multivariate Cox’s regression analysis revealed that an AFP level of > 400 ng/mL (hazard ratio [HR]: 3.150, 95% confidence interval [CI]: 1.644–6.035, P = 0.001) and a sorafenib treatment period of < 2 month (HR: 3.966, 95% CI: 2.118–7.466, P < 0.001) were independent risk factors associated with poor prognosis. **Conclusions:** Our results indicated that survival rate is significantly longer in patients receiving sorafenib + TACE than in those with sorafenib alone. However, as most of our patients (88%) received sorafenib therapy for less than 6 months, the effect of sorafenib may be underestimated. Thus, further prospective randomized trials are required to confirm our findings.

# 1190 Translational study for liver carcinogenesis and developing personalized targeted treatment

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**Background/Aims:** Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer and the second leading cause of cancer-related death worldwide. Most of the liver cancer cases occur in 15 Asian countries. China has more than half of the newly diagnosed liver cancer cases in the world. Recurrence, metastasis, and chemoresistance are major obstacles to improving the prognosis of HCC. **Methods:** Combining gene expression profiles of HCC samples with or without early recurrence and established cell lines with epithelial or mesenchymal phenotype, some key factors like EDIL3 were identified as a novel regulator of epithelial–mesenchymal transition, which contributes to angiogenesis, metastasis, and recurrence of HCC. The expression of EDIL3 was evaluated by quantitative polymerase chain reaction, western blotting, and immunohistochemistry. The function of EDIL3 and targeted treatment strategies were investigated in liver cancer cells in vitro and orthotopic xenograft mouse model of HCC in vivo. **Results and Discussion:** EDIL3 induces epithelial–mesenchymal transition and promotes HCC migration, invasion, and angiogenesis in vitro. Mechanistically, overexpression of EDIL3, which was regulated by downregulation of miR-137 in HCC, triggered the activation of extracellular signal-regulated kinase (ERK) and transforming growth factor (TGF)-β signaling through interactions with αvβ3 integrin. Blocking ERK and TGF-β signaling overcomes EDIL3-induced angiogenesis and invasion. Using the orthotopic xenograft mouse model of HCC, we demonstrated that EDIL3 enhanced the tumorigenic, metastatic and angiogenesis potential of HCC in vivo. **Conclusions:** Therefore, it is promising for combating liver cancer through translation study and personalized therapy. EDIL3-mediated activation of TGF-β and ERK signaling could provide personalized therapeutic implications for HCC.
Hepatocellular carcinoma (HCC) is a common disorder worldwide with a rising incidence in Egypt due to high prevalence of HBV-related and HCV-related chronic liver disease. α-Fetoprotein (AFP)-L3 and simplified HCC-α-fetoprotein routine test (HCC-ART) could help in early detection of HCC. However, their diagnostic accuracy was not previously compared among Egyptian patients. **Aim:** This study aimed to compare the diagnostic role of simplified HCC-ART and AFP-L3 in Egyptian patients with HCC. **Methods:** Serum levels of AFP and AFP-L3 were determined in 47 patients with HCC and 17 patients with liver cirrhosis admitted to Kasr Al-Aini Hospital–Cairo University. All HCC patients were diagnosed by the non-invasive criteria applied to cirrhotic patients according to 2012 EASL guidelines. AFP and AFP-L3 were assessed by the ELISA technique in all participants. AFP-L3% was defined as the percentage of AFP-L3 over the total AFP. A simplified HCC-ART was calculated (age [years] × log AFP × AAR [AST/ALT] × ALP/albumin [g/L]). The performance characteristics for the diagnosis of HCC were obtained using receiver operating characteristic (ROC) curves in study populations with a special emphasis on patients with 20 < AFP < 200 ng/mL. **Results:** All HCC patients had elevated AFP; 19 (40.4%) patients had AFP > 200 ng/mL, and 28 (59.6%) patients had an AFP of 20–200 ng/mL, while 15/17 (88.2%) non-HCC patients had AFP ≤ 200 ng/mL. Among the whole study population (n = 64), ROC yielded that the simplified HCC-ART and AFP at cut-off values of 63.4 and 62.5 ng/mL were able to diagnose HCC patients with higher sensitivity and specificity for HCC-ART (83% and 53%) compared with serum AFP (78.7% and 47%), respectively. Areas under the curve of AFP, simplified HCC-ART, and AFP-L3 were 0.7 (P < 0.05), 0.64 (P < 0.01), and 0.49 (P > 0.05), respectively, with a significant difference between AFP-L3 and simplified HCC-ART (P < 0.05). On the other hand, among the subset of patients with AFP ranging from 20 to 200 ng/mL (liver cirrhosis ± HCC, n = 43), areas under the curve of AFP-L3 and HCC-ART for HCC were 0.72 (P = 0.017) and 0.59 (P > 0.05), respectively. At a cut-off value of 10.9% for AFP-L3, HCC was diagnosed with 82% sensitivity and 67% specificity (Fig. 1). However, there was no significant difference between AFP-L3 and HCC-ART for HCC diagnosis among this subgroup. **Conclusion:** Simplified HCC-ART could be a helpful score in HCC diagnosis. AFP-L3 could improve the diagnostic performance particularly in patients with AFP below the diagnostic cut-off level for HCC, that is, 200 ng/mL. **Keywords:** α-Fetoprotein L3, diagnosis, Egypt, hepatocellular carcinoma, simplified HCC-ART, tumor marker.
# 1227 Nucleos(t)ide analog therapy is associated with reduced hepatocellular carcinoma recurrence after radiofrequency ablation

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Efforts should be made to reduce the risk of tumor recurrence after radiofrequency ablation (RFA) for hepatocellular carcinoma (HCC). We aimed to investigate the association between nucleos(t)ide analog (NA) therapy for hepatitis B virus (HBV) and the risk of HCC recurrence following RFA. Using the Taiwan National Health Insurance Research Database between July 1, 2004, and December 31, 2012, we screened 48,807 patients with newly diagnosed HBV-related HCC. We identified 850 patients (200 patients who used NAs for more than 90 days and 650 patients who never used NA after RFA) who received RFA as a potentially curative treatement. Patients in the NA-treated cohort were randomly matched 1:2 with patients in the untreated cohort by age, gender, cirrhosis, and the time period between RFA and initiation of NA therapy. Finally, 148 patients were recruited in the NA-treated group and 296 in the untreated group. The HCC recurrence rate of the NA-treated group was significantly lower than that of the untreated group (2-year recurrence rate: 43.0%, 95% confidence interval [CI]: 34.5–51.4% vs 55.2%, 95% CI: 49.2–61.1%; P < 0.01). In a modified Cox regression analysis, NA therapy was independently associated with a decreased risk of HCC recurrence (hazard ratio 0.68, 95% CI: 0.50–0.92; P = 0.01). Multivariate stratified analyses verified the association of NA therapy and decreased HCC recurrence in all patient subgroups. **Conclusion:** Nucleos(t)ide analog therapy was associated with a decreased risk of HCC recurrence among patients with HBV-related HCC following RFA.

# 1238 Ultrasound-guided biopsy of hepatic cystic lesions with a thick wall

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**Aims:** This study aimed to assess the security and accuracy of US-guided biopsy of cystic lesions with a thick wall in liver. **Methods:** Fifteen patients with hepatic cystic masses were enrolled in this study from June 2012 to April 2015. We compared the pathology by US-guided biopsy with the postoperative. Patient selection included the following criteria: (i) the thickness of the cystic mass wall is more than 1 cm; (ii) the puncture path should be through normal hepatic tissues; and (iii) the thick wall of cystic masses should be parallel with the ultrasonic sound beam. In the process of US-guided biopsy, we performed the following: (i) detect the internal texture and adjacent tissue of the tumor in different sections; (ii) select those cyst walls that have a different blood supply to puncture; (iii) according to the direction of the cyst wall, select puncture site and approach; (iv) detect blood vessels in the tumor and peripheral blood vessels and bile duct; and (v) use color Doppler to detect whether there is bleeding. A coagulant was used in the cystic cavity to stop bleeding. **Results:** (i) US-guided biopsy of liver was performed in 15 patients successfully. (ii) The bleeding of one patient was stopped by using a coagulant in the cystic cavity. (iii) There was no serious complications after the implantation in other patients. (iv) The pathological results of US-guided biopsy agreed with postoperative pathologic results. **Conclusion:** (i) US-guided biopsy is less invasive, safe, and effective for tumor, especially for cystic tumor. (ii) Complications after US-guided biopsy can be treated in time.

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Correction added on 5 December 2015, after Online publication. Corresponding author is J QU.

# 1255 Assessment of percutaneous radiofrequency ablation treatment with Soloist and LeVeen needles for hepatocellular carcinoma patients

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**Introduction:** Hepatocellular carcinoma (HCC) is a common disease in the world as well as in Vietnam. Radiofrequency ablation (RFA) is a local therapy to destroy tumor tissue by heat. **Materials and Methods:** This is an interventional longitudinal study on HCC patients having ≤3 tumors with each tumor being ≤3 cm in size or with a single tumor of up to 5 cm and having Child Pugh A or B. The study was conducted in the Gastroenterology Department of Bach Mai Hospital from November 2011 to April 2015. **Results:** One hundred and twenty-seven patients with a mean age of 58.1 ± 10.3 underwent 368 times of RFA with the mean ablation times being 2.9 ± 1.5 in which 81 were treated only by RFA and 46 patients were treated by RFA combined with transarterial chemoembolization. HBV was the predominant cause of HCC with a rate of 67.7%. Eight patients underwent artificial ascites with a mean volume of 2125 ± 231 mL of 5% glucose, and two patients underwent artificial pleural effusion with a mean volume of 1100 ± 141 mL of 5% glucose due to difficult locations. The procedure was safe with the complication rate being 1.1% including hemotorax, ascites, pleural effusion, and hypervagal reaction, which were treated well by internal medicine. Fever and abdominal pain were recorded in 13.6% ablation times. After 1 month of the first RFA, 117 patients had complete and partial responses according to modified Response Evaluation Criteria in Solid Tumors (92.1%); after 9 months, 105 patients had complete and partial responses (82.7%). Forty-nine patients (38.6%) had better clinical response with gain weight and less fatigue. During follow-up time (18.1 ± 7.5 months), 5 patients died (3.9%); 22 patients had a new lesion (17.3%), 3 patients had portal vein thrombosis (2.3%), 1 patient had abdominal lymph node (0.8%), and 1 patient had tract seeding (0.8%). **Conclusion:** Radiofrequency ablation with Soloist and LeVeen needles is a safe technique and effective in improving treatment response and quality of life of HCC patients. **Keywords:** hepatocellular carcinoma (HCC), radiofrequency ablation (RFA).
# 1260 Expression of endoglin (CD105) in hepatocellular carcinoma with its clinicopathological and prognostic significance analysis

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**Background and Aims:** Hepatocellular carcinoma (HCC) is a highly vascularized tumor with intense angiogenesis, but the molecular mechanisms regulating angiogenesis have not been fully understood. We clarified the relation of CD105 expression with HCC and explored its importance with HCC prognosis comprehensively. **Methods:** A total of 112 hepatocellular carcinoma patients were analyzed. Immunohistochemical staining for the CD105 was performed in tumor and non-tumor specimens. We further compared the relation of CD105 with clinicopathological parameters by immunohistochemical staining. We also analyzed 30 pairs of fresh tissue specimens including a tumor part and a non-tumor part in 30 hepatocellular carcinoma patients using the quantitative real-time polymerase chain reaction and western blot and analyzed the expression of endoglin with clinicopathological parameters. **Results:** We demonstrated that CD105 was more abundant in the non-tumor part of liver in HCC patients. And the well-differentiated HCC and early-stage HCC and lower serum α-fetoprotein level had higher microvessel density of CD105 expression. And a higher CD105 expression had a lower tumor recurrent rate after operation. In western blot, the early-stage and smaller HCCs had a higher CD 105 expression. The quantitative real-time polymerase chain reaction also showed a higher CD 105 expression in the non-tumor part than in the tumor part. **Conclusions:** CD105 has an important role in HCC angiogenesis, and this study provides evidence for HCC prognosis related with CD105 expression. We obtained similar results and validated them by immunohistochemical staining and quantitative real-time polymerase chain reaction and western blot.

# 1265 Fighter or genomics? Surviving a decade of liver cancer conservatively

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**Introduction:** An estimated 695,900 liver cancer deaths occurred worldwide in 2008. Based on US statistics, the 5-year survival rate is only 15%. The low survival rate is attributable to concomitant liver cirrhosis, which is itself is fatal. **Case Description:** We present a case of a 65-year-old lady who survived a decade despite being diagnosed with liver cancer in a cirrhotic liver. She had chronic hepatitis C infection but achieved sustained viral response following therapy with pegylated interferon and ribavirin in 2005. A year later, she was diagnosed with liver cancer during surveillance. The cancer measured 2.2×2.6×1.7 cm in segment 2. Surgery was not an option because of her poor liver reserve. She was not keen on further treatment and opted for conservative therapy. A repeated computed tomography scan after 5 years revealed the tumour had doubled in size to 4.2×5.8×4.2 cm with other new lesions. Regular monitoring of α-fetoprotein showed a steady rise from the initial hundreds to thousands and finally >10,000 ng/mL. She remained asymptomatic until her 10th year when she started experiencing liver decompensation. Despite a known poor survival outcome, she defied all odds to live a decade with a European Cooperative Oncology Group score of 1 despite no cancer treatment. **Conclusion:** Liver cancer is highly heterogeneous, and cancer genomics may hold the key to explaining the aggressiveness and indolence of certain cancer subtypes. By unlocking this, we may one day individualize liver cancer treatment. Some may not require aggressive treatment regimes where the benefits and risks need to be weighed against survival prognosis.

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# 1290 Building of a scoring model based on preoperative plasma fibrinogen level for predicting tumor recurrence after liver transplantation for hepatocellular carcinoma

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**Objective:** Elevated plasma fibrinogen (FBG) level is associated with tumor progression and poor patient outcomes in several cancers. However, the prognostic value of FBG in hepatocellular carcinoma (HCC) patients undergoing liver transplantation (LT) is unclear. The aim of this study was to investigate the prognostic value of preoperative plasma FBG level in HCC patients after LT and build a scoring model based on FBG for predicting tumor recurrence after LT. To our knowledge, this is the first report discussing the prognostic value of preoperative plasma FBG level in HCC patients after LT. **Methods:** We analyzed the outcome of 99 patients who underwent LT for HCC at our institution. Clinical and pathological factors were evaluated by Kaplan–Meier analysis, and survival curves were compared using the log-rank test. Cox multiple-regression analysis was performed to determine the parameters predicting HCC recurrence and patient survival. The optimal cut-off value for elevated level of preoperative FBG was determined using a receiver operating characteristic curve analysis. A scoring model was built by giving a value of 0 or 1 to independent risk factors selected by Cox regression analysis. **Results:** Preoperative FBG levels were significantly higher in patients with tumor recurrence (3.27 g/L) compared with those in patients without recurrence (2.34 g/L) (P<0.001). A cut-off value for elevated FBG level of 2.68 g/L was defined using receiver operating characteristic curve analysis. There were significant differences in disease-free survival between the elevated FBG group and normal FBG group (78.4% vs 37.2%, P=0.001). Patients with macrovascular invasion and α-fetoprotein >400 ng/mL also had significantly higher preoperative plasma FBG concentration than the others. Macrovascular invasion, tumor number >3, and FBG ≥2.68 g/L were independent risk factors of HCC recurrence after LT. A scoring model was built to predict the risk of tumor recurrence, with a sensitivity of 68.3% and a specificity of 87.5%. **Conclusion:** Pretransplant elevated plasma FBG level significantly increases the risk of tumor recurrence in patients after LT for HCC. The scoring model we built based on FBG level and tumor number strongly correlates to tumor recurrence and may aid in the selection of patients that would most benefit from transplantation for HCC.
# 1385 Prognostic factors of transarterial chemoembolization/transarterial embolization for hepatocellular carcinoma patients with prolonged survival of more than 3 years
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Background: The advancements in transarterial management of non-resectable hepatocellular carcinoma, including transarterial embolization (TAE) and transarterial chemoembolization (TACE), are used as palliative therapies. The aim of this study is to evaluate the survival rate of patients subjected to TAE/TACE and to propose a new opinion. Method: A total of 112 patients of hepatocellular carcinoma, who were managed with TAE/TACE and radiofrequency ablation (RFA) and/ or ultrasound-guided alcohol injection (USGAI) and survived for 3 years or more till the year 2014, were studied. To explore factors influencing their survival, age, number of procedures (including RFA and USGAI) in 1 year, the frequency of procedures in 1 year, Barcelona Clinic Liver Cancer stage, Model for End-stage Liver Disease scores, spleen size, and all blood data related to liver were analyzed. Results: The survival rate was statistically significantly higher if patients were younger than 70 years old (log-rank test, \( P = 0.026 \)) and have had more than three times of TAE/TACE procedures within 1 year (\( P = 0.019 \)), prothrombin time of \( \leq 12 \) s (\( P = 0.010 \)), international normalized ratio of \( \leq 1.2 \) (\( P = 0.012 \)), alkaline phosphatase of \( \leq 95 \) U/L (\( P = 0.037 \)), Barcelona Clinic Liver Cancer staging of A (\( P = 0.007 \)), and an average interval between each procedure of \( > 8 \) months (\( P = 0.034 \)). Conclusion: The survival outcomes of patients presenting with early staging, less severe coagulopathy and liver dysfunction, and increasing number of procedures within the given time frame showed comparable improvements.

# 1490 A pilot safety study of natural killer cells from sibship to treat the recurrence of hepatocellular carcinoma after liver transplantation
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Objective: Natural killer (NK) cells have been thought to play a pivotal role in innate immunity. However, the safety and efficacy of NK cells for the treatment of hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT) are unknown. In this study, we investigated whether the injection of activated NK cells (CD3+CD56+ cells) from a sibship with the same blood type is safe for the treatment of HCC recurrence after LT. Method: Six patients with HCC recurrence after LT were eligible and enrolled in this study. The patients received injections of \( 5 \times 10^6 \) NK cells from the sibship with the same blood type four times at a frequency of once every 2 weeks. Lymphocytes were extracted from the peripheral blood mononuclear cells and cultured with interleukin-2 and other cytokines for 2 weeks. The purity of lymphocytes was assessed by flow cytometric analysis, and only the CD3+CD56+ cells greater than 70% were used. The adverse effects, laboratory tests, and overall survival were assessed. Results: No serious adverse effects and laboratory abnormalities were identified as related to the treatment of NK cells. Five patients were alive in the follow-up period of 2–6 months, while one died of liver failure due to tumor progression after 2 months of NK cell infusion. There was no graft-versus-host disease in all six patients during follow-up. Conclusion: In this study, we have demonstrated for the first time to our knowledge that NK cells from sibships with the same blood type can be used safely as adoptive immunotherapy for the treatment of HCC recurrence after LT.

# 1511 Expression of β2-arrestin 1 in the course of mice non-alcoholic fatty liver disease progressing to hepatocellular carcinoma
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Aims: This study aimed to investigate the expression of β-arrestin 1 and its possible function in the course of non-alcoholic fatty liver disease (NAFLD) progressing to hepatocellular carcinoma. Materials and Methods: C57BL/6 mice were fed with chow diet and high-fat diet (HFD) for 9, 24, and 48 weeks, and the incidence of hepatocellular carcinoma was observed at the end of 48 weeks. Expressions of β-arrestin 1 in the liver tissue of mice were detected by western blot and real-time reverse transcription–polymerase chain reaction. Results: The liver of mice exhibited the typical appearance of fatty liver after 9 weeks of HFD. At the 48th week or the end-point of study, the incidence of hepatocellular carcinoma was 0/23 in the chow diet group and 4/22 in the HFD group with a statistically significant difference (\( P < 0.05 \)). Compared with the chow diet group, the HFD group had statistically increased β-arrestin 1 protein expression of liver tissue at 9 weeks (\( P < 0.05 \)), and the level of β-arrestin 1 protein was positively correlated to the duration of HFD (\( r = 0.949 \), \( P = 0.000 \)). Furthermore, the expressions of β-arrestin 1 protein in tumor tissue was dramatically higher than that of fatty liver tissue from the same period of HFD (\( P < 0.05 \)). The change of β-arrestin 1 mRNA exhibited the same tendency. The order from lowest to highest in mRNA level of β-arrestin 1 was liver tissue from mice fed with chow diet for 9 weeks, liver tissue from mice fed with HFD for 9, 24, and 48 weeks, and tumor tissue from hepatocellular carcinoma (all \( P < 0.05 \)). Conclusions: It is easy to develop NAFLD in mice fed with HFD, and there is a higher incidence of hepatocellular carcinoma in NAFLD mice. β-Arrestin 1 might play an important role in the course of NAFLD progressing to hepatocellular carcinoma.

Keywords: β-Arrestin 1; hepatocellular carcinoma; non-alcoholic fatty liver disease (NAFLD).
# 1533 Increased risk of hepatocellular carcinoma in chronic hepatitis C patients with new-onset diabetes: A nationwide cohort study

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**Background:** The impact of diabetes for hepatocellular carcinoma (HCC) development in chronic hepatitis C patients remains controversial. We aimed to investigate the risk of HCC in CHC patients who develop new-onset diabetes.

**Methods:** We conducted a nationwide cohort study by using the Taiwanese National Health Insurance Research Database, which comprised data from >99% of the entire population. Among the randomly sampled one million enrollees, 6251 adult CHC patients were identified from 1997 to 2009. Diabetes was defined as new onset in patients who were given the diagnosis in the years 1999–2009 but not in 1997–1998. The cohorts of CHC with new-onset diabetes (n = 1100) and 1:1 ratio age-matched, gender-matched, and inception point (onset date of diabetes)-matched non-diabetes (n = 1087) were followed up from the inception point until the development of HCC, withdrawal from insurance, or December 2009. **Results:** After adjustment for competing mortality, patients with new-onset diabetes had a significantly higher cumulative incidence of HCC (relative risk = 1.544, 95% confidence interval CI = 1.000–2.387, modified log–rank test, P = 0.047) as compared with those without. After adjustment for age, gender, cirrhosis, hyperlipidemia, CHC treatment, diabetes treatment, comorbidity index, obesity, and statin therapy by the Cox proportional hazard model, diabetes was still an independent predictor for HCC (hazard ratio HR = 1.906, 95% CI = 1.102–3.295, P = 0.021). The risk for HCC was increased in those who were 40–59 years old, independent of other variables (HR = 3.086, 95% CI = 1.045–9.112, P = 0.041) and after adjustment for competing mortality (modified log–rank test, P = 0.009). **Conclusions:** Chronic hepatitis C patients who develop diabetes are at an increased risk of HCC over time.

# 1547 The NIACE score: An additional prognostic tool that applies to any hepatocellular carcinoma treatment modality

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**Background:** Nowadays, therapeutic options in hepatocellular carcinoma (HCC) are based on the Barcelona Clinic Liver Cancer (BCLC) staging system algorithm. However, each BCLC stage comprises a wide spectrum of tumors, and patients’ prognosis is variable after treatment. **Aim of the Study:** This study aimed to refine the stratification of patients after curative or palliative treatment of HCC, by establishing a new, simple prognostic score. **Methods:** The score was defined by a regression model based on an advanced HCC BCLC C population (n = 161) and validated with several cohorts at different stages (BCLC C n = 377, BCLC B n = 104, and BCLC A n = 128). It was then assessed with HCC patients according to the administered treatment (surgery n = 248/RFA, TACE n = 321, sorafenib n = 285). Five centers took part in this study. **Results:** Five variables had independent prognostic values: the number of nodules, the infiltrating nature of the HCC, α-fetoprotein serum level, Child–Pugh score, and European Cooperative Oncology Group performance status grade. They were integrated into a new score (NIACE) ranging from 0 to 7, correlated to survival, whatever the BCLC stage of the HCC (A, B, or C) and the administered treatments are. Through the use of different threshold values, this score allows us to define two populations having different survivals within each HCC treatment modality. **Conclusion:** The NIACE score is a simple additional tool that allows us to define different prognostic subgroups after curative or palliative treatment of HCC. This finding could have clinical implications for the management of patients with HCC.

# 1553 The Child–Turcotte–Pugh numeric score of 6 or more has influence on survival in patients with hepatocellular carcinoma after curatively hepatic resection

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**Background/Aims:** Surgery is one of the preferred methods for curative intervention of HCC. Risk factors of mortality and tumor recurrence are major issues after curative hepatectomy. Child–Turcotte–Pugh (CTP) score is a scoring system to assess the severity of liver cirrhosis and a part of the
Barcelona Clinic Liver Cancer staging system. Most patients who underwent surgical resection of HCC belong to CTP classification A or early B. However, few articles discussed the role of the CTP numeric score in these patients. This study aimed to investigate the prognostic factors of HCC after liver resection in the Far Eastern Memorial Hospital. **Methods:** From March 2006 to January 2011, 178 patients who underwent curative hepatectomy (for HCC) in the Far Eastern Memorial Hospital were included and followed till January 2014. CTP scores were assessed in spite of liver cirrhosis or not. We used the Kaplan–Meier method to analyze their survival and recurrence. Demographics, CTP scores, tumor factors, and pathologic characteristics were tested by log–rank test. Variables in univariate analyses with \( P < 0.1 \) were subjected to multivariate Cox regression modeling. Because the biochemical variables, including albumin, total bilirubin, prothrombin time, and ascites, are parameters of CTP, we analyzed CTP score and parameters of CTP by different methods in multivariate analysis. In method 1, variables including CTP score and classification were analyzed, but the parameters of CTP were excluded. In method 2, parameters of CTP and other variables were evaluated excluding CTP score and classification. **Results:** Of the 178 patients, 135 patients were male, and 43 patients were female. The median age was 60.38 years, and the median follow-up duration was 40 months (1–95 months). One hundred twenty-seven patients (71.35%) had liver cirrhosis. One hundred fifty-five (87.08%) and 21 (11.80%) patients belonged to Child classifications A and B, and the highest CTP score was 9 in 3 patients. Hepatitis B/C virus and both infections were detected in 95 (53.37%), 44 (24.72%), and 9 (5.2%) patients. The multivariate analysis of variants that predict recurrence and survival were in Tables 1 and 2. **Conclusions:** (i) Child–Turcotte–Pugh \( \geq 6 \) was a poor survival factor in patients after curative resection of HCC. Albumin \( \leq 3.5 \text{ g/dL} \), the major component of CTP \( \geq 6 \), was a poor prognostic factor in survival. Major branch portal venous thrombosis, in only three patients in our study, was a poor recurrent prognostic factor.

### Table 1 Multivariate analysis of variants that predict recurrence

| Variables | Hazard ratio | 95% confidence interval | \( P \)-value |
|-----------|--------------|-------------------------|--------------|
| \( \alpha \)-Fetoprotein 20 | 2.376 | 1.451–3.889 | 0.001 |
| Portal venous thrombosis Stage 1 | 1.00 | | |
| Stage 2 | 1.597 | 0.873–2.921 | 0.129 |
| Stage 3 or 4 | 3.713 | 2.003–6.885 | <0.001 |

*The 1-year, 3-year, and 5-year recurrence rates are 55.24%, 63.74%, and 65.04%, respectively.

*Portal venous thrombosis (\( P = 0.02 \)) and tumor size > 5 cm (\( P = 0.042 \)) were factors for very early recurrence (recurrence < 1 year).*

### Table 2 Multivariate analysis of variants that predict survival

| Variables | Hazard ratio | 95% confidence interval | \( P \)-value |
|-----------|--------------|-------------------------|--------------|
| Child score 5 | 1.00 | | |
| Child score \( \geq 6 \) | 2.948 | 1.774–4.899 | <0.001 |
| Stage 1 | 1.00 | | |
| Stage 2 | 3.543 | 1.632–7.693 | 0.003 |
| Stages 3 + 4 | 6.83 | 3.16–13.903 | <0.001 |
| Indocyanine green, 15 min > 10% | 1.713 | 1.015–2.890 | 0.044 |
| Albumin 3.5 | 2.255 | 1.306–3.893 | 0.004 |
| Stage 1 | 1.00 | | |
| Stage 2 | 2.839 | 1.330–6.060 | 0.007 |
| Stages 3 + 4 | 5.868 | 2.835–12.146 | <0.001 |

*The 1-year, 3-year, and 5-year survival rates are 74.50%, 56.38%, and 39.46%, respectively.

*Of the 61 patients with CTP \( \geq 6 \), most of the patients (\( n = 36, 57.38% \)) had albumin \( \leq 3.5 \text{ g/dL} \) (ascites in 50.82%, total bilirubin \( \geq 2.0 \text{ mg/dL} \) in 14.75% patients).

*The CTP classification (A vs B) did not reach statistical significance (\( P = 0.485 \), univariate).*

# 1652 Hepatocellular carcinoma, NIACE score: An aid to the decision-making process before the first transarterial chemoembolization

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**Background:** NIACE score (which stands for nodules [N], infiltrative tumor [I], \( \alpha \)-fetoprotein [A], Child–Pugh [C], European Cooperative Oncology Group performance status [E]) (American Association for the Study of Liver Diseases 2014 [P1329] and EASL 2015 [P0376]) defines two populations with different survival. Transarterial chemoembolization (TACE) is recommended for intermediate-stage HCC (Barcelona Clinic Liver Cancer [BCLC] B). In clinical practice, it is used to treat more advanced HCC or earlier stages not suitable for surgery/radiofrequency ablation or recurrent after surgery. **Aim of the Study:** This study aimed to evaluate the NIACE score as an aid to the decision-making process before the first TACE in order to determine the patients who may not benefit from TACE. **Patients and Methods:** Patients treated with TACE as the main treatment in our institution between 01/2007 and 12/2013 were included, including HCC with segmental portal vein thrombosis. Patients who had additional treatment after TACE (surgery/radiofrequency ablation and transplantation), involved in the establishment of the NIACE
score, and had metastatic HCC and HCC with main portal vein thrombosis were excluded. The results were confirmed in an external cohort treated with TACE during the same period. Likelihood ratio, Akaike information criterion, and area under the receiver operating curves were used to determine the best model. Results: The internal cohort included 230 patients, with a median age of 67 (58.5–74) years and European Cooperative Oncology Group performance status of 0/1 (100%); patients were mainly cirrhotics (95%), classified as Child–Pugh A (66%) or Child–Pugh B (29%), related to a viral etiologies (48%) or alcohol 33%, and classified as BCLC A (39%), B (40%), or C (21%). HCCs were multi-nodular (41%) or infiltrating tumors (19%). Thirty-three percent of the patients had an elevated α-fetoprotein level of ≥ 200 ng/mL, and 58% had esophageal varices. The median overall survival (OS) of the group was 22.3 (10.2–36.5) months. The score’s variation was correlated to survival. With a threshold value < 3, the score distinguished between two populations having different median OS: NIACE < 3 (n = 160), 28 (26–35) months versus NIACE ≥ 3 (n = 70), 9.6 (7–12) months, P = 0.001. Concerning the external cohort including 91 BCLC A and B HCC patients from Nancy, treated by TACE, the median OS of the group was 24.9 (20.9–32.5) months. By applying a NIACE < 3 threshold, the median OS of the NIACE < 3 group was 27 (23–26) months versus 13 (13–23) months for the NIACE ≥ 3 group, P = 0.0015. Conclusion: In this multicentric study involving HCC patients treated with TACE as the main treatment, NIACE score distinguishes subgroups with different prognoses. Patients with a score of NIACE > 3 do not seem to benefit from TACE treatment. These results should be confirmed in a prospective study.

# 1667 How to guide sorafenib for advanced hepatocellular carcinoma? Usefulness of NIACE score
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Background: Sorafenib is the first Food and Drug Administration-approved therapy for patients with advanced HCC. It is a treatment option for intermediate-stage HCC (Barcelona Clinic Liver Cancer [BCLC] B) not suitable or refractory to transarterial chemoembolization (Bruijx J et al., J. Hepatol., 2012). The prognosis of patients treated with sorafenib is variable. The NIACE score (American Association for the Study of Liver Diseases 2014 [P1329] and European Association for the Study of the Liver 2015 [P0376]), ranging from 0 to 7, is correlated to survival, whatever the BCLC stage of the HCC (A, B, or C) are. It includes parameters such as the infiltrating nature of the HCC at any stage of the disease and the AFP level ≥ 200 ng/mL. Aim of the Study: This study aimed to define among HCC patients treated with sorafenib subgroups with different prognoses using the NIACE score. Patients and Methods: All patients treated with sorafenib as the main therapeutic modality between 01/2008 and 12/2013 in four institutions (Marseille n = 139, Nancy n = 83, Bordeaux n = 119, and Rennes n = 83) were included. We excluded patients involved in the development of the score and patients who had additional treatment (transarterial chemoembolization, surgery/radiofrequency ablation, or transplantation) with sorafenib. Results: The four cohorts, that is, 424 patients, had common characteristics: age, male sex, majority of Child–Pugh A cirrhosis, infiltrating nature of HCC, portal vascular invasion, elevated α-fetoprotein level ≥ 200 ng/mL in 50% of cases. The median duration of sorafenib administration in the four cohorts varied from 3.7 (1.3–8.1) to 6.9 (3.8–11.3) months; less than 20% of patients stopped the treatment during the first month. By applying the score, there were subgroups of different prognoses, and the score’s variation was correlated to survival. The NIACE score with a threshold value < 3 corresponded to two groups with different median overall survival into the three external cohorts: Nancy, NIACE < 3 (n = 28), 16 (14–25) months versus NIACE ≥ 3 (n = 55), 6 (4–8) months, P < 0.0001; Rennes, NIACE < 3 (n = 37), 10.6 (4.1–17.1) months versus NIACE ≥ 3 (n = 46), 5.1 (2.9–7.4) months, P < 0.0001; and Bordeaux, NIACE < 3 (n = 44), 11.3 (8.1–15.9) months versus NIACE ≥ 3 (n = 75), 6.0 (4.3–7.6) months, P < 0.0001. The median duration of sorafenib administration in the four cohorts varied from 2.2 (0.7–4.1) months to 4.2 (2.6–7.1) for patients with a NIACE score > 3 versus 6.0 (3.9–13.1) months to 9.9 (6.8–21.5) months for patients with a NIACE score < 3. The median survival of patients with NIACE score > 3 was similar to a group of untreated patients. Conclusion: In this multicenter series of HCC treated with sorafenib as a main treatment, NIACE score distinguishes subgroups with different prognoses. Patients with a NIACE score > 3 do not seem to benefit from treatment with sorafenib.

# 1673 Increasing incidence of and mortality by hepatocellular carcinoma and decreasing mortality by liver diseases in Korea: Nationwide whole-population data analyses
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Background and Aims: The annual mortality rate by chronic liver diseases and hepatocellular carcinoma (HCC) that are associated with hepatitis B and C has been shown to be reduced by antiviral treatments. However, the prolonged life expectancy of patients with chronic viral hepatitis may increase the cumulative incidence of and mortality by HCC. Methods: Data on incidence rates of HCC were obtained from the Korea Central Cancer Registry, which compiles nationwide data on all newly diagnosed cancers. Data on cause-specific mortality and on liver transplantation were obtained from the Korean National Death Registry (Statistics Korea) and Korea National Organ Sharing, respectively. Results: The mean age at death by liver diseases and HCC significantly increased between 1998 and 2013 (56.3 vs 64.8 years; β=0.65, P < 0.001, and 60.0 vs 63.9 years; β=0.30, P < 0.001, respectively). Between 1998 and 2013, the mortality rate by liver diseases and viral hepatitis significantly decreased (25.4/100,000 people vs 14.7/100,000 people; β=−0.77, P < 0.001). The incidence rate of liver mortality by HCC significantly increased during the same period (28.2/100,000 people vs 32.9/100,000 people; β=0.45, P < 0.001, and 20.0/100,000 people vs 22.6/100,000 people; β=0.11, P = 0.01). The trends in mortality rates by liver diseases and HCC were consistently observed after adjusting for liver transplantation and mortality by alcoholic disease. Conclusion: During the recent 15 years when the antiviral treatments for hepatitis B and C have been introduced, life expectancy of patients with
chronic liver disease has increased in Korea, a hepatitis B virus endemic area, which may be associated with the increasing cumulative incidence and mortality rates by HCC. These results suggest that HCC is becoming the main cause of death in patients with chronic viral hepatitis.

### 1683 Hepatocellular carcinoma, NIACE score: A simple tool to better distinguish patients at risk of relapse after surgery

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**Background:** Surgery is the reference treatment of HCC. Despite patient selection being linked to underlying cirrhosis and late detection, patients’ prognosis is variable after surgery. NIACE score (which stands for nodules [N], infiltrative tumor [I], α-fetoprotein [AFP] [A], Child–Pugh [C], European Cooperative Oncology Group performance status [E]) (American Association for the Study of Liver Diseases 2014 [P1:329] and EASL 2015 [P10:376]) allows us to define subgroups with different prognoses whatever the BCLC stage of HCC (A, B, or C) are. **Aim of the Study:** This study aimed to identify among operated HCC or HCC treated by radiofrequency ablation subgroups with different prognoses, using the NIACE score.

**Patients and Methods:** We selected Barcelona Clinic Liver Cancer (BCLC) A, B, and C HCC patients treated by surgical resection in our service between 01/2007 and 12/2013. We excluded patients who participated in the development of the NIACE score and those who are transplanted patients. The results were confirmed in an external cohort treated exclusively by surgery. Likelihood ratio, Akaiki information criterion, and area under the receiver operating curves were used to determine the best model.

**Results:** Internal cohort included 104 patients, with a median age of 71 (58; 75) years; patients were mostly cirrhotic (70%); related to viral etiologies (40%), alcohol 19%, and metabolic syndrome 28%; and classified as Child–Pugh A (64%) and B (6%) and BCLC A (64%), B (28%), and C (8%). The median size of operated tumors was 30 mm (25; 57); 7% of HCC were multi-nodular; 20% of patients had an elevated AFP of ≥200 ng/mL. The mean overall survival (OS) was 55.4 ± 3.0 months. The NIACE ≤1 threshold is the one with the best likelihood ratio (13.2423, P = 0.0003). Application of this threshold makes it possible to discriminate between two groups having different mean OS (NIACE ≤1, 66.3 ± 2.6 months, vs NIACE > 1, 25.7 ± 2.9 months, P < 0.0001) and different mean time until progression (NIACE ≤1, 26.9 ± 16.3 months, vs NIACE > 1, 9.2 ± 9.7 months, P < 0.0001). External cohort was made of 144 BCLC A, B, and C HCC patients; the mean OS was 51.6 ± 3.9 months. By applying a NIACE ≤1 threshold, the mean OS of the NIACE ≤1 group was 66 ± 6 versus 41 ± 5 months for the NIACE > 1 group, P < 0.0001. The score also distinguished between two BCLC B HCC patient populations having significantly different median OS: 50 (27–78) versus 16 (9–36) months, P = 0.0002. **Conclusion:** There was a significant difference survival between patients having a low score, which include not only BCLC A HCC but also BCLC B HCC, and the others patients. Without referring to the stage of the disease, survival is probably influenced by the infiltrating nature of the tumor and a significantly high AFP level. NIACE is a simple score, which is able to distinguish between subgroups with different prognoses, within an HCC population treated by surgery.

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**# 1688 Hepatectomy for malignancy confined to segment VII**

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**Introduction:** Despite advancement in surgical technique, resection of hepatic malignancy located in Couinaud’s segment VII remains challenging because of its deep location. Full mobilization of the right liver is necessary to facilitate resection. The most common surgical procedure for HCC is posterior sectionectomy and wedge resection for metastasis. **Material and Method:** Between August 2008 and March 2015, 127 consecutive patients received hepatectomy for HCC, metastasis, cholangiocarcinoma, and others. Twenty-seven patients received hepatectomy for malignancy confined to segment VII. The operation procedure selected was based on background liver function, tumor size, and tumor number. **Result:** Fifteen patients with HCC received posterior sectionectomy, and two patients with huge HCC had right hepatectomy. The remaining 10 patients with metastasis received wedge resection or posterior sectionectomy. **Conclusion:** For malignancy located in segment VII, full mobilization of the right liver is essential for safe hepatectomy. The procedure may range from wedge resection, posterior sectionectomy to right hepatectomy depending upon the background liver function.

**Keywords:** hepatectomy, posterior sectionectomy, segment VII.

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**# 1690 The effect of confluent hepatic fibrosis on hepatectomy**

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**Introduction:** Despite advancement in surgical technique, resection of hepatic malignancy located in Couinaud’s segment VII remains challenging because of its deep location. Full mobilization of the right liver is necessary to facilitate resection. The most common surgical procedure for HCC is posterior sectionectomy and wedge resection for metastasis. **Material and Method:** Between August 2008 and March 2015, 127 consecutive patients received hepatectomy for HCC, metastasis, cholangiocarcinoma, and others. Twenty-seven patients received hepatectomy for malignancy confined to segment VII. The operation procedure selected was based on background liver function, tumor size, and tumor number. **Result:** Fifteen patients with HCC received posterior sectionectomy, and two patients with huge HCC had right hepatectomy. The remaining 10 patients with metastasis received either wedge resection or posterior sectionectomy. **Conclusion:** For malignancy located in segment VII, full mobilization of the right liver is essential for safe hepatectomy. The procedure may range from wedge resection, posterior sectionectomy to right hepatectomy depending upon the background liver function.

**Keywords:** hepatectomy, posterior sectionectomy, segment VII.
Introduction: Confluent hepatic fibrosis (CHF) is a mass-like fibrosis seen in some patients with advanced fibrosis. The morphological changes were attributed to selective volume reduction, especially middle hepatic venous (MHV) drainage area. The long length of MHV with its relatively large drainage area may account for the selective volume reduction. The topographical change in the surface anatomy of such liver may cause confusion in major hepatectomy. Material and Method: Between August 2008 and March 2015, 127 consecutive patients received hepatectomy for hepatocellular carcinoma (HCC), metastasis, cholangiocarcinoma, and others. Seven patients (5.5%) demonstrated CHF. All cases with CHF occur in HCC patients. The correlation of preoperative imaging and the resected specimen was investigated. Result: The surface anatomy of the liver showed atrophic change with capsular retraction. It is mostly seen in the MHV drainage area. Conclusion: Topographic confusion may occur for hepatectomy of liver with CHF. Preoperative imaging study may provide useful information for distinction of surgical boundaries. Keywords: confluent hepatic fibrosis, hepatectomy.

#1752 Unusual presentation of metastatic thymic carcinoma in liver: A case report
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A thymic carcinoma, basaloid type, is a rare neoplasm and also an unusual case with extra-thoracic metastasis. Most patients presented with dyspnea, chest pain, and cough initially. Asymptomatic patients account for less than

Figure 1 Abdominal ultrasonography revealed one mix to hyperechoic tumor lesion around 4.8 × 5.0 cm in the right lobe of the liver. S5–S8. There is no obvious blood flow in the liver tumor under Doppler ultrasonography.

Figure 2 Abdominal CT revealed a 5.5 × 4.4 cm heterogeneous lesion with central high density at hepatic subphrenic area.
one-third in all cases. The clinical outcome for advanced stage of thymic carcinoma depends on complete resection. However, complete surgical resection is not always possible in cases of advanced-stage thymic carcinoma because of local regional invasion.

We reported a 61-year-old man who had a medical history of neurofibroma involving the thoracolumbar spine and underwent resection because of paraplegia in 2008 and 2010. One hepatic mass was found accidentally by abdominal ultrasound on November 2014. On abdominal ultrasonography, this huge mass was homogeneous hyperechogenicity (Fig. 1). Computed tomography (CT) of the abdomen (Fig. 2) presented that this metastatic mass had soft tissue density with central calcification. Fluorodeoxyglucose (FDG) positron emission tomography was performed to search for the primary site of malignancy, and lobulated FDG hypermetabolic lesions were located in the anterior mediastinum (Fig. 3). Chest CT presented a lobulated soft tissue density mass with central necrosis, and perifocal lymphadenopathy occupied anterior mediastinum. The patient underwent resection of the thymic tumor followed by curative partial hepatectomy. It was proved to be thymic basaloid carcinoma with liver metastasis (Fig. 4). After surgical intervention, he received concomitant chemoradiotherapy 1 month later. The patient was still alive 6 months after the appearance of the liver metastasis.
(a) there was prominent palisading of the tumor cells around the neoplastic islands and nests. The sections reveal a malignant tumor composed of ovoid to short-spindle neoplastic cells with a high nuclear cytoplasmic ratio and frequent mitoses arranged in cystic or solid patterns from surgical specimen of thymus (hematoxylin-and-eosin stain, magnification 100×).

(b) Microscopically, the liver parenchyma shows infiltration of basaloid tumor cells with high nuclear cytoplasmic ratio and occasional mitotic figures, consistent with metastatic thymic carcinoma of liver (hematoxylin-and-eosin stain, magnification 40×).

**Aims**: This study aimed to investigate the influence of HBV DNA elevation on HCC recurrence and the preventive role of antiviral therapy. **Methods**: One hundred forty-four patients who had Barcelona Clinic Liver Cancer stage 0 or A and received surgical resection as primary therapy were enrolled. HBV DNA elevation was defined as reactivation in patients without preoperative antivirals or virologic breakthrough in patients with preoperative antivirals. **Results**: Overall 1-year, 3-year, and 5-year recurrence was 20.1%, 33.3%, and 45.1%, respectively. In multivariate analysis for risk factors of recurrence, multiple tumor and HBV DNA elevation, ALT ≥ 30, were independently associated with HCC recurrence. Multiple tumor and HBV DNA elevation were independent risk factors for HCC recurrence irrespective of preoperative antiviral therapy. In multivariate analysis for risk factors of HBV DNA elevation, age < 50 years, no preoperative antivirals, and HBV DNA ≥ 2000 remained as risk factors. Risk factors for HBV DNA elevation were further analyzed in patients without preoperative antivirals. Age < 50 years, HBV DNA ≥ 2000 IU/mL, hepatitis B e antigen positivity, and delayed antiviral therapy were independent risk factors for HBV DNA elevation. **Conclusion**: Hepatitis B virus DNA elevation after resection increases the risk of HCC recurrence irrespective of preoperative antivirals. However, HBV DNA elevation is an independent risk factor for recurrence in patients without preoperative antivirals. Therefore, antiviral therapy should be considered to prevent HBV DNA elevation and HCC recurrence, especially in patients with age < 50 years and/or HBV DNA ≥ 2000 IU/mL and/or hepatitis B e antigen positivity.

**# 1766 Enhanced liver fibrosis score predicts hepatocellular carcinoma in Singapore Chinese Authors**: WM LOO[1]; LZ ONG[2]; YY DAN[1]; WP KOH[3] **Affiliations**: [1]Division of Gastroenterology and Hepatology, National University Hospital, Singapore [2]Division of Laboratory Medicine, National University Hospital, Singapore [3]Duke-NUS Graduate Medical School Singapore, Singapore

**Background**: The enhanced liver fibrosis (ELF) test is based on three extracellular matrix markers associated with liver fibrosis: hyaluronic acid, tissue inhibitor of metalloproteinase-1, and propeptide of type III procollagen. While epidemiologic studies suggest that the ELF score can predict transplant-free survival in patients with cirrhosis, the use of ELF score as a predictor of hepatocellular carcinoma (HCC) has not been examined. **Methods**: We examined the association between ELF scores and HCC risk using a matched case-control set of 61 cases and 61 controls nested within the Singapore Chinese Health Study, a population-based prospective cohort of Chinese men and women (45–74 years), who were recruited during 1993–1998 in Singapore. Blood from cases was collected before cancer diagnosis, and controls were matched by age, gender, and time of blood taking. **Results**: Hepatocellular carcinoma cases had significantly higher serum levels of hyaluronic acid, tissue inhibitor of metalloproteinase-1, propeptide of type III procollagen, and ELF scores than controls (all \(P < 0.001\)). An optimal cut-off of 10.2 for ELF score distinguished between cases and controls with an area under the receiver operating characteristic curve of 0.82 (95% confidence interval, 0.75–0.89) and with a sensitivity of 72% and a specificity of 80%. Compared with lower scores, an ELF score of 10.2 or above was associated with a 26-fold increase in risk of HCC (odds ratio [OR] = 25.75, \(P = 0.002\)). The risk estimate was much higher among individuals negative for serology markers.
of chronic infection with HBV or HCV (OR = 27.75, P = 0.002) than among those who were positive (OR = 3.94, P = 0.23). **Conclusion:** Our data demonstrated that the ELF score is a potent predictive marker of non-viral hepatitis-related HCC, potentially allowing for personalized treatment and surveillance.

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# 1788 Androgen receptor expression decreases recurrence of hepatocellular carcinoma after liver resection

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**Background and Rationale:** Although liver resection and liver transplantation surgery for hepatocellular carcinoma (HCC) are effective curative treatment modalities, the recurrent rate still remains high. It is particularly high in patients with specific types of cancer stem/progenitor cells in circulating tumor cells (CTC). Androgen and androgen receptor (AR) signaling was suggested as an HCC metastasis suppressor in rodent HCC models. However, whether AR is associated with recurrence in HCC patients who received liver resection is unknown. This translational research describes AR function as a cancer recurrence suppressor in molecular and cellular levels.

**Methods:** Circulating tumor cells from patients with HCC who underwent liver resection were obtained, and primary tumors were collected to associate gene expressions with disease outcomes. Liver-specific AR knockout mouse were introduced into two spontaneous HCC mouse models (carcinogen and hepatitis B virus related) to delineate AR role in gene expressions. Three HCC cell lines were introduced into two spontaneous HCC mouse models (carcinogen and hepatitis B virus related) to delineate AR role in gene expressions. Three HCC cell lines were introduced into two spontaneous HCC mouse models (carcinogen and hepatitis B virus related) to delineate AR role in gene expressions. Three HCC cell lines were introduced into two spontaneous HCC mouse models (carcinogen and hepatitis B virus related) to delineate AR role in gene expressions.

**Main Result:** Here, we found the expression of AR in HCC CTC was negatively associated with the HCC recurrence/progression after liver resection. Mechanism dissection suggested that AR might decrease HCC recurrence/progression via altering three signals. First, AR could suppress the expression of CD90, the CTC cancer stem/progenitor cell marker of HCC recurrence, in a spontaneous HCC mouse model and human HCC cells via modulation of the histone-3H2A. Second, AR could reprogram HCC cell from growth promotion to migration suppression via global transcriptome shift. Third, AR could promote CTC anoikis via increasing cellular amorphosis (dysregulated cytoskeletal adsorption). **Conclusion:** Together, these results illustrated the mechanistic insight showing AR expression might be the gatekeeper for the recurrence/progression of HCC after liver resection. Therefore, targeting AR in pre-surgery downstaging procedures might be effective as a secondary prevention against HCC recurrence.

**Keywords:** AR, CD90, CTC, HCC, recurrence.

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# 1811 MicroRNA-200a/b influenced curcumin therapeutic effects in hepatocellular carcinoma cells

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**Background:** MicroRNAs (miRNAs) play an essential role in regulating gene expression in normal and malignant cells. Expression of the miRNA-200 (miR-200) family has been correlated to malignancy in cancers. However, whether miR-200a/b plays a role in curcumin-mediated treatment of hepatocellular carcinoma (HCC) is unknown. **Methods:** We performed miRNA array analyses in two different HCC cell lines (HepG2 and Hep5). The expression patterns of miR-200 family members were assessed with real-time polymerase chain reaction. We overexpressed miR-200 family members using a lentiviral system and selected stably transduced clones with antibiotics. The anticancer effects of curcumin on J5-200a, J5-200b, and J5 control cells were assessed by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay, flow cytometry cell cycle analysis, and TUNEL assay. **Results:** We found that HepG2 cells, which were more resistant to curcumin treatment than Hep5 cells, expressed higher levels of miR-200a/b. The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay revealed that the overexpression of miR-200a/b in Hep5 cells conferred enhanced resistance to curcumin treatment compared with the control cells. By cell cycle analysis and TUNEL assay, we found that apoptosis was increased dramatically in J5 control cells compared with J5-200a and J5-200b cells after curcumin treatment. Finally, we evaluated the levels of Bcl-2, Bax, and Bad and found a decrease of Bcl-2 levels and increase of Bad levels in the J5 control cells treated with curcumin. The expression levels of miR-200a/b might determine the therapeutic efficacy of curcumin on HCC cells. **Conclusions:** In this study, we dissected the role of the miR-200 family of miRNAs in the antitumor effects of curcumin on HCC. The findings from this investigation may provide important novel and potentially therapeutic insight into the application of curcumin for the treatment of liver cancer.

**Keywords:** Curcumin, miR-200, HCC, apoptosis, cell cycle.
**# 1825 Propofol-based deep sedation for percutaneous radiofrequency ablation in sick elderly patients with hepatocellular carcinoma in a developing country**

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**Background and Aims:** The aim of this study was to evaluate and compare the clinical efficacy of propofol-based deep sedation for percutaneous radiofrequency ablation (RFA) in sick (American Society of Anesthesiologists [ASA] physical status I and II) elderly patients in a teaching hospital in Thailand. **Method:** We retrospectively analyzed the patients on whom gastrointestinal endoscopy had been performed during the period of January 2010 to December 2012 in Siriraj Hospital. The patients’ characteristics, pre-anesthetic problems, anesthetic techniques, drugs, duration of anesthesia, and anesthesia-related complications were assessed and summarized. **Results:** During the study period, there were 400 RFA procedures. Median age was 63.0 ± 11.4 years. The majority of them were male (69.0%) and classified in American Society of Anesthesiologists class II (68.3%). The most common pre-anesthetic problems were liver disease (57.5%), hypertension (46.8%), hematologic disease (37.3%), and diabetes mellitus (35.3%). Intravenous sedation (99.3%) was a common technique. The mainly used anesthetic agents were propofol, fentanyl, and midazolam. The anesthetic duration ranged from 15 to 270 min. The overall anesthesia-related complication rate was 23.8%. Hypotension (16.5%) was the most frequent anesthetic complication. **Conclusion:** Almost all of the RFA procedures and intravenous sedation technique can be used effectively. However, clinical signs should be carefully observed, and the anesthetic personnel had to optimize the patients’ conditions for safety and beware of complications.

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**# 1846 Response at first chemoembolization is a strong predictor of favorable outcome in hepatocellular carcinoma**

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**Background/Aim:** Transarterial chemoembolization (TACE) is the recommended treatment for patients with Barcelona Clinic Liver Cancer staging system stage B hepatocellular carcinoma (HCC). However, real-world practice varies from these American Association for the Study of Liver Diseases guidelines. In this study, we try to assess factors determining good response (whether partial or complete response) at first TACE and outcome. **Methods:** From January 2010 to May 2011, 474 patients with newly diagnosed HCC were treated at the Chang Gung Memorial Hospital, Linkou Medical Center; 299 patients underwent TACE with on-demand policy. According to the modified Response Evaluation Criteria in Solid Tumors guideline, we categorized patient into four groups: complete response (CR), partial response (PR), progressive disease, and stable disease. The primary outcome was CR after a series of TACE using either the conventional method or DC-BEAD®. The results are expressed as median (interquartile range) values. Categorical variables were analyzed with Pearson’s chi-squared test. Numerical variables were compared with independent Student’s t-tests. Logistic regression analysis was applied for the predictors of CR after a series of TACE. All tests were two-tailed, and the level of statistical significance was set as P < 0.05. Analysis was
# 1874 Viral genotypes and associated risk factors of hepatocellular carcinoma in India

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**Objective:** This study aims to investigate the etiological relationship among hepatitis B virus (HBV), hepatitis C virus (HCV), and alcohol as risk factors in a cohort of hepatocellular carcinoma (HCC) patients from India. The clinical and biochemical profiles and tumor characteristics in the HCC cases were also evaluated. **Methods:** A total of 357 consecutive cases of HCC fulfilling the diagnostic criteria from the Barcelona-2000 EASL conference were included in the study. The blood samples were evaluated for serological evidence of HBV and HCV infection, viral load, and genotypes using serological tests, reverse transcription–polymerase chain reaction, and restriction fragment length polymorphism. **Results:** The male/female ratio for the HCC cases was 5.87:1. Majority of the HCC patients (33.9%) were 50–59 years of age, with a mean age of 4 ± 13.23 years. More than half of the cases (60.8%) had underlying cirrhosis at presentation. Among the HCC patients, 68.9% were HBV related, 21.3% were HCV related, 18.8% were alcoholic, and 18.2% were of cryptogenic origin. The presence of any marker positive for HBV increased the risk for developing HCC by almost 27 times (odds ratio [OR]: 27.33; [12.87–59.71]). An increased risk of 10.6 times was observed for HCC development for cases positive for any HCV marker (OR: 10.55; [3.13–42.73]). Heavy alcohol consumption along with HCV RNA positivity in cirrhotic patients was found to be a risk for developing HCC by threefold (OR: 3.17; [0.37–70.71]). **Conclusions:** Patients of chronic HBV infection followed by chronic HCV infection were at higher risk of developing HCC in India. Chronic alcohol consumption was found to be a risk factor in cirrhotic cases only when it was associated with HCV RNA positivity. Most of the patients had a large tumor size (> 5 cm) with multiple liver nodules, indicating an advanced stage of the disease, thus making curative therapies difficult.

# 1899 Hepatitis B virus-associated hepatocellular carcinoma: Study from Central India

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**Background:** Hepatitis B virus (HBV) affects approximately 350 million people worldwide and poses a risk of hepatocellular carcinoma (HCC) in these individuals. **Aim:** This study aimed to investigate the HBV genotype and profile of HCC patients in Central India. **Materials and Methods:** A prospective study was conducted from May 2013 to May 2015 in patients admitted in our center (n = 29). Diagnosis of HCC was based on the Barcelona-2000 EASL conference and American Association for the Study of Liver Diseases 2009 updated guideline recommendations. Detailed history and physical examination were noted, and complete hemogram, liver function test, α-fetoprotein, and computed tomography abdomen were performed in all patients. Hepatitis B surface antigen, HBV-DNA (quantitative), and HBV genotype were also performed in these patients. We studied genotypes A–F in our study by the polymerase chain reaction method. **Results:** Mean age of presentation was 56.17 ± 11.65 years. Male-to-female ratio was 13:1. Abdominal pain (79.3%), anorexia (62.1%), and weight loss (55.2%) were the most common symptoms, while ascites (72.4%), splenomegaly (51.7%), and hepatomegaly (41.4%) were the most common signs in these patients. Cirrhosis was present in 86.2% cases. Risk factors associated with HCC include smoking and alcohol consumption, which were present in 37.9% and 17.2%, respectively. Approximately half of patients had Child C liver cirrhosis. Occult HBV infection was present in 17.2%, and AFP levels above diagnostic range (≥ 400 ng/mL) were present in 51.7% patients. Hypoglycemia was noted in four patients. Multifocal HCC was present in 58.6% patients. Portal vein thrombosis and metastases were seen in 31% and 37.9% patients, respectively. One-year mortality was 79.3%. Single genotypes were present in 66.5%, and the rest had mixed genotypes. Genotype D (37.9%) was most common followed by genotypes B + D (27.6%). Genotypes A and A mix (A + D) and genotypes D and D mix (A + D and B + D) had reduced mortality as compared with other genotypes (genotype A + A mix, P = 0.017; genotype D + D mix, P = 0.034). **Conclusion:** Hepatitis B virus-related HCC was most commonly seen in the fifth decade of life, predominantly affecting male patients with underlying cirrhosis. Genotype B + D was noticed for the first time in the Indian subcontinent in these patients. These findings will have therapeutic and prognostic implications among these patients.

# 1913 Genetic variants and serum levels of major histocompatibility complex I chain-related A in predicting hepatocellular carcinoma development in chronic hepatitis C patients post antiviral treatment: A longitudinal follow-up study

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**Objective:** The median age was 63.1 years (54.9–72.3), 72.6% were men, and 89.0% had chronic virus (HBV or HCV) infection. The median size of the largest target lesion was 3.5 cm (2.0–6.2). There were 64.9% of patients who had less than three tumors when diagnosed, and 50.8% patients had unilobar tumor extent. Median overall survival from index TACE was 31.9 months (14.3–47.8). Overall, 171 (57.2%) patients could achieve response (whether PR or CR) at first TACE. By multivariate analysis, no ascites (odds ratio [OR]: 2.38, 95% confidence interval [CI]: 1.29–4.41, P = 0.006), tumor numbers plus size less than seven (within up-to-seven criteria) (OR: 2.71, 95% CI: 1.63–4.51, P < 0.001), and no macrovascular invasion (OR: 3.91, 95% CI: 1.91–8.00, P < 0.001) appeared to be good predictors of approaching good response at first TACE. Patients who could have good response at first TACE had a higher probability to achieve complete response (53.2% vs 8.6%, P < 0.001) and better survival rate (1 year: 89.5% vs 64.1%, 2 years: 72.5% vs 41.4%, 3 years: 57.9% vs 28.1%, P < 0.001). **Conclusions:** In our study, within-up-to-seven criteria, no ascites, and no macrovascular invasion are the significant factors in determining good response at first TACE. Patients who could achieve good response at first TACE had a good prognosis.
Poster liver

Background/Aims: Genome-wide association study has demonstrated that a genetic variant of major histocompatibility complex class I chain-related A (MICA) determines hepatitis C virus (HCV)-related hepatocellular carcinoma (HCC). It is unclear whether the genetic variants have an impact on HCC development in the post-treatment cohort. Methods: Major histocompatibility complex class I chain-related A rs2596542 single-nucleotide polymorphism (SNP) and the serum level (sMICA) were selected to test its associations with HCC development in patients who have received antiviral therapy. Results: Fifty-eight (8.2%) of the 705 patients developed HCC after antiviral therapy with a median follow-up period of 48.2 months (range: 6–129 months). Cox regression analysis including sMICA as a covariant revealed that the strongest factor independently associated with HCC was liver cirrhosis (hazard ratio [HR]/confidence intervals [CI]: 8.02/3.474–18.528, P < 0.001), followed by non-sustained virological response (SVR) (HR/CI: 2.11/1.112–3.994, P = 0.02), low platelet counts (HR/CI: 0.992/0.986–0.998, P = 0.01), and high sMICA levels (HR/CI: 1.001/1.000–1.002, P = 0.008). The effect of MICA SNP in HCC existed only in cirrhotic patients without an SVR, of which factors independently associated with HCC development were high sMICA levels (HR/CI: 5.26/2.03–13.61, P = 0.001) and MICA rs2596542 A allele carriage (HR/CI: 4.09/1.43–11.75, P = 0.009). The carriage of risk A allele or GG genotype with sMICA > 175 ng/mL provided the best accuracy of 79% and negative predictive value of 100% in predicting HCC. None of the 14 GG genotype carriers whose sMICA < 175 ng/mL developed HCC. The incidence of HCC did not differ between patients with or without the risk factors in terms of MICA SNP and sMICA among the other subpopulations. Conclusions: Cirrhotic patients with MICA risk allele carriage and those without risk allele but with high sMICA levels possessed the highest risk of HCC development once they failed antiviral therapy. The finding provided insight for prioritization candidates for retreatment and closer follow-up strategies toward the population.

Keywords: EGF, HCC, IL-28, MICA, PNPLA3, sMICA, SNP, SVR, treatment

# 1929 Association between vascular endothelial growth factor and severity of hepatocellular carcinoma staging

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Background: Serum vascular endothelial growth factor (VEGF) examination can be reflected to predict the severity of hepatocellular carcinoma (HCC), although there is no consensus among experts about the severity of HCC staging and serum VEGF levels. Aim: We determine the association between serum VEGF levels and severity of HCC. Methods: This is a cross-sectional study and conducted at the Cipto Mangunkusumo Hospital. Statistical analysis was performed using ANOVA. Post-hoc analysis will be performed using the Tukey–Schaffe test. Results: There were 61 HCC subjects included in this study. No subjects had Barcelona Clinic Liver Cancer (BCLC) stage 0. The mean VEGF serum level was 288.26 ± 156.6 pg/mL in patients with BCLC stage A, 434 ± 164.8 pg/mL in patients with BCLC stage B, 785.57 ± 194.25 pg/mL in patients with BCLC stage C, and 1537.97 ± 660.62 pg/mL in patients with BCLC stage D. One-way ANOVA showed P < 0.001 between mean serum VEGF levels and the severity in all BCLC stages. Post-hoc Tukey–Schaffe test showed significant statistical difference between BCLC stages A and C (P < 0.05), BCLC stages A and D (P < 0.001), BCLC stages B and D (P < 0.001), and BCLC Stages C and D (P < 0.001). There were no significant statistical differences between patients with BCLC stages A and B and between BCLC stages B and C. Discussion: VEGF serum was said to be correlated to the severity of HCC, and high levels were usually found in patients with vascular invasion or metastasis, thus indicating a poor prognosis in patients with HCC. Therefore, VEGF has the potential to assist in predicting tumor differentiation and vascular invasion. Conclusion: We found that increased levels of serum VEGF were associated with the severity of HCC based on BCLC staging classification, especially in patients with BCLC stage B and upwards.

Keywords: BCLC, HCC, VEGF.

# 1930 Targeting aldehyde dehydrogenase 2: New therapeutic potentials for prevention of alcohol-related hepatocellular carcinoma?

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Background: Acetaldehyde is a major cause of alcohol hangover symptoms and may exert pivotal roles in developing cirrhosis and hepatocellular carcinoma from chronic alcoholic liver disease. This cytotoxic aldehyde is primarily metabolized by aldehyde dehydrogenase. Recently, a variety of anti-hangover products are commercially available; however, almost none of them has been proven to show enhanced activity of aldehyde dehydrogenase in a live subject. We aimed to investigate a specific product of interest. Methods: The enzyme activities of the anti-hangover candy were examined by in vitro and in vivo experiments to measure the amount of NADH formation which is generated through catalytic conversion of alcohol and acetaldehyde. A powder sample of a commercial anti-hangover product (KISLip®, PICO Entech, South Korea) was used as the experimental substance. In vivo examination tested the ethanol and acetaldehyde concentration in blood of rats with oral infusion of experimental substance
before or after ethanol intake. Results: In vitro measurements of the activities of alcohol dehydrogenase and aldehyde dehydrogenase within the anti-hangover substance were 1.84 and 0.28 unit/g, respectively. The enzyme activities in experimental rats were significantly increased after substance gavages. Particularly, the cases with an oral intake of substance 220 mg/kg after 1 h of ethanol intake have shown more meaningful and obvious decreases in acetaldehyde concentration in blood (Fig. 1).

Conclusions: Oral intake of anti-hangover substance (KISiLip®) has significantly enhanced aldehyde dehydrogenase activity within rat circulation. Further research on animal model of alcoholic liver disease using this substance is recommended.

# 1952 Transcatheter arterial chemoembolization with hydrophilic microsphere—A porcine study

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**Background/Aim:** Hepatoma is the second leading cause of cancer death in the world. Most patients were diagnosed at an intermediate stage. Transcatheter arterial chemoembolization is the most commonly used treatment modality for these patients. We develop the microspheres to improve treatment response. Methods: We used pharmaceutical excipients that were generally regarded as safe or could be used as implants in humans to make emulsions. A two-flow method with modification was applied to produce microspheres. The sizes of our microspheres were adjustable by a sieving method, ranging from 100 to 750 μm based on clinical needs. The hydrophilic microspheres were loaded with doxorubicin. Under anesthesia, the piglets were embolized with hydrophilic microsphere via left/right hepatic and splenic artery by interventional radiologists. Serial blood tests and CT scan were performed to evaluate its efficacy and safety. All piglets were sacrificed 35 days later to obtain embolized liver and spleen tissue for histological examination. Results and Discussion: Ten piglets were treated with novel microsphere loaded with doxorubicin. After sacrifice, we can see significant embolization effects in embolized liver and spleen. The drug levels are not detected in blood, but in the embolized liver and spleen parenchyma. Significant degradation of the microsphere and tissue necrosis can be observed in pathological examinations. Transient elevation of WBC, GOT, and GPT were noted at 24 h after embolization. In addition, our microspheres are radiopaque and biodegradable. Conclusion: Transcatheter arterial embolization with novel microspheres loaded with doxorubicin is safe and effective in porcine study. Further clinical trial is needed to evaluate its safety and efficacy in clinical application.

# 1954 Hepatic actinomycosis mimicking a neoplasm—Case report

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**Introduction:** Actinomycosis is a rare bacterial infection that manifests as acute on chronic inflammation with suppuration. Actinomyces Israelii is the commonest species isolated and found as a commensal in gastrointestinal and female genital tracts. Diagnosis of deep-seated actinomycotic abscess is difficult as it mimics neoplasms in imaging. Antibiotic of choice is conventional penicillin, and 4–6 weeks’ parenteral followed by 6 months’ oral treatment is recommended to prevent recurrence. **Case Report:** A 42-year-old healthy person presented with abdominal pain and fever for 10 days’ duration. Examination revealed an acute abdomen and evidence of sepsis. Hematological and biochemical investigations were in favor of an acute inflammatory condition due to a pyogenic infection. Radiological evaluation was suspicious of a hepatic neoplasm or an abscess (Fig. 1). Aspirate of the cystic areas of the lesion was negative for an infective etiology, but biopsy of solid areas showed histopathological evidence of actinomycosis (Fig. 2). Patient was started on benzyl penicillin and then converted to coamoxiclave and clindamycin (based on microbiology opinion) due to practical problems of long-term parenteral penicillin therapy. The patient was treated intravenously for 2 weeks and discharged on oral antibiotics for 4 weeks. Repeat imaging was planned in 1 month, but patient was lost to follow up. **Discussion and Conclusion:** Hepatic actinomycosis should be considered an important differential diagnosis in patients with features of sepsis and evidence of hepatic neoplasm in imaging. Surgical interventions are not indicated if the patient is not deteriorating but should be followed up with imaging to exclude concomitant neoplasm.

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**Figure 1** Multiloculated contrast-enhancing mass lesion in CT.
Background/Aims: Although sorafenib is the standard therapy for advanced hepatocellular carcinoma (HCC), the treatments vary in these patients. Accordingly, we evaluated the effect of different treatment strategies on overall survival (OS) in HCC cases. Methods: A retrospective study of advanced HCC patients receiving sorafenib was conducted. The primary outcome was the OS. Prognostic factors were assessed using Cox multivariate analysis. Results and Discussion: A total of 658 patients (mean age 54.4 years, 83.5% male) were analyzed; 275 were treated with sorafenib monotherapy, 20 with sorafenib followed by transarterial chemoembolization (TACE), 126 with a combination of the two, and 237 with TACE followed by sorafenib. The baseline characteristics of these groups were comparable. However, patients treated with combination therapy had more portal vein invasion (52.3%, \( P < 0.001 \)). The sorafenib treatment duration was shorter in the TACE followed by the sorafenib group (81.9 days, \( P=0.004 \)). The median OS was comparable (11.3 months for sorafenib monotherapy, 19.3 months for sorafenib followed by TACE, 16.2 months for the combination, and 13.5 months for TACE followed by sorafenib; \( P=0.22 \)). However, in subgroup analysis of portal vein invasion cases, the combination (25.7 months, \( P < 0.001 \)) and TACE followed by sorafenib (14.0 months, \( P=0.011 \)) treatments were associated with better OS than sorafenib monotherapy (5.5 months). In a multivariate model, the Child–Pugh stage (odds ratio [OR], 1.83, \( P=0.005 \)), sorafenib treatment duration (OR, 0.96, \( P < 0.001 \)), and TACE (OR, 0.24, \( P < 0.001 \)) were associated with better survival. Conclusions: In patients with portal vein invasion, TACE performed concurrently or before sorafenib medication is associated with better survival.
**Background and Study Aims:** The poor prognosis of hepatocellular carcinoma (HCC) is due to high recurrence rate mainly caused by intrahepatic or extrahepatic metastasis. Paxillin, the most important adaptors in focal adhesion, is known to play an essential role in mediating the signal pathway for HCC progression. Within the paxillin superfamily, hydrogen peroxide inducible clone 5 (Hic-5) is the most homologous to paxillin. Moreover, both adaptors play distinct but complementary roles in tumor progression of breast cancer. Our previous clinical and preclinical study demonstrated the statistic correlation of Hic-5 expression with HCC metastasis and the critical role of Hic-5 in the HCC progression. **Patients and Methods:** First, whether Hic-5 was a powerful prognosis marker of HCC progression was validated by more than a hundred clinical HCC samples. Second, whether Hic-5 played an essential role in HCC progression was confirmed both in *in vitro* and *in vivo* using more patient-derived HCC cell lines. Third, whether Hic-5 could be an ideal therapeutic target for HCC progression was investigated by *in vivo* RNA interference technology. **Results:** By screening 145 HCC clinical samples, we found the Tyr31 phosphorylated paxillin and Hic-5 increased in about 40.7% and 48.3% tissues, respectively. Moreover, about 34.5% HCC tissues exhibited simultaneous elevation of both proteins. Whether Hic-5 was indeed overexpressed within the HCCs was examined *in situ*. Immunohistochemistry (IHC) of Hic-5 on tissue sections of two Hic-5-overexpressing HCCs, denoted as HCC-Hic-5 I and HCC-Hic-5 II, revealed that Hic-5 was distributed within the tumor (but not the non-tumor parts) region as indicated by hematoxylin/eosin stain and IHC of an HCC maker GPC3 on the parallel tissue sections. We also demonstrated that, by RNA interference technology, depletion of Hic-5 suppressed tumor progression of HCC329 (one in-house highly metastatic clinical HCC cell line) *in vivo*. **Conclusions:** The presence of Hic-5 in HCC cells indicates high potential of metastasis and thus poor prognosis. Depletion of Hic-5 suppressed HCC tumor progression. Hic-5 serves as both a prognosis marker and therapeutic target for hepatocellular carcinoma. **Keywords:** hepatocellular carcinoma, hydrogen peroxide clone 5, paxillin, tumor progression.

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**# 2050 Efficacy and safety of transarterial chemoembolization in patients with advanced stages of hepatocellular carcinoma**

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**Background/Aims:** TACE is the standard of care for patients with intermediate–stage HCC. However, TACE is sometimes unavoidably utilized in patients with more advanced stages. This study was aimed to determine the efficacy and safety of TACE in patients with intermediate and advanced stages of HCC according to the Barcelona Clinic Liver Cancer (BCLC) system. **Methods:** Data of consecutive HCC patients with BCLC-B and BCLC-C who underwent selective TACE between 2008 and 2012 at a tertiary center were analyzed. **Results:** One hundred ten HCC patients were included: mean age 54 years, 53% HBV positive, 23% Child–Pugh B, and 89% tumor size ≥5 cm. There was no significant difference in overall survival between the BCLC-B (*n* = 56) and BCLC-C groups (*n* = 54): median survival 9.6 versus 7.7 months, respectively; *P* = 0.535. Progressive disease by modified RECIST was more common in BCLC-B than in BCLC-C (31.5% vs 10.7%, *P* = 0.007). Pretreatment MELD score (HR 1.1; 95% CI: 1.02–1.19), TACE-related complications (HR 1.95; 95% CI: 1.21–3.15), and portal vein thrombosis/invasion (PVT) (HR 3.37; 95% CI: 3.37–6.98) were independent factors for survival in a multivariate analysis. The median survival of patients with (*n* = 40) and without PVT was 5.6 and 11.2 months (*P* < 0.001), respectively. There was no difference in survival between patients with (*n* = 31) and without extranecstatic metastases (9.6 vs 8.5 months, respectively; *P* = 0.784). The incidence of TACE-related complications was similar (*P* < 0.05, Table 1).

**Conclusions:** The overall survival and adverse events following TACE were comparable between HCC patients with BCLC-B and BCLC-C. These findings support the use of TACE as an option for selected patients with BCLC-C

**Table 1** Characteristic of 110 HCC patients who underwent TACE

| Characteristic | BCLC-B (*n* = 56) | BCLC-C (*n* = 54) | *P*-value |
|---------------|------------------|------------------|----------|
| Male          | 80.4%            | 83.3%            | 0.686    |
| Age (year)    | 58 ± 11          | 54 ± 11          | 0.047    |
| HBV positive  | 53.6%            | 51.9%            | 0.857    |
| CTP class A/B | 80.4%/19.6%      | 74.1%/25.9%      | 0.432    |
| AFP (mg/dL)   | 9719 ± 16 735    | 13 806 ± 20 974  | 0.238    |
| No. of tumor  | 28.6%/71.4%      | 24.1%/75.9%      | 0.605    |
| (single/multiple) |           |                  |          |
| Portal vein invasion | 0%             | 74.1%            | NA       |
| Extrahepatic metastasis | 0%             | 57.4% (18 LN, 7 lung, NA |
| No. of TACE   | 2 (1–3)          | 2 (1–3)          | 0.762    |
| Complete and partial response | 62.5% | 26.9% | 0.001 |
| Stable disease| 23.2%            | 33.3%            | 0.238    |
| Progressive disease | 10.7% | 31.5% | 0.007 |
| Post-TACE liver decompensation | 30.4% | 29.6% | 0.934 |
| Post-TACE liver failure | 1.8%  | 5.6%  | 0.291 |

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**# 2052 Microvascular ultrasonographic images for liver tumor vascular signal detection**

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**Background/Aims:** Tumor vascular patterns provide important information for differential diagnosis. Both color Doppler ultrasound (CDUS) and power Doppler ultrasound (PDUS) could detect the vascular signals in and around the tumors. However, microvessels with slow vascular flow
velocity could not be well demonstrated by CDUS/PDUS. Microvascular ultrasonographic images are developed for detecting microvessels with slow flow velocities. Our study aims to demonstrate the efficacy in vascular signal detection in comparison with CDUS and PDUS. Materials and Methods: From Mar. 2015 to Jul. 2015, 17 patients with detected liver tumors were enrolled retrospectively for the study. The ultrasound examination was performed with a Toshiba SSA-500 ultrasound machine. Tumor vascular signal was examined by conventional CDUS and PDUS. Microvascular signals are examined by color superb micro-vascular imaging (cSMI) and monochrome superb microvascular imaging (mSMI).

Results: By CDUS, vascular signals are detected in intra-tumoral areas in 1/17 patients and at the peri-tumoral margin in 9/17 patients. By PDUS, vascular signals are detected in intra-tumoral areas in 2/17 patients and at the peri-tumoral margin in 8/17 patients. By cSMI, vascular signals are detected in intra-tumoral areas in 4/17 patients and at the peri-tumoral margin in 16/17 patients. By mSMI, vascular signals are detected in intra-tumoral areas in 5/17 patients and at the peri-tumoral margin in 13/17 patients. cSMI could detect vascular signals in three patients without signal in CDUS and in two patients without signal in PDUS. Discussion: A higher vascular signal detection rate was obtained by both cSMI and mSMI images. With the advance of ultrasound data processing, lower motional artifact could be eliminated, and better image quality could be obtained. Conclusion: Microvascular ultrasonographic images could effectively detect both intra-tumoral and peripheral vascular signals. It showed less motional artifact and better detection ability than conventional CDUS and PDUS.

Keywords: color Doppler, microvascular ultrasonography, power Doppler.

# 2055 Successful treatment for hepatocellular carcinoma with extrahepatic lymph node metastasis by sorafenib combined with radiofrequency ablation and radiation therapy: A case report

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Introduction: Hepatocellular carcinoma (HCC) is the most common primary liver tumor and is generally associated with hepatitis B or C virus-related cirrhosis in Taiwan. Radiofrequency ablation (RFA) is an effective treatment against small solitary HCC. A multiple-electrode switching RFA system may achieve satisfactory control for HCCs larger than 3 cm. Patients with advanced HCC and extrahepatic metastasis are not good candidates for resection or locoregional treatments. Radiation therapy can provide local control for lymph node metastasis but cannot improve the prognosis. Sorafenib is associated with survival benefits in advanced HCC. Combination of sorafenib with other treatment modalities such as transarterial chemoembolization, RFA, or radiotherapy for HCC has shown additive effects or advantages. Case Description: A 62-year-old woman presented with HCV-related HCC which metastasized to a precaval lymph node. Both intrahepatic and extrahepatic lesions were larger than 5 cm. The intrahepatic HCC in S8 was treated with RFA using a multiple-electrode switching system. Radiation therapy was performed on lymph node metastasis. The patient concomitantly received a finite course of sorafenib. The intrahepatic HCC had been completely ablated, and the lymph node metastasis regressed. The patient has a recurrence-free survival for more than 3 years. With combination therapies of sorafenib, RFA, and radiotherapy, satisfactory outcomes can be achieved for advanced HCC with extrahepatic metastasis.

# 2070 Washout appearance could be a more important factor in prediction of small hepatocellular carcinoma with an atypical image pattern

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Introduction: The importance of washout appearance has been overlooked for years in detecting early HCC, but it might be more sensitive than traditional arterial-phase enhancement. Materials and Methods: From 2005 to 2013, a total of 229 HCC high-risk patients with 430 nodules (±2 cm) were recruited in the study. All nodules did not meet the criteria of LI-RADS (v.2014) in image diagnosis of HCCs (i.e., both arterial-phase enhancement and washout appearance in equilibrium phase) using MDCT/CE-MRI. Liver biopsy is performed for all nodules to make a definite diagnosis. Results: The rolled-in tumor size ranged from 0.4 to 2.0 cm in diameter. Of 430 recruited nodules, 206 of them (47.9%) are diagnosed as HCC. Most of them are well-differentiated HCC (78.6%), and others are moderately differentiated, except for one that was poorly differentiated. Sensitivity and specificity of solely washout appearance are 37.4% and 76.8%, respectively, and those of solely arterial-phase enhancement are 19.9% and 88.4%, respectively. The sensitivity of the washout appearance is significantly higher than arterial-phase enhancement (P < 0.001) in detecting small HCC. The results are illustrated in Table 1.

Reference:

1 European Association for the Study of the Liver, European Organisation for Research and Treatment of Cancer. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. J. Hepatol. 2012; 56: 908–43.

Table 1

|                     | HCC  | Total |
|---------------------|------|-------|
|                     | (+)  | (−)   |
| Washout appearance  | 77   | 52    | 129  |
| (+)                 | 129  | 172   | 301  |
| Arterial-phase enhancement | 41   | 26    | 67   |
| (+)                 | 165  | 198   | 363  |
| Total               | 206  | 224   | 430  |
Radiotherapy for hepatocellular carcinoma with portal vein thrombosis: Stereotactic ablative radiotherapy versus conventionally fractionated radiotherapy

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Aims: This study aimed to analyze the treatment results of hepatocellular carcinoma (HCC) with portal vein thrombosis using CyberKnife stereotactic ablative radiotherapy (SABR) or conventionally fractionated radiotherapy (CFRT). Material and Methods: We treated 98 patients who had HCC with portal vein thrombosis, using CyberKnife SABR (40 patients) or CFRT (58 patients). The mean dose of SABR is 42 Gy, 7–12 Gy per fraction. The mean dose of CFRT is 43 Gy, 2–2.5 Gy per fraction. Results: At the last follow up, 93 patients died. The median survival in SABR and CFRT group was 8.3 and 3.6 months, respectively. In the SABR group, there were 10% complete response (Fig. 1), 43% partial response, 43% stable disease, and 3% disease progression. In the CFRT group, there were 9% complete response, 24% partial response, 38% stable disease, and 29% disease progression. Nine (23%) patients in the SABR group and 4 (7%) patients in the CFRT group recanalized the portal vein and then received TACE, \( P = 0.025 \). Patients receiving SABR had a significantly higher survival rate, compared with those receiving CFRT (1-year survival: 40% vs 17%; 2-year survival: 19% vs 13%, \( P = 0.04 \), Fig. 2). Conclusions: SABR is superior to CFRT for patients with portal vein thrombosis in terms of recanalization rate and survival outcome. Further large, multicenter prospective study is feasible.
### Table 1  Patient characteristics

| Variable                | SABR No. of patients (%) | cRT No. of patients (%) | P-value |
|-------------------------|--------------------------|-------------------------|---------|
| No. of patients         | 40 (100)                 | 58 (100)                | 0.479   |
| Age (years) Mean (SD)†  | 59.4 (13.33)             | 57.8 (9.87)             | 0.639   |
| Sex                     |                          |                         |         |
| Male                    | 30 (75.0)                | 41 (70.7)               |         |
| Female                  | 10 (25.0)                | 17 (29.3)               |         |
| Liver disease           |                          |                         | 0.877   |
| HBV                     | 23 (67.7)                | 37 (64.9)               |         |
| HCV                     | 11 (32.5)                | 12 (21.1)               |         |
| HBV and HCV             | 1 (2.5)                  | 1 (1.8)                 |         |
| Non-virus               | 5 (12.5)                 | 7 (12.3)                |         |
| ECOG                    |                          |                         | 0.616   |
| 0–1                     | 33 (82.5)                | 50 (86.2)               |         |
| 2                       | 7 (17.5)                 | 8 (13.8)                |         |
| AJCC                    |                          |                         | 0.922   |
| IIIB                    | 27 (67.5)                | 38 (65.5)               |         |
| IVA                     | 7 (17.5)                 | 12 (20.7)               |         |
| IVB                     | 6 (15)                   | 8 (13.8)                |         |
| Child                   |                          |                         | 0.156   |
| A                       | 25 (62.5)                | 25 (43.1)               |         |
| B                       | 12 (30.0)                | 28 (48.3)               |         |
| C                       | 3 (7.5)                  | 5 (8.6)                 |         |
| CLIP                    |                          |                         | 0.373   |
| ≤3                      | 25 (62.5)                | 31 (53.4)               |         |
| > 3                     | 15 (37.5)                | 27 (46.6)               |         |
| Tumor size (cm)         |                          |                         | 0.164   |
| ≤10                     | 27 (67.5)                | 31 (53.4)               |         |
| > 10                    | 13 (32.5)                | 27 (46.6)               |         |
| α-Fetoprotein (%)       |                          |                         | 0.808   |
| < 400                   | 19 (47.5)                | 29 (50.0)               |         |
| ≥400                    | 21 (52.5)                | 29 (50.0)               |         |
| Total dose (Gy) Mean (SD)† | 42 (7.36)           | 43 (15.55)              | 0.528   |
| Fractions               |                          |                         | < 0.001 |
| Mean (SD)†              | 4.91 (0.83)              | 21.64 (7.926)           |         |
| EQD2 (Gy)               |                          |                         | < 0.001 |
| Mean (SD)†              | 67.06 (15.14)            | 45.82 (15.34)           |         |

†t-test.

CLIP, Cancer of the Liver Italian Program; cRT, conventional radiotherapy; ECOG, European Cooperative Oncology Group; AJCC, American Joint Committee on Cancer; HBV, hepatitis B virus; HCV, hepatitis C virus; SABR, stereotactic ablative radiotherapy; SD, standard deviation.
follow-up duration was 31.9 (14.3–47.8) months. By comparison of the 18 patients defined as TACE failure with those defined as non-failure, smoking (66.7% vs 40.6%, \( P = 0.03 \)), BCLC stage C (77.8% vs 42%, \( P = 0.011 \)), higher platelet count (131K vs 108K, \( P = 0.028 \)), larger tumor size (7.4 vs 3.5 cm, \( P = 0.006 \)), up-to-seven criteria (72.2% vs 46.3%, \( P = 0.033 \)), macrovascular invasion (38.9% vs 15.3%, \( P = 0.009 \)), and post-TACE fever (66.7% vs 35.9%, \( P = 0.009 \)) were unfavorable factors. By multivariate analysis, beyond BCLC stage B3/B4/C (OR: 5.624, 95% CI: 1.580–20.01, \( P = 0.008 \)) and post-TACE fever (OR: 3.364, 95% CI: 1.208–9.373, \( P = 0.020 \)) were independent predictors of TACE failure. **Conclusions:** In our study, advanced BCLC staging and post-TACE fever are independent predictive factors of TACE refractoriness. Patients who encountered these factors may consider other treatment modalities for poor efficacy.

**# 2120 Serum level of CCL4 is the only predictor for non-responder in GT-1 chronic hepatitis C patients with favorable interleukin-28B genotype when treated with peginterferon/ribavirin**

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**Background:** The chemokines/cytokines play important roles in the pathogenesis of chronic hepatitis C. However, their clinical characteristics and implications in treatment responses to pegylated interferon plus ribavirin treatment have not been fully illustrated yet. **Aims:** This study aims to investigate the predictability of the baseline serum concentrations of the chemokines/cytokines for the treatment responses to PegIFN/ RBV for CHC. **Methods:** Patients with chronic genotype-1 hepatitis C infection who had been treated with PegIFN/RBV were enrolled. HCV genotyping and quantitation were performed. Sustained virological response (SVR), relapse, and non-responder (NR) were assessed according to international definitions. IL-28B genotyping was performed as well. Serum samples were analyzed by cytometric bead array. The seven analyzed chemokines and cytokines were CXCL9–11, CCL3–4, IL-10, and IFN-\( \gamma \). **Results and Discussion**

There were 65 CHC GT-1 patients enrolled, including 27 (41%) with sustained viral responses, 16 (25%) relapsers, and 22 (34%) null responders. The patients with advantageous IL-28B genotype (rs12979860 cc genotype) were 49 (75%), and it was significantly higher in patients with SVR when compared with relapsers and NR (\( P = 0.002 \)). The baseline serum levels of CXCL10, CXCL11, CCL3, CCL4, IL-10, and IFN-\( \gamma \) were significantly higher in patients with NR when compared with SVR and relapsers (CXCL10: \( P = 0.002 \); CXCL11: \( P = 0.001 \); CCL3: \( P = 0.048 \); CCL4: \( P = 0.013 \); IL-10: \( P = 0.041 \); IFN-\( \gamma \): \( P = 0.021 \)). However, the serum levels of CXCL9 were significantly lower in patients with NR than SVR when compared with SVR and relapsers (\( P < 0.001 \)). The predictors for NR in all these patients were IL-28B genotype (OR: 1.09, \( P = 0.002 \)) and CXCL10 (OR: 0.995, \( P = 0.034 \)). However, in patients with advantageous IL-28B genotype, CCL4 became the only predictor for NR (OR: 0.957, \( P = 0.013 \)). **Conclusions:** The baseline serum level of CCL4 is the only predictor for NR in GT-1 CHC patients with favorable IL-28B genotype when treated with PegIFN/RBV.

**# 2141 Liver resection for hepatocellular carcinoma in cirrhotic patients with preoperative indocyanine green 15-min retention \( \geq 30\% \)**

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**Purpose:** Indocyanine green 15-min retention rate (ICG R15) has been a guide for liver resection feasibility. Generally, ICG R15 \( \geq 30\% \) means a considerable liver dysfunction. The role of liver resection and transplantation for hepatocellular carcinoma (HCC) in cirrhotic patient remained controversial. This study reviews our result of liver resection, especially to the HCC in cirrhotic patient whose ICG R15 \( \geq 30\% \). **Patient and Methods:** A retrospective review of a prospectively collected data of liver resection for HCC in cirrhotic patients in 1993–2014 was carried out. According to preoperative ICG R15, these cirrhotic patients were divided into two groups, group 1 with preoperative ICG R15 < 30% (n = 1023) and group 2 with \( \geq 30\% \) (n = 115). Clinicopathological characteristics, early postoperative results, and long-term survival rate were compared. Those whose HCC fulfilled the Milan criteria for liver transplantation between both groups were selected for survival analysis (n = 522 for group 1 and n = 84 for group 2).

**Results:** Group 2 patients had characterized by older age (\( P = 0.001 \)), smaller tumor size (\( P = 0.0001 \)), shorter operative time (\( P = 0.0012 \)), higher Child–Pugh grade, and smaller resection weight (\( P = 0.0001 \)). The blood loss amount, complication rates and 90-day mortality, and pathological characteristics did not significantly differ. Five-year disease-free (DF) and overall survival rates (OS) for groups 1 and 2 were 44.9% and 41.8% (\( P = 0.784 \)) and 51.4% and 46.8% (\( P = 0.937 \)) respectively. However, for those whose HCC fulfilled the Milan criteria, DF and OS for group 1 (n = 522) and group 2 (n = 84) were 60.5% and 49.4% (\( P = 0.023 \)) and 77.3% and 65.1%, respectively. **Conclusions:** The HCC in selective cirrhotic patients requiring preoperative ICG R15 \( \geq 30\% \) is worthwhile for liver resection. However, for HCC that fulfilled the Milan criteria, transplantation may be first considered when their ICG R15 \( \geq 30\% \).
width. From Jan 2011 to Jan 2014, nine HCC cases with abutting major hepatic veins (HV) or portal veins (PV) (9 juxta-vessel HCC; JV) were retrospectively compared with nine Barcelona Clinic Liver Cancer stage A-matched cases (10 HCC with no adjacent vessels; NJV). SMI was maintained at >0.5 for each RFA procedure in both groups. RFA was performed with a multi-prong probe (AngioDynamics), and the heating protocol was defined according to the manufacturer's guide. The time ratio (TR) was defined as the "actual heating time/manufacturers’ reference time" for a complete RFA procedure. The higher the TR indicated, the stronger the HSE. The mean RFA TRs of both patient groups were compared, as well as the 1YLR rates. The tumor sizes are 3.02 ± 0.65 and 2.89 ± 0.58 cm in the JV group and NJV group, respectively. The SMI is 0.68 ± 0.31 versus 0.91 ± 0.27 (P = 0.102) in the JV and NJV groups. 

**Result:** (i) The resultant TR is 1.34 ± 0.47 versus 0.99 ± 0.33 (P = 0.033 < 0.05) in the JV group and NJV group, respectively. This indicates HSE does exist and significantly prolong the TR in the JV group. 

**Conclusion:** The "SMI > 0.5" precondition overcomes the HSE, resulting in a comparably good complete eradication rate and low 1YLR.

### # 2154 New subclassification system showed different survival in Barcelona Clinic Liver Cancer C hepatocellular carcinoma patients receiving sorafenib treatment

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**Background and Aim:** Barcelona Clinic Liver Cancer (BCLC) staging system links the stage of HCC status to a specific treatment strategy. The BCLC-C stage comprises a highly heterogeneous patient population. In this study, we aimed to stratify patients with advanced hepatocellular carcinoma (HCC) into different sub-stages and to identify possible prognostic predictors that might influence the overall survival amount of patients receiving sorafenib treatment. 

**Method:** We retrospectively reviewed data from August 2012 to May 2015 in the National Cheng Kung University Hospital of Taiwan. A total of 271 patients who were diagnosed as advanced HCC (BCLC stage C) receiving sorafenib were included. Patients’ data were collected including etiology of HCC, baseline and on treatment change of serum AFP levels, survival (days) in C1:C2:C3 stages are 397 ± 29 versus 231 ± 29 versus 121 ± 22 days, respectively (all P < 0.01) (Fig. 1). The Cox regression analysis identified non-viral hepatitis (P ≤ 0.01), high baseline AFP (e.g., AFP > 400) (P < 0.01), and poor AFP response to sorafenib (P < 0.01) as prognostic factors to the survival of patients with advanced HCC.

**Conclusion:** According to our study, the BCLC-C sub-staging system showed different survival in these heterogeneous population. The etiology of liver disease and the baseline and on treatment change of serum AFP levels were also related to patients’ survival.

| BCLC  | C1  | C2  | C3  |
|-------|-----|-----|-----|
| Branch or Mets | +  | –  | –  |
| Main or B + M   | –  | +  | +  |
| CTP score       | 5–6| 5–6| 7–9|

# 2156 Hepatic arterial infusion chemotherapy for hepatocellular carcinoma resistant to transarterial embolization

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**Background:** Hepatocellular carcinoma (HCC) is prevalent in Taiwan. Surgical resection and local treatment can be curative for early HCC, but prognosis in advanced HCC or patients with disease progression after transarterial embolization (TAE) is very poor. In the Sorafenib Hepatocellular Carcinoma Assessment Randomized Protocol and Asia-Pacific trials, sorafenib has been acknowledged as a standard treatment for advanced HCC or TAE-resistant HCC; however, it is limited by high costs, a low response rate around 3%, and high adverse event rates. The response rate of hepatic arterial infusion chemotherapy (HAIC) for advanced HCC is 28% in our previous study, but the efficacy in HCC resistant to TAE is unclear. 

**Aims:** This study aims to evaluate the efficacy and safety of HAIC for HCC resistant to TAE. 

**Methods:** From 2004 to 2013, we retrospectively reviewed the data of HCC patients who received TAE prior to HAIC. 

**Results:** A
Background: Hepatocellular carcinoma (HCC) is one of the most common malignancies, with an increasing incidence, and is the third leading cause of cancer. But the role of autophagy in the prognosis and metastasis of human HCC tissues is not well known.

Aims: The study aims to explore the expression of markers of autophagy genes using immunohistochemistry (IHC) in human HCC tissues. We also investigate the autophagy markers associated with clinicopathological characteristics and prognosis. Methods: We retrospectively analyzed 200 patients diagnosed with HCC by histology after surgical resection at the Chung Hua Christian Hospital, Chung Hua, and Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, from 2009 to 2014. The demographic data, recurrence, and survival were collected until December 2014. The expressions of autophagy-related markers (LC3, beclin-1, and p62) were analyzed by IHC staining using HCC tumor tissues and non-tumor tissues. Results: Two hundred HCC patients were included. The average age was 62.8 years old, and the rate of male is 74%. The rates of hepatitis B virus (HBV), hepatitis C virus (HCV), HBV + HCV, and non-HBV/non-HCV are 48%, 28%, 4%, and 20%, respectively. Median survival was 26.3 months (range 3–42 months). The positive rate of LC3 was significantly higher in HCC tumor tissues than in non-tumor tissues (85.5 vs 50.0%, P < 0.001). In HCC, The disease-free survival was significantly correlated with BCLC stage and LC3 tumor part staining in univariate Cox regression analysis. Furthermore, the disease-free survival was significantly correlated with LC3 tumor part staining (P = 0.008) in multivariate Cox regression analysis. The strong positive LC3 staining is significantly associated with increasing disease-free survival rates by Kaplan–Meier survival analysis (P = 0.038). Conclusions: Our results show that the expression of autophagy marker, LC3, might be a strong prognostic factor of disease-free survival in HCC patients who underwent liver resection.
# 1024 Alterations in the portal venous system in idiopathic non-cirrhotic portal hypertension: a prospective long-term follow-up study

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**Background/Aim:** Idiopathic non-cirrhotic portal hypertension (INCPH) is a group of diseases that are characterized by an increase in portal pressure, due to intrahepatic or prehepatic lesions, in the absence of cirrhosis of the liver. INCPH includes extrahepatic portal vein obstruction (EHPVO) and non-cirrhotic portal fibrosis (NCPF). The natural history of INCPH is still not clear. **Aim and Method:** The aim of the present study was to determine prospectively the changes in the portal venous system in patients with NCPH. Patients with a diagnosis of NCPF and EHPVO registered since 2001 were serially followed at a yearly interval for changes in liver size, in its echotexture, and in the intrahepatic and extrhepatic portal venous systems. Baseline demographic details, liver function test, and comorbid illness including virological profile were noted. Patients with comorbid illness and those with known etiology of cirrhosis were excluded from the study. **Results:** There were 34 patients with NCPF (M:F 1:1.8) and 30 patients with EHPVO (M:F ratio 1.6:1). The mean age was 24.9 and 41.2 years, respectively. During follow-up, 20 out of 34 and 16 out of 30 patients with NCPF and EHPVO respectively had no progression of disease. Fourteen patients with EHPVO progressed to cirrhosis over a mean period of 5.21 years. Eight patients developed ascites and required diuretics. Fourteen patients with EHPVO progressed to NCPF over the mean period of 8.6 years, and 12 patients further progressed to cirrhosis over a mean period of 5.1 years. Overall, 40% of patients with EHPVO progressed to cirrhosis over a mean period of 13.7 years. **Conclusion:** Idiopathic non-cirrhotic portal hypertension is a spectrum wherein EHPVO progresses to NCPF and further to cirrhosis over a period of 13.7 years at least in a proportion of patients. So our report clearly emphasizes that INCPH is a spectrum of disease, so these patients should be monitored periodically to observe the changes in the portal venous system.

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# 1088 A retrospective study on non-invasive predictors of esophageal varices in patients with liver cirrhosis, a Makati Medical Center experience

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**Introduction:** Esophageal varices and gastrointestinal bleeding are serious complications of liver cirrhosis and portal hypertension. Non-invasive parameters would be valuable in early detection, prevention, and management of these conditions. **Methodology:** A retrospective cross-sectional study on 101 cirrhotic patients was undertaken from January to December 2013. Diagnosis was based on clinical history and biochemical and ultrasonographic findings. Parameters tested for the presence of varices were platelet count, ultrasonographic bipolar spleen diameter, platelet count/spleen diameter ratio, Child-Pugh, and serum albumin levels. Esophagogastroduodenoscopy was done on all patients. Data were gathered from the medical records. **Exclusion Criteria:** These included the following: active bleeding, previous endoscopic sclerosis or band ligation of esophageal varices, previous surgery for portal hypertension or transjugular intrahepatic portosystemic stent shunt placement, hepatocellular carcinoma, spontaneous bacterial peritonitis, or portal vein thrombosis, schistosomiasis, and liver abscess. Data were tabulated, and descriptive analysis was performed with a P value ≤ 0.05. Receiver operating characteristic curves were applied to the variables. Statistical Package for Social Sciences (SPSS version 17) was used in computation. **Results:** The platelet count/spleen diameter ratio showed a trend for association with esophageal varices, but this did not reach statistical significance (odds ratio 54.8, 95% confidence interval [CI] 0.20–150, P = 0.16). The best predictive cut-off of the platelet/spleen diameter ratio in this study was derived to be at ≤ 1.86. This had a positive predictive value of 89% (95% CI 80.4–94.9) and negative predictive value of 33% (13.3–59%). The sensitivity of this cut-off was at 86% (95% CI 76.9–92.6%). The rest of the parameters were not predictive. **Conclusion:** In our study, these parameters were not able to predict the presence of esophageal varices. Platelet count/spleen diameter ratio only showed a non-statistically significant trend for association with esophageal varices. At present, esophagogastroduodenoscopy remains the gold standard in evaluating their presence and the risk of bleeding.

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# 1140 Evaluation of health-related quality of life in liver cirrhosis patients in Singapore

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**Background:** Patients with liver cirrhosis experience symptoms and concerns that negatively impact their quality of life. This study aims to examine the health-related quality-of-life (HRQL) in patients with liver cirrhosis. **Methods:** A cross-sectional study was conducted in the gastroenterology wards and clinics of the Singapore General Hospital. Thirty-five cirrhotic patients and 24 chronic hepatitis patients were recruited as case and control groups, respectively. Patients with significant comorbidities were excluded. The Chronic Liver Disease Questionnaire (CLDQ) was used to assess the HRQL of these patients, and mean CLDQ score was used as the primary outcome measure. **Results:** Cirrhotics were older and had lower educational status compared to non-cirrhotic controls. Of cirrhotics, 57% were Child A, 29% Child B, and 14% Child C. Overall mean CLDQ scores were lower in cirrhotics compared to controls (5.04 ± 1.12 vs 5.84 ± 1.07, P = 0.008) with 49% of cirrhotics having poor HRQL (defined as mean CLDQ score ≤ 5) compared to 21% of controls. Significant differences were found in the activity, emotional, and worry domains but not in the abdominal, fatigue, and systemic symptom domains. CLDQ scores in cirrhotics < 60 years old were significantly lower than those in > 60 (4.38 ± 0.94 vs 5.42 ± 1.05, P = 0.006), whereas there was no age effect in the controls. Younger cirrhotics had poorer HRQL in the abdominal symptoms (P < 0.001), fatigue (P = 0.011), systemic symptoms (P = 0.049), and emotional (P = 0.005) domains. **Conclusion:** Cirrhotics have poorer HRQL compared to chronic hepatitis patients, particularly in emotional and worry domains. Multidisciplinary care for cirrhotics should focus on identifying and alleviating concerns and anxieties. Younger cirrhotics have worse HRQL especially in abdominal symptoms and emotional domains.
# 1196 To study the role of oxidative stress in cirrhosis

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**Introduction:** Oxidative stress is defined as an imbalance between pro-oxidant and anti-oxidant mechanisms in our body. Oxidative stress has been implicated in the pathogenesis of liver cirrhosis, among other conditions like atherosclerosis, and pulmonary fibrosis. Aim: We studied oxidative stress in patients with cirrhosis by measuring serum superoxide dismutase (SOD), serum catalase, and serum thiobarbituric acid reactive substance (TBARS) and compared these with those in normal healthy controls. Design: This is a case–control prospective study.

**Materials and Method:** Thirty patients of proven cirrhosis along with 20 age-matched and sex-matched healthy controls were included in our study. Exclusion criteria were coexisting diabetes, chronic kidney disease, coronary artery disease, recent acute illness, hospital admission, and use of anti-oxidant drugs and statins. Beside routine investigations, serum SOD, serum TBARS, and serum catalase levels were measured by standard methodology and compared with those in controls. Statistical Analysis: Continuous variables were recorded as mean ± SD, and ANOVA test was used to evaluate P values among the groups. Results: Cirrhotic patients showed a significant increase in serum TBARS (0.267 ± 0.1330) and serum catalase (3.502 ± 0.458) when compared to controls (0.0964 ± 0.018621 and 2.0278 ± 0.016, respectively), with a P value < 0.001. There was a significant decrease in level of SOD (2.74 ± 0.6449) compared with that controls (4 ± 0.380058), with a P value < 0.001. Conclusion: This study indicates that there is increased lipid peroxidation and oxidative stress as observed by an increased level of serum TBARS catalase with a decreased level of SOD levels. As more studies continue to emerge regarding the role of oxidative stress in disease development and the mechanisms underlying cellular toxicity, these findings will lead to more rational anti-oxidant therapeutic approaches. Further large clinical trials are necessary to confirm whether drugs targeting oxidative stress like anti-oxidant supplementation become a magical pill for treatment of cirrhosis and its complication.

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# 1399 No mortality difference following treatment with terlipressin or somatostatin in gastric variceal hemorrhage patients

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**Introduction:** Somatostatin and terlipressin, both being vasoactive drugs, play a role in the control of variceal bleeding. However, no study has investigated the use of various vasoactive drugs specifically in controlling gastric variceal bleeding so far. **Background and Aims:** This work aims to study the effects of vasoactive agents on mortality related to bleeding from gastric varices in cirrhosis patients. **Methods:** The National Health Insurance Database, derived from the Taiwan National Health Insurance Program, was used to enroll 311 cirrhotic patients who received gastric variceal sclerosing therapy and vasoactive agents for gastric variceal bleeding and who were hospitalized from January 1, 2007, to December 31, 2007. **Results:** In total, 311 cirrhosis patients who accepted sclerotherapy for active gastric variceal bleeding were enrolled in this study. Among them, 218 patients accepted terlipressin, and 93 patients accepted somatostatin. The overall 30-day mortality rate was 13.2% (41/311). A total of 78 (25.1%) patients received second-look endoscopy, but only 12 (7%) patients needed a second course of sclerotherapy. The overall 30-day mortality rates for patients treated with terlipressin and somatostatin were 13.3% and 12.9%, respectively, which showed no statistically significant differences between outcomes in the two vasoactive agent treatment groups (*P* = 1,000). The risk of 30-day mortality was significantly higher in patients with hepatocellular carcinoma (hazard ratio [HR]: 3.257, 95% confidence interval [CI]: 1.640–6.469, *P* = 0.001), acute renal failure (HR: 6.261, 95% CI: 2.376–16.499, *P* < 0.001), or hepatic encephalopathy (HR: 3.091, 95% CI: 1.430–6.680, *P* = 0.004). **Conclusions:** Mortality rates did not differ significantly between cirrhosis patients with acute gastric variceal bleeding who received somatostatin or terlipressin as adjuvants to endoscopic treatment.

# 1500 The predicting factors for mortality after hip surgery in cirrhotic patients

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**Background/Aim:** Cirrhosis increases the risk of osteoporosis and fracture. However, there are sparse data about outcome of hip fracture in cirrhotic patients. We investigated the predictors for mortality in cirrhotic patients with hip fracture who underwent surgery. **Methods:** A total of 40 cirrhotic patients with hip surgery were retrospectively enrolled between 2006 and 2013. The cause of cirrhosis, Child–Turcotte–Pugh (CTP), Model for End-stage Liver Disease (MELD) score, operation record, perioperative
Poster liver

complication, hospital length of stay, and in-hospital and 1-year mortality after hip fracture were investigated. Results: Six patients (15%) died after hip surgery. Serum platelet, CTP and MELD score at the time of admission, and the duration of intensive care unit stay after surgery were associated with in-hospital mortality. On multivariate analysis, CTP and MELD score were independent factors predicting in-hospital mortality (CTP score: relative risk, 9.73; 95% confidence interval [CI], 1.06–89.39; \( P = 0.044 \); MELD score: relative risk, 1.482; 95% CI, 1.051–2.088; \( P = 0.025 \)). The area under the receiver operating characteristic curve of MELD score was 0.944 (\( P = 0.001 \); 95% CI, 0.864–1.023). MELD score \( \geq 17.5 \) was associated with in-hospital mortality (sensitivity 83.3% and specificity 94.1%). One year after surgery, 20 patients (50%) died. Body weight, serum blood urea nitrogen, MELD score, and the cause of cirrhosis (alcohol) were associated with 1-year mortality. On multivariate analysis, the cause of cirrhosis (alcohol) was the only independent factor predicting 1-year mortality after surgery (relative risk, 6.189; 95% CI, 1.051–2.088; \( P = 0.025 \)). Conclusion: Child–Turcotte–Pugh and MELD score were important predictors for in-hospital mortality after hip surgery in cirrhotic patients. Especially in alcoholic cirrhotic patients, long-term prognosis was poor, although the hip surgery was performed successfully.

Keywords: hip fracture, liver cirrhosis, mortality.

# 1515 Vitamin D₃ treatment has comparative portal hypotensive effects as propranolol by decreasing intrahepatic resistance in cirrhotic rats

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Background and Aim: Vitamin D₃ improves portal hypertension (PH) through the activation of vitamin D receptor (VDR) and calcium sensing receptor (CaSR) in cirrhotic rats. Propranolol is a nonselective β-blocker that is recommended for the treatment of PH. The present study aims to investigate the detailed systemic and hepatic mechanisms of vitamin D₃ and propranolol, alone or in combination, in cirrhotic rats. Methods: Common bile duct-ligated and thioacetamide cirrhotic rats were treated with vehicle, propranolol (30 mg/kg/day), vitamin D₃ (0.5 μg/100 g/day, twice weekly), or propranolol + vitamin D₃ separately. Results: Significantly, propranolol and vitamin D₃ produced a similar magnitude of reduction in portal venous pressure (PVP) in cirrhotic rats through different mechanisms: whereas propranolol decreased PVP by reducing splanchnic hyperemia and cardiac index, vitamin D₃ decreased PVP by decreasing intrahepatic resistance (IHR). However, propranolol plus vitamin D₃ did not further decrease PVP in cirrhotic rats. Notably, a marked decrease in hepatic VDR and CaSR expressions was noted in cirrhotic human/rat livers compared to non-cirrhotic human/rat livers. In cirrhotic rats, vitamin D₃ administration decreased IHR by inhibiting the renin–angiotensin system, hepatic oxidative stress, inflammation/fibrosis, angiotensin II (ANGII) production, CaSR-mediated ANGII hyperresponsiveness, and ANGII-induced hepatic stellate cell contraction and correcting hepatic endothelial dysfunction through upregulation of hepatic VDR, CaSR, and endothelial nitric oxide synthase expressions. Conclusion: Chronic vitamin D₃ treatment alone results in comparative portal hypotensive effects as propranolol alone in cirrhotic rats with PH. Taken together, chronic vitamin D₃ administration was an ideal alternative strategy to effectively improve PH without unwanted systemic side effects.

Keywords: anadamide, tumor necrosis factor-α, systemic side effects.

# 1516 Inhibition of hepatic tumor necrosis factor-α attenuates anandamide-induced vasoconstrictive response in cirrhotic rat livers

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Background: Increased anandamide, an endocannabinoid which interacts with both cannabinoid CB₁ and CB₂ receptors, can induce hepatic vasoconstrictive responses which contribute to the increased intrahepatic resistance (IHR) in cirrhotic rats. Chronic endotoxemia and subsequent release of tumor necrosis factor-α (TNF-α) are suggested to result in increased anandamide in cirrhotic livers. Thalidomide, inhibiting TNF-α effectively, has been used clinically in states of chronic TNF-α elevation with encouraging results. Aim: This study wants to explore the possible effects of thalidomide on hepatic endocannabinoids and microcirculation of cirrhotic rats. Methods: Portal venous pressure (PVP), superior mesenteric arterial blood flow (SMA BF), hepatic TNF-α, interleukin (IL)-6, protein expression of CB₁ and CB₂ receptors, and thromboxane synthase (TXS) were measured in bile duct-ligated (BDL) rats receiving 1 month of vehicle (BDL-V) or thalidomide (BDL-thalido). Degree of hepatic fibrosis was also assessed. In liver perfusion system, IHR and concentration–response curves of portal perfusion pressure to anandamide were evaluated. Results: In BDL-thalido rats, PVP, IHR, and hepatic levels of TNF-α and IL-6, protein expression of CB₁ and CB₂ receptors, and thromboxane synthase (TXS) were lower than in BDL-V rats. In BDL-thalido rat livers, the attenuation of vasoconstrictive response to anandamide was associated with an upregulation of CB₁ receptor and a downregulation of CB₂ receptors. Nevertheless, SMA BF was not different between BDL-thalido and BDL-V rats. Conclusions: Thalidomide decreased the PVP and IHR through the prevention of hepatic fibrosis, attenuation of anandamide-induced constrictive response, and a decrease in the production of TNF-α, IL-6, and TXA₂ in the liver of rats with biliary cirrhosis in this study. Discussion: Using biliary cirrhosis rat’s model, we found that inhibition of hepatic TNF-α by administration of thalidomide decreased the PVP and IHR through the prevention of hepatic fibrosis, attenuation of hepatic anandamide-induced constrictive response via upregulation of hepatic CB₁ receptor and a downregulation of hepatic CB₂ receptors, and a decrease in the production of TXA₂.

Keywords: anadamide, tumor necrosis factor-α, vasoconstriction.
# 1589 Higher body mass index is associated with higher liver necroinflammation in chronic hepatitis B viremic patients with persistently normal alanine aminotransferase

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**Background:** The histology manifestations of patients with chronic hepatitis B viremia and persistently normal alanine aminotransferase (PNALT) remain unclear and need to be investigated. **Aim:** The study aimed to evaluate the liver histology and the predictors of histologic abnormalities in patients with PNALT. **Material and Methods:** Patients aged between 18 and 65 with PNALT were enrolled for further screening. The definition of PNALT was at least two alanine transferase (ALT) values less than the upper limit of normal range within 1 year that were at least 3 months apart before enrollment. Patients with hepatitis B virus (HBV) DNA level more than 2000 IU/mL were included and then received liver biopsy. The Knodell necroinflammation grades and Ishak fibrosis stages were used for histologic evaluation. **Results:** In total, 380 CHB patients were enrolled from screening, and 81 patients received liver biopsy. The 81 patients included 33 HBeAg-positive patients and 48 HBeAg-negative patients. The distribution of the Knodell necroinflammation grades was as follows: 55.5% were minimal (score 0–3), 42.0% mild (score 4–6), 2.5% moderate (score 7–9), and 0% severe (score 10–14). The distribution of the Ishak fibrosis stage was as follows: 75.4% minimal (stage 0–1), 21.0% significant (stage 2–3), and 3.7% advanced (stage 4–6). Univariate analysis showed body mass index (BMI) was a predictor for Knodell necroinflammation score >3, but age, ALT, HBV DNA level, and NAS were not. Multivariate logistic regression analysis showed BMI was still a significant predictor (OR: 1.307, P = 0.002, CI = 1.103–1.547) for Knodell necroinflammation score >3. However, multivariate analysis showed no factors associated with significant fibrosis. **Conclusion:** A higher BMI significantly influenced the necroinflammation. It may indicate that non-alcoholic fatty liver disease contributes to histology abnormalities in chronic hepatitis B viremic patients with PNALT.

# 1607 Plasma levels of matrix metalloproteinase 2 and 9 in male and female patients with cirrhosis of different etiologies

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**Introduction:** Liver fibrosis and cirrhosis may be reversible in some circumstances. Reliable diagnostic tests are necessary for monitoring hepatic fibrogenesis. Matrix metalloproteinase (MMP)-2 and MMP-9 are two of the major MMPs in the circulation and may be most relevant to hepatic fibrosis. The behavior of MMPs may be significantly different in men and women and may also differ in cases of cirrhosis of various etiologies. This study aimed to evaluate the manifestations of MMP-2 and MMP-9 in liver cirrhosis of different etiologies in men and women and to compare these patterns with those of healthy controls. **Materials and Methods:** We measured MMP-2 and MMP-9 levels in plasma samples from 112 patients with cirrhosis and 112 age-matched and gender-matched healthy controls. We then correlated these MMP levels with gender and disease etiology. **Results:** Plasma MMP-2 concentrations in patients showed a trend towards increasing values with cirrhosis severity and were markedly increased in patients regardless of gender and etiology compared with healthy controls (P < 0.0001). Plasma mean MMP-9 levels were comparable in patients with cirrhosis and controls but increased with disease severity. They were significantly lower in patients, female patients, and male patients with mild cirrhosis than in controls, female controls, and male controls (P = 0.001, 0.041, and 0.009, respectively). MMP-2 and MMP-9 concentrations were not significantly different between genders among controls and among various patient subgroups. **Conclusions:** Plasma MMP-2 level may be a useful diagnostic marker for monitoring hepatic fibrogenesis in patients with disease of different etiologies.
# 1653 Platelet replacement is not necessary before endoscopic variceal band ligation in patients with cirrhosis and severe thrombocytopenia

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**Background and Aims:** It is not clear whether platelet replacement transfusion is necessary to prevent post-procedural bleeding before endoscopic variceal band ligation (EBL) in patients with cirrhosis and severe thrombocytopenia. **Methods:** In this historical cohort study, we analyzed the data of 79 EBL sessions which have been performed in 42 patients with cirrhosis and a platelet count of less than 50,000/mm³. The number of unexpected visits, post-procedural bleeding, and red blood cell transfusion was compared between the EBL sessions with and without prophylactic platelet replacement transfusion. **Results:** Platelet replacement transfusion was done before 61 sessions and was not done before 18 sessions of EBL. Mean age (55 vs 58 years) and platelet count (38,330 vs 40,670/mm³) were not different between the two groups at baseline (P = 0.27 and P = 0.13, respectively). The number of unexpected visits (12 [19.7%] vs 1 [5.6%]), post-procedural bleeding (3 [4.9%] vs 0 [0.0%]), and red blood cell transfusion (5 [8.2%] vs 1 [5.6%]) was minimal and was not significantly different between the platelet transfusion and no transfusion groups (P = 0.16, P = 0.34, and P = 0.71, respectively). **Conclusion:** In patients who have cirrhosis and severe thrombocytopenia, platelet replacement transfusion may not be necessary to prevent post-procedural bleeding.

# 1678 The clinical significance of ⁹⁹mTc lung perfusion imaging in patients with liver cirrhosis

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**Aims:** Liver cirrhosis is one of the most common causes of mortality in China. We evaluated the clinical manifestations and imaging of ⁹⁹mTc lung perfusion in cirrhosis patients with various complications, investigated the relationships between ⁹⁹mTc lung perfusion and portal hypertension, and assessed the roles of ⁹⁹mTc lung perfusion in severity of the conditions. **Methods:** The clinical records of 14 patients diagnosed with liver cirrhosis were reviewed. ⁹⁹mTc lung perfusion imaging was conducted in all patients. **Results and Discussion:** Six males and eight females, the medium age of whom was 55.5 years (24–77), were included in this study. Eight cases showed positive lung perfusion imaging. The Child–Pugh classification was from A to C, and the shunt rate in pulmonary perfusion was from 5.4% to 39.3%. No patients revealed clinical manifestations of hepatopulmonary syndrome. Thirteen patients had varices bleeding. Eleven patients had ascites. Compared with the negative group, patients in the positive group were inclined to have a higher Child–Pugh score and higher incidence of gastric varices. In abdominal ultrasound and computed tomography (CT) scanning, the average diameter of the portal vein was 14.03 and 16.00 mm in the positive and negative groups, respectively. The average thickness of the spleen was 4.95 and 5.33 cm in the positive and negative groups, respectively. The average minimum platelet count was 55.38 * 10⁹/L in the positive group and 50.33 * 10⁹/L in the negative group. Thrombosis in the portal vein was found in three cases in the positive group and two cases in the negative group. **Conclusions:** The positive results of ⁹⁹mTc lung perfusion scanning might have certain relationships with Child–Pugh classification, gastric fundus varices, ascites, and the degree of thrombocytopenia in cirrhosis patients. Besides, it might be negatively correlated with the diameter of portal vein. It might have an important role in the assessment of severity of liver cirrhosis and predicting the degree of portal hypertension.
Figure 1. Typical lung perfusion imaging and CT scanning from positive and negative groups. (a) Lung perfusion imaging of case no. 6; see positive shunt (shadow in systemic circulation). (b) CT of case no. 6. (c) Lung perfusion imaging of case no. 3, with negative result. (d) CT of case no. 3. Notably, this case had more serious portal vein dilation and splenomegaly compared with case no. 6. Arrowhead: systemic circulation shunt. Arrow: portal vein. Star: spleen.
**Table 1 Clinical data**

| No. | Gender | Age | Hush | Child classification | Child score | Varices | Ascites | Splend diameter | Portal vein thrombosis | Vein spleen thickness | MinPLT |
|-----|--------|-----|------|----------------------|-------------|---------|---------|-----------------|------------------------|-----------------------|-------|
| 1   | M      | 71  | –     | A                    | 5           | E       | –       | 22              | –                      | 5.5                   | 44    |
| 2   | F      | 62  | –     | B                    | 8           | E       | +       | 16              | –                      | 5.5                   | 32    |
| 3   | F      | 27  | –     | B                    | 8           | E       | +       | 16              | –                      | 6.7                   | 51    |
| 4   | M      | 53  | –     | B                    | 9           | E + G   | +       | 13              | +                      | 4.5                   | 60    |
| 5   | M      | 46  | –     | A                    | 5           | E       | –       | 18              | +                      | 5.2                   | 90    |
| 6   | F      | 71  | –     | A                    | 6           | E + G   | +       | 11              | –                      | 4.6                   | 25    |
| 7   | M      | 61  | +     | C                    | 11          | E + G   | +       | 15              | +                      | 4                     | 64    |
| 8   | M      | 55  | +     | A                    | 6           | E       | +       | 15.7            | –                      | 6.2                   | 46    |
| 9   | F      | 56  | +     | A                    | 5           | E + G   | –       | 12              | +                      | Not valid             | 75    |
| 10  | F      | 24  | +     | A                    | 10          | E + G   | +       | 14              | –                      | 4.7                   | 32    |
| 11  | F      | 75  | +     | B                    | 9           | E + G   | +       | 11.5            | –                      | 5.1                   | 52    |
| 12  | F      | 77  | +     | C                    | 12          | G       | +       | 12              | –                      | Not valid             | 45    |
| 13  | F      | 51  | +     | A                    | 6           | E       | +       | 14              | –                      | 4.4                   | 40    |
| 14  | M      | 49  | +     | B                    | 7           | E + G   | +       | 18              | +                      | 5.3                   | 89    |

E, esophageal varices; E + G, esophageal and gastric varices; G, gastric fundus varices.

**# 1693 Transient elastography (FibroScan): 2 years’ experience from Karachi, Pakistan**

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**Introduction:** Transient elastography (FibroScan) is a new, non-invasive, rapid, and reproducible method allowing evaluation of liver fibrosis by measurement of liver stiffness, and its accuracy to confirm fibrosis in non-alcohol fatty liver disease (NAFLD) and cirrhosis is confirmed by VW Wong et al.² We here present our data of previous 2 years as a continuation of our previously presented data in Asian Pacific Digestive Week 2014. We carried out this study to validate the benefits of this novel modality in our population, specifically when FibroScan facility is only available at very few centers in the Sindh province of Pakistan. **Objective:** This study aims to assess the indications and results of FibroScan patients in our population. **Study Design:** This is a cross-sectional study in 267 patients attending Medlink Clinics in Karachi, Pakistan. **Results:** In our study, of 267 patients, there were 196 (73%) males, with age ranging from 15 to 84 years. Mean age was 43 years. Main indications were chronic hepatitis in 131 (49%) patients and NAFLD in 114 (42.7%) patients. The remaining 22 (8.2%) patients had various indications like chronic alcohol abuse and primary sclerosing cholangitis and were referred for assessment of liver fibrosis before chemotherapy. Among this group, 111 (41.6%) patients had significant fibrosis, F3–F4. Ninety-seven (36.4%) patients had F1–F2 stage of fibrosis, while 59 (22.2%) patients had F0 stage. Chronic hepatitis was the most common underlying etiology, accounting for 49% of the patients, of which 45% (59 patients) had advance fibrosis on FibroScan. NAFLD was the second most common indication in which 37% (42 patients) had advance fibrosis. **Conclusion:** Transient elastography is a promising non-invasive method for staging of liver fibrosis. In our study of 267 patients, 41% had advanced fibrosis, which is helpful in planning further management of these patients. Additionally, patients with a lesser degree of fibrosis should be closely followed up and advised early treatment to prevent further deterioration of liver disease.

**# 1711 Improvement of bloated feeling and nutritional status by tolvaptan in cirrhotic patients with ascites**

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**Background/Aims:** Tolvaptan had been approved in cirrhotic patients with ascites and insensitive response to conventional diuretics in Japan. The objectives were to investigate the improvement of symptom and nutritional status by tolvaptan use in cirrhotic patients. **Methods:** Support Team Assessment Schedule (STAS-J) which consists of five grades was used to evaluate bloated feeling. Its symptomatic responder was defined as improvement of one grade or more. Controlling nutritional status (CONUT) is based on serum albumin level, total lymphocyte count, and total cholesterol level. CONUT, which consists of 13 grades, was used to evaluate nutritional status. Body weight and serum electrolyte were measured; further, concomitant use of drugs and dietary intake were recorded. Additionally, the predictive factors which affected the symptomatic responder of tolvaptan were confirmed. **Results:** Eligible for enrollment were 32 patients with liver cirrhosis including males/females (12/20), 68.3 ± 14.4 years old, with Child–Pugh classification B/C (10/22) and Child-Pugh score of 10.2 ± 1.5. Reduction in body weight was 4.0 ± 3.7 kg. The STAS-J score was significantly increased vs 10.1 ± 1.9, P < 0.01, respectively. Dietary intake in responders significantly increased (P < 0.01). Serum sodium concentration at baseline was the most reliable
predictive factor (responder, 137.3 ± 5.6 mEq/L, vs non-responder, 133.7 ± 5.9 mEq/L, \( P < 0.001 \), respectively); further, branched amino acid use and low-dose loop diuretics use (< 20 mg daily) were extracted. Conclusion: Patients who improved bloated feeling by tolvaptan increased dietary intake and improved nutritional status. Serum sodium was the most reliable predictive factor which affected the improvement of bloated feeling.

# 1754 Transient elastography, liver fibrosis, body mass index, non-alcoholic fatty liver disease, and chronic viral hepatitis

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Introduction: It has been suggested from prospective studies that excess body weight may result in a substantial increase in the risk of liver fibrosis. Transient elastography (FibroScan) is a novel non-invasive modality which has now been proven to assess liver fibrosis with high sensitivity. We conducted this study to assess the stage of liver fibrosis on FibroScan in patients with a body mass index (BMI) of more than 28, irrespective of the underlying cause of liver disease. Objective: The purpose of this study was to compare the results of FibroScan in patients with high BMI > 28 versus low BMIs < 28. Study Design: This is a cross-sectional study. Setting: This study was performed in Medlink Clinics, Karachi, Pakistan. Sample Size and Collection: A total of 254 patients were enrolled, of which 93 had a BMI of more than 28. Results: In our study, there were 254 patients; the main indications were non-alcoholic fatty liver disease, chronic hepatitis B or C, and alcohol abuse. Ninety-three patients had a BMI of more than 28. Study Design: This is a cross-sectional study.

Sample Size and Collection: A total of 254 patients were enrolled, of which 93 had a BMI of more than 28. Results: In our study, there were 254 patients; the main indications were non-alcoholic fatty liver disease, chronic hepatitis B or C, and alcohol abuse. Ninety-three patients had a BMI of more than 28, and 67 were male. Age ranged from 19 to 72 years, and mean age was 43.4. In patients with a BMI more than 28, 55 (59%) patients had significant fibrosis (F3–F4) on FibroScan, and 23 (24.7%) patients had F2 stage, while 15 (16.1%) had F0 fibrosis. One hundred sixty-one patients had BMI > 28, 122 were male, and mean age was 43.8. Among these, only 50 patients (31%) had significant fibrosis (F3–F4) on FibroScan, and 71 (44%) patients had F2 stage, while 40 (24.8%) had F0 fibrosis.

Conclusion: In our study, 59% patients with a BMI of more than 28 were found to have significant fibrosis as compared to only 31% patients with low BMI, giving a P-value of 0.00002. We conclude that patients with high BMI should be evaluated early with FibroScan, irrespective of the underlying disease.

# 1771 Initial experience with injection. Darbepoetin and injection pegfilgrastim in liver cirrhosis patients

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Introduction: Dysregulated erythropoietin plasma levels may play a role in the pathophysiology of chronic liver disease because chronic anemia is frequently observed in patients with liver cirrhosis. Some reports have used regular erythropoietin and filgrastim in liver cirrhosis patients with benefits to patients. There is no report of use of long-acting erythropoietin (darbepoetin alpha) and pegylated filgrastim (pegfilgrastim) in patients with liver cirrhosis. Aims and Methods: This work aims to study the benefits of darbepoetin and pegfilgrastim in patients with advanced liver disease (Child C status). Prospective patient inclusion and all the hematological, biochemical, ultrasound, and clinical parameters were recorded. Patients with active bleeding, confirmed hepatoportal syndrome, hepatoma, portal vein thrombosis, and splenic vein thrombosis were excluded from the study. The study started from October 2014 onwards. Patients started on injection darbepoetin alpha 200 μg and injection pegfilgrastim 6 mg subcutaneously every 15 days, with a total of three injections, and a minimum of 3 months’ follow up was planned. Improvement in hematological, coagulation, biochemical, clinical parameters, and Child score was analyzed. For statistical analysis, the median was calculated for nonparametric variables, and a Kruskal–Wallis nonparametric test was done on SPSS version 12 statistics software. Results and Discussion: A total of 12 patients were included in study, and three were lost to follow up, all of whom were male. Etiology of cirrhosis was non-alcoholic fatty liver disease in two, hepatitis B virus cirrhosis in one, hepatitis C virus in one, and alcohol in eight patients. Median age was 54 years (range 50–66 years). There was an improvement in median hemoglobin from 8.7 to 10.6 g % (Z value 1.96, P value 0.05), total leukocyte count improved from 4700 to 7100/mm³ (Z value 2.13, P value 0.033), platelet count improved from 60 000 to 188 000/mm³ (Z value 2.668, P value 0.008), international normalized ratio improved from 1.8 to 1.4 (Z value 2.668, P value 0.008), serum albumin improved from 2.1 to 2.4 g/dL (Z value 2.028, P value 0.043), and Child score improved from 10 to 8 (Z value 2.694, P value 0.007). There was no significant improvement in serum creatinine, sodium, potassium, calcium, bilirubin, total protein values and clinical scores of ascites, and hepatic encephalopathy. One patient developed fever with respiratory tract infection which led to decompensation, which affected all the reports. High cost of medicine was the limiting factor to include more patients in study. Conclusion: Initial data suggest that darbepoetin alpha and pegfilgrastim are significantly effective in improving hemoglobin, total leukocyte count, platelet count, international normalized ratio, serum albumin, and Child score of the patients with advanced liver cirrhosis.
Predicting risk factors for rebleeding, infections, and mortality in cirrhotic patients with peptic ulcer bleeding— Nationwide cohort study

**Authors:** SHIH-CHENG YANG[1]; SENG-KEE CHUAH[1, 2]; CHIEN-NING HSU[3]; CHIH-MING LIANG[1]; CHENG-KUN WU[1]; WEI-CHEN TAI[1, 2]; TSUNG-HSING HUNG[4]; SENG-HOWE NGUANG[5]; LAN-TING YUAN[6]; JIUNN-WEI WANG[7]; KUO-LUN TSENG[7]; WEI-CHIH SUN[8]; PING HSU[8]; DENG-CHYANG WU[7]; ON BEHALF OF TAIWAN ACID-RELATED DISEASE (TARD) STUDY GROUP

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**Introduction:** Cirrhosis is associated with poor outcomes in peptic ulcer bleeding (PUB) and very few large population-based studies in the literature. This nationwide cohort study aimed to elucidate the association between cirrhosis and recurrent PUB, mortality by analyzing the Taiwan National Health Insurance Research Database. **Methods:** Data of 1997–2008 were extracted from the National Health Insurance Research Database in Taiwan. A total of 18,646 discharges with PUB as a diagnosis were identified. Patients <20 years of age and patients who underwent bleeding with endoscopic treatment within 180 days before index, varices bleeding, gastric resection, varotomy, or gastric cancer before index hospitalization discharge were excluded (n = 533). In this population-based cohort study, 737 cirrhotic patients, 1044 chronic hepatitis patients, and 13,794 normal controls were compared. **Results:** In this study, cirrhotic patients had significantly higher incidences of recurrent PUB than chronic hepatitis patients and controls (12.48% in cirrhosis, 6.7% in chronic hepatitis, and 5.61% in controls, P < 0.0001). By Cox proportional hazard regression analysis, cirrhosis was independently associated with increased risk of recurrent PUB (hazard ratio: 2.42; 95% confidence interval [CI]: 1.88–3.21, P < 0.0001) after adjusting for age, gender, Charlson score, and ulcerogenic medication. Male gender, repeated endoscopic therapy, infection, severe ulcer bleeding, and use of aspirin were risk factors for in-hospital recurrent PUB in all patients. Age, male gender, Charlson score ≥2, severe ulcer bleeding, and use of aspirin/nonsteroidal anti-inflammatory drugs were risk factors for in-hospital death in all patients. Mortality of PUB with concomitant cirrhosis was higher than that in the chronic hepatitis group and controls (P = 0.01 and P = 0.04, respectively). In multivariate analysis, the presence of cirrhosis independently increased long-term mortality (hazard ratio: 1.97; 95% CI: 1.68–2.32, P < 0.0001), but not in-hospital death. Patients with cirrhosis received more transcatheter arterial embolization for recurrent PUB compared with the other two groups (7.6% vs 2.6% vs 0.7%, respectively). Hospitalization costs and length of stay also were increased in patients with cirrhosis. **Conclusions:** This study suggests that cirrhotic patients are associated with a significantly higher risk of recurrent PUB. Liver cirrhosis is also associated with long-term risk of mortality after hospital discharge.

Activation of microRNA-29a in activated hepatic stellate cells modulates its profibrogenic phenotype through inhibition of histone deacetylases 4

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**Background:** Recent studies have shown that microRNA-29 (miR-29) is significantly decreased in liver fibrosis and that its downregulation influences the activation of hepatic stellate cells (HSCs). In addition, inhibition of the activity of histone deacetylases 4 (HDAC4) has been shown to strongly reduce HSC activation in the context of liver fibrosis. **Objectives:** In this study, we examined whether miR-29a was involved in the regulation of HDAC4 and modulation of the profibrogenic phenotype in HSCs. **Methods:** We employed miR-29a transgenic mice (miR-29aTg mice) and wild-type littermates to clarify the role of miR-29a in cholestatic liver fibrosis, using the bile duct ligation (BDL) mouse model. Primary HSCs from both mice were treated with a miR-29a mimic and antisense inhibitor in order to analyze changes in profibrogenic gene expression and HSC activation using real-time quantitative reverse transcription–polymerase chain reaction, immunofluorescence staining, western blotting, and cell proliferation and migration assays. **Results:** After BDL, overexpression of miR-29a decreased collagen-I and HDAC4 and activated HSC phenotype through inhibition of the HDAC4 function. Overexpression of miR-29a and HDAC4 RNA interference decreased the expression of fibrotic genes, HDAC4 signaling, and HSC migration and proliferation. In contrast, knockdown of miR-29a with an antisense inhibitor increased HDAC4 function, restored HSC migration, and accelerated HSC proliferation. **Conclusions:** Our results indicate that miR-29a ameliorates cholestatic liver fibrosis after BDL, at least partially, by modulating the profibrogenic phenotype of HSCs through inhibition of the HDAC4 function.
# 1789 Low air temperature increases the risk of esophageal variceal bleeding: A population and hospital-based case-crossover study in Taiwan

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**Background and Aims:** Studies concerning seasonal variations and the impact of air temperature on esophageal variceal bleeding have yielded conflicting results. We aimed to explore the impact of air temperature on the occurrence of variceal bleeding. **Methods:** A case-crossover study design was employed, and two cohorts were used, including the NHI-EVB cohort from the National Health Insurance Research Database of Taiwan from January 1, 1999, to December 31, 2010, and the VGH-EVB cohort from the Taipei Veterans General Hospital, from May 4, 2002, to December 31, 2010. A conditional logistic regression model was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). **Results:** In total, 2542 cases from the NHI-EVB cohort and 220 cases from the VGH-EVB cohort were analyzed. Our analysis showed that low air temperature increased the risk of variceal bleeding regardless of age, sex, decompensated cirrhosis, Child–Pugh classification, etiology of liver disease, and concomitant hepatocellular carcinoma: the lag effect was also observed. The ORs per 5 °C decrease in daily mean air temperature were 1.144 (95% CI, 1.031–1.235) for the NHI-EVB cohort and 1.307 (95% CI: 1.059–1.658) for the VGH-EVB cohort. Esophageal variceal bleeding in patients with small varices, end-stage liver disease score ≥ 15, or those using non-selective beta blockers was not influenced by air temperature. **Conclusions:** Patients have higher risk of esophageal variceal bleeding at low air temperature regardless of age, sex, Child–Pugh classification, decompensated cirrhosis, and concomitant hepatocellular carcinoma and can be protected by use of non-selective beta blockers.

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**# 1834 Acoustic radiation force impulse sonography-based non-invasive prediction of esophageal varices**

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**Background:** For varices detection, although esophagogastroduodenoscopy (EGD) screening is an affordable medical strategy and suggested with a practice guideline by the American Association for the Study of Liver Diseases for cirrhosis patients, the true EGD screening rate is still not high. Different results have been shown in esophageal varices prediction using acoustic radiation force impulse (ARFI) in literature. **Aims:** To determine spleen stiffness (SS) values in clinically diagnosed cirrhosis patients by using ARFI for EV prediction. **Method:** From December 2013 to March 2014, we measured liver stiffness and spleen SS by ARFI sonography in 118 patients with chronic liver disease. Eighty-five patients were clinically diagnosed with liver cirrhosis, and the other 33 were diagnosed with chronic liver disease. In cirrhosis patients, half of them ever received EGD within 1 year before ARFI examination. Variables found to be associated with the presence of esophageal varices on univariate analysis (P < 0.05) were entered into the multivariate logistic regression analysis. The optimal cut-off value for esophageal varices prediction was calculated under the receiver operating characteristic curve. **Result:** In the cirrhosis group, spleen stiffness was higher in patients with EV (3.43 ± 0.44 m/s, n = 26) than NEV (3.03 ± 0.68 m/s, n = 16; P = 0.043). SS and spleen diameter meet significant difference in multivariate analysis for EV prediction (P = 0.035 and P = 0.037, respectively), shown in Table 1. Based on area under the receiver operating characteristic curve analysis, for EV prediction, spleen diameter with the optimal cut-off value of 10.69 cm showed a sensitivity of 96.2% and specificity of 56.3%; SS with the optimal cut-off value of 2.82 m/s showed a sensitivity of 96.2% and specificity of 50% (Fig. 1). A relaxed new cut-off criterion, spleen diameter ≥ 10.69 cm or SS ≥ 2.82 m/s, was introduced with 100% negative predictive value and 100% sensitivity. **Conclusion:** Spleen diameter and SS together can provide powerful diagnostic performance in selecting cirrhosis patients who have EV formation.
Table 1  Variables between EVs and non-EVs patients

| Variables                        | EV (n = 26) | NEV (n = 16) | Univariate analysis (P value) | Multivariate analysis |
|---------------------------------|-------------|--------------|------------------------------|-----------------------|
| Age (y), mean ± SD              | 54.50 ± 11.39 | 59.25 ± 8.53 | 0.204                        |                       |
| Sex (male/female)               | 23/3        | 11/5         | 0.223                        |                       |
| BMI (kg/m2); mean ± SD          | 24.71 ± 3.00 | 22.90 ± 2.76 | 0.095                        |                       |
| MELD score; mean ± SD           | 10.90 ± 3.65 | 12.43 ± 5.06 | 0.630                        |                       |
| Underlying disease, n           |             |              |                              |                       |
| HBV                             | 11          | 5            | 0.331                        |                       |
| HCV                             | 4           | 5            |                              |                       |
| Alcohol                         | 11          | 6            |                              |                       |
| AST (IU/L), mean ± SD           | 48.87 ± 27.75 | 33.06 ± 14.25 | 0.032 | 1.03 (0.95 – 1.13) | 0.460 |
| ALT (IU/L), mean ± SD           | 36.08 ± 19.33 | 22.50 ± 9.92 | 0.011 | 1.08 (0.96 – 1.21) | 0.206 |
| T/B (mg/dl), mean ± SD          | 1.95 ± 2.75  | 1.21 ± 0.89  | 0.094 |                       |                       |
| ALB (gm/dl), mean ± SD          | 3.70 ± 0.65  | 4.01 ± 0.49  | 0.111 |                       |                       |
| Platelet count (x 10^4/μl), mean ± SD | 9.28 ± 3.97 | 12.67 ± 6.22 | 0.092 |                       |                       |
| APRI                            | 1.57 ± 1.01  | 0.99 ± 0.96  | 0.012 | 0.30 (0.06-1.60) | 0.159 |
| Spleen diameter, cm, mean ± SD  | 13.68 ± 2.48 | 10.81 ± 2.14 | <0.001 | 1.78 (1.04-3.07) | 0.037 |
| Median LS (m/s)                 | 2.46 ± 0.54  | 2.04 ± 0.78  | 0.037 | 1.35 (0.26-6.93) | 0.72  |
| Median SS (m/s)                 | 3.43 ± 0.44  | 3.03 ± 0.68  | 0.043 | 7.12 (1.15-44.05) | 0.035 |

MELD score, model for end-stage liver disease

Figure 1

Source of the Curve
- Spleen Diameter
- SS median
# 1847 Differences of gastric pH between patients with mild and severe portal hypertensive gastropathy due to liver cirrhosis

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Introduction: One of the causes of upper gastrointestinal bleeding in patients with liver cirrhosis is the presence of portal hypersensitive gastropathy (GHP). GHP prevalence in patients with liver cirrhosis is quite high but there was still inconsistency regarding the studies about gastric pH in cirrhosis patient. The aim of this study is to find the difference of gastric pH in liver cirrhosis patient with mild and severe portal hypertensive gastropathy. Method: Cross-sectional method with consecutive sampling to all liver cirrhotic patients who came to Clinic of Gastroenterology and Hepatology in Cipto Mangunkusumo hospital was done from March to May 2014. Sixty two liver cirrhosis patients with portal hypertensive gastropathy underwent endoscopy to measure degree of gastropathy based on McCormack classification and measured mean basal gastric pH with pH-metric. Results: There are 50 (80.6%) male subject and 12 (19.4%) female subject participating in this study. Portal hypertensive gastropathy mostly caused by hepatitis C (56.5%), hepatitis B (32.3%), non hepatitis (8.1%) and alcohol (3.2%). Mean of gastric pH in all liver cirrhosis patients with portal hypertensive gastropathy was 2.13. The mean gastric pH in liver cirrhosis patient with mild portal hypertensive gastropathy 2.00 is lower than the gastric pH in severe portal hypertensive gastropathy 2.25 with significant differences (P < 0.05). Conclusion: The gastric pH in liver cirrhosis patient between mild and severe portal hypertensive gastropathy are significantly different.

Keywords: gastric pH, liver cirrhosis, portal hypertensive gastropathy, pH-metric

# 1878 Can non-invasive aspartate aminotransferase-to-platelet ratio index score in cirrhosis replace invasive hepatic venous pressure gradient?

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Background: Portal hypertension leads to complications of cirrhosis, both bleeding as well as non-bleeding. Hepatic Venous Pressure Gradient (HVPG) is the only recommended means to measure portal hypertension and prognosticate cirrhosis, but is invasive. There is a need for a simple, non-invasive marker to measure portal hypertension. Aspartate aminotransferase/platelet ratio index (APRI) is a good simple non-invasive marker of hepatic fibrosis. Very little data available on correlation of non-invasive APRI with invasive HVPG for portal hypertension. Aim: To compare non invasive APRI score with invasive HVPG for portal hypertension and determine usefulness of APRI in portal hypertension Methods: The study included all consecutive patients of cirrhosis satisfying study protocol, between ages 18 and 70 years, who underwent HVPG and simultaneous APRI measurement. Results: This study included 147 patients with median age 52.39 ± 10 years; 120(81.6%) males. The etiology of cirrhosis were alcohol 69 (47%), viral 20 (13%), cryptogenic 46(31%) and others 12(8%). Mean CTP score and mean MELD score were 7.69 ± 1.91 and 13.29 ± 4.90 respectively. The median HVPG was 17.90 ± 4.74 mmHg. The maximum Youden’s index was 0.4676 which corresponded to a cut-off value of 0.946 of APRI. The ROC curve to study the performance of APRI for predicting high portal pressure (HVPG > 12 mmHg) had area under curve 0.712 (P = 0.001). An APRI of 0.946 had a sensitivity 71.76%, specificity 75%, positive predictive value 95.92%, negative predictive value 24.49%, and diagnostic accuracy 72.10% for predicting HVPG > 12 mmHg. There was significant difference (Spearman’s rho = 0.370; P ≤ 0.001) with in median APRI between patients with HVPG ≤ 12 mmHg (APRI 0.83 [0.32–3.33]) and those with HVPG > 12 mmHg (APRI 1.40 [0.29–12.22]), respectively. Conclusion: APRI score of 0.946 seems to have an acceptable accuracy for prediction of high portal pressure. APRI is a simple, non invasive and cost-effective parameter for diagnosis of high portal pressure in patients with cirrhosis. APRI correlates well with HVPG in patients of cirrhosis.

Keywords: Cirrhosis, HVPG, APRI, Portal hypertension.

# 1928 Overexpression of heparin-binding epidermal growth factor-like growth factor mediates liver fibrosis in transgenic mice

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Background/Aims: Liver fibrosis is a common consequence of chronic liver injury that is induced by a variety of etiological factors. The present study aimed to test the hypothesis that heparin-binding epidermal growth factor-like growth factor (HB-EGF) is a potential target of liver fibrosis. Materials and Methods: HB-EGF transgenic (TG) mice and wild-type (WT) mice were used. Liver fibrosis was induced by intraperitoneally injection of carbon tetrachloride (CCL4). H&E, Sirius red, and α-SMA immunohistochemical staining were performed in the liver sections of TG and WT mice. Primary hepatic stellate cells (HSCs) isolated from two types of mice were used. The proliferative capacity and the degree of apoptosis of primary HSCs were evaluated. RT-PCR was used to test for mRNA levels of α-SMA, collagen 1α1, TIMP-1 and MMP-13 both in the liver sections and the primary HSCs. The protein levels of EGFR, p-EGFR, ERK and p-ERK in the liver sections were detected by Western blot. Results: The mRNA levels of HB-EGF, α-SMA, collagen 1α1, and TIMP-1 were elevated in TG mice compared to WT mice. Liver fibrosis in TG mice was more significantly amplified with more deposition of collagen and increased expression of α-SMA and fibrogenic genes. Compared with WT mice, increased protein levels of p-EGFR and activated ERK were found in TG mice. HSC from TG mice showed enhanced activation and reduced apoptosis as well. Conclusions: HB-EGF overexpression contributes to the progression of liver fibrosis and exerts profibrotic roles. Therefore, HB-EGF is a potential therapeutic target in liver fibrosis.
# 1945 Sorafenib induces autophagic cell death and apoptosis in hepatic stellate cell via the JNK and Akt signaling pathways

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Background/Aims: Increasing hepatic stellate cell (HSC) death is an attractive approach for limiting liver fibrosis. The multiple tyrosine kinase inhibitor sorafenib has recently demonstrated anti-fibrotic effects in vitro and in vivo. However, the precise molecular mechanism through which sorafenib mediates this activity is unknown. Methods: We investigated the mode of cell death induced by sorafenib and its underlying mechanism in primary rat HSC and human LX2 cells. Apoptosis and autophagy were monitored by using morphological methods, such as transmission electron microscopy and immunofluorescence. Western blot analysis confirmed these findings. Results: Sorafenib induced apoptosis in a dose dependent manner in LX2 cells. Ultrastructural analysis revealed that rat HSCs treated with sorafenib accumulated residual digested material and empty or autophagic vacuoles. Incubating LX2 cells with lysosomal protease inhibitors increased the accumulation of LC3-II, indicating that sorafenib enhances autophagic flux in HSCs. This conclusion was confirmed by the observed upregulation of Beclin 1, Atg7, and Atg5. In LX2 cells treated with sorafenib, expression of cleaved-PARP increased significantly, whereas levels of LC3-II peaked at 12 h and reverted to baseline by 24 h. These findings indicate that autophagy may precede apoptosis. Inhibition of autophagy in LX2 cells via 3-MA treatment or siRNA-mediated knockdown of Atg5 resulted in a marked increase in apoptosis. Finally, Sorafenib induced programmed cell death by attenuation and activation of Akt/mTOR/Beclin 1, Atg7, and JNK signaling, respectively. Conclusion: These results demonstrate that sorafenib-induced cell death is mediated autophagic cell death and apoptosis, which could potentially result in novel anti-fibrosis therapies.

# 1953 Portal vein thrombosis does not significantly influence the therapeutic effect of endoscopic therapy for second prevention of gastroesophageal variceal bleeding in cirrhotic patients

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Aims: To investigate whether PVT affect the therapeutic effects of endoscopy therapy for secondary prevention of gastroesophageal variceal bleeding in cirrhotic patients. Methods: 574 patients matched the inclusion criteria whose clinical data were collected retrospectively. Patients were followed up to November 16th 2014 or date of deceased. Kaplan Meier survival analysis was conducted to describe an 8-week/overall rebleeding rate. Cox proportional hazards analysis was used to compare patients who had PVT at the time of inclusion (n = 119) with those who did not (n = 455), after adjusting for important baseline characteristics. Among those initially diagnosed with PVT, changes of PVT were also observed to further investigate subsequent impact. Results: 59 (10.3%) patients (PVT group: 16/119, Non-PVT group: 43/455) developed gastroesophageal variceal rebleeding within 8 weeks after endoscopic therapy. During a mean follow-up period of 33.7 months, 230(40.1%) patients (PVT group: 43/119, Non-PVT group: 187/455) developed gastroesophageal variceal rebleeding. Compared to patients without PVT, patients with PVT had a similar risk of 8-week rebleeding (adjusted hazard ratio [AHR], 1.62; 95% confidence interval [CI], 0.88–2.98; P = 0.12) and overall rebleeding rate (adjusted hazard ratio [AHR], 0.96; 95% confidence interval [CI], 0.67–1.36; P = 0.80). During the follow-up period, PVT worsened in 13.45% (16/119), improved in 35.29%, and was stable in 13.45% of patients. Those with progressed PVT had a higher 8-week rebleeding and overall rebleeding rate (11.7% vs 25.0%, P = 0.099; 34.0% vs 50.0%, P = 0.092), but no statistical significance was incurred. Conclusion: Among cirrhotic patients who received endoscopic therapy for preventing gastroesophageal variceal rebleeding, the presence of PVT does not significantly influence the therapeutic effect.

# 2003 Predictors of mortality in patients with cirrhosis admitted at intensive care unit at Cardinal Santos Medical Center

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Introduction: Cirrhosis is the final stage of all chronic liver diseases. It has been a significant source of morbidity and mortality. The over-all prognosis for patients with cirrhosis admitted to ICU remains poor. Many clinical and biochemical parameters have been suggested in order to predict more accurately the prognosis of cirrhotic patients and correctly assess their survival rate. The objective of the study is to identify predictors of mortality in patients with cirrhosis admitted to ICU. Methodology: This is a retrospective study of patients with cirrhosis admitted at medical intensive care unit (MICU) at Cardinal Santos Medical Center (CSMC) between June 1, 2009 to June 30, 2014. Data on age, gender, etiology of liver disease, number of years diagnosed with cirrhosis, indication for ICU admission, length of ICU stay were recorded. Laboratory parameters recorded were platelet count, blood urea nitrogen, creatinine, sodium, AST, ALT, total bilirubin, INR, albumin, arterial bicarbonate, pH, partial arterial pressure of oxygen (PaO2) and inspired oxygen concentration (FiO2). The severity of liver disease was graded by the Child Pugh, MELD and MELD-Na scores using parameters recorded on the day of admission. For comparison of continuous variables t test comparison of independent means and chi-square test to compare categorical variables were used. Results: A total of 51 cirrhotic patients were admitted at the Cardinal Santos Medical Center Medical Intensive Care Unit between June 1, 2009 to June 30, 2014. Majority were male with Hepatitis B virus infection as the most common etiology of cirrhosis. The most common indication for ICU admission was encephalopathy. The overall mortality rate in the ICU was 39.22% in which the common cause of death was multi-organ failure (45%). Mean MELD, MELD-Na and Child Pugh scores were 42, 44 and 11 respectively. Non-survivors had significantly used a mechanical ventilator (35.29%), needed an inotropic support (31.37%) and had undergone renal replacement therapy (25.49%). Laboratory findings showed that non-survivors had significantly lower venous pH and bicarbonate values than the survivors. Conclusion: This study confirms that the prognosis for cirrhotic patients admitted to the MICU is poor. MELD, MELD-Na is associated with lower survival. Non-survivors had significantly lower venous pH and bicarbonate values and used a mechanical ventilator, needed an inotropic support and had undergone renal replacement therapy.
# 2017 The hemodynamic profile during liver transplantation: Review and a highly simplified model

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**Author Contributions:** Hsieh CB and Feng AC contributed equally to this work. Hsieh CB and Feng AC designed the study and Feng AC wrote the paper. Fan HL, Chen TW, and Yu JC collected the data and reviewed the references in detail. Hsieh CB and Yu JC performed the final verification.  
**Aim:** The correlation between portal vein flow and portal vein pressure is not yet confirmed. This hypothesis is established to identify the correlation between different hemodynamic parameters during liver transplantation.  
**Methods:** The hypothesis of “hepatic energy” is derived from the fluid mechanics and the law of energy conservation. The kinetic energy consumed by the liver graft can be calculated as the sum of kinetic energy inflow of portal vein and hepatic artery minus the kinetic energy outflow from hepatic vein. After a serial substitution, the final equation is: Power of kinetic energy consumption by the liver graft = portal vein pressure × portal vein flow + mean arterial pressure × hepatic artery flow – central venous pressure × (portal vein flow + hepatic artery flow). We utilized data obtained from published studies to evaluate the kinetic energy status in a healthy population, cirrhosis, acute hepatic failure, and liver transplantation with full-size, partial, and small-for-size grafts.  
**Results:** The range of the energy power index in the healthy population was 22,750–45,500. 17,276–39,963 of liver transplantation with full-size grafts, 11,116–25,227 of partial graft, and 10,754–26,534 of smaller left-lobe grafts. The simulated diseased models were all located out of the calculated range according to the graft-to-recipient weight ratio.  
**Conclusion:** The hepatic energy consumed by the liver graft and its safe margin according to the graft-to-recipient weight ratio is considered as a potential prognostic factor and also a possible indicator for graft inflow modulations not based on portal vein pressure or portal vein flow separately.  
**Keywords:** energy metabolism, hemodynamics, hydrodynamics, liver circulation, liver transplantation.

# 2163 A scoring model for prediction of relapse among chronic HCV patients with rapid virologic response to peginterferon/ribavirin treatment  

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**Background and Aims:** Rapid virological responses (RVR) to peginterferon/ribavirin (peg-IFN/RBV) are predictive of sustained virological response (SVR) in hepatitis C virus (HCV) infection. A number of HCV patients with RVR did not achieve a SVR. We aimed at finding a simple score to identify the predictors of relapse after treatment will help in better selection of patients and avoidance of unnecessary side effects.  
**Methods:** 818 HCV-infected, treatment-naive patients receiving pegIFN/RBV, the feasibility of predicting treatment failure using the baseline and on-treatment factors to explore the risk score for HCV patients with a RVR.  
**Results:** The multi-variable logistic regression analysis showed that independent predictors of relapse were AST ≤ 40 IU/L, low platelet count, HCV genotype 1, high viral load, and clinical liver cirrhosis. A scoring model for prediction of relapse was calculated based on the regression coefficients of each predictor. The ROC curve for prediction of relapse by the score showed that the area under the curve (AUC) is 71.2. A cut-off value of 15% had 73.49% sensitivity, 60.62% specificity, 92.57% negative predictive value and 25.52% positive predictive value.  
**Conclusions:** A scoring model using AST ≤ 40 IU/L, low platelet count, HCV genotype 1, high viral load, and clinical liver cirrhosis during therapy can efficiently predict relapse.

# 1022 Sequential treatment with lamivudine and peginterferon therapy in patients with E antigen-positive chronic hepatitis B and high viral load  

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**Background:** The aim of this study was to assess the therapeutic response of sequential therapy, lamivudine (LAM) followed by PEG-IFN, in the patients with e antigen-positive chronic hepatitis B (CHB) and high viral load.  
**Methods:** CHB patients who have positive e antigen, HBV DNA greater than 10^7 IU/mL, ALT levels greater than 2 times the upper limit, and treatment naive were included. Those with concurrent hepatitis C or HIV infection, liver cirrhosis or decompensated liver disease, or pregnancy were excluded. The enrolled cases received therapy with PEG-IFN monotherapy for 48 weeks (PEG-IFN group) or sequential therapy with lamivudine (LAM) for 4 weeks followed by PEG-IFN therapy for 48 weeks (LAM/peg-IFN group).  
**Results:** There were 10 patients in each group, and there were no differences in characteristics between the two groups. The positive response ratio of end-of-treatment (EOT) was 30% and 10% in the PEG-IFN group and the LAM/PEG-IFN group. Sustained off-treatment virological responses (SVR) at 12 weeks after EOT were 40% and 10%, at 24 weeks after EOT were 30% and 20% in the PEG-IFN group and the LAM/PEG-IFN group, respectively. The therapeutic responses between the two groups showed no differences.  
**Conclusion:** In CHB patients who have positive e antigen and a high viral load at baseline, similar therapeutic responses were noted between the sequential therapy group and the PEG-IFN monotherapy group. Further research with a higher number of patients and a prolonged LAM course are needed to confirm the efficacy of this approach.
# 1067 Population pharmacokinetic analysis of ledipasvir/sofosbuvir fixed-dose combination tablet in Taiwanese subjects with chronic genotype 1 hepatitis C virus infection

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**Background:** Administration of ledipasvir (LDV)/sofosbuvir (SOF) fixed-dose combination tablet (FDC) once daily for 12 weeks achieved an overall SVR12 rate of 98% (83/85) in treatment-naive and treatment-experienced Taiwanese patients with chronic genotype 1 HCV infection. Phase 3b: GS-US-337-0131. Pharmacokinetic (PK) data were collected in the study to examine the relationship between demographic variables and exposure response and to compare results to studies conducted across various regions.

**Methods:** Treatment-naive (N = 42) and treatment-experienced (N = 43) Taiwanese subjects were enrolled to receive LDV/SOF 90 mg/400 mg FDC for 12 weeks. Intensive and sparse samples were collected to evaluate the pharmacokinetics of LDV, SOF and GS-331007 (predominant circulating metabolite). Individual PK parameters were estimated using previously established population PK models for LDV, SOF, and GS-331007. The effect of demographic variables on LDV, SOF, and GS-331007 exposure was evaluated. 

**Results:** Table 1 presents steady-state exposure for LDV, SOF, and GS-331007. Compared to historical data, the percentage geometric mean ratios (GMRs) (90% confidence intervals) for Taiwanese/US subjects; this increase was not considered clinically relevant. SOF and GS-331007 exposures were similar between the two populations.

**Conclusion:** There were no clinically relevant differences in the PK of LDV/SOF in Taiwanese subjects compared to historical data. PK results in conjunction with safety and efficacy data support the use of LDV/SOF 90 mg/400 mg 12 weeks for the treatment of GT1 HCV infection in Taiwanese patients.

| Parameter | Taiwanese population | LDV/SOF USFDA population | %GMR (90% CI) | NDA |
|-----------|---------------------|--------------------------|---------------|-----|
| **AUC**<sub>τ</sub> (ng*h/mL) | | | | |
| LDV<sup>4</sup> | 11,600 (52.0) | 8530 (60.8) | 141 (127, 156) |
| SOF<sup>5</sup> | 446 (42.6) | 364 (61.4) | 127 (116, 138) |
| 303 (47.3) | 247 (69.2) | 129 (116, 1430) |
| **AUC**<sub>τ</sub> (ng*h/mL) | | | | |
| GS-331007<sup>7</sup> | 1440 (26.1) | 1380 (34.0) | 106 (97.8, 114) |
| **Cmax** (ng/mL) | | | | |
| LDV | 731 (27.0) | 659 (34.0) | 113 (101, 125) |
| SOF | 303 (47.3) | 247 (69.2) | 129 (116, 1430) |
| **AUC**<sub>τ</sub> (ng*h/mL) | | | | |
| GS-331007<sup>7</sup> | 12,500 (21.1) | 12,500 (29.2) | 102 (96.9, 108) |
| **Cmax** (ng/mL) | | | | |
| LDV | 792 (21.5) | 736 (28.2) | 109 (104, 115) |

Data reported to three significant figures.

†One subject withdrew from the study on day 2, did not have PK samples collected and is not included in the PK analysis.

‡N = 2113 (LDV/SOF USFDA population).

§N = 36 (Taiwanese population) or 1542 (overseas LDV/SOF population).

# 1068 Treatment with the single-tablet regimen ledipasvir/sofosbuvir for 12 weeks results in 100% sustained virologic response in Japanese patients with chronic genotype 1 hepatitis C virus infection

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**Aim:** This open-label, Phase 3 study evaluated the efficacy and safety of ledipasvir 90 mg/sofosbuvir 400 mg Fixed-Dose Combination (LDV/SOF FDC) ± ribavirin (RBV) administered orally, once daily for 12 weeks in treatment-naive and treatment-experienced Japanese subjects with chronic genotype 1 hepatitis C virus (HCV) infection. 

**Methods:** Eligibility requirements included: age ≥ 20 years; HCV-RNA ≥ 10² IU/mL; platelets ≥50,000/μL. Primary endpoint was Sustained Virologic Response 12 weeks after treatment completion (SVR12). 

**Results:** 341 Japanese patients were enrolled (166 treatment-naïve and 175 treatment-experienced). Mean age was 59 years; 42% were male; 22% had cirrhosis; mean baseline HCV-RNA was 6.6 log₁₀ IU/mL. All patients in both arms had HCV RNA < LLOQ at weeks 4–12 of treatment. SVR12 was achieved in 100% of patients in the LDV/SOF group and 98% (167/170) of patients in the LDV/SOF + RBV group. In the LDV/SOF + RBV group, one subject relapsed, one discontinued RBV due to a RBV-related rash, and one died due to cardiac arrest. All treatment-experienced patients achieved SVR12.
regardless of previous HCV regimen or previous treatment response. Treatment-emergent adverse events (TEAEs) were reported by 65% of patients in the LDV/SOF arm and 75% in the LDV/SOF + RBV arm, with the most frequent being nasopharyngitis (29% and 24%, respectively) and anemia (2% and 14% respectively). Most TEAEs were mild to moderate in severity. Conclusions: LDV/SOF FDC ± RBV for 12 weeks achieved SVR12 in 99% of patients. LDV/SOF for 12 weeks provides a highly effective, well-tolerated, interferon- and RBV-free treatment for Japanese patients with chronic HCV GT1 infection.

### # 1076 Sofosbuvir in combination with ribavirin for 12 weeks achieves 97% sustained virologic response in Japanese patients with chronic genotype 2 hepatitis C infection

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**Aim:** This open-label, single-arm Phase 3 study evaluated the efficacy and safety of sofosbuvir (SOF) 400 mg administered orally, once daily with weight-based ribavirin (RBV; 600–1000 mg/day) in Japanese patients with chronic genotype 2 hepatitis C virus (HCV) infection. Methods: Treatment-naive and treatment-experienced Taiwanese subjects with chronic genotype 2 HCV infection were randomized (90 treatment-naïve and 63 treatment-experienced). Mean age was 57 years (range 25–74), 54% (83/153) female, 79% (121/153) IL-28B-CC, 11.1% (17/153) had cirrhosis. All patients achieved undetectable HCV RNA by Week 4 and completed the full 12 weeks of treatment. SVR12 was 96.7% (148/153); there were no virologic breakthroughs but 5 patients relapsed. SVR12 was 98% and 95% in treatment-naïve and treatment-experienced patients, respectively. Adverse events were generally mild, and laboratory abnormalities were infrequent and consistent with the safety profile of RBV. No AEs led to treatment discontinuation. Conclusions: Treatment-naive and treatment-experienced Japanese patients with chronic GT-2 HCV infection, including those with compensated cirrhosis, achieved high rates of SVR12 with 12 weeks of an IFN-free, all-oral regimen of SOF + RBV. The regimen was safe and well-tolerated with no treatment discontinuations and an AE profile consistent with that observed with RBV. The data suggest that SOF + RBV may offer an improved, IFN-free treatment for Japanese patients with chronic GT-2 HCV infection.

### # 1077 Sofosbuvir population pharmacokinetics in Taiwanese subjects with chronic genotype 2 hepatitis C virus infection

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**Background:** Administration of sofosbuvir (SOF) + ribavirin (RBV) once daily for 12 weeks achieved an overall SVR12 rate of 100% (87/87) in treatment-naïve and treatment-experienced genotype 2 HCV-infected Taiwanese patients with or without cirrhosis (Phase 3b: GS-US-334-0115). Pharmacokinetic (PK) data were collected in the study to examine the relationship between demographic variables and exposure response and to compare results to studies conducted across various regions. Methods: Treatment-naïve (N = 43) and treatment-experienced (N = 44) Taiwanese subjects were enrolled and received SOF 400 mg + RBV (weight-based dosing) for 12 weeks. Sparse samples were collected to evaluate the pharmacokinetics of SOF and GS-331007 (predominant circulating metabolite). Exposure estimates for SOF and GS-331007 were generated for each subject, with measureable concentrations of SOF or GS-331007, using previously established population PK models. The effect of demographic variables on SOF and GS-331007 exposure was evaluated. Results: Table 1 presents steady-state exposure for SOF and GS-331007. Compared to historical data (overseas Phase 2/3 population), SOF and GS-331007 exposures were similar between the two populations. Within the Taiwanese study population, no clinically relevant differences were observed in the PK of SOF or GS-331007 based on CLcr, age, sex, BMI, cirrhosis, prior treatment experience, or SVR12 outcome. Conclusion: SOF and GS-331007 exposures were similar in Taiwanese subjects compared to historical data. PK results in conjunction with safety and efficacy data support the use SOF 400 mg + RBV (weight-based dosing) for the treatment of GT2 HCV infection in Taiwanese patients.

| Table 1 |
| Mean (%)CV PK parameter | Taiwanese population | SOFUSNDA Phase 2/3 population | %GMR (90%CI) Taiwanese/SOFUSNDA |
|-------------------------|----------------------|-----------------------------|-----------------------------|
| SOF AUCtau (ng*h/mL)    | N = 44               | N = 838                      | 97.8 (89.7, 107)             |
|                          | 972 (23.7)           | 1030 (36.5)                  |                             |
| Cmax (ng/mL)            | 567 (24.8)           | 511 (32.5)                   | 115 (104, 127)               |
| GS-331007               | N = 87               | N = 1695                     |                             |
| AUCtau (ng*h/mL)        | 8680 (22.1)          | 7120 (30.7)                  | 123 (117, 131)               |
| Cmax (ng/mL)            | 740 (26.6)           | 582 (36.3)                   | 132 (123, 142)               |

PK parameters are presented up to three significant digits.
# 1198 The hepatitis C virus genotype distribution in southeastern Taiwan

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**Introduction:** The hepatitis C virus (HCV) infection is a serious public health problem in the world. In Taiwan, the most prevalent genotype was 1b, followed by genotypes 2a and 2b. The regional difference of genotype distribution might exist within different areas in Taiwan. The racial diversity of Taitung is heterogeneity and is a distinguishing feature. How the racial differences influence the genotype distribution is not well studied. The aim of this study is to determine the HCV genotype distribution and clinical implication in southeastern Taiwan. **Methods:** In this retrospective study, we included total 343 patients who had treated with peginterferon-alpha plus ribavirin from Nov 2009 to Mar 2015. The data of genotypes, races, HCV viral load, and laboratory examination were collected and analysed (Table 1). **Results/Discussion:** The predominant HCV genotype in southeastern was type 1 (43.7%, including type 1b 36.4%), followed by type 2 (37.0%, including type 2a 26.8%) (Fig. 1). The prevalence of genotype 6 (5.2%) in southeastern Taiwan seems higher than other area, but there is no difference between indigenous and non-indigenous people. Taiwanese indigenous people belong to Austronesian families. The Austronesian people are mainly in the South Pacific islands, including Taiwan, Vietnam, the Philippines, Malaysia, and so on. HCV genotype 6 is restricted to South China, Southeast Asia and in migrant patients from endemic countries [4]. The association between Austronesian people and genotype distribution was still unclear. **Conclusions:** In southeastern area, HCV genotype 6 appeared slightly higher than general population in Taiwan. The prevalence of genotype 1 in indigenous people is lower than in non-indigenous people. Further investigations are needed to determine the possible explanations of these differences.

# 1202 Hepatitis C virus suppresses interferon-stimulated production of immunoproteasomes by the protein kinase R pathway

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**Background:** Hepatitis C virus (HCV) is known to evade host’s immune responses efficiently. In virus-infected cells, antigen is processed by proteasome complex and presented to CD8+ T cells by major histocompatibility complex (MHC) class I. Interferon (IFN) switches conventional proteasomes to immunoproteasomes, which are more suitable for generation of MHC class I epitopes. Herein, we studied the effect of HCV infection on immunoproteasome production and its mechanism. **Methods:** JFH-1 (genotype 2a) HCV cell culture system was used for in vitro infection of Huh-7.5 cells. Huh-7.5 cells were treated with IFN-γ to induce immunoproteasome production. The expression of immunoproteasome subunits was evaluated by immunoblots and real-time PCR. The expression of protein kinase R (PKR) was silenced with lentiviruses that express small hairpin RNAs, and immunoproteasome induction was examined in PKR silenced cells. The peptide digestion was assessed in each cell group by mass spectrometry. **Results:** IFN-γ induced the expression of immunoproteasome subunits (immunosubunits) such as β1i (LMP2), β2i (MECL-1), and β5i (LMP7). However, IFN-γ-induced immunosubunits expression was attenuated in HCV-infected cells. While this attenuation in HCV-infected cells was observed at the protein level, it was not at the mRNA level. This result suggests that IFN-γ-induced immunosubunits expression is hampered during translation in HCV-infected cells. The expression of immunosubunits was restored by PKR silencing in HCV-infected cells, demonstrating that the PKR pathway is responsible for the suppression of immunosubunits expression in HCV-infected cells. This attenuated immunoproteasome expression by HCV infection resulted in decreased peptide production. **Conclusions:** HCV suppresses IFN-stimulated expression of immunoproteasome subunits through PKR.
pathway. Suppression of immunoproteasome production might contribute to immune evasion of HCV by altering generation of MHC class I epitopes.

# 1259 Distribution pattern of hepatitis C virus in eastern Peninsular Malaysia for the past decade

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Introduction: Analysis of the Hepatitis C Virus (HCV) genotype spread in a particular area has a crucial impact on public health. Genotyping is essential before initiating treatment. Methods: This is a hospital-based cohort of 133 chronic hepatitis C patients, collected prospectively among subjects attending Hospital Tengku Ampuan Afzan, Kuantan, within an area of eastern Peninsular Malaysia. We assessed the rate and distribution of HCV genotypes during two consecutive periods, from 2005 to 2006 and from 2013 to 2014, according to age, gender, race and risk factors. Results: The results are illustrated in Table 1. Genotypes 3 and 1 were predominant before initiating treatment. A particular area has a crucial impact on public health. Genotyping is essential before initiating treatment.

Table 1

| Affiliation                                                                 | Race      | Gender | Age (mean ± SD) | Risk factors |
|----------------------------------------------------------------------------|-----------|--------|-----------------|--------------|
| First cohort (2005/2006)                                                   |           |        |                 |              |
| Second cohort (2013/2014)                                                  |           |        |                 |              |
| N (%)                                                                     | N (%)     |        |                 |              |
| Gender                                                                     | Race      | N (%)  |                  |              |
| Male                                                                       | Malay     | 46 (70.8) | 41 (63.1)       | 27 (41.5)    |
| Female                                                                     | Chinese   | 19 (19.2) | 20 (30.8)       | 19 (29.2)    |
| Race                                                                       | Indian    | 4 (6.2) | 4 (6.2)         | 8 (12.3)    |
| Age (mean ± SD)                                                           | Others    | 1 (1.5) | 1 (1.5)         | 11 (16.9)   |
| Risk factors                                                               |           | 1 (1.5) | 1 (1.5)         | 11 (16.9)   |
| Unknown                                                                    | IVDU      | 27 (41.5) | 19 (29.2)       | 22 (32.4)   |
| Blood transfusion                                                          | Sexual promiscuity | 19 (29.2) | 8 (12.3)       | 32 (47.1)   |
| Sexual promiscuity                                                        | Genotype  | 11 (16.9) | 11 (16.9)       | 7 (10.3)    |
| 1                                                                          |           | 21 (32.3) | 21 (32.3)       | 21 (30.9)   |
| 3                                                                          |           | 38 (58.5) | 38 (58.5)       | 45 (66.2)   |
| 4                                                                          |           | 4 (6.1) | 4 (6.1)         | 1 (1.5)    |
| 6                                                                          |           | 2 (3.1) | 2 (3.1)         | 1 (1.5)    |

# 1270 Treatment efficacy of tenofovir in treating drug-resistant chronic hepatitis B

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Background/Aims: The purpose of this study is to evaluate the predictive factors by examining the treatment effects and responses in patients with chronic hepatitis B after a 6-month period of tenofovir rescue therapy. Methods: The medical records of 68 patients who had undergone a six-month treatment of tenofovir were analyzed. Those patients had previously been identified with drug resistance mutations from September 2012 through August 2014. The virological response showed a decrease in a value of less than 201U/mL of HBV DNA and the Partial virological response showed a decrease in value over a 1log baseline of HBV DNA, while throughout the trial, HBV DNA was continuously detected. Results: After 24 weeks 36 patients (53%) showed a virologic response, and 29 patients (43%) showed a partial virological response. Compared with virological response patients, the partial virological response patients showed a higher HBeAg positive rate (P < 0.001) of HBV DNA with the baseline (P < 0.001) and showed a significant difference. The results of the analysis showed that the amount of HBV DNA (P < 0.001) was independent factor to predict virological response at 24 weeks after tenofovir rescue therapy. Conclusions: Tenofovir rescue therapy showed a positive therapeutic effect in drug-resistant chronic hepatitis B patients. And baseline low HBV DNA levels and HBeAg negative status is useful in predicting the virological response of tenofovir rescue therapy.

# 1384 Validation of increased liver size by ultrasonography after nucleos(t)ides analogs for treatment of chronic hepatitis B—A non-invasive exam for evidence of liver histological improvement

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Background: To evaluate the stage of liver damage prior to, during and after treatment of patients of Chronic Hepatitis B (CHB), liver biopsy has been the most reliable method of ascertaining the stages of liver damage; albeit not without the disadvantage of being invasive. Histological improvement and regression of liver fibrosis or cirrhosis after long-term use

Poster liver
of nucleos(t)ides analogs (NUCs) have been reported. The aim of present investigation is to evaluate the feasibility of parameters demonstrated in ultrasonography as evidences to validate histological improvement of liver after NUCs therapy in CHB patients. Methods: A total of 181 patients of CHB, who were subjected to long-term NUCs treatment, in Cathay General Hospital, were used as the basis of this study; every patient having had tests at the baseline and the endpoint of treatment period. The study population was divided into three groups, cirrhotic, non-cirrhotic, and healthy hepatitis B virus (HBV) carrier. The changes in the percentages of liver size, liver edge, spleen size, platelet count, and platelet count/spleen diameter (PC/SD) ratio were obtained, and compared with the mean differences of different stages of liver damage. Results: The mean averages of liver sizes, liver edges, spleen sizes, platelet count, and PC/SD ratio in healthy CHB carriers, non-cirrhotic and cirrhotic patients, were 7.33, 6.93 and 6.34 cm; 39.09, 35.98 and 37.74; 8.69, 9.09 and 10.79; 212.52, 166.03 and 125.58; and 2477.22, 1880.58 and 1329.08 respectively; thus exhibiting that could be seen as developing to cirrhosis. Decrease in spleen size exhibited a linear relationship when compared with the treatment period (coefficient of determination, \( R^2 = 0.905 \)). Conclusions: Comparing outcomes of healthy HBV carrier, non-cirrhotic, and cirrhotic patients, demonstrated histological improvement of liver after NUCs therapy in CHB patients.

**# 1400 Association of a sustained virologic response with a reduced progression rate to esophageal varices in cirrhotic patients with chronic hepatitis C**

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**Introduction:** Chronic hepatitis C (CHC) is an important cause of liver cirrhosis. Esophageal variceal (EV) is a potentially fatal complication in cirrhotic patients. The achievement of a sustained virologic response (SVR) through interferon-based therapies can slow the progression of liver fibrosis. It is important to know the association of a SVR with a reduced progression rate to EV in cirrhotic patients with CHC. Background and Aims: To study the effect of SVR on the progression of EV in compensated cirrhotic patients with CHC. **Methods:** Ninety-eight treatment-naive CHC compensated cirrhotic patients who underwent combination treatment of pegylated-interferon (PEG-IFN)/ribavirin, from January 2005 to December 2011, were enrolled in this retrospective study. All the patients were examined with abdominal ultrasonography and liver biochemistry at baseline, the end of treatment, and every 3–6 months post-treatment. The frequency of surveillance endoscopies in cirrhotic patients was according to the EV guideline of AASLD. Results: The mean age of 98 cirrhotic patients without baseline esophageal varices was 58.0 ± 10.5 years. The average following-up time of each patient was 4.43 years (standard deviation: 1.74 years, range: 1.13 – 9.27 years). Fifty-seven patients (58.2 %) achieved a SVR. Nineteen patients (9.2%) were diagnosed with EV post-treatment. The adjusted hazard ratios (HR) of the occurrence of EV in patients without SVR and alcohol related were 10.3 (95% confidence interval [CI]: 1.10 – 94.9, \( P = 0.041 \)) and 11.5 (95% CI: 1.49 – 88.71, \( P = 0.019 \)), respectively. The cumulative incidence of EV was significantly higher in patients without SVR (5-year cumulative incidence: 22.4%, 95% CI: 4.9–40.0%) compared to the patients with SVR (5-year cumulative incidence: 3.9%, 95% CI: 0–9%). Conclusions: In cirrhotic HCV-infected patients, SVR is the major predictor in EV development, whereas alcoholism might be a potent predictor of EV progression among these patients.

**# 1429 Baseline factors associated with increased sustained virologic response rates in 123 treatment-naive chronic hepatitis C virus genotype 1 patients treated with a shortened 12-week simprevir plus pegylated interferon and ribavirin regimen: A multivariate analysis**

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**Introduction:** A Phase 3, open-label study of SMV (150 mg q.i.d) + PR was conducted in Europe, in 163 treatment-naive chronic HCV genotype 1 patients with mild-to-moderate fibrosis (F0–F2, Metavir score) to investigate safety and efficacy of a 12-week SMV + PR regimen. This pre-planned, multivariate analysis aimed to determine factors associated with SVR12, and identify patients who may benefit from a shortened treatment regimen. Methods: Patients with HCV RNA < 25 IU/mL (detectable/undetectable [using Roche COBAS® TaqMan® assay, LLOQ: 25 IU/mL, LLOD: 15 IU/mL]) at Week 2, and < 25 IU/mL undetectable at Week 4 and 8, were eligible for the 12-week regimen and were included in the univariate/multivariate analyses to determine factors influencing either SVR or relapse. Results: Overall, 75% (123/163) of patients were eligible for 12 weeks of therapy. Of these, 65% (80/123) achieved SVR12; 39 relapsed and 4 did not have SVR12 data. SVR12 rates varied according to baseline and on-treatment factors including IL-28B genotype (CC: 94% [30/32]; CT: 53% [39/73]; TT: 61% [11/18], respectively). Univariate/multivariate analyses of baseline factors associated with SVR12 and/or relapse are shown in Table 1. The observed safety profile of SMV + PR was consistent with previous studies. Conclusions: Early on-treatment response patients with IL-28B CC genotype, mild fibrosis (F0–F1), and lower baseline HCV RNA levels are more likely to achieve high SVR12 rates with a 12-week SMV + PR regimen. In the non-CC patient population, mild fibrosis and lower baseline HCV RNA levels were associated with SVR on this shortened regimen.
Table 1  Factors associated with SVR and viral relapse determined by univariate and multivariate analyses in patients eligible for 12 weeks of therapy

| Baseline factor  | Univariate analysis | Final multivariate analysis |
|------------------|---------------------|----------------------------|
|                  | N       | Odds ratio (95% CI) | P-value | Odds ratio (95% CI) | P-value |
| Baseline viral load(Log10 HCV RNA IU/mL) | 123 | 0.53 (0.29,0.95) | 0.0339 | 0.24 (0.10,0.57) | 0.0012 |
| IL-28B genotype CC | 123 | 12.3 (2.77,54.5) | 0.0010 | 31.1 (5.77,168) | < 0.0001 |
| Metavir fibrosis score F0-F1 | 122 | 4.45 (1.85,10.7) | 0.0009 | 6.96 (2.25,21.5) | 0.0007 |
| Baseline viral load(Log10 HCV RNA IU/mL) | 91 | 0.19 (0.08,0.46) | 0.0002 | 0.17 (0.06,0.43) | 0.0002 |
| Metavir fibrosis score F0-F1 | 91 | 6.37 (2.09,19.4) | 0.0011 | 8.02 (2.23,28.8) | 0.0014 |
| Relapse, all patients | | | | |
| Baseline viral load(Log10 HCV RNA IU/mL) | 122 | 2.30 (1.21,4.38) | 0.0109 | 6.73 (2.50,18.1) | 0.0002 |
| IL-28B genotype CC | 122 | 0.04 (0.01,0.34) | 0.0027 | 0.01 (0.00,0.12) | 0.0001 |
| Metavir fibrosis score F0-F1 | 121 | 0.22 (0.09,0.54) | 0.0008 | 0.12 (0.03,0.40) | 0.0007 |
| Relapse, non-CC patients | | | | |
| Baseline viral load(Log10 HCV RNA IU/mL) | 90 | 5.86 (2.32,14.8) | 0.0002 | 6.70 (2.48,18.1) | 0.0002 |
| Metavir fibrosis score F0-F1 | 90 | 0.18 (0.06,0.52) | 0.0016 | 0.14 (0.04,0.49) | 0.0021 |

Week 2 viral response was associated with SVR in the univariate analysis of the full population (odds ratio 2.52 [1.13, 5.60], P = 0.0235), but not in the multivariate analysis (odds ratio 1.92 [0.70, 5.29], P = 0.2068). Similar results were found for the association of Week 2 viral response with SVR in the non-CC population and with relapse in both populations analysed. HCV genotype subtype, race, sex and baseline BMI were not associated with SVR in either the full or non-CC patient populations.

# 1432 Patient-reported outcomes in Asian patients with chronic hepatitis C treated with ledipasvir and sofosbuvir

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Background: Prevalence of chronic hepatitis C (CH-C) infection in Asian patients ranges between 1% and 20%. Treatment regimens for CH-C have a negative impact on patient-reported outcomes (PRO). Our aim was to assess the PRO impact of interferon (IFN)-free ribavirin (RBV)-free regimens in Asian CH-C patients. Methods: PRO data were collected from 12 multinational phase 3 clinical trials (2012–2015) of sofosbuvir (SOF)-based regimens. At baseline, during and post-treatment, patients completed 4 validated PRO questionnaires which were compared across treatments. Results: Out of 4485 CH-C patients with PROs, 106 were Asian (55.7% male, 69.8% treatment-naïve, 17.0% cirrhotic). Fifteen received IFN-free RBV-free LDV/SOF treatment and 90 received IFN- and/or RBV-containing SOF-based regimen. The Asian CH-C patients were younger, had lower BMI and rates of psychiatric comorbidities (anxiety, depression, sleep disorders; all P < 0.05). Also, their baseline SF-36 physical functioning scores were lower (by −5.6% on a normalized 0–100% PRO scale, P = 0.001). During treatment, Asian CH-C patients receiving IFN and/or RBV regimens experienced decreased PRO scores (up to −19.6%, P < 0.050) while those receiving LDV/SOF experienced some improvement (+9.0% in general health of SF-36, P = 0.03). After achieving sustained virologic response 12 (SVR-12), PRO scores improved regardless of treatment (up to +9.3%, P = 0.0003). In multivariate analysis, use of LDV/SOF was independently associated with higher PRO scores during and after treatment (betas +15.0% to +29.3%, P < 0.05). Predictors of PRO impairment included depression, type 2 diabetes, and cirrhosis (P < 0.05). Conclusions: The use of IFN- and RBV-free LDV/SOF regimens leads to PRO improvement in Asian patients during treatment and after achieving SVR-12.

# 1439 Three cases of the hepatitis C patients that presented hyperkalemia during daclatasvir and asunaprevir combination therapy

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Introduction: Daclatasvir (DCV) and asunaprevir (ASV) have both shown good overall safety and antiviral potency in laboratory and early human studies in the hepatitis C virus (HCV) patients, but as main side effects of its therapy there have not been the report of a renal damage and the hyperkalemia. We report three cases in which the HCV patients that...
presented hyperkalemia after DCV, ASV therapy introduction relatively early this time. **Case Report:** Case 1: A 76-year-old female with HCV genotype 1b infection cirrhosis and a null response to pegylated interferon-α and complicated with hypertension and diabetes mellitus, started DCV, ASV therapy. A slight renal function disorder and hyperkalemia (5.6 mEq/L) developed after start of therapy three weeks later. Case 2: A 69-year-old female treatment-naïve with HCV genotype 1b infection cirrhosis complicated with hypertension and diabetes mellitus, started DCV, ASV therapy. A slight renal function disorder and hyperkalemia (5.4 mEq/L) developed after start of therapy one week later. Case 3: A 73-year-old male treatment-naïve with chronic hepatitis C genotype 1b complicated with hyperkalemia (5.8 mEq/L) without a renal dysfunction from start one week later. All patients improved hyperkalemia by a potassium diet and the diuretic dosage, polytransfusion use one or two weeks later. As a main side effect of DCV, ASV therapy, ALT increase 17.6%, AST increase 14.1%, headache 12.9%, fever 11.8% are reported. All three cases were complicated with hypertension and took all causes renin angiotensin system repressor. The aldosterone-producing restraint with the adrenal gland with the RAS repressor is considered as the main reason of the hyperkalemia. DCV, ASV might reduce the potassium excretion with the kidney directly or indirectly with RAS repressor, and it is necessary to note not only the liver damage but also the hyperkalemia symptom during DCV, ASV therapy.

# 1457 Prolonged entecavir therapy improves liver fibrosis estimated by aspartate aminotransferase-to-platelet ratio index in majority of naive patients with a partial virological response

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**Background/Aims:** No data are available about the long-term changes in non-invasive tests of liver fibrosis in chronic hepatitis B (CHB) patients with detectable hepatitis B virus (HBV) DNA after 48 weeks. **Methods:** In a single center cohort study, we retrospectively investigated the long-term changes in liver fibrosis of entecavir treatment for more than 48 weeks in 284 nucleos(t)ide-naïve CHB patients, particularly those with partial virological response (PVR). Serial changes of aspartate aminotransferase to platelet ratio index (APRI) and fibrosis 4 (FIB-4) were analyzed using a linear mixed model. **Results and Discussion:** Seventy-one of 284 (25%) nucleos(t)ide-naïve patients without pretreatment cirrhosis had a detectable HBV DNA at week 48 (PVR). The mean follow-up duration after PVR was 35.0 ± 23.8 months. During prolonged entecavir therapy, 47 (66.2%) patients achieved virological response, and 5 (7.0%) developed genotypic resistance to entecavir. After excluding patients with entecavir resistance (n = 5), who switched to tenofovir due to insufficient virologic suppression (n = 4), and who had been followed up less than 1 year after PVR (n = 8), we finally analyzed non-invasive fibrosis tests of 54 patients. After considering age and gender as fixed effects, APRI values improved significantly with prolonged entecavir treatment (coefficient −0.15, P < 0.0001). The change in FIB-4 values was not significant throughout the time course of entecavir treatment (coefficient 0.003, P = 0.74). **Conclusions:** With continuous prolonged entecavir treatment, liver fibrosis estimated by APRI has been evolved in CHB patients with PVR who had not develop entecavir resistance.

# 1475 Entecavir combined short-term intravenous hepatitis B immune globulin to prevent hepatitis B recurrence after liver transplantation

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**Objective:** Combination Hepatitis B Immune Globulin (HBIG) and the nucleoside analog prophylaxis has become the standard of care for the prevention of HBV recurrence after liver transplantation for HBV-related diseases. However, HBIG is costly and inconvenient to the patients. In this prospective, randomized, single-center study, we aimed to evaluate the efficacy of a new hepatitis B prophylaxis regimen. **Methods:** A total of 46 consecutive chronic hepatitis B patients transplanted were included in this study. All patients received the long-term treatment with Entecavir. Control group (30 patients) received combination therapy with long-term low-dose intramuscular HBIG while experimental group (16 patients) received a short-term high-dose intravenous HBIG three to four times within one month after liver transplantation based on HBV DNA level. No HBIG was administered after one month of combination treatment in experimental group which received a subsequent Entecavir monotherapy. Viral load and liver function were detected at regular intervals during follow-up. The detection threshold for the HBV DNA was 100 IU/mL. Hepatitis B recurrence was defined as HBV DNA > 1000 IU/mL during follow-up beyond one month after transplant. **Results:** There were 17 cases with HBV DNA positive before liver transplantation in control group while 8 cases in experimental group. All patients were alive with a good liver function within 6–12 months in the follow-up after transplantation. There was no HBV recurrence during the follow-up time. **Conclusion:** HBIG cessation 1 month after liver transplantation with subsequent entecavir monotherapy provides an effective prophylaxis against HBV recurrence compared with long-term HBIG therapy.

# 1476 Aspartate aminotransferase-to-platelet ratio index and sustained virologic response are associated with occurrence of hepatocellular carcinoma among hepatitis C cirrhotic patients receiving pegylated interferon plus ribavirin

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**Background and Aims:** The aim of this study was to evaluate the clinically significant predictors for hepatocellular carcinoma (HCC) development among hepatitis C virus (HCV) cirrhotic patients receiving combination therapy. **Methods:** One hundred and five compensated cirrhosis patients who received pegylated interferon (peg-IFN) plus ribavirin between January 2005 and December 2011 were enrolled. All the patients were examined with abdominal sonography and liver biochemistry at baseline, the
end of treatment, and every 3–6 months post-treatment. The occurrence of HCC was evaluated every 3–6 months post-treatment. Results: A total of 105 patients were enrolled (mean age 58.3 ± 10.4 years). The average follow-up time for each patient was 4.38 y (SD 1.73 years; range 1.13–9.27 years). Fifteen (14.3%) patients developed HCC during 463 person-years of follow up. Thirteen of them had high baseline aspartate aminotransferase to platelet ratio index (APRI) (i.e., an APRI > 2.0). Multivariate analysis showed that those without sustained virologic response (SVR) (HR 5.795; 95% CI 1.370–24.5; P = 0.017) and high APRI (HR 5.548; 95% CI 1.191–25.86; P = 0.029) had a significantly higher risk of HCC occurrence. The cumulative incidence of HCC was significantly higher (P = 0.009) in patients without SVR (3-year cumulative incidence 21.4%; 95% CI 7.4–35.5%; 5-year cumulative incidence 11.2–51.1%) compared to those with SVR (3- and 5-year cumulative incidence 6.2%; 95% CI 0–1.3%). Further, the cumulative incidence of HCC was significantly higher (P = 0.006) in patients with high APRI (3-year cumulative incidence 8.2%; 95% CI 0–1.0%) compared to those with low APRI (3- and 5-year cumulative incidence 4.2%; 95% CI 0–2.2%). Conclusions: In HCV-infected cirrhotic patients who received combination therapy, APRI and SVR are two major predictors of HCC development.

# 1492 The incidence and predictors of hepatitis B surface antigen loss and hepatocellular carcinoma development after the cessation of lamivudine and entecavir treatment in chronic hepatitis B patients

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Background: It remained unclear the incidence and predictors of HBsAg loss and hepatocellular carcinoma (HCC) development after the cessation of nucleos(t)ide analogs (NA) therapy. Aims: To investigate the incidence and predictors of HBsAg loss and HCC development after stopping NA treatment in chronic hepatitis B (CHB) patients. Patients and Methods: From 2004 to 2012, 485 CHB patients (177 HBeAg-positive, 308 HBeAg-negative) (97 cirrhosis) received lamivudine (n = 198) or entecavir (n = 287) treatment and have stopped the treatment at least 12 months were recruited. All patients fulfilled the stopping criteria of the APASL 2008 or 2012. Results: In 177 HBeAg-positive patients, the cumulative rates of HBsAg loss in years 3, 5 and 8 were 5.6%, 11.7% and 19.2%, respectively, after stopping NA treatment. Cox regression analysis showed that old age, lower baseline HBV DNA and end-of-treatment qHBsAg were independent predictors for HBsAg loss. In 308 HBeAg-negative patients, the cumulative rates of HBsAg loss in years 3, 5 and 8 were 14.5%, 26.8% and 44% respectively, after stopping NA treatment. Cox regression analysis showed that HBV genotype C and lower end-of-treatment qHBsAg levels were independent predictors for HBsAg loss. For all patients, the cumulative rates of HBsAg loss in patients who had end-of-treatment qHBsAg < 100, 100–300, 300–1000, > 1000 IU/mL in year 8 were 76.8%, 58%, 25.4% and 7.2% respectively. For all patients, the cumulative rates of new HCC development in year 10 (follow-up period included re-treatment duration) in non-cirrhotic and cirrhotic patients were 2.3% and 32.5% respectively. Cox regression analysis showed that old age, cirrhosis and longer treatment duration were independent predictors for new HCC development. The end-of-treatment qHBsAg levels or HBsAg loss after stopping NA treatment was not a significant factor for HCC development. Conclusions: The end-of-treatment qHBsAg was a useful predictor for HBsAg loss after stopping lamivudine and entecavir treatment.

Keywords: hepatitis B virus, HBsAg, lamivudine, entecavir, hepatocellular carcinoma

# 1523 Frequency and severity of depression in patients taking combination interferon and ribavirin for hepatitis C treatment at a tertiary care hospital in Karachi

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Pakistan carries one of the world’s highest burdens of chronic hepatitis and mortality due to liver failure and hepatocellular carcinomas. Depression is among the most common chronic illnesses. Prevalence of depressive disorders is 34% in Pakistan. Depression is serious side effect of combination interferon and ribavirin therapy which may leads to suicide attempts, timely diagnosis and treatment can prevent this problem. This prompted me to collect data representing our patients on interferon and ribavirin, so as to give a better understanding of the problem and improve the quality of life. Design: Cross-sectional study in 245 patients attending Gastroenterology out-patient department. Patients aged > 18 years of either gender taking combination interferon and ribavirin for Hepatitis C treatment were included in this study. Patients with known psychiatric illnesses or taking antidepressant medicines were excluded from the study. Patients were asked to fill the Siddiqui Shah Depression Scale (SSDS) questionnaire, (In National Language of Pakistan). Patients were categorized as follows according to the number of points they scored in SSDS:

| Score | Description |
|-------|-------------|
| < 26  | No depression |
| ≥ 26 to 36 | Mild depression |
| ≥ 37 to 49 | Moderate depression |
| ≥ 50  | Severe depression |

Result: Gender distribution shows predominance of male 59.2%. Average age was 36.4 (±8.8) years. Out of 245 cases, depression was seen in 50 patients (20.4%). In 50 depressed patients, 58% patients had mild symptoms, 32% had moderate and 10% had severe depressive symptoms. Proportion of depression was high in females 22% as compared to 19.3% males. Depression was highest in age between 21 and 40 years; average age was 27.9 ± 9.9 years. Conclusion: Depression is a major factor leading to non-compliance with treatment. Prompt diagnosis and treatment of depression using antidepressant therapy can safely and effectively used not only to treat depression but also to keep patients compliant to antiviral treatment of chronic hepatitis C.

# 1534 Acute exacerbation of hepatitis C in hepatocellular carcinoma patients receiving chemotherapy

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Background: Acute hepatitis C exacerbations could occur in cancer patients carrying HCV when receiving systemic chemotherapy. No study has been conducted illustrating hepatitis C exacerbation in advanced HCC patients receiving systemic chemotherapy. Aim: Report and analyze clinical factors related to hepatitis C exacerbation in HCV-related advanced HCC who underwent systemic chemotherapy using 5-fluorouracil, cisplatin, and mitoxantrone (FMP) from 2008 to 2014 were retrospectively analyzed. Results: Nine patients developed acute hepatitis C exacerbations defined by HCV-RNA level increased ≥ 10-fold and alanine transaminase (ALT) level increased fivefold or more of the upper normal limit. Three patterns of clinical courses were observed including single exacerbation (n = 5), fluctuated flares (n = 3), and delayed exacerbation (n = 1). Prior to chemotherapy, patients with subsequent acute exacerbations were less likely to have ascites (11.1% vs 53.8%; P = 0.028) and harboring a lower baseline ALT (44.1 ± 28.5 U/L vs 72.6 ± 19.2 U/L; P = 0.007). Univariate analysis revealed unfavorable prognostic factors as ECOC stage > 0 (P = 0.034), presence of ascites (P = 0.002), and higher bilirubin level (P < 0.001). Interestingly, despite a high risk of hepatic failure, occurrence of hepatitis C exacerbation was associated with a favorable overall survival (P = 0.027; 22.8 vs 5.4 months). Conclusions: Patients with lower baseline ALT and/or absence of ascites had a higher risk of hepatitis C exacerbation when receiving systemic chemotherapy. The hepatitis flares could lead to liver failure but were associated with a better overall survival.

# 1548 Prevalence of hypophosphatemia in chronic hepatitis B virus infection with nucleos(t)ide analogs: A large sample cross-sectional study in China

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Introduction: Adverse effects affecting kidney consist of a decrease of glomerular filtration rate and/or a proximal renal tubular dysfunction. Confirmed hypophosphatemia is one of the indications for tubular function abnormality; however, few data are available on the prevalence of hypophosphatemia in chronic hepatitis B virus infection (CHB) with nucleos(t)ide analogs (NAs). Patients and Methods: Seven hundred and seventeen patients were undergoing NA mono-therapy (57 lamivudine, 225 adefovir, 159 telbivudine, and 276 entecavir) for more than 48 months, while 293 patients were not treated by any NAs. Hypophosphatemia was defined as serum phosphate < 0.8 mmol/L. Chi-squared test and univariate and multivariate logistic regression analyses were performed with the SPSS software. Results: Among the 1010 patients analyzed, 78% were men, the mean age was 42 ± 14 years, the average treatment time was 54 ± 19 weeks, the mean serum creatinine level was 0.94 ± 0.20 mg/dL, the estimated glomerular filtration rate (eGFR) (CKD-EPI) was 97.6 ± 17.2. Prevalence of hypophosphatemia in lamivudine, adefovir, telbivudine, entecavir, and NA-naïve patients was 3.5%, 17.8%, 2.5%, 4.3%, and 2.4% respectively. The chi-squared test showed that the difference among the hypophosphatemia rates among the five groups was statistically significant (\(\chi^2 = 62.904, P < 0.001\)). In a multivariate analysis (P; odds ratio, 95% confidence interval), the independent predictors of hypophosphatemia were adefovir use (vs NA naïve, P = 0.003, 3.972; 1.598–9.874), eGFR < 60 (vs eGFR ≥ 90, P = 0.02, 6.961, 1.357–35.705), cirrhosis (vs none, P = 0.006, 2.386, 1.280–4.448), male (vs female, P = 0.003, 23.699, 2.977–188.660), older age (P = 0.018, 1.039, 1.006–1.072), and higher aspartate aminotransferase (AST) (P = 0.045, 1.020, 1.000–1.039). Conclusion: In CHB patients, exposure to ADV, moderate decrease in eGFR, cirrhosis, older age, and higher AST are associated with an increased risk of hypophosphatemia, which might indicate tubular function abnormality. Therefore, close monitoring of tubular function parameters should be recommended to patients receiving ADV.

Keywords: adefovir, chronic HBV, hypophosphatemia, nucleos(t)ide analogs.

# 1549 Loss to follow-up of patients with chronic hepatitis B: What are the reasons?

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Background and Aim: Regular surveillance for the patients with chronic hepatitis B (CHB) is important. However, many patients are not on regular surveillance in clinical practice. This study was to understand the reasons for loss to follow-up (LTFU) from a long-term regular surveillance program in China. Materials and Methods: All the outpatients came from a long-term cohort study of CHB in south China. All are educated about the importance of regular surveillance and informed consent before being registered. Data of 487 patients LTFU from May 31, 2008, to May 31, 2014, were examined. Telephone interviews were used to understand their reasons for LTFU by a simple question—“What is the reason for not returning for scheduled surveillance in the chronic hepatitis clinic?” The study is descriptive. Results: Overall, 487/2094 (23.3%) patients were LTFU. Of the 487, 236 patients were contacted for tracing, 216 were untraceable, and 35 were dead. Of the 236, the period of loss to follow-up ranges from 1 to 5 years. Focusing on the answers, the following reasons for missed visits are given: (i) 53 cases (22.4%, 53/236) attended to other doctors or tried to have alternative treatment(s) including traditional Chinese medicine (4.7%, 11/236); (ii) 45 cases (19.1%, 45/236) felt healthy, thinking it is needless to be surveyed; (iii) 40 cases (16.9%, 40/236) had no time or experienced inconvenience in work for the regular surveillance; (iv) 33 cases (14.0%, 33/236) migrated or went on a business trip from our health center; (v) 25 cases (10.6%, 25/236) complained about the distance; (vi) 22 cases (9.3%, 22/236) misunderstood or lacked information of the treatment; and (vii) 21 cases (8.9%, 21/236) visited doctors or tried to have alternative treatment(s) including traditional Chinese medicine (4.7%, 11/236). Conclusion: LTFU patients have reasons according to poor attitude on CHB instead of social or financial reasons. This study shows the basic information for better understand the nature of CHB patient compliance to regular surveillance. Further efforts are need to improve patient compliance.

Keywords: chronic hepatitis B, compliance, lost to follow-up, outpatient.
# 1561 Hyperlactatemia/lactic acidosis caused by telbivudine during the treatment for chronic hepatitis B: Six case reports and treatment experience

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Introduction: Creatine kinase (CK) elevations is the most common side effect resulting from telbivudine, while hyperlactatemia or lactic acidosis is rare but fatal. Here, we report six cases of hyperlactatemia/lactic acidosis caused by telbivudine 600 mg/day regularly during the treatment for chronic hepatitis B (CHB). The clinical features of the six patients were summarized so as to make diagnosis and appropriate therapy for the cases.

Table 1: Characteristics and laboratory test results of patients

| Patient ID | Age (year) | Duration (month) | Lactate | BE | Bicarbonate | CK | MGB | LDH | HBV-DNA |
|------------|------------|------------------|---------|----|-------------|----|-----|-----|---------|
| 1          | 23         | 12               | 15      | 6.88 | -31.6       | 899 | 429.5 | 922 | 2.53E+03 |
| 2          | 19         | 5                | 9.5     | 7.35 | -5.5        | 2155| 137.6 | 1371| 7.47E+06 |
| 3          | 35         | 3                | 2       | 7.38 | -0.8        | 2216| 324  | 299 | 5.21E+03 |
| 4          | 33         | 7                | 6.7     | 7.35 | 2.4         | 2140| 968.1| 339 | 1.70E+05 |
| 5          | 26         | 8                | 7.3     | 7.4  | 0.5         | 1566| 296.5| 394 | 1.33E+04 |
| 6          | 33         | 9                | 8       | 7.35 | 8           | 1196| 114.5| 237 | 3.27E+06 |

# 1645 Efficacy of tenofovir disoproxil fumarate therapy after suboptimal response to entecavir in chronic hepatitis B patient—A community hospital’s experience

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Background: Entecavir is a potent drug for treating chronic hepatitis B (CHB), but some patients have suboptimal response (SOR) to entecavir. The efficacy of tenofovir disoproxil fumarate (TDF) for chronic hepatitis B patients with suboptimal response to entecavir was evaluated.

Methods: From Jul. 2011 to Dec. 2014, adult CHB patients with SOR to ETV were retrospectively included in this study. Complete virologic response was defined as an achievement of serum hepatitis B virus (HBV) DNA level < 15 IU/mL by the real-time polymerase chain reaction method during treatment (measured every 24 weeks). SOR was defined as a detectable HBV DNA≥ 15 IU/mL after more than 24 weeks of oral antiviral therapy in an adherent patient. Those patients with SOR to ETV were switched to TDF monotherapy. Safety assessment was based on the serum creatinine levels.

Results: A total of six CHB patients who experienced SOR to ETV were switched to TDF in this study. The mean age was 42.8 years (range, 31–67). Five of six patients were male. The mean duration of ETV treatment was 116 weeks (range, 60–204). The mean baseline DNA was 7.9 log_{10} IU/mL. The mean HBV DNA level at time of switching was 4.18 log_{10} IU/mL. At a median duration of 93.1 weeks of TDF treatment, 50% (3/6) of patients achieved CVR. One patient achieved CVR early at 24 weeks after TDF treatment (whose hepatitis B e antibody was positive and had lower hepatitis B surface antigen [17 IU/mL] level at baseline). Another two patients achieved complete virologic response (CVR) at 48 and 72 weeks. Three patients who did not achieve CVR had higher DNA levels at baseline (9, 6.9, and 7.6 log_{10} IU/mL). Their DNA levels at time of switching to TDF were 1.83, 2.52, and 7.79 log_{10} IU/mL, respectively. Their DNA level was suppressed significantly after TDF treatment (15 IU/mL at 96 weeks, 104 IU/mL at 72 weeks, and 147 IU/mL at 120 weeks). No patient developed renal impairment during TDF treatment.

Conclusion: Tenofovir disoproxil fumarate might be an effective and safe rescue therapy in CHB patients with SOR to ETV therapy. Further study is necessary to elucidate this conclusion.
# 1647 Low frequency of drug-resistant virus did not affect the therapeutic efficacy in daclatasvir plus asunaprevir therapy in patients with chronic hepatitis C virus genotype 1

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**Background:** The efficacy of a direct-acting antiviral agent is compromised by the development of drug resistance. The associations between resistance-associated virus (RAV) and therapeutic outcomes have not been well understood. **Patients and Methods:** Thirty patients with hepatitis C virus (HCV) genotype 1b were enrolled and treated for 24 weeks with asunaprevir (ASV) and daclatasvir (DCV). Viral sequences in non-structural (NS) regions 3 and 5A in serum and liver tissue before treatment were examined with direct sequencing, next-generation sequencing, and the polymerase chain reaction (PCR)-invader method to evaluate the importance of drug resistance in the prediction of the outcomes of ASV plus DCV therapy. **Results:** Of 30 patients (17 naive patients, 5 interferon-intolerant patients, and 8 non-responders), 25 patients (83.3%) achieved sustained virological response (SVR) 24 weeks after the treatment. Viral breakthrough occurred in three naive patients and one non-responder. One naive patient experienced viral relapse. Among 25 patients without RAV, 24 obtained SVR, whereas 5 patients had RAV with a 1.3–88% frequency, resulting in various therapeutic outcomes. For HCV compartments, similar RAVs were detected in serum and liver tissue for a patient obtaining SVR despite HCV NS5A Y93H, and another developed viral breakthrough although no RAV was detected. Direct sequencing could not detect RAVs in low frequency (1.3–12%) for three of four patients. **Conclusions:** Low frequency of RAVs might not affect the outcomes of ASV plus DCV therapy. Deep sequencing and PCR-invader methods can detect clinically significant RAVs for ASV plus DCV therapy.

# 1651 Telaprevir-based and simeprevir-based interferon triple therapy for patients with hepatitis C

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**Background/Aims:** Since 2011, combinations of non-structural 3/4 protease inhibitors, telaprevir or simeprevir, with ribavirin and peginterferon have been available in Japan as standard of care for patients with hepatitis C virus genotype 1. We aimed to compare clinical and adverse effects of these inhibitors-based therapies. **Methods:** Fifty-four patients were treated with 2250 or 1500 mg/day of telaprevir (T-group) and 31 with 100 mg/day of simeprevir (S-group), with combinations of ribavirin and peginterferon-α-2a or peginterferon-α-2b for 24 weeks. Protease inhibitors were given for the initial 12 weeks. Doses of these drugs were modified by attending physicians. Clinical and laboratory data were monitored throughput and at 6 months after the treatment. **Results:** Mean age was 3.1 years old, and liver fibrosis was advanced in the S-group than in the T-group. Seven patients from the T-group and two from the S-group withdrew from the protocol because of adverse events. Forty-three of T-group (79.6%) and 24 of S-group patients (77.4%) achieved sustained virologic response (SVR). Two of four patients in the T-group and one of five in the S-group who were non-SVR had viral breakthrough. Adverse events such as skin rash, appetite loss, and nausea were more severe in the T-group than in the S-group. Elevations in serum creatinine and uric acid were seen in the T-group, and the rise in serum bilirubin and alkaline phosphatase was seen only in the S-group, which all returned to normal after stopping protease inhibitors. **Conclusion:** Telaprevir-based and simeprevir-based triple therapy had comparably high SVR rates when the treatment was completed. But severe adverse events limited the effect of treatment in telaprevir-based therapy.

# 1654 Comparison of continuing or modification telbivudine treatment on estimated glomerular filtration rate in patients with chronic hepatitis B—4-year real-world study

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**Background:** Telbivudine therapy resulted in improved estimated glomerular filtration rate (eGFR), while other nucleos(t)ide analogs (NUCs) were associated with decreased or stationary eGFR. We do not know the outcome of eGFR in patients with a modification during the telbivudine treatment. **Aims:** The aim of this real-world observation is to compare continuing or modification treatment of telbivudine on eGFR at the fourth year. **Methods:** The treatment was according to the Taiwan National Health Insurance clinical practice. Renal functions (eGFR) were recorded at the beginning, treatment modification, and the fourth year on Modification of Diet on Renal Disease calculation. Fifteen patients continued the medication at year 4 without evidence of resistance, while 19 patients were added on or shifted to other NUCs when resistance appeared. **Results:** At the end of the fourth year, the rates of renal function improved (>10% increasing eGFR) and were higher at 73.4% in the combined group than at 31.6% in the modification group (P = 0.016). Among the patients who received telbivudine without evidence of resistance, eGFR improved in the checking point and at the fourth year. If there was a treatment modification with adding on or switching from telbivudine, eGFR did not change significantly in the checking point and the fourth year. Detailed data were listed in Table 1. **Conclusions:** There was no eGFR improvement at the checking point due to resistance existence; the eGFR improvement may relate to treatment and virologic response. When the resistance was overcome by adding on or switching from telbivudine, the eGFR cannot maintain the improvement and even declines.
Table 1 Comparison of continuing or modification treatment of telbivudine treatment on estimated glomerular filtration rate

|                  | Continue (n = 15) | Modification (n = 19) | P value |
|------------------|-------------------|----------------------|---------|
| Age (mean)       | 45.7              | 45.5                 | 0.952   |
| Age (> 50 years) (%) | 40%              | 45%                  |         |
| Male (%)         | 12                | 8                    | 0.901   |
| Hepatitis B e antigen (+) (%) | 4%              | 10%                  | 0.127   |
| Favor baseline DNA level | 14            | 93.3%                | 0.613   |
| (3-year) improvement | 7              | 46.7%                | 0.968   |
| (4-year) improving | 11              | 73.3%                | 0.016   |
| (3-to 4-year) improvement | 6              | 40%                  | 0.1     |

# 1665 Risk of hepatocellular carcinoma and mortality among treated patients with chronic hepatitis B versus chronic hepatitis C

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**Background:** Limited data are available on whether the effect of antiviral treatment differs on the risk of hepatocellular carcinoma (HCC) and mortality between patients with chronic hepatitis B (CHB) and those with chronic hepatitis C (CHC). Methods: We compared CHB patients treated with entecavir between 2007 and 2011 (n = 2000) and CHC patients treated with peg-interferon and ribavirin between 2004 and 2011 (n = 733). Virologic response (VR) was defined as HBV DNA < 15 IU/mL at 1 year of treatment for CHB or the achievement of sustained VR for CHC. Data were collected for up to 6 years and analyzed by multivariable Cox proportional hazards model. Results: Virologic response was achieved in 1520 (76.0%) and 475 (64.8%) patients in CHB and CHC cohorts, respectively. During the follow-up period, 203 (7.4%) patients developed HCC, and 118 (4.5%) died or received a liver transplant. Multivariable analyses showed that CHB patients were associated with a significantly higher risk of HCC than CHC patients (hazard ratio [HR], 1.62; P = 0.02), but with a similar risk of death or transplantation (HR, 0.77; P = 0.31). Among patients with VR, CHB patients were again associated with a higher risk of HCC (HR, 2.62; P = 0.003) and a similar risk of death or transplantation (HR, 0.91; P = 0.81). However, among patients without VR, there were no differences between the two groups in terms of HCC and death or transplantation. Conclusions: Chronic hepatitis B patients with VR were associated with a similar risk of death or transplantation, but a higher risk of HCC compared with CHC patients with sustained VR.

# 1735 Interleukin-28B polymorphism and ITPA gene variations in hepatitis C genotype 1 patients treated with pegylated interferon and ribavirin

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**Background:** A retrospective review of data suggests there was a 73.0% sustained viral response (SVR) rate among our patients with chronic hepatitis C with genotype 1 infection (CHC-GT1) treated with dual therapy (DT) using pegylated-interferon and ribavirin. It is known that IL-28B polymorphism can predict response to treatment, with CC genotype associated with favorable response, and ITPA gene deficiency protecting against ribavirin-associated hemolysis that sometimes necessitates the decrease in ribavirin dosage, which affects SVR. We aim to determine the gene frequency in our treated CHC-GT1 population and correlate it with their treatment outcome. Methods: All CHC-GT1 patients who were treated with DT over the past 10 years were identified by available medical records and approached by letter of invitation for blood sampling for IL-28B and ITPA genotyping. Medical records were reviewed to verify previous treatment course and response, including anemia development and erythropoietin use. Results: Forty-two patients (83.3% males) were recruited. Mean age was 45 ± 12.9 years at time of treatment. Thirty-three (78.6%) had IL-28B (rs12979860) CC genotype, of which 25 (75.8%) obtained SVR. Only 3/9 (33.3%) patients with IL-28B (rs12979860) CT genotype achieved SVR. There were 3.0%/24.2%/72.7% of patients with AA/AC/CC ITPA (rs1127354) genotype, respectively. Of those with ITPA (rs1127354) AA/AC/CC, 0.0%/45.5%/30.0% had anaemia, respectively, requiring dose attenuation of ribavirin and/or erythropoietin. Of those with IL-28B (rs12979860) CC, 77.8% of patients with ITPA (rs1127354) AA and AC had SVR compared to 67.7% with ITPA (rs1127354) CC. Conclusion: This study suggests IL-28B and ITPA genotyping can better inform our CHC-GT1 patients for decision making for treatment. This is relevant in our population that has a relatively high prevalence of IL-28B CC genotype when access to newer therapeutic options remains a challenge.

# 1755 The efficacy and the adverse effect in the early stage of daclatasvir and asunaprevir combination therapy for chronic hepatitis C virus genotype 1b infection in Miyazaki, Japan

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**Purpose:** It is reported that the daclatasvir and asunaprevir combination therapy is able to get a highly therapeutic effect beyond the combination therapy with protease inhibitor, peginterferon-α, and ribavirin in patients with genotype 1b hepatitis C virus. In this study, we aimed to clarify the antiviral effect and adverse event in the early stage of daclatasvir and asunaprevir combination therapy. **Method:** A total of 146 patients were enrolled at five centers in Miyazaki Prefecture, Japan, from September 2014 to March 2015. Antiviral effects including rapid virological response
Introduction: Dengue is one disease entity with different clinical presentations and often with unpredictable clinical evolution and outcome. It is the most frequent arbovirus disease in the world and the most important one in terms of morbidity and mortality. With rising disease burden, atypical manifestations have increased as well, which are missed most often due to lack of awareness. We present one atypical dengue infection with severe hepatis, acalculous cholecystitis, and normal platelet count.

Case Report: A 19-year-old Bangladeshi student without any past history was admitted to ward due to fever, nausea, vomiting, jaundice, and epigastralgia for 1 week. He denied any drug or alcohol history. Generally, he is jaundiced and lethargic. His blood test results were as follows: aspartate aminotransferase (AST) 2502 U/L, alanine aminotransferase (ALT) 2331 U/L, total bilirubin (Bil[T]) 242.6 μmol/L, direct bilirubin (Bil[D]) 216.4 μmol/L, alkaline phosphatase 195 U/L, albumin 38 g/L, international normalized ratio (INR) 1.89, prothrombin time (PT) 20.3 s, activated partial thromboplastin time (APTT) 33 s, platelet 181 000 μL, hepatitis marker hepatitis B surface antigen (–), hepatitis C virus antibody (–), hepatitis A virus antibody (–), and leptospirosis IgM (–). Abdomen ultrasound was done with acalculous cholecystitis and bilateral pleural effusion. During hospitalization, blood investigation of ANA, C-ANCA, and P-ANCA, anti-mitochondrial antibodies, anti-HIV, and blood film for malarial antigen showed negative results. On day 3 of admission, dengue blood tests were taken: dengue NS-1 Ag (–), dengue IgM (+), and dengue IgG (–). Adequate intravenous normal saline hydration fluid replacement and prophylactic antibiotics were given. The patient was hospitalized for 13 days and discharged. One week later, he was followed up in a clinic, and his blood test results were as follows: AST 57 U/L, ALT 138 U/L, Bil(T) 45.7 μmol/L, Bil(D) 35.8 μmol/L, INR 1.23, PT 14.7 s, APTT 31 s, platelet 452 000 μL. This patient had recovered uneventfully with great improvement.

Discussion: The most common dengue fever symptoms are fever, myalgia, headache, rash, arthralgia, and epigastralgia. Rare manifestations are severe hepatitis, hepatic failure, dengue encephalitis, renal failure, and acalculous cholecystitis. The exact pathogenesis of dengue hepatitis is unknown. It could be either virus direct cytotoxicity to hepatocytes or its immune-mediated injury leading to stimulating apoptosis and microvesicular steatosis and to severe dengue hepatitis. The elevation in the level of AST enzyme is normally greater than the elevation in the level of ALT in dengue patients during the first week of infection, and this is an uncommon phenomenon in patients with hepatitis A, B, or C. Dengue-related acalculous cholecystitis resolves spontaneously with supportive care in majority of cases.

Conclusion: Clinical doctors should be alert to detect and manage the atypical manifestations of dengue fever. Clinical vigilance about these presentations is vital for dengue early treatment.

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# 1782 Review on the use of pegylated interferon-α and ribavirin for treatment of chronic hepatitis C in Hong Kong
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Background/Aims: Despite the advent of direct-acting antivirals (DAAs) in chronic hepatitis C virus (HCV) infection, combination therapy using pegylated interferon-α and ribavirin (PR) is still the current standard of care in Hong Kong. Our aim is to investigate its use in Hong Kong. Methods: A total of 723 anti-HCV-positive patients who attended the outpatient clinic of the Department of Medicine, Queen Elizabeth Hospital, from January 2002 to March 2014 were reviewed for their characteristics and reasons for declining treatment. A total of 143 patients received combination therapy. Their characteristics, response to treatment, and side effects of treatment were retrospectively analyzed. Results: A total of 143 patients (99 male and 44 female) with a median age of 50 received PR-based combination therapy. Treatment uptake rate was 19.8%. Genotypes 1 and 6 were the commonest. Intravenous drug abuse was the commonest mode of acquisition of HCV (54.9%). The overall sustained virologic response (SVR) rate was 72.7%. Genotype 6 infection performed significantly better than genotype 1 infection (89.3% vs 62.5%; P=0.008). Multivariate analysis identified non-genotype 1 infection, low baseline HCV RNA level, those without prior history of combination therapy, and those who completed ≥80% of treatment as predictors of SVR. Side effects occurred in 88.1%. Thirty-two patients (22.4%) terminated treatment early due to side effects. Conclusion: The treatment of chronic hepatitis C infection using standard PR-based combination therapy was quite successful with an SVR rate of 72.7%. Further studies concerning use of DAAs and their cost-effectiveness will be needed to provide an insight for the best medical care for treating hepatitis C in Hong Kong.
Introduction: In Taiwan, injecting drug use has been the main route of transmission of the human immunodeficiency virus (HIV) since 2005, and hepatitis B virus (HBV), hepatitis D virus (HDV), and HIV have similar transmission routes. This has become an important public health issue. The aim of this study is to explore the conditions of HDV infections between injecting drug users (IDUs) with and without HIV infection in Southern Taiwan. Materials and Methods: In this study, we enrolled 87 IDUs, including 27 anti-HDV seronegative IDUs and 60 anti-HDV seropositive IDUs and also analyzed the results of liver function tests, CD4 cell counts, anti-HIV, and HIV RNA. Result: The prevalence of anti-HDV seropositivity among hepatitis B surface antigen (HBsAg)-seropositive IDUs was 68.97% (60/87) in this study, and the prevalence of anti-HDV seropositivity was 84.21% among HBsAg-seropositive IDUs with HIV infection and 40.0% among IDUs without HIV infection. Anti-HIV seropositivity was related to anti-HDV seropositivity (odds ratio = 9.34, 95% confidence interval = 2.67–31.59, P < 0.001). No significant difference between CD4 cell count, HIV RNA viral load, and anti-HDV was noted in this study. Conclusions: The prevalence of HDV infection among IDUs is higher than that in non-IDUs, and due to anti-HDV seropositivity being significantly related to anti-HIV seropositivity, HDV infection among IDUs is still important. We suggest that for IDUs, HBsAg and anti-HDV should be monitored closely. Keywords: hepatitis B virus, hepatitis D virus, human immunodeficiency virus, injecting drug users, Taiwan.
# 1868 Clinical, biochemical, and virological differentiation in acute hepatitis B and chronic hepatitis B with acute exacerbation

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**Background and Aims:** Many areas of the world including Korea, China, and Taiwan are known as endemic areas for hepatitis B virus infection. In these countries, it is difficult to distinguish acute hepatitis B (AHB) from chronic hepatitis B with acute exacerbation (CHB-AE) due to their similar serological profiles and clinical features. Distinction between AHB and CHB-AE is clinically important to decide the initiation of antiviral therapy. The aim of this study was to investigate clinical, biochemical, and virological differentiation in patients with AHB and CHB-AE. **Methods:** A total of 59 patients with immunoglobulin M antibody to hepatitis B core antigen seropositivity from January 2005 to December 2014 were enrolled. The subjects were divided into the AHB group (n=40) and the CHB-AE group (n=19) according to previous history of hepatitis B infection or results of radiologic examination through a review of their medical records. Clinical, biochemical, and virological features were analyzed and compared between both groups retrospectively. **Results:** The presence of jaundice and hepatitis B envelope antibody (HBeAb) seropositivity in the AHB group were significantly higher than that in the CHB-AE group (72.5% vs 42.1%; P=0.042; and 60.0% vs 26.3%; P=0.002, respectively). Levels of serum HBV DNA significantly differed between the AHB group and the CHB-AE group (4.9 vs 6.7 log_{10} IU/mL; P=0.000). In addition, levels of serum α-fetoprotein significantly differed in the two groups (5.5 vs 135.5 ng/mL; P=0.001). However, no significant difference in seropositivity rates of hepatitis B surface antigen and hepatitis B envelope antigen was observed between both groups (90.0% vs 100%; P=0.294; and 55.0% vs 78.9%; P=0.133, respectively). In addition, levels of hepatitis B surface antigen (ratio of the optical density of the sample to the cut-off value < 20) were not significantly different from the AHB group and CHB-AE group (2041.2 vs 2078.6; P=0.756). **Conclusions:** This study showed that the presence of jaundice and HBeAb seropositivity as well as the levels of serum HBV DNA and α-fetoprotein might be used to distinguish between patients with AHB and patients with CHB-AE.

# 1869 Boceprevir-based triple therapy to rescue hepatitis C virus genotype 1/hepatitis B virus dually infected patients refractory to peginterferon-plus-ribavirin combination therapy in Taiwan

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**Introduction:** Recent study showed that the risk of hepatocellular carcinoma incidence is even higher among hepatitis B virus (HBV)/hepatitis C virus (HCV)-co-infected persons than those with HBV or HCV mono-infection. Previous studies showed that the peg-interferon (IFN)/ribavirin (RBV) has been effective in the treatment of HCV-dominant, treatment-naive patients with HCV/HBV dual infections. The aim of this study is to explore the safety and efficacy of boceprevir-based triple therapy to rescue HCV genotype 1/HBV dually infected Taiwanese patients refractory to peg-IFN-plus-RBV combination therapy. **Materials and Methods:** We enrolled 12 eligible patients who agreed to join this clinical trial from Kaohsiung Medical University Hospital and National Taiwan University Hospital from March 2014 to December 2014. These 12 patients were classified according to whether patients suffered from liver cirrhosis and the response of previous peg-INF/RBV therapy (relapser, partial responder, and null responder). **Result:** Seven relapsers and five null responders were among these 12 subjects. Eight male and 10 HCV genotype 1b subjects were enrolled in this study. No event of death happened in this study, and two SEA were noted. Anemia (1/6), but no neutropenia and thrombocytopenia, was also noted. Until now, one of three relapers reaches the sustained virological response 12, and the percentage of undetectable HCV RNA was more than 70% during the period of therapy regimen. **Conclusions:** Even though this study is in progress, we think that from the preliminary data, boceprevir-based triple therapy to rescue HCV genotype 1/HBV dually Infected patients refractory to peg-IFN-plus-RBV combination therapy is effective and under consideration. **Keywords:** boceprevir, hepatitis B virus, hepatitis C virus, Taiwan.

# 1918 Clinical usefulness of measurement of neutrophil-to-lymphocyte ratio

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**Objective:** This study aims to investigate the association between neutrophil-to-lymphocyte ratio (NLR) values and different disease states in hepatitis B virus-infected patients. **Methods:** A total of 67 patients with chronic hepatitis B (CHB), 40 patients with chronic severe hepatitis B (CSHB), and 45 normal healthy persons (control group) were enrolled into this study. NLR, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TBIL), direct bilirubin (DBIL), and prothrombin time activity (PTA) were detected. **Results:** The levels of NLR in the CHB, CSHB, and control groups were 1.930 ± 1.09, 4.313 ± 2.62, and 1.523 ± 0.524, respectively. NLR values in patients with CSHB were significantly higher than those in healthy controls; statistical difference was found (all P < 0.001). Moreover, NLR values of CSHB patients were higher than those of CHB, and the NLR level was negatively associated with PTA. Increased NLR values were clinically associated with severe liver disease. The results are illustrated in Table 1. **Conclusion:** Neutrophil-to-lymphocyte ratio values are increased in CHB and CSHB patients, which are associated with its severity. **Keywords:** hepatitis B, neutrophil to lymphocyte ratio.
# 1943 Change of insulin resistance in hepatitis C virus-infected patients receiving pegylated interferon plus ribavirin

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**Background:** Hepatitis C virus (HCV) infection can lead to increased insulin resistance, but the dynamics of insulin resistance in HCV-infected patients receiving pegylated interferon plus ribavirin remain elusive.

**Methods:** The prospective study enrolled HCV-infected patients who received pegylated interferon plus ribavirin. Patients were classified according to the attainment of sustained virological response (SVR). The insulin resistance was measured by homeostatic model assessment insulin resistance (HOMA-IR). The change of HOMA-IR at baseline, the end of treatment, and 24 weeks after the end of treatment was compared in patients who achieved SVR and those who did not. **Result:** A total of 65 patients participated in this study, of which 46 (71%) achieved SVR. Overall, the HOMA-IR changed significantly during antiviral therapy. However, only patients who achieved SVR had significant off-therapy reduction of HOMA-IR. In those without SVR, the HOMA-IR measured 24 weeks after treatment completion did not differ from baseline values. The results were illustrated in Tables 2 and 3. **Discussion:** This study, which was conducted in an ethnic Chinese population, corroborates the causative role of HCV in impairing glucose homeostasis and implicates the clinical effectiveness of viral eradication. Remission of insulin resistance may derive from improvement of liver fibrosis after viral clearance. There are limitations about sample size and standardized therapeutic duration. **Conclusion:** Dual therapy with pegylated interferon plus ribavirin ameliorated insulin resistance in HCV-infected patients, but the off-therapy improvement of insulin resistance was limited to those who attained SVR.

**# 1932 Long-term efficacy of peginterferon/ribavirin with and without lamivudine therapy for hepatitis B e antigen-positive hepatitis B and C dual infection**

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**Background:** The optimal therapeutic strategy for hepatitis B virus (HBV) e antigen (HBeAg)-seropositive and hepatitis C virus (HCV) dually infected patients remains unknown. We aimed to elucidate the effectiveness of peginterferon (peg-IFN)/ribavirin (RBV) with and without lamivudine (LAM) combination therapy in clinical settings.

**Patients and Methods:** Nine patients seropositive for HBV surface antigen, HBeAg, antibodies to HCV, and HCV RNA for >6 months were treated with peg-IFN/RBV with (n = 5) and without (n = 4) a 12-month LAM add-on therapy at treatment week 12. The treatment duration of peg-IFN/RBV was 24 weeks (HCV genotype 1 [HCV-1] with rapid virological response [RVR] or HCV-2) or 48 weeks (HCV-1 without RVR). Primary end-points included HBeAg loss and HBV DNA (male/female) and HBeAg seroconversion, developed HBeAg seroreversion at 15 months.

**Discussion:** For HBeAg-positive HBV/HCV dually infected patients, peg-IFN/RBV was effective for HCV eradication. Add-on LAM therapy might promote HBeAg loss in clinical settings.

**Keywords:** dual infection, HBeAg positive, hepatitis B, hepatitis C, lamivudine.

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### Table 1 Clinical characteristics of studied subjects

|                  | Healthy controls (n = 45) | CHB (n = 67) | CSHB (n = 40) |
|------------------|--------------------------|-------------|--------------|
| Age (year)       | 38 ± 10                  | 33 ± 10     | 43 ± 13      |
| Gender (male/female) | 35/10                   | 55/12       | 36/4         |
| NLR              | 1.523 ± 0.524            | 1.930 ± 1.09*| 4.313 ± 2.62***|
| AST (U/L)        | 21.36 ± 5.42             | 243.9 ± 280.4***| 525.2 ± 587.9***|
| ALT (U/L)        | 23.82 ± 13.21            | 403.3 ± 393.70***| 808.4 ± 831.30***|
| TBIL (μmol/L)    | 11.91 ± 3.67             | 22.69 ± 15.95***| 240.9 ± 113.50***|
| DBIL (μmol/L)    | 3.39 ± 1.36              | 10.69 ± 10.98***| 144.5 ± 64.50***|
| PTA (%)          | 88.91 ± 13.65            | 27.85 ± 7.88 |

Data are expressed as mean ± standard deviation.

*P < 0.05, **P < 0.001 compared with healthy controls.

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### Table 2 Change of HOMA-IR during the antiviral treatment among study participants

|                  | Baseline | End of therapy | 24 weeks off therapy |
|------------------|----------|----------------|---------------------|
| Overall          | 3.7 (1.6–10.0) | 1.5 (0.8–2.9) | <0.0001 | 1.6 (0.9–3.1) | 0.0001 |
| SVR              | 3.6 (1.5–9.9) | 1.4 (0.6–2.7) | 0.001  | 1.3 (0.7–2.6) | <0.0001 |
| No SVR           | 3.9 (2.2–10.0) | 2.1 (0.8–4.8) | 0.002  | 2.2 (1.9–4.7) | 0.46  |

†Values calculated by the Wilcoxon matched-pairs signed-rank test, with the baseline measurement as the reference for comparison.

HOMA-IR, homeostatic model assessment insulin resistance; SVR, sustained virologic response.
Table 3  Change of BMI during the antiviral treatment among study participants

|                | Baseline | End of therapy | 24 weeks off therapy | \( p^* \) |
|----------------|----------|----------------|---------------------|-----------|
| Overall        | 25.1     | 23.2           | > 0.0001            | 24.6      | 0.01      |
| (n = 65)       | (23.5–26.3) | (21.3–25.1)     | (22.7–26.7)         |           |
| SVR            | 24.4     | 22.9           | > 0.0001            | 24.3      | 0.1       |
| (n = 46)       | (22.7–25.8) | (21.2–24.8)     | (22.6–25.6)         |           |
| No SVR         | 26.0     | 24.3           | 0.0001              | 25.9      | 0.03      |
| (n = 19)       | (24.6–28.9) | (22.5–26.6)     | (22.7–29.4)         |           |

\( P \)-values calculated by the Wilcoxon matched-pairs signed-rank test; with the baseline measurement as the reference for comparison.

BMI, body mass index; SVR, sustained virologic response.

# 1947 Hepatitis B surface antigen carriage among Filipino preschool children in Lapu-Lapu City, Cebu

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Introduction: Hepatitis B infection is a major public health problem in the Philippines. Although hepatitis B virus (HBV) vaccination has been started in our country for more than two decades, there are no published data regarding the hepatitis B surface antigen (HBsAg) prevalence and immunity level among children. Materials and Methods: We tested for HBsAg on serum samples from children aged 4–6 years. HBsAg-negative samples were tested for total hepatitis B core antibody (anti-HBc). All HBsAg-negative and anti-HBc-negative samples were tested for hepatitis B surface antibody (anti-HBs). Results were compared with data from a study conducted in 1991. Results: A total of 454 randomly selected children were tested. HBsAg prevalence was 0.22% (1/454) among the total population and 0.3% (1/365) among the fully immunized children. Four (1.1%) were reactive to total anti-HBc, indicative of post hepatitis B infection. There was a statistically significant decrease in HBV infection from 131/532 (24.6%) to 1/454 (0.22%), \( P \)-value 0.0001, when the current study was compared to the 1991 study. Detectable anti-HBs of 176/365 (48%) showed a decrease in the seropositivity when compared to 182/214 (85%) in 1991, \( P \)-value 0.0001. Conclusion: Hepatitis B virus vaccination resulted in a significant decrease in HBsAg prevalence. A significant portion of fully immunized children had no protective anti-HBs but were not infected either.

Keywords: Asia, children, HBsAg, prevalence, the Philippines

# 1965 Clinical chronic hepatitis C: peginterferon I ± 2a/ribavirin/simeprevir combined therapy: Device of individual medical treatment for elderly patients, including interferon I2 for carcinogenic prevention

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Aim: Despite the high sustained virologic response (SVR) rate in interferon (IFN)-free therapy, IFN was also used by priority for carcinogenic prevention. PegIFN-α/REB/simeprevir with an excellent therapeutic effect is employed as the main treatment for elderly patients, because the side effects are equivalent to those of pegIFN-α/REB. IFN-β preceding prescription is also considered as an independent medical treatment. We investigated the safety and efficacy of these treatments. Background and Method: Between April 2007 and January 2015, 195 patients were introduced to peg-IFN-α. Twenty-one underwent peg-IFN-α/REB/simeprevir (≥ 60 years old: 13), and 51 underwent peg-IFN-α2a/REB (≥ 60 years old: 30, ≥ 59 years old: 21); we compared each groups. Among peg-IFN-α2a, Gr1, and IFN-β preceding prescription, 47 (60.3 years old, M:F = 21:26) and 44 patients without IFN-β (55.8, 23:21) are also compared. Side effects like fatigue, alopecia, appetite loss, and depression were scored (0–3). Result: Peg-IFN-α/REB/simeprevir (58.8, 10:11) had HCV-RNA 6.0 log IU/mL and alanine aminotransferase (ALT) 57.3 IU/L. The virus-negative rate was 21.4% (2 weeks), 60.0 (4 weeks), 78.9 (8 weeks), 88.9 (12 weeks), and 91.7 (end treatment response [ETR]), and the SVR12 was 83.3% (5/6). Peg-IFN-α2a/REB (≤ 59/≥ 60 years old) showed pretreatment HCV-RNA (6.2/6.0), ALT (63/49), and SVR (47/64/3.3). Side Effects: The scores of fatigue (simeprevir: 1.14/α2a: 29.5/α2a: 60.0 old; 0.7/α2a: 60.0 old), appetite loss (0.8/0.6/0.8/0.7), alopecia (0.48/0.5/0.7/0.7), and depression (0.29/0.4/0.4) were shown. Others are itching (61.2%/22.2%/75.9%), eruption (61.2/25.0/56.6%), fatigue (22.6/25.1/26.6), and SVR (23.5–25.1) can be also introduced to individual treatment including IFN-β.

# 1966 HIV/hepatitis B virus co-infection: Are there any magic bullets?

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Background: Co-infection with the human immunodeficiency virus (HIV) can affect the progression of hepatitis B (HBV) infection. The condition is associated with complex viral–host interaction and enhanced viral replication. Case Description (Methods and Results): A 54-year-old man acquired HIV infection 17 years ago. He was given combivir and a protease inhibitor. He achieved satisfactory HIV viral load suppression with lamivudine-containing antiretroviral therapy (ART). HBV co-infection was diagnosed 10 years later. The addition of adefovir demonstrated slow HBV viral load reduction (4 log) with virological breakthrough 15 months later. HBV viral resistance testing showed rtL80V, rtL180M, and rtM204I/V mutations. In concordance with more recent HIV therapeutic recommendations, the regimen was changed to Truvada-containing ART. There was again HBV virological breakthrough 42 months post therapy. A similar partial viral suppression was noted with the addition of entecavir (ETV). Pegylated interferon would be the sole remaining therapeutic option. Discussion: Compliance may not be the issue as HIV remained well suppressed, prompting a search for alternative reasons for virological breakthrough. Kiriños et al. reported tenofovir monotherapy should be effective for at least 6 years without significant mutation selection. This regimen is also reported to be the best combination for patients with lamivudine-resistant hepatitis B. ETV resistance requires at least three mutations: rtL180M + rtM204F and either rtT184S or
rtS202I/G or rtM250V. This patient has only the rtL180M + rtM204V mutation. Emtricitabine is also reported to have anti-HBV properties but only in the absence of M184V HIV mutation. The “recalcitrant” HBV in this case study suggests the possibility of other undiscovered pathways.

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# 1991 Applying non-invasive assessment of liver fibrosis in chronic hepatitis B patients with equivocal indication for antiviral therapy

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Objective: This study aims to evaluate whether blood-based biomarkers and acoustic radiation force impulse (ARFI) could spare liver biopsy to guide treatment in chronic hepatitis B (CHB) patients with equivocal indication for antiviral therapy. Study Design: This is a cross-sectional analysis of prospective biochemical, sonographical, and histological data. Methods: This study enrolled 101 CHB patients with viral DNA > 2000 IU/mL, but alanine aminotransferase (ALT) was mildly elevated between onefold and twofold above the upper normal limit (Table 1). Those with cirrhosis, hepatic decompensation, and malignant disease were excluded. All participants underwent liver biopsy and ARFI. The performance of ARFI, aspartate aminotransferase (AST) to platelet ratio index (APRI), and fibrosis-4 (FIB-4) score to identify patients with significant liver fibrosis was analyzed. Results: Liver fibrosis was Metavir F0 in 2 (2.0%), F1 in 43 (42.6%), F2 in 34 (33.7%), F3 in 16 (15.8%), and F4 in 6 (5.9%) patients. The stage was correlated with ARFI (ρ, 0.38; P = 0.0001) (Fig. 1), APRI (ρ, 0.25; P = 0.012), and FIB-4 (ρ, 0.28; P = 0.004). The C statistics of ARFI, APRI, and FIB-4 for fibrosis stage ≥ 2 were 0.70 (95% confidence interval [CI], 0.59–0.80) (Fig. 2), 0.62 (95% CI, 0.51–0.73) (Fig. 3), and 0.64 (0.53–0.75) (Fig. 4), respectively. Cut-off values for 95% sensitivity and 95% specificity to predict significant liver fibrosis were 0.97 and 1.36 m/s for ARFI, 0.36 and 1.0 for APRI, 0.63 and 2.22 for FIB-4, respectively. A combination of these cut-off points could spare a total of 44 patients (43.6%) from liver biopsy. Conclusions: A combination of ARFI, APRI, and FIB-4 can spare liver biopsy in approximately 40% of non-cirrhotic CHB patients with equivocal indication for antiviral treatment.

Table 1  Characteristics of participants

| Characteristics | All (n = 101) |
|----------------|-------------|
| Age (years)    | 45.7 ± 9.6  |
| Male gender, n (%) | 80 (79.2%) |
| Positive hepatitis B e antigen, n (%) | 22 (21.8%) |
| HBV DNA (log IU/mL) | 5.5 ± 1.5 |
| AST (IU/L) | 40.2 ± 12.1 |
| ALT (IU/L) | 53.2 ± 11.6 |
| α-Fetoprotein (ng/mL) | 4.1 ± 3.2 |
| Creatinine | 1.1 ± 0.16 |
| APRI | 0.57 ± 0.25 |
| FIB-4 | 1.41 ± 0.82 |
| ARFI | 1.2 ± 0.25 |

Figure 1 Correlation of ARFI with fibrosis.

Figure 2 ARFI to predict significant fibrosis.

Figure 3 APRI to predict significant fibrosis.
Clinical characteristics of chronic hepatitis C in elderly patients

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Background/Aims: Data considering chronic hepatitis in elderly patients are scarce. Therefore, the present study aimed to elucidate clinical characteristics of the elderly patients with chronic hepatitis C.

Methods: A total of 1388 patients with chronic hepatitis C from January 2004 to December 2014 were reviewed retrospectively. Among the enrolled patients, 668 (48.1%) patients were over 65 years old.

Results: The distribution of genotypes was as follows: 1.8% of genotype 1a; 39.3% of genotype 1b, 3.1% of genotype 1c, 0.6% of genotype single 1, 2.4% of genotype 2a, 38.1% of genotype 2a/2c, 11.3% of genotype single 2, 0% of genotype 3, 1.2% of genotype 4, 0% of genotype 6, and 2.4% of non-applicable. Liver cirrhosis, decompensation, and hepatocellular carcinoma all occurred more frequently in the elderly compared to the non-elderly patients (26.5% vs 17.2%/14.8% vs 6.0%/6.8% vs 3.4%, P < 0.001). Fifty (7.5%) elderly patients received antiviral treatment with pegylated interferon and ribavirin compared to 257 (35.7%) non-elderly patients (P < 0.001). The proportion of treatment discontinuation was 18.0% (9/50) in the elderly versus 19.1% (49/256) in the non-elderly (P = 1.000). The sustained virologic response (SVR) rate of treated patients was 52.0% (26/50) in the elderly versus 64.6% (166/257) in the non-elderly (P = 0.294).

Discussion: Treatment attempt was lower in the elderly patients compared to the non-elderly patients. However, treatment discontinuation rate, cytopenia, and the SVR rate were similar between the elderly and non-elderly patients.

Cohort effect on seroprevalence of hepatitis B virus and hepatitis C virus in Taiwan

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Background: The seroprevalence of hepatitis B surface antigen (HBsAg) and antibody for hepatitis C virus (anti-HCV) varied among different age groups. The lower seroprevalence of HBsAg in the aged group might be due to spontaneous seroclearance in the nature of course of hepatitis B virus infection. In addition to spontaneous seroclearance, we hypothesized that cohort effect might influence the seroprevalence of HBsAg.

Materials and Methods: The study cohort was composed of 403,811 subjects who were ≥20 years old and received our outreach screening programs in the period of 1996–2013. Blood samples were obtained from subjects and sent for aspartate aminotransferase, alanine aminotransferase, HBsAg, anti-HCV, and α-fetoprotein tests. Results: In the age group 20–29, the HBsAg-positive rate was 24.1% in birth_cohort 1960–1969, while it was 16.8% in birth_cohort 1970–1983. In the age group of 60–69, the anti-HCV-positive rate was 7.9% in birth_cohort 1920–1929 and 8.1% in birth_cohort 1930–1939, while it was 5.9% in birth_cohort 1940–1949. For both HBsAg and anti-HCV, there were trends that seroprevalence decreased in the younger cohort (Fig. 1). Multiple logistic regression showed that male gender, younger age, and earlier birth year were associated with positive HBsAg. Older age and earlier birth year were associated with positive anti-HCV.

Conclusions: The prevalence of HBsAg and anti-HCV was influenced by birth cohort effect.
**# 2022 Serum beta-2 microglobulin level: A possible marker for disease progression in Egyptian patients with chronic hepatitis C virus-related liver diseases**

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**Methods:** This is an analytical cross-sectional study including 92 subjects divided into four equal groups: group 1, chronic HCV; group 2, HCV cirrhosis; group 3, HCC on top of HCV; group 4, healthy controls. History taking, clinical examination, routine labs, and abdominal ultrasound were done to all patients. Polymerase chain reaction (PCR) and Metavir score of the liver were analyzed. Serum HBV DNA was measured by COBAS AMPLICOR HBV monitor (limit: < 20 IU/mL) and HBsAg by Roche Elecsys® II kit (limit: < 0.05 IU/mL). The 1-year rate of clinical relapse (hepatitis B virus [HBV]-DNA > 2000 IU/mL plus alanine aminotransferase [ALT] > 2× upper limit of normal [ULN]) after cessation of entecavir (ETV) therapy by the Asian Pacific Association for the Study of the Liver (APASL) stopping rule (treatment > 2 years, HBV DNA undetectable > 1 year) in hepatitis B e antigen (HBeAg)-negative chronic hepatitis B patients was 45%, of which 25.6% occurred within 6 months. **Aim:** This study aims to investigate events after cessation of tenovir (TDF) therapy. **Patients and methods:** Thirty-four HBeAg (−) patients who stopped TDF therapy by the APASL stopping rule were followed up every 1–3 months for > 6 months. Baseline age, gender, cirrhosis, ALT, genotype, hepatitis B surface antigen (HBsAg) and HBV DNA levels, duration of therapy, and consolidation therapy were analyzed. Serum HBV DNA was measured by COBAS AMPLICOR HBV monitor (limit: < 20 IU/mL) and HBsAg by Roche Elecsys® II kit (limit: < 0.05 IU/mL). **Results:** Of these 34 patients, mean age was 51.8 year, 82.4% were male, and 14 (41.2%) were cirrhotic. The 1-year cumulative clinical relapse rate was 46%, of which 93.3% occurred within 6 months and 13.3% developed decompensation. The features are compared with reported data off-ETV therapy (Table 1). Cox regression analyses revealed that end-of-treatment HBsAg level ≥ 300 IU/mL (odds ratio [OR]: 4.62, 95% confidence interval [CI]: 1.087–19.678, P = 0.038) and cirrhotic patients (OR: 4.553, 95% CI: 1.478–14.023, P = 0.008) are independent factors for clinical relapse. **Conclusion:** Clinical relapse occurred much earlier and tended to be more severe after cessation of TDF than ETV. Close monitoring during the first 6 months, especially monthly in the first 4 months, is mandatory after cessation of TDF treatment.

**Keywords:** APASL guideline, ETV, HBeAg negative, stopping treatment, TDF.
# 2065 Regional differences of hepatitis C virus genotype and clinical characteristics of chronic hepatitis C in Jeollanam-do province

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**Background/Aims:** The prevalence of hepatitis C virus (HCV) infection in Korea has a characteristic geographic variation. According to the National Health Insurance database, Jeollanam-do showed the second highest age-adjusted prevalence ratio, 1.48. However, data about HCV genotypes distribution in Jeollanam-do are scarce. Therefore, the present study aimed at determining HCV genotypes distribution among 1388 HCV RNA-positive individuals from Jeollanam-do province. **Methods:** In total, 1388 patients who were positive for HCV RNA were analyzed from January 2004 to December 2012. **Results:** Out of the 1388 HCV RNA-positive patients, 794 (57.2%) were male and 594 (42.8%) were female. The distribution of genotypes was as follows: 3.6% genotype 1a, 43.4% genotype 1b, 1.3% genotype 1c, 0.9% genotype single 1, 4.9% genotype 2a, 33.5% genotype 2a/2c, 8.8% genotype single 2, 0.5% genotype 3, 0.5% genotype 4, 0.9% genotype 6, and 1.6% others. Antiviral treatment was received by 307 (22.1%) patients. The sustained virologic response (SVR) of enrolled patients was 62.5%. The SVR rate was 48.9% for genotype 1, 75% for genotype 2, and 57.1% for others. **Discussion:** The most common HCV genotype in Jeollanam-do is type 1b. Regional difference in genotypes was observed in Jeollanam-do province. This study may facilitate treatment options and preventive strategies in Jeollanam-do province.

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# 2071 ROG, GATA3, and T-bet mRNA levels in peripheral blood mononuclear cells in patients with chronic hepatitis B

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**Aims:** The purpose of this study was to investigate the role of ROG, GATA3, and T-bet in the progression of chronic hepatitis B (CHB). **Methods:** We determined the mRNA levels of ROG, GATA3, and T-bet in peripheral blood mononuclear cells (PBMCs) from 135 patients with CHB (mild group 45; moderate group 42; serious group 48) and 15 healthy controls (control group) by real-time quantitative PCR. Statistic analysis was performed with the SPSS 16.0. **Results:** The levels of T-bet of CHB patients were higher than those of healthy controls (P < 0.05). The differences between each of the two hepatitis groups was also statistically significant (P < 0.05). ROG levels of serious patients were higher than those of healthy controls, the mild group, and the moderate group (P < 0.05); but there was no difference between these three groups (P > 0.05). The expression of GATA3 in the moderate group and serious group was higher than that in healthy controls and the mild group (P < 0.05). The value of T-bet/GATA3 in three CHB groups was higher than that in the control group (P < 0.05); but the differences between each of the two hepatitis groups were not found (P > 0.05). ROG levels were not correlated with the value of T-bet/GATA3 in CHB groups. **Conclusions:** The levels of ROG, GATA3, and T-bet in PBMCs in CHB patients were obviously upregulated, which might be involved in the progression of chronic hepatitis B. ROG plays an important role of correcting and maintaining the new balance of Th1/Th2. **Keywords:** chronic, GATA3, hepatitis B, ROG, T-bet, transcription factor.

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**Table 1**

| Time to relapse | ALT (N < 36 U/L) × ULN | Total bilirubin > 2 (mg/dL) | Decompensation |
|----------------|------------------------|-----------------------------|-----------------|
|                | Median (range, days)   | 5–10 | 10–20 | > 20 |                |                  |
| TDF (N = 34)   | 12                     | 72 (41–183) | 53.3% | 93.3% | 416.5 (123–1800) | 25% | 41.7% | 25% | 3 (20%) | 2 (9.1%) |
| ETV (N = 96)   | 43                     | 230 (79–368) | 2.3% | 26.6% | 376 (76–1338) | 21.4% | 40.5% | 16.7% | 3 (5%) | 1 (2.3%) |

**P value**

|                  | 0.000 | 0.00 | 0.00 | 0.308 | 0.736 | 0.076 | 0.053 |

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# 2074 ROG, GATA3, and T-bet mRNA levels in peripheral blood mononuclear cells in patients with hepatitis B-induced acute-on-chronic liver failure

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**Aims:** The purpose of this study was to investigate the role of ROG, GATA3, and T-bet in the progression of hepatitis B-induced acute-on-chronic liver failure (HBV-ACLF). **Methods:** We determined the mRNA levels of ROG, GATA3, and T-bet in peripheral blood mononuclear cells (PBMCs) from 45 patients with HBV-ACLF (HBV-ACLF group) and 15 healthy controls (control group) by real-time quantitative polymerase chain reaction. Statistic analysis was performed with the SPSS 16.0. **Results:** The levels of ROG of HBV-ACLF patients and healthy controls were 0.98 ± 0.27 and 0.64 ± 0.19 (P < 0.05), respectively; GATA3 levels of HBV-ACLF patients and healthy controls were 0.73 ± 0.15 and 0.58 ± 0.22 (P < 0.05), respectively; and the levels of T-bet of HBV-ACLF patients and healthy controls were 0.78 ± 0.29 and 0.46 ± 0.17 (P < 0.05), respectively. Compared with healthy controls, HBV-ACLF patients had higher ratios of ROG/GATA3 and T-bet/GATA3 (P < 0.05). Furthermore, the levels of ROG negatively correlated with GATA3 in patients with HBV-ACLF. However, ROG levels were not correlated with the value of T-bet/GATA3 in the HBV-ACLF group. **Conclusions:** The levels of ROG, GATA3, and T-bet in PBMCs in patients with HBV-ACLF were obviously upregulated, which might be involved in the progression of HBV-ACLF. **Keywords:** GATA3, liver failure, ROG, T-bet, transcription factor.
# 2103 Improved screening rate of viral hepatitis B in cancer patients via hospital-based screening reminder system: A single-center experience

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**Introduction:** Reactivation of hepatitis B virus (HBV) infection in immunosuppressed cancer patients undergoing cytotoxic chemotherapy is a serious clinical problem. It may cause interruption of chemotherapy and lead to liver death or death. Screening for HBV surface antigen (HBsAg) and antiviral prophylaxis are recommended for HBsAg-positive cancer patients receiving cytotoxic chemotherapy. The aim of this study is to evaluate the screening rate of HBV infection before systemic chemotherapy after the use of a hospital-based screening reminder system. **Methods:** Between September 2012 and November 2014, a total of 311 female patients with breast cancer in Chang Gung Memorial Hospital at Linkou, Taiwan, were enrolled in this study. These patients were assessed before receiving systemic chemotherapy and divided into three stages. The first stage (N=93) before May 2013 was no reminder or alert system before chemotherapy. The second stage (N=118) between June 2013 and February 2014 was an optional alert system for reminding physicians to check HBsAg. The third stage (N=100) after March 2014 was a compulsory alert system for the request of a serological profile including HBsAg, hepatitis B core antibody (anti-HBc), and hepatitis B surface antibody (anti-HBs). The screening rate of HBV serological markers was assessed according to the three stages mentioned previously. **Results:** Using implementation of this compulsory reminder system, an overall screening rate of HBsAg is 89% (89/100) as shown in Table 1. The use of the reminder system before chemotherapy had increased the screening rate from less than 70% to 89% for HBsAg and from 0% to 84% for anti-HBc. **Conclusions:** This study demonstrates the feasibility of implementing a reminder system to increase the screening rate of HBV infection. The system allows physicians to identify patients at a higher risk for HBV reactivation and to provide prophylactic measures according to current guidelines. The rate of antiviral prophylaxis and HBV reactivation will be evaluated in further study.

| Table 1 | Screening rate of HBV in three stages |
|---------|-------------------------------------|
|         | Screening HBsAg, anti-HBc, and anti-HBs, N (%) |
|         | No screening, HBsAg, anti-HBc, and anti-HBs, N (%) |
|         | N (%) | N (%) | N (%) |
| First stage | 28 (30.1%) | 65 (69.9%) | 0 (0%) | 2 (2.2%) |
| (09/2012–05/2013) |         |         |         |         |
| Second stage | 21 (17.8%) | 97 (82.2%) | 38 (32.2%) | 18 (15.3%) |
| (06/2013–02/2014) |         |         |         |         |
| Third stage | 11 (11%) | 89 (89%) | 84 (84%) | 76 (76%) |
| (03/2014–11/2014) |         |         |         |         |

# 2125 Role of interleukin-28B genetic variants in hepatitis C virus-related liver disease severity in patients with different viral genotypes

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**Background:** The role of host interleukin-28B (IL-28B) in liver disease severity in patients of chronic hepatitis C (CHC) is conflicting. Its impact on Asian patients with different viral genotypes remains elusive. **Aims:** This study aims to elucidate the effect of IL-28B genetic variants in a large Asian cohort with different viral genotypes. **Methods:** A total of 1288 biopsy-proven CHC patients were enrolled for testing the association of liver fibrosis and IL-28B rs8099917 genotype. **Results:** Hepatitis C virus (HCV) genotype 1 (HCV-1) infection accounted for 59.4% of the patients, and the remaining 518 patients (40.6%) were with non-HCV-1 infection (the majority were with HCV-2 infection). Of the 1084 patients with IL-28 genotype available, 928 (85.6 %) patients were with TT genotype. Univariate analysis revealed that patients with advanced liver fibrosis (F3–F4) were older, had lower platelet counts, had higher α-fetoprotein and alanine aminotransferase levels, had higher proportion of diabetes, rs8099917 non-TT genotype carriage, aspartate aminotransferase-to-platelet ratio index, and FIB-4 level. Logistic regression analysis revealed that factors associated with advanced liver fibrosis included age (odds ratio [OR]/95% confidence intervals: 1.023/1.009–1.037, P = 0.001), diabetes (OR/95% confidence intervals: 1.736/1.187–2.539, P = 0.004), α-fetoprotein (OR/95% confidence intervals: 1.007/1.002–1.012, P = 0.009), platelet count (OR/95% confidence intervals: 0.991/0.988–0.993, P < 0.001), and rs8099917 non-TT genotype carriage (OR/95% confidence intervals: 0.585/0.400–0.856, P = 0.006), while patients were divided based on their viral genotype. Factors independently associated with advanced liver fibrosis in patients with HCV-1 infection included diabetes (OR/95% confidence intervals: 2.379/1.452–3.896, P = 0.001), α-fetoprotein (OR/95% confidence intervals: 0.995/0.986–0.994, P < 0.001), platelet count (OR/95% confidence intervals: 0.529/0.328–0.854, P = 0.009). On the other hand, factors independently associated with advanced liver fibrosis in patients with non-HCV-1 infection included age (OR/95% confidence intervals: 1.039/1.016–1.063, P = 0.001) and platelet count (OR/95% confidence intervals: 0.990/0.986–0.995, P < 0.001). **Conclusions:** An unfavorable IL-28B genotype was associated with advanced liver disease. The genetic effect was restricted to patients with HCV-1 infection.
Distinct viral evolution and quasispecies dynamics between hepatitis B e antigen seroconverters and non-seroconverters in response to interferon-based therapy

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**Background/Aims:** Hepatitis B e antigen (HBeAg) seroconversion is the therapeutic goal in HBeAg-positive chronic hepatitis B (CHB) patients receiving interferon (IFN) treatment, but the underlying viral evolution and quasispecies dynamics across the entire genome and their impact on clinical outcomes are not fully clear. **Methods:** With the polymerase chain reaction amplicon-based deep-sequencing strategy, we performed nearly whole-genome deep sequencing for serial samples (four time points) of 30 HBeAg-positive CHB patients receiving IFN treatment. All samples were barcoded and pooled for sequencing in two runs. **Results:** The viral genetic diversity of the entire HBV genome, particularly in non-overlapping regions, increased along with time and was larger in patients undergoing HBeAg seroconversion (Fig. 1). Interestingly, patients who underwent HBeAg seroconversion but remained highly viremic exhibited low viral genetic diversity. Furthermore, the genetic diversity was negatively correlated with levels of HBV viral load \(r = -0.608, P < 0.001\) and HBeAg \(r = -0.709, P < 0.001\). Additionally, the viral evolution rate of HBeAg seroconverters with low viremia was faster than that in patients without HBeAg seroconversion. The number of nucleotides with a significant frequency change, defined as greater than 50%, was more in patients with HBeAg seroconversion. We also identified certain amino acid changes that were associated with HBeAg seroconversion. Finally, the network analysis of HBV evolution revealed distinct evolution patterns between HBeAg seroconverters and non-seroconverters. **Conclusion:** Deep sequencing identifies characteristic viral evolution patterns of IFN-induced HBeAg seroconversion and may provide mechanistic insight and novel biomarkers for IFN treatment response in HBeAg-positive CHB patients.

# 2152 Incidence of resistance-associated variant and early viral dynamics in patients of chronic hepatitis C treated with daclatasvir and asunaprevir: A preliminary report from a single site of Taiwan

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**Background/Aim:** The all-oral, ribavirin-free, direct-acting antiviral regimens are the current trend of therapy in patients with chronic hepatitis C virus (HCV) infection. The fixed-dose combination of daclatasvir (a pan-genotypic NS5A inhibitor) and asunaprevir (an NS3 protease inhibitor) achieves excellent sustained virologic response in the clinical trials. This study is to investigate the incidence of resistance-associated variant (RAV) and the efficacy of this regimen in the real world. **Methods:** There were 34 patients of chronic hepatitis C (CHC), genotype 1b, who received an RAV test. Among those with no RAV, 18 patients received a 24-week, twice-daily, fixed-dose combination of daclatasvir (30 mg) and asunaprevir (200 mg) and had been treated for greater than 4 weeks. Treatment was discontinued in cases of virologic breakthrough, defined as a confirmed increase in HCV-RNA of 1 log10 IU/mL or greater from nadir or confirmed increase in HCV-RNA to greater than or equal to the assay lower limit of quantitation (LLOQ: 15 IU/mL) after a previous decline to less than the LLOQ. The presence of cirrhosis was established by a liver biopsy or a FibroScan value greater than 12.6 kPa within 1 year. HCV-RNA was quantified using the Roche HCV COBAS TaqMan Test v2.0 (LLOQ 15 IU/mL; limit of detection, 10 IU/mL). Genotype and subtype were determined by the VERSANT HCV genotype 2.0 line probe assay. Resistance testing was performed by population-based sequencing (sensitivity, 25%) of NS3, NS5A, and NS5B at baseline and on samples with HCV-RNA of 1000 IU/mL or greater. Statistics were assessed by SPSS, version 16.0. **Results:** The 34 patients were 62.6 ± 9.8 years old and included 15 males (44.1%), 26 experienced (66.5%), and 24 cirrhotics (70.6%). Six (17.6%) of them had RAV. Those with RAV were older (median: 75.4 vs 60.0 years, \(P = 0.002\)), were experienced (100% vs 71.4%, \(P = 0.297\)), and had greater amount of HCV-RNA (median of log10 7.21 vs 6.18, \(P = 0.003\)). Age was the only associated factor of RAV by multivariate logistic regression \(P = 0.013\). Among the 28 patients with no RAV, 18 patients had received the combination therapy for longer than 4 weeks. They were 61.9 ± 7.6 years old, and 9 (50%) were male. Thirteen (72.2%) were treatment experienced, and 13 (72.2%) were cirrhotics and had a log10 increase in HCV-RNA to greater than or equal to the assay lower limit of quantitation (LLOQ: 15 IU/mL) after a previous decline to less than the LLOQ.
Clinical characteristics of studied subjects

| Health status       | n = 45     | n = 67     | n = 30     |
|---------------------|------------|------------|------------|
| Age (year)          | 38 ± 10    | 33 ± 9     | 41 ± 12    |
| Gender (male/female)| 35/10      | 36/6       | 30/12      |
| NLR                 | 1.523 ± 0.525 | 1.882 ± 1.189 | 4.884 ± 2.918 |
| INR                 | 1.095 ± 0.1392 | 2.775 ± 0.6898 |
| MELD score          | 7.184 ± 3.798  | 28.74 ± 5.689    | 92.47 ± 63.94 |
| TBIL (μmol/L)       | 14.80 ± 6.087  | 44.21 ± 40.678   | 428.3 ± 140.0 |
| Creatinine (μmol/L) | 72.58 ± 15.62  | 68.56 ± 15.37   | 92.47 ± 63.94 |

Data are expressed as mean ± standard deviation.

**P<0.001 compared with healthy controls; **P<0.001 compared with CHB.

# 2157 Clinical usefulness of measurement of neutrophil-to-lymphocyte ratio in hepatitis B virus-related acute-on-chronic liver failure

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Background: Neutrophil-to-lymphocyte ratio (NLR) values, a marker of subclinical inflammation that is largely overlooked, are a newly recognized risk marker in patients with tumor, but its role in hepatitis B virus (HBV)-related acute-on-chronic liver failure (ACLF) has not been explored. The present study was designed to investigate whether the NLR values can provide diagnostic information in HBV-related ACLF.

Methodology/Principal Findings: One hundred and thirty-eight patients, including 63 with chronic hepatitis B (CHB), 30 with ACLF, and 45 healthy controls were enrolled. A blood sample from individual patients was collected at admission to examine liver function, international normalized ratio, and renal function. NLR values at admission in patients with ACLF (4.884 ± 2.918, P < 0.001) were significantly higher than those in healthy controls (1.523 ± 0.524).

Conclusion: Neutrophil-to-lymphocyte ratio values are significantly increased in ACLF patients. In patients with hepatitis B, NLR values have a relationship with Model for End-stage Liver Disease (MELD) scores (r = 0.6859, P < 0.001).

Keywords: ACLF, neutrophil-to-lymphocyte ratio.

# 2161 Hepatitis B surface antigen level as a predictor of liver fibrosis in hepatitis B e antigen-positive patients with chronic hepatitis B virus infection

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Background and Aims: Preliminary data suggest lower serum hepatitis B surface antigen (HBsAg) level is associated with more severe liver fibrosis in hepatitis e surface antigen (HBeAg)-positive patients. We evaluated the association of HBsAg level with biochemical, virological, and histological features in asymptomatic patients with chronic hepatitis B virus (HBV) infection. Methods: Hepatitis B surface antigen levels were measured at baseline in 481 asymptomatic, treatment-naïve patients with chronic HBV infection. Subjects were followed up prospectively (median, 12; range, 8–36 months). Phases of HBV infection were defined after regular monitoring of HBV-DNA and transaminases. Liver histology was scored using the Metavir system. Results: Hepatitis B e antigen-positive (n, 126) patients were significantly younger than HBeAg-negative patients (n, 355), median age 26 versus 30 years, P < 0.01. HBV genotype could be determined in 350 patients, 240 (68.57%) had genotype D, and 100 (28.57%) had genotype A. HBsAg level had modest correlation with serum HBV DNA (r = 0.6 vs 0.4 in those who are HBeAg positive and negative, respectively). HBeAg-positive patients with fibrosis score ≥ F2 showed significantly lower median serum HBsAg levels and serum HBV DNA levels compared with patients with F0–F1 scores (median, range; 4.51, 2.99–6.10 vs 5.06, 4.13–5.89, P < 0.01, and 8.39, 3.85–10.60, P < 0.01, respectively). Significant inverse correlation of HBsAg levels was found with liver fibrosis in the HBeAg-positive group (r = −0.76; P < 0.001). HBsAg level cut-off value of 4.7 log10 IU/mL predicted moderate to advance fibrosis (≥ F2) with 92% sensitivity, 85% specificity, and 91% negative predictive value. Conclusion: Lower HBsAg levels might reflect the status of advanced liver fibrosis in HBeAg-positive chronic hepatitis B subjects.

Keywords: chronic HBV infection, chronic hepatitis B, HBsAg quantification, hepatic fibrosis, liver fibrosis.
**# 1049 Incidence of drug-induced liver injury among government tertiary hospital patients on anti-Koch treatment**

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**Introduction:** Tuberculosis (TB) remains a major global health problem. Anti-TB drugs have proven effective against TB; however, they can induce various adverse events, of which hepatotoxicity is the most serious. Anti-TB drug-induced liver injury (ATLI) is emerging as a significant threat to TB control, though limited data are available at present. This study aims to estimate the incidence of ATLI and understand its clinical features.

**Methodology:** This was a single-center, prospective study which consisted of a cohort of TB patients who received directly observed treatment, short course, at East Avenue Medical Center from December 2013 to May 2014. Only 285 patients who were at least 18 years of age were included. Clinical and laboratory features of ATLI were monitored for the treatment duration.

**Results:** We monitored 240 TB patients; 52 were dropped from the study, while 188 continued. Nine patients developed ATLI with a cumulative incidence of 4.8% (95% confidence interval, 2.4–7.19%). Nausea and abdominal pain were the most frequently observed signs and symptoms. Three (33.33%) ATLI patients had severe hepatotoxicity, seven (77.7%) recovered, one (11.11%) failed to respond to treatment with continued elevation of aminotransferases, and one (11.11%) died as a result of ATLI.

**Conclusion:** For this cohort, ATLI incidence was higher compared to data from China and Canada, comparable with Hong Kong and Singapore, but lower than Taiwan. The presence of comorbidities showed a trend of increasing ATLI; however, further analysis only showed those with liver and biliary diseases to be statistically significant. A larger cohort of patients is suggested.

**Keywords:** antituberculosis-induced liver Injury, drug-induced liver injury, tuberculosis.

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**# 1056 Intrahepatic cholestasis in hyperthyroidism**

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**Introduction:** The relation of jaundice to hyperthyroidism can be presented in three clinical possibilities: hyperthyroidism is the underlying cause of jaundice, a chronic liver disease patient liver function deteriorates with deep jaundice, and a hyperthyroidism patient develops jaundice. The mechanism underlying jaundice observed in hyperthyroidism is not clear, but different functional and histological hepatic changes have been reported in patients with hyperthyroidism. Liver function test abnormalities in hyperthyroidism can be mainly divided into two types; hepatocellular pattern and intrahepatic cholestasis pattern. High levels of thyroxine hormones, the hypermetabolic state, thyroid hormones’ direct toxic effect on hepatic tissue, and hyperthyroidism medication can cause jaundice in hyperthyroidism patients. **Case Description:** A 25-year-old female with uncontrolled hyperthyroidism who had intrahepatic cholestasis was examined. Further examinations did not find chronic or acute viral...
hepatitis, hepatic congestion, hepatic injury, hepatotoxic side effects of anti-thyroid medications propylthiouracil (PTU) as a cause for her intrahepatic cholestasis. After PTU medications, her condition improved, total, direct, and indirect bilirubin of 25.20, 20.10, and 5.10 mg/dL decreased to 13.63, 10.39, and 3.24 mg/dL, respectively.

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Regelmann MO, Miloh T, Arnon R, Morotti R, Kerkar N, Rapaport R. Graves' disease presenting with severe cholestasis. Thyroid. 2012; 22(4): 437–9.

# 1103 Cytoprotective effect of hyaluronic acid-modified sphingosine-1-phosphate on experimental hepatic ischemia–reperfusion injury
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Background/Aims: Liver sinusoidal endothelial cells (LSECs) play an important role in hepatic ischemia–reperfusion (I/R) injury. We report that sphingosine-1-phosphate (S1P) has an anti-apoptotic effect on LSECs. It is difficult to target single-agent S1P to LSECs because S1P receptors are widely expressed in many organs. We developed a formulation of direct combination of hyaluronic acid (HA) and S1P (HA-S1P), and we investigated whether HA-S1P has cytoprotective effects in hepatic I/R injury.

Methods: Sprague-Dawley rats were divided into four groups as follows: control, HA, S1P, and HA-S1P groups. After the administration of each agent via the tail vein, rat livers were subjected to 20 min of total ischemia followed by 2 h of reperfusion. After reperfusion, the following investigations were performed: alanine aminotransferase (ALT), histological findings, TUNEL staining, and transmission electron microscopy, as well as the expression of proteins associated with apoptosis, hepatoprotection, and S1P accumulation. Results and Discussion: Sphingosine-1-phosphate accumulated more in the liver of the HA-S1P group than in the S1P group. Serum ALT levels, TUNEL-positive hepatocytes, and expression of cleaved caspase-3 were significantly decreased in the HA-S1P group. In transmission electron microscopy, the sinusoidal endothelial lining was preserved in the HA-S1P group. Moreover, HA-S1P increased the protein levels of heme oxygenase-1 more than in the S1P group. Conclusion: In this study, it was suggested that HA-S1P exhibits cytoprotective effects in the liver through the inhibition of LSEC apoptosis. These data indicate that HA-S1P can be an effective agent for hepatic I/R injury.

# 1264 Missed opportunities in the diagnosis and treatment of non-alcoholic fatty liver disease
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Background: In Singapore, with rising obesity, non-alcoholic fatty liver disease (NAFLD) will become the leading cause of chronic liver disease. However, NAFLD remains underdiagnosed, and controversies on the best way of diagnosis exist. This study aims to examine such missed opportunities (defined as subjects with reported NAFLD but not clinically diagnosed/intervened or NAFLD cases not picked up on radiology) and identify independent predictive factors for NAFLD.

Methodology: In this...
cross-sectional study, 1000 consecutive subjects appointed at the University Digestive Centre of a Singapore tertiary medical center in 2011 were included (Fig. 1). To identify NAFLD intervention, 238 eligible subjects were reviewed for liver function test performed within 3 months of their liver imaging. Two designated radiologists also reviewed the images to ascertain the presence of NAFLD against standardized, validated criteria. Discrepancies in NAFLD identification between the original and reviewed reports were identified. Independent predictive factors for NAFLD were determined using multiple logistic regression. Results: Of the subjects with NAFLD (original report), 35.3% (n = 41) had no intervention within 3 months. Among the scans reviewed, 11.3% (n = 26) were found to be negative for NAFLD on the original report but positive on review. Significant independent predictive factors of NAFLD are diabetes mellitus (P = 0.046, odds ratio [OR] = 2.416, 95% confidence interval [CI] = 1.017–5.741), and aspartate aminotransferase > 30 U/L (P = 0.047, OR = 2.087, 95% CI = 1.009–4.317). Conclusion: Missed opportunities for early intervention are significant among study subjects. A common criterion is useful in standardizing radiological NAFLD identification. Multivariate analysis allows NAFLD to be predicted by combining various risk factors.

Figure 1
*Electronic medical records.
**NAFLD group (NAFLD on original and/or reviewed radiological report).
***Control group (no NAFLD on original and reviewed radiological reports).

Keywords: diagnosis, imaging, missed opportunities, non-alcoholic fatty liver disease (NAFLD), risk factors of NAFLD.
# 1293 Diagnosis and management of peritoneal chylous leakage after liver transplantation

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**Objective:** Peritoneal chylous leakage after liver transplantation (LT) is an uncommon complication, and the optimal treatment remains unclear. The aim of this study was to investigate the diagnosis and management of peritoneal chylous leakage after LT in our liver transplant institute. **Methods:** Between June 2012 and April 2014, 241 patients received LT at our institution. The clinical data of the patients with peritoneal chylous leakage were collected and analyzed retrospectively. The diagnosis of chylous leakage is based on the presence of milky and creamy ascites with a positive result of chylous test. **Results:** Nineteen patients were diagnosed with peritoneal chylous leakage after LT (mean 10.8 days after LT). The incidence of the chylous leakage after LT was 7.9%. All patients received conservative treatment, which involved the cessation of oral diet, total parenteral nutrition and somatostatin, and passive peritoneal drainage. No patients received laparotomy. One patient, whose peritoneal drainage had been removed, was treated with catheter drainage guiding by ultrasonography. Eighteen patients healed with no further complications. One patient died 44 days after transplantation due to multidrug-resistant Acinetobacter baumannii pneumonia, which was considered unrelated to the formation of chylous leakage because the amount and quality of the drainage decreased gradually and the drain was removed 21 days after LT. **Conclusion:** Peritoneal chylous leakage after LT is not a rare complication. Combination treatment with total parenteral nutrition and somatostatin is an effective method to therapy peritoneal chylous leakage after LT.

# 1312 Liver volume changes after biliary decompression are different between malignant and benign biliary obstruction

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**Background and Aims:** Liver volume assessment could be an effective tool for the evaluation of liver regeneration not only in liver resection but also after stenting in malignant biliary obstruction. The mechanism of liver regeneration from liver damage is very complicated and different in various hepatic or biliary diseases. We aimed to use liver volumetry to compare liver volume changes after decompression of biliary obstruction by bile duct cancer and stone disease. **Methods:** A retrospective analysis was done of 60 patients with bile duct cancer who underwent biliary metal stenting and 20 patients with common bile duct stone who underwent endoscopic retrograde cholangiopancreatography stone removal. Liver volumes were measured by liver volume extraction software with baseline and follow-up computed tomography images at 4–20 weeks after stenting or stone removal. **Results:** Of the enrolled 60 bile duct cancer patients, 31 were treated for hilar bile duct cancer and 29 for distal bile duct cancer. Overall mean follow-up duration was 11.7 ± 4.9 and 9.4 ± 4.8 weeks in bile duct cancer and stone group, respectively. In the bile duct cancer group, liver volume increased after biliary stenting 17.4 ± 24.1% (189.5 ± 253.5 mL) from baseline (1230.7 ± 343.8 mL) to follow-up (1420.2 ± 406.2 mL) (P < 0.001). In contrast, in the bile duct stone group, liver volume decreased after stone removal 11.2 ± 11.8% (143.8 ± 179.5 mL) from baseline (1388.1 ± 314.2 mL) to follow-up (1244.3 ± 390.9 mL) (P < 0.001). **Conclusions:** Liver volume assessment might be a useful tool for evaluating liver regeneration and stent efficacy. Biliary stenting markedly increased liver volume in both hilar and distal bile duct cancer. However, in biliary stone disease, biliary decompression by stone removal results in a significant decrease of liver volume. Our data suggest that liver regeneration from decompression of malignant biliary obstruction seems to be different from that of benign disease. Further study should be guaranteed to understand the mechanism of liver regeneration or repair by decompression of malignant or benign biliary obstruction.

# 1339 Sarcopenic obesity and the risk of elevated alanine aminotransferase in elderly adults: The role of insulin resistance

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**Introduction:** It is unclear to what extent insulin resistance modulates the relationship between sarcopenic obesity and risk of elevated alanine aminotransferase (ALT) levels. **Materials and Methods:** We measured the value of the homeostatic model assessment insulin resistance (HOMA-IR) in 1432 participants aged 65 years and older from the 2009 Korea National Health and Nutrition Examination Survey. Subjects were classified as normal, sarcopenic, obese, or sarcopenic–obese based on measures of body mass index and appendicular skeletal muscle mass divided by weight. The sarcopenic, obese, and sarcopenic–obese groups were significantly associated with higher HOMA-IR values (P for trends < 0.001). **Results:** Compared with the normal group, the sarcopenic–obese group had 3.41 greater odds (95% confidence interval, 1.89–6.16) of an elevated ALT level, but the obese and sarcopenic groups had no significantly elevated odds. Adjusting for other participant factors did not substantially affect the results. The addition of the HOMA-IR value decreased the estimate of the sarcopenic–obese group by 64%, and the estimate became insignificant. The HOMA-IR value remained as an independent predictor of the outcome in the model. **Conclusions:** Sarcopenic obesity is correlated with insulin resistance and elevated ALT levels in elderly adults. Insulin resistance plays a major role in modulating the association between sarcopenic obesity and elevated ALT levels.
**# 1374 Aggravation of liver function of autoimmune hepatitis by artemisia capillaries—Three case reports**  
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**Background:** Artemisia capillaries (AC) has been used to treat inflammatory and hepatic disorders such as hepatic injury, hepatic fibrosis, and hepatitis. We report on the three cases of patients with autoimmune hepatitis (AIH) to describe the possibility of AC aggravating autoimmune hepatitis.  
**Case Report:** Three patients diagnosed with AIH have been treated with predonine. To try to put AIH under more strict control, I prescribed AC to them. Laboratory data got worse after they took AC for about 1 month. Therefore, I stopped prescribing AC. About 2 weeks later, their laboratory date improved. In this period, another drug was prescribed, and the dose of steroid was not changed. And there were no factors of aggravating liver functions.

I show the course of liver function as below.

|                | Aspartate aminotransferase | Alanine aminotransferase |
|----------------|-----------------------------|----------------------------|
|                | Before AC                   | After AC                   | After stopping AC            |
| Patient 1      | 97/270                      | 247/415                    | 98/259                      |
| Patient 2      | 36/61                       | 57/114                     | 46/88                       |
| Patient 3      | 108/68                      | 287/169                    | 112/66                      |

**# 1383 The major changes of Gilbert’s syndrome and UGT1A1 gene abnormalities in Mongolians are of western type**  
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**Background:** Hereditary abnormalities of uridine diphosphoglucuronate-glucuronosyltransferase 1A1 (UGT1A1) gene is identified as a major cause of unconjugated hyperbilirubinemia. Asian and Caucasian populations have different genetic profiles for UGT1A1, while abnormalities of the UGT1A1 gene in the Mongolian population remain uninvestigated.  
**Methods:** Between 2007 and 2014, 8 in 99 Mongolian adults visiting the Liver Unit of the Cathay General Hospital developed indirect hyperbilirubinemia. We genotyped the TATA box promoter region of the UGT1A1 gene for the A(TA)nTAA (6) or A(TA)nTAA (7) promoter variant, and the coding region for nucleotide mutations (nt)-211 G to A (G71R), nt-686 C to A (P229Q), nt-1091 C to T (P364L), and nt-1456 T to G (Y486D).  
**Results:** Two patients were homozygous for the nt-211 G > A mutation, and two patients were heterozygous for the 6/7 promoter genotype and the nt-211 G > A mutation, whereas four patients were with homozygous 7/7 genotype and were diagnosed with Gilbert’s syndrome. The percentage of 7/7 genotype patients (50%) was comparable with Caucasian, African, and Indian populations but significantly higher than other Asian countries. We did not identify any Mongolian patient with nt-686 C to A, nt-1091 C to T, or nt-1456 T to G mutations, which are common in Asian countries but not in the Western population. One patient with homozygous nt-211 G > A mutation developed severe indirect hyperbilirubinemia during the initial phase of the combined interferon and ribavirin therapy.  
**Conclusion:** The prevalence of UGT1A1 abnormalities in Mongolians are more similar to the Western population than the Asian population, whereas the high prevalence of nt-211 G > A mutation is similar to Asians.

**# 1610 An unusual case of hepatitis B flare in a patient with metastatic pheochromocytoma**  
**Authors:** KALAIYARASI KALIYAPERUMAL; CHARLES VU  
**Affiliation:** Tan Tock Seng Hospital, Singapore

**Background:** The exact interplay of endogenous cortisol and hepatitis B reactivation is not entirely understood. The possible postulated mechanisms include a persistent immunocompromised state predisposing to a flare and/or the activation of the glucocorticoid responsive elements in the hepatitis B viral (HBV) genome leading to HBV replication and gene expression.  
**Methodology/Results:** We present an interesting case of a 71-year-old man with metastatic pheochromocytoma co-secreting adrenocorticotropic hormone, who presented with a hepatitis B flare. This occurred in the setting of a rising cortisol level and a recent initiation of ketocconazole for chemical adrenalectomy. Entecavir was started for the patient with subsequent normalization of the liver function test.  
**Conclusion:** The role of endogenous cortisol excess in the reactivation of hepatitis B is less well understood and studied, compared to exogenous steroid intake. By highlighting this unusual case, we hope to alert physicians to this potential association. Screening for hepatitis B and antiviral therapy may help to prevent a hepatitis B flare and liver decompensation.

**# 1618 An unusual case of spontaneous bacterial peritonitis in a patient with peritoneal carcinomatosis**  
**Authors:** YANG ZJ; KALIYAPERUMAL KK  
**Affiliation:** Gastroenterology and Hepatology, Tan Tock Seng Hospital, Singapore

**Background/Aim:** This study aims to describe a case of spontaneous bacterial peritonitis (SBP) occurring in a patient with malignant ascites from underlying pancreatic adenocarcinoma.  
**Methods:** A 57-year-old Indian gentleman, presented to the Emergency Department with new-onset ascites of 1-week duration, loss of weight, and fever. Physical examination revealed tense, tender ascites with no signs of chronic liver disease or heart failure. Abdominal paracentesis done demonstrated yellow and turbid fluid with the following results: a corrected polymorphonuclear cell count of 2430 (74% neutrophils) and a serum ascites albumin gradient of 12 mmol/L. Ascitic fluid gram stain and cultures were negative.  
**Results:** A diagnosis of culture-negative SBP was made, and he was started on antibiotics. Fluid cytology showed metastatic adenocarcinoma. A computer tomography scan revealed a pancreatic body mass with hepatic and peritoneal metastases. There was no radiological evidence of cirrhosis, splenomegaly, or varics. He was subsequently referred to medical oncology for chemotherapy.  
**Conclusion:** The majority of SBP tends to occur in cirrhotic ascites, but is rare in malignant ascites. To our knowledge, only a few have been reported in current literature. We chose this case to highlight the unusual presentations of SBP in non-cirrhotic ascites so that physicians will maintain a high index of suspicion for early institution of treatment.
We postulate that lymphatic hypertension from disseminated intra-abdominal nodal malignancy may predispose to rupture of smaller lymphatics and showering of incumbent intestinal flora into the ascitic fluid, similar to cirrhotic ascites. However, further studies are needed to evaluate this.

# 1628 The influence of sympathetic nervous system inhibition on anorexia and hepatic expressions of cytokines, chemokines, and heme oxygenase-1 in carbon tetrachloride-treated mice

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Background/Aims: We reported that sympathetic nervous system (SNS) ablation prevents the progression of carbon tetrachloride (CCl4)-induced acute liver injury in mice by attenuating enhanced lipid peroxidation. However, the CCl4-induced anorexia and detailed protective mechanisms of the SNS ablation need to be further investigated. Methods: Acute liver injury was induced in mice with and without chemical sympathectomy by a single injection of CCl4. Enteropathy-associated anorexia was assessed. Liver injury and expressions of cytochrome P450 2E1 (CYP2E1), heme oxygenase-1 (HO-1), cytokines, and chemokines in the liver were measured. Results and Discussion: Chemical sympathectomy prevented CCl4-induced ileal villous edema-associated anorexia (Fig. 1). Expressions of CYP2E1, a pro-oxidant, and HO-1, an anti-oxidant, were increased after chemical sympathectomy. Attenuated injury in sympathectomized mice was associated with raised HO-1, not CYP2E1, expression. These results suggest that chemical sympathectomy failed to prevent suicidal degradation of CYP2E1 (Fig. 2). Moreover, chemical sympathectomy modulated the CCl4-induced inflammatory responses within the liver, including interleukin (IL)-1α, IL-10, leptin, tissue inhibitor of metalloproteinase-2, soluble tumor necrosis factor receptor I, granulocyte-macrophage colony-stimulating factor, CCL3, CCL5, CCL9, CCL11, and CXCL11 (Fig. 3). To the best of our knowledge, this is the first demonstration of expression of CCL9, a mouse CC chemokine and strong chemoattractant for bone marrow cells, in the liver. Conclusions: These results indicate SNS ablation prevents enteropathy-related anorexia and acute hepatic injury associated with HO-1 expression in CCl4-treated mice. We also suggest that SNS may be providing a permissive microenvironment affecting expressions of cytokines and chemokines in hepatocytes.

Keywords: carbon tetrachloride, chemokines, cytokines, heme oxygenase-1, sympathetic nervous system.
**Reference:**

1 Yang M, Odgren PR. Molecular cloning and characterization of rat CCL9 (MIP-1gamma), the ortholog of mouse CCL9. *Cytokine* 2005; 31: 94–102.

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**# 1648 Clinical and histological differences between drug-induced autoimmune hepatitis and classical autoimmune hepatitis**

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**Background:** The exact etiology of autoimmune hepatitis (AIH) is uncertain, but it can be triggered in susceptible persons by drugs. An increasing number of drug-induced AIH (DIAIH) cases were reported, but they remain poorly characterized. We aim to compare the clinical and histological characteristics of DIAIH and classical AIH.

**Methods:** Consecutive cases fulfilling AIH simplified criteria diagnosed between 2008 and 2013 in Singapore General Hospital were included. DIAIH was defined as patients fulfilling standardized diagnostic criteria but also had identifiable drug suspected of triggering AIH. Histology was reviewed by three independent liver pathologists blinded to the cases. Known features of AIH and drug-induced liver injury such as plasma cells, rosettes, emperipolesis, inflammation, eosinophils, cholestasis, bile duct damage, and fibrosis staging were assessed for each case.

**Results:** Sixty-two patients were included. Of these, nearly a quarter (24.5%) fulfilled the study definition of DIAIH. Nitrofurantoin was implicated in one case of DIAIH, whereas the rest were associated with traditional Chinese medicine use. Classical AIH patients were more likely to present with advanced fibrosis (Metavir > 2) than DIAIH patients (*P* = 0.02). Histology features were otherwise not
significantly different between AIH and DIAIH. Clinically, DIAIH patients were more likely to present with severe jaundice (bilirubin > 320) and prolonged prothrombin time > 15 s. DIAIH patients were less likely to require long-term treatment (P = 0.03). Conclusion: Histological features were similar and not helpful in differentiating DIAIH from classical AIH, although DIAIH patients were significantly less likely to present with advanced fibrosis. Clinically, DIAIH patients were significantly more likely to present with liver synthetic dysfunction but less likely to require long-term immunosuppressive treatment.

# 1664 The first-line antiviral agents for viral hepatitis B: A clinical physician’s perspective in medical economic at a medical center
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Background/Aim: The American Association of the Study of Liver Diseases, European Association of the Study of the Liver, and Asian Pacific Association for the Study of the Liver, and World Health Organization guidelines all recommend initial treatment with entecavir (ETV) or tenofovir (TDF) for chronic hepatitis B patients. TDF and ETV may be similarly effective and safe. However, most economic benefit studies come from insurance and social perspectives. In this report, we like to know laboratory test items and the impact of time costs when clinicians prescribe these drugs in outpatient departments. Methods: Randomly, we selected patients who received a first prescription TDF or ETV in 2014. Patients with malignancy and hospitalization were excluded. The laboratory test items were recorded from last to after-visit date of the clinicians prescribing. We also tried to analyze visit times of patients. Results: Fifty-two patients were included: 30 with ETV and 22 with TDF. All patients had hepatitis B virus DNA, alanine aminotransferase, and aspartate aminotransferase results before taking an antiviral agent. The proportion of creatinine test was 17% versus 68%, and blood urea nitrogen test was 0% versus 32% (ETV vs TDF). The ETV group did not have electrolyte reports. Serum phosphate and urinalysis were checked in 5% and 23% patients with TDF. The time of visits had a great difference that could not be parsed for time cost. Discussion/Conclusion: There were many limitations in this observation. However, clinicians are still concerned about the safety of renal impairment in TDF. Comparing patients with ETV treatment, clinicians did more tests and might take more time to check and explain the data for these patients. This prescription of TDF will have more hidden costs than ETV in clinical practice.

# 1674 Diabetes: Its impact on liver diseases
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Background and Aims: The strong epidemiological evidence suggests risk of chronic liver disease, cirrhosis, hepatocellular carcinoma (HCC) and increased mortality due to liver disease in patients of diabetes. This study was undertaken to determine the impact of diabetes on the entire spectrum of liver diseases. Methods: We evaluated all patients presenting to our liver clinic or getting hospitalized from January 2010 to December 2012 for presence of diabetes and type of liver disease at presentation. Included in the study were 3715 patients (median age: 46 years, range: 12–95 years, 2737 males). Results: Prevalence of diabetes was 19.21%. Forty percent of diabetic patients had fatty liver. Thirty-nine percent of diabetics had cirrhosis at presentation versus 20% of non-diabetics (P < 0.001). Among the diabetics with acute hepatitis, 22% had severe or fatal hepatitis. Sixteen percent of chronic hepatitis C patients (non-cirrhotic) had diabetes as compared against 9% of chronic hepatitis B patients. Thirty-two percent of our cirrhotic patients had diabetes. More than 40% of those with diabetes and cirrhosis had non-alcoholic steatohepatitis-associated or cryptogenic cirrhosis. Only 9% of diabetic cirrhotics belonged to Child’s C class as against 19% of non-diabetic cirrhotics. Of patients with HCC, 39% had diabetes at presentation, whereas incidence of new-onset HCC was 3.9% within the diabetics. A higher proportion of diabetics with HCC belonged to Barcelona Clinic Liver Cancer stage A (50%). Conclusion: Our study showed a significant association between type 2 diabetes mellitus and a spectrum of liver diseases ranging from acute hepatitis to acute liver failure, cirrhosis, fatty liver disease, and HCC.

# 1720 Optimal timing of portoenterostomy for biliary atresia
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Background: Early intervention before 60 days of age with a portoenterostomy (PE) is the current standard of care for patients with biliary atresia (BA) to have a better prognosis. However, the prognosis of BA with PE performed at different ages of life varies among different reports. Methods: The National Health Insurance (NHI) was implemented in Taiwan in 1995 and covers most of the population (>99%). We use the NHI database to investigate the prognosis of BA at different timing of PE performed. Results: We identified 327 new BA cases during the years from 1996 to 2003. The 5-year survival rate with native liver was lowest in the cases without receiving PE (3.7%) and the cases with PE after 90 days old (36.5%). There was no difference between the groups receiving PE before 30 days old (59.1%), 30–45 days old (52.6%), 45–60 days old (44.3%), and 60–90 days (52.7%). The 5-year survival rate with native liver was significantly different before 90 days and after 90 days old (50.8% vs 36.5%, P = 0.041). The 5-year overall survival rate was not significantly different among PE performed before 30, 30–45, 45–60, and 60–90 days old and after 90 days old (P > 0.05). Conclusions: The timing of PE performed before 30, 30–45, 45–60, and 60–90 days old does not have a different prognosis in native and overall 5-year survival. BA cases
without PE and those receiving PE after 90 days have the worst native liver survival rates.

**# 1802 The clinical and ultrasonic characteristics of hepatic angiosarcoma**

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**Objective:** This study aims to analyze the clinical and ultrasonic characteristics of hepatic angiosarcoma. **Method:** The ultrasound and clinical data of four patients with hepatic angiosarcoma were analyzed retrospectively. **Result:** Four patients were hospitalized because of right upper-quadrant pain, nausea, and inappetence, two of whom were with fever and fatigue and the rest were with backaches. Among the four cases, only one had positive hepatitis B surface antigen as well as positive e antibody and core antibody, the other three were with positive hepatitis B surface antigen and negative e and core antibody. Serum α-fetoprotein of four patients was in the normal range. The lesions in four patients were all single, one of which was in the left hepatic lobe and the remaining three were in the right hepatic lobe. Ultrasound showed the lesions in four cases were all big, the biggest of which was more than 5.0 cm and the maximum diameter of the other three was larger than 10 cm. Three lesions were quasi-circular, and one lesion was oval. Lesion borders had no clear vision, and interior echoes were inhomogeneous. Non-echo areas were all found in three cases. Color Doppler flow imaging showed sparse point and linear blood signal in interior. **Conclusion:** The clinical feature and laboratory examination lacked specificity. The ultrasonographic features showed regular morphology, not very clear borders, and inhomogeneous interior echoes, most of which were with little non-echo areas. The ultrasound test was aiming to find abnormal lesions in the liver, and the diagnosis should be confirmed by pathological results. **Keywords:** angiosarcoma, liver, ultrasonic examination.

**# 1839 Clinical characteristics of pyogenic liver abscess caused by Escherichia coli versus Klebsiella pneumoniae**

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**Introduction:** Pyogenic liver abscess is a serious condition with a high mortality rate that represents a diagnostic and therapeutic challenge. The objective of this study was to compare differences in underlying disease, clinical manifestations, characteristic features of liver abscesses, antibiotic resistances, and outcome between *Escherichia coli* (EC groups) and *Klebsiella pneumoniae* (KP groups) liver abscess. **Materials and Methods:** In total, 259 patients were enrolled, and each group included 136 (KP groups n = 112, EC groups n = 24) patients. We reviewed the medical records retrospectively including etiology, underlying diseases, characteristics of the liver abscess, laboratory and microbiologic findings, treatment, and outcome of the patients. **Results:** Patients in the EC group were more likely to have infection sources from benign biliary diseases (P = 0.001), biliary malignancy (P < 0.001), history of cholecystectomy (P = 0.027). The low hemoglobin level was higher in the EC group (P = 0.002). Elevated alkaline phosphate level was higher in the EC group (P = 0.006). Decreased albumin level was higher in the EC group (P = 0.037). Multi-drug-sensitive KP was most common among isolates of the KP group, whereas the EC group usually has a multi-drug-resistant EC in this study (P < 0.001). The overall mortality rate in this study was 4.2% (11/259), with 2.7% (3/112) in the KP group and 8.3% (2/24) in the EC group. **Conclusions:** In contrast to patients with *K. pneumoniae*, patients with *E. coli* liver abscesses were more likely to be older and female and have anemia, a high level of alkaline phosphatase, a low level of serum albumin, biliary disease, a history of cholecystectomy, and multi-drug-resistant organisms.

**# 1853 The application of liver stiffness measurement in healthy residents through a community-based screening program in Taiwan**

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**Background/Aim:** Liver stiffness measurement (LSM) by transient elastography (TE) is a non-invasive and useful tool to evaluate liver fibrosis in chronic liver diseases. The study aimed to investigate the usefulness of TE and to identify factors that associated with significant liver fibrosis in a community-based population. **Methods:** We conducted a hepatitis screening program from Aug 2014 to May 2015 in two remote villages of Southern Taiwan. All participants received questionnaire evaluation, blood tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST), hepatitis B surface antigen, and anti-hepatitis C virus antibody, abdominal sonography, and LSM by FibroScan®. Residents with any one of following criteria were excluded: hepatitis B virus infection, hepatitis C virus infection, more than moderate alcohol drinking, and failure to obtain valid or reliable LSM. **Results and Discussion:** There were 605 residents who participated in the program. After exclusion, 376 residents were enrolled. Significantly higher liver stiffness was observed in residents with female gender (P = 0.035), diabetes mellitus (P = 0.001), and increment of body mass index (BMI; P = 0.001). Nineteen residents (5.1%) exhibited significant fibrosis (liver stiffness ≥ 8 kPa). Univariate analysis showed body weight ≥ 70 kg, BMI ≥ 28 kg/m², abnormal ALT, abnormal ALT, and diabetes mellitus were factors associated with significant fibrosis. Only abnormal ALT and BMI ≥ 28 kg/m² were two independent factors under multivariate analysis. **Conclusion:** Liver stiffness measurement by TE is a useful screening tool in the community. Residents who had no viral hepatitis or consumed less than moderate alcohol and exhibited obesity or abnormal ALT may be considered a substantial group with significant fibrosis in the community.
# 1897 Amiodarone as an autophagy promoter improved liver regeneration and survival in mice after 90% massive hepatectomy

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**Background:** The use of pharmacological interventions offers the potential for improved hepatocyte proliferation and liver regeneration following partial hepatectomy (PHx). Autophagy, a process that results in cellular degradation, has been found to be involved in the human liver disease. **Aims:** This study aims to investigate the role of autophagy in the regulation of liver regeneration after PHx. Furthermore, pharmacological modulation of autophagy could be an effective approach to promote liver regeneration and survival after 90% massive PHx. **Methods:** We administrated autophagy enhancers to C57BL/6 mice intraperitoneally: amiodarone and chloroquine. This was followed by a 70% PHx or 90% PHx or sham operation. The survival rate was collected. Furthermore, activation of autophagy, level of hepatocyte proliferation, and blood levels of liver enzyme were also measured. **Results:** Autophagy was activated in the early stages of liver regeneration following 70% PHx. Moreover, amiodarone was associated with a significant enhancement of autophagy, hepatocyte proliferation, and liver growth, along with reduced liver injury and the termination of liver regeneration due to increased proliferating cell nuclear antigen and cyclin D1 protein levels but decreased transforming growth factor-β1 expression after 70% PHx. The promotion of autophagy appeared to selectively increase the removal of damaged mitochondria. Finally, amiodarone improved liver regeneration, survival, and liver injury after 90% PHx. **Conclusion:** Pharmacological enhancement of autophagy by amiodarone could be a novel strategy for promoting liver regeneration, hepatocyte proliferation, and survival and alleviating liver injury after 90% massive PHx.

**Keywords:** amiodarone, autophagy, liver regeneration, massive partial hepatectomy, survival.

# 1976 Efficacy of prothrombin complex concentrate in hepatobiliary disorders patients with coagulopathy who underwent invasive procedures

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**Background:** Prothrombin complex concentrates (PCC) containing prothrombin, factors VII, IX, and X, and the inhibitors proteins C and S have been used as an emergent reversal for oral anticoagulation therapy. The use of PCC in hepatobiliary disorder patients who need to undergo invasive procedure has not been well studied as the patients are usually accompanied by coagulopathy. **Objective:** This study aims to evaluate the efficacy of PCC treatment to control or prevent bleeding complications in patients with hepatobiliary disorders who undergo invasive procedures. **Method:** This was a prospective, open-label, non-randomized, before-and-after study in patients with hepatobiliary disorders who underwent invasive procedures accompanied by liver impairment and received PCC injection (Cofact®, Sanquin, the Netherlands). Patients with coagulopathy from various causes were recruited consecutively. Data collected were the episodes of bleeding, liver function test, and the international normalized ratio (INR) calculated before and 1 h after PCC therapy. The primary end-point was INR change after treatment, while secondary endpoints included bleeding control and bleeding event after treatment. **Results:** Thirty patients (17 men and 13 women) were enrolled. Patients’ mean age was 57 ± 15.5 years. Liver cirrhosis was found in 14 (46.7%) patients. The procedures consist of liver biopsy, liver abscess aspiration, abdominal paracentesis, therapeutic upper gastrointestinal endoscopy, endoscopic retrograde cholangiopancreatography and percutaneous transhepatic biliary drainage. After treatment, 25 (83.3%) patients showed decreased median INR from 1.6 to 1.3 (P < 0.001, Wilcoxon’s signed-rank test). Five patients failed to show INR reduction. No new bleeding event related to the invasive procedures. Despite the reduction of INR, two patients passed away due to ongoing severe bleeding from gastric malignancies. **Conclusion:** Prothrombin complex concentrate treatment is effective to control and prevent bleeding complications in patients with hepatobiliary disorders who underwent invasive procedures.

**Keywords:** international normalized ratio (INR), liver cirrhosis, liver coagulopathy, liver dysfunction, mortality, prothrombin complex concentrate.

# 1983 Associations between vitamin D level and serum aminotransferase concentration in Korea using nationwide survey

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**Background:** Recently, vitamin D has been recognized to have nonskeletal actions. The aim of this study was to investigate the association between vitamin D level and serum aminotransferase concentration in general
Korean adults using the Korea National Health and Nutrition Examination Surveys. Methods: Serum 25(OH)D levels were measured and then categorized into deficient (≤ 20 ng/mL), insufficient (> 20–30 ng/mL), and sufficient (≥ 30 ng/mL) groups. Elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) concentrations were defined as > 30 IU/L for men and > 19 IU/L for women. The association between vitamin D level and aminotransferase concentration was tested by chi-squared tests and multiple logistic regression analyses. Results: The prevalence of elevated ALT was 25.0%, 24.7%, and 22.6% in deficient, insufficient, and sufficient groups, respectively. The proportions of individuals with elevated AST were 30.0%, 31.5%, and 34.5% in deficient, insufficient, and sufficient groups, respectively. Compared to the deficient group of vitamin D, subjects with higher serum vitamin D levels had significantly lower risks for elevated ALT concentration (insufficient group: adjusted odds ratio [aOR] = 0.87, 95% confidence interval [CI] = 0.79–0.96, sufficient group: aOR = 0.76, 95% CI = 0.62–0.94) in the high-risk group for liver injury. Conclusions: Higher vitamin D level was significantly associated with the lower risks of elevated ALT concentration in Korea.

# 1986 Gilbert syndrome in an adolescent male with coexisting glucose-6-phosphate dehydrogenase deficiency: A case report
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Background: Gilbert syndrome is the most prevalent inherited disorder of unconjugated hyperbilirubinemia with reduced expression of promoter glucuronosyltransferase 1 (UGT1A1) gene. In Southeast Asia and Pacific Islands, prevalence is less than 5% of the population. Surveys have shown a correlation between Gilbert syndrome and glucose-6-phosphate dehydrogenase (G6PD) deficiency. The presence of a UGT1A1 promoter gene variant is attributed to the development of hyperbilirubinemia in G6PD deficiency. Clinical Description: We present a case of a 16-year-old, male, with jaundice, and diagnosed G6PD deficiency at birth. Interval history was unremarkable. Patient engaged in strenuous sports activity accompanied by episodes of missed meals. Subsequently, he developed jaundice, tea-colored urine, fatigue, and anorexia. He had no history of alcohol or drug intake, fever, and concurrent illness. On examination, he showed hepatomegaly without other stigmata of liver disease. Liver biochemistry revealed elevated serum total bilirubin (335 μmol/L) with a predominance of unconjugated bilirubin (263 μmol/L). Hepatobiliary tree ultrasound, viral hepatitis markers, complete blood count, and liver function tests were unre- markable: serum glutamic pyruvic transaminase (70.8 U/L), alkaline phosphatase (71 IU/L), albumin (4.5 g/dL), prothrombin time (13.5 s, international normalized ratio 0.98). UGT1A1 gene mutation test was not done due to unavailability in the country. Consequently, diagnosis by exclusion of Gilbert syndrome was made. Patient was managed conservatively and improved. Conclusion: In a patient with G6PD deficiency with jaundice and unconjugated hyperbilirubinemia, a diagnosis of Gilbert syndrome is highly considered. The associated co-inheritance of a variant promoter UGT1A1 gene is strongly correlated with coexisting G6PD deficiency proven in studies. Identification of this condition will warrant directed diagnostic approach and management.

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# 2077 Evaluation focal liver lesion with contrast-enhanced ultrasound—A preliminary report
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Background: Conventional ultrasound (US) is a feasible and easy tool to detect focal liver lesion (PLL). The accurate diagnosis of PLL may be difficult when the lesion is not a simple hepatic cyst. Contrast-enhanced ultrasound (CEUS) is an excellent and safe tool for assessment of the vascular characteristics of PLL and has great potential in the detection and characterization of hepatic tumors. The enhancement patterns of lesions can be studied during all vascular phases (arterial, portal venous, late, and postvascular phases) that are similar to computed tomography (CT) and magnetic resonance imaging (MRI) but in real time and under full control of the US operator. Methods: From June 2015 to July 2015, 20 patients (16 male/4 female) who had PLL disclosed by US were evaluated by CEUS. Contrast agents with Definity® (Lantheus Medical, Billerica, MA, USA)
were used with dose adjustment by weight. Sixty-five percent of patients (13/20) had also received other image studies such as CT or MRI. We follow the practical guideline from Dr. Claudon for diagnosis of FLL (Claudon et al., Ultraschall. Medn 2013; 34: 11–29). **Results:** Sixteen of the 20 patients were male. Two patients did not receive CEUS study due to uncertainty of heart disease and suboptimal baseline US study. Fifty percent of the patients (10/20) were diagnosed as hepatocellular carcinoma (HCC) by CEUS, and six patients were confirmed by either CT or MRI with the diagnosis of HCC. Four patients were diagnosed as hemangioma with typical peripheral enhancement during arterial phase and centripetal fill-in during portal phase and late phase. All four hemangiomas were confirmed either by CT or MRI. Two patients were diagnosed as focal nodular hyperplasia that presented with typical finding with a hyperenhancing pattern from the center in the arterial phase then rapid fill out. Two patients had inconclusive CEUS finding. All patients tolerated the examination well without side effects. **Conclusion:** CEUS can be a potential tool for diagnosis of FLL, especially in patients with renal impairment who are not suitable for CT or MRI with contrast imaging study. In this preliminary study, only one patient diagnosed as HCC had been confirmed by pathologic result. Further study is needed to compare CEUS, CT, or MRI and pathologic findings.