



Report of novel approaches for portal hypertension: SNG of the 26th Conference of Asian Pacific Association for the Study of the Liver

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The 2017 Asian Pacific Association for the Study of the Liver (APASL) was held in Shanghai, China (Figures 1,2). With 5,228 participants, the 26th conference was marked by an extensive exchange of views on new development in both clinical practice and academic research. The major themes of the meeting were viral hepatitis, alcoholic hepatitis, the drug-induced liver damage, liver fibrosis, cirrhosis, liver cancer and liver transplantation. A wide range of topics were covered by a series of oral presentations, poster sessions, and discussion. This report highlights the major themes discussed in the APASL Working Party on Portal Hypertension by summarizing the main topics and discussion points. The principal contents of the meeting were novel technologies and development in the diagnosis and treatment of portal hypertension.

Noninvasive predictors of portal hypertension

Portal hypertension accounts for the presence of collateral circulation and hyperdynamic circulatory syndrome leading to a series of related complications such as gastrointestinal bleeding, esophageal varices (EV), ascites, hepatorenal syndrome, spontaneous bacterial peritonitis (SBP) and hemorrhage. Hepatic venous pressure gradient (HVPG) more than 12 mmHg correlates with the occurrence of EV bleeding, while HVPG more than 22 mmHg is linked to a high mortality rate in patients with alcoholic cirrhosis. Moreover, a higher value of 30 mmHg is considered to be relevant to the occurrence of SBP. In contrast, improvement of portal hypertension with a decrease in portal pressure was demonstrated to improve the prognosis of cirrhotic patients.

Gamal Shiha (Mansoura University CEO, Egyptian Liver Research Institute and Hospital, Mansoura, Egypt)

emphasized the importance of portal pressure measurement in patients with alcoholic cirrhosis. Although HVPG remains the gold standard for the diagnosis of portal hypertension, due to its invasiveness and limitations, safe and reproducible non-invasive methods are now urgently needed.

Evaluation by biochemical tests and morphological parameters

The platelet count/spleen diameter ratio (Plt/Spl) was shown to have a high predictive value for the presence of EV. Combination of the Lok index and the Forn's index was useful in excluding clinically-relevant EV with a high negative predictive value (>90%). Current results showed that the grade of the portal pressure cannot be detected using simple non-invasive laboratory tests, but they may be useful for patients with suspected clinically significant portal hypertension (CSPH, defined as HVPG ≥ 10 mmHg). Thus, endoscopy examination cannot currently be replaced by simple non-invasive serum markers for a majority of patients in clinical practice.

There are many morphological parameters performed by ultrasound techniques, able to indicate the presence of portal hypertension, considered non-invasive such as the presence of collateral vessels, spleen enlargement and ascites, the change in the portal vein parameters (increase in diameter, disappearance of caliber variation during respiration, decrease in blood flow velocity, increase in the congestion index) as well as the increase in hepatic and splenic arterial resistance indices, and decrease in the damping index of hepatic veins. Measurement combining portal vein blood flow velocity, diameter of portal vein and hepatic artery and splenic artery resistance index was

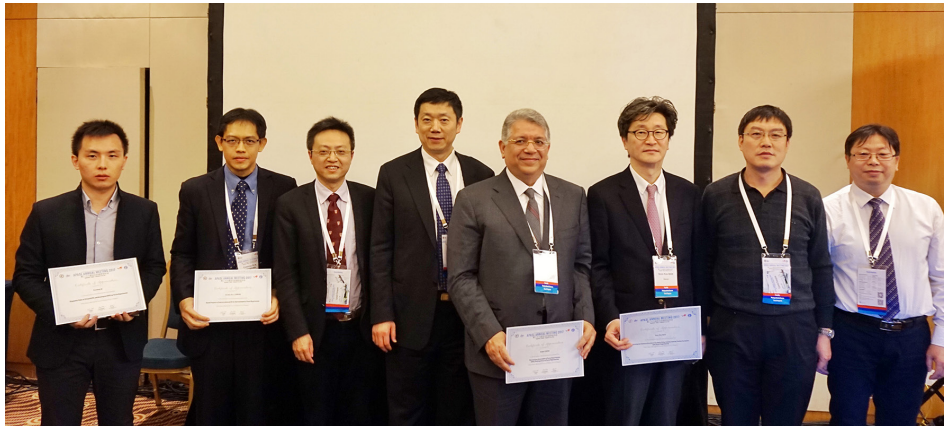


Figure 1 Meeting picture.

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Figure 2 Academic Committee of CHESS.

shown to be helpful in clinical monitoring for patients with cirrhosis and portal hypertension. As for the emerging technique, contrast-enhanced ultrasonography, it offered more options in the evaluation of the grade of portal hypertension by the analysis of the transit time of microbubble contrast agent through the liver.

Evaluation of portal hypertension by the measurement of liver stiffness (LS)

Studies have shown that LS is comparable to HVPG in detecting clinical decompensation and complications associated with portal hypertension. At present, investigations demonstrated that transient elastography (TE) could be offered as a screening tool for CSPH in patients with compensated cirrhosis. Particularly, TE value ≥ 21 kPa is equivalently accurate as HVPG ≥ 10 mmHg in predicting first clinical decompensation in compensated cirrhotic patients. Furthermore, Prof. Gamal Shiha reported the utilization of FibroScan in predicting EV with an area under the receiver operating characteristic curve (AUC) of 0.777 in a cohort of 150 cirrhotic patients performed in Egyptian Liver Research Institute and Hospital. New elastography techniques, emerging as additional alternatives, seem to overcome some of the limitations of the traditional TE, providing more options for physicians and patients with cirrhosis and portal hypertension in recent years.

Evaluation of portal hypertension by the measurement of spleen stiffness (SS)

SS measurement was demonstrated to have a close correlation with the degree of portal hypertension ranging from early stages to late stages of cirrhosis. In particular, SS less than 54 kPa could be employed as an indicator for excluding the risk of portal hypertension related complications in the following two years. The combination of SS, Doppler splenic resistance indices, platelet count and spleen size was proved to have a better predictive ability for the presence of portal hypertension compared to that of a single parameter. A prospective study performed with LS-spleen diameter to platelet ratio score (LSPS) showed promising results in detecting the presence of variceal bleeding. With a cutoff ≥ 5.5 , a higher cumulative incidence rate of esophageal variceal bleeding was indicated. LSPS and the portal hypertension risk score (LS, sex, and spleen diameter/platelet count ratio) were regarded as the most accurate non-invasive parameters for the identification

of CSPH in cirrhotic patients. In conclusion, LS and SS measurements along with Doppler ultrasound techniques provide a feasible method with a relatively high accuracy for excluding CSPH while HVPG measurement remains necessary for accurate identification of the progression of portal hypertension. Further analyses of factors and strategies in non-invasive prediction of portal hypertension are needed to be continued.

Histological subclassification of cirrhosis using Laennec scoring system correlated with portal hypertension

Soon Koo Baik (Yonsei University, Wonju College of Medicine, Wonju, South Korea) discussed the role of histological subclassification of cirrhosis using Laennec scoring system in predicting the occurrence of portal hypertension and focused on the discrimination power for assessing anti-fibrotic effects. He reported that the histological subclassification of cirrhosis was correlated with functional stages supported by the significant correlations among Child-Pugh score, MELD score and Laennec scoring system. Nowadays, cirrhosis is considered potentially reversible with the removal of harmful factors. Thus, discrimination ability to assess anti-fibrotic effects for cirrhosis is urgently required. Many studies have shown that effective anti-viral treatments of hepatitis B and C could result in reduction of liver fibrosis. Attempt to evaluate the effect of anti-fibrosis drug for liver cirrhosis would be highly restricted by lack of sub-histological classification. After anti-fibrosis treatment, F4C may be improved to F4A in Laennec scoring system, but scores of the conventional classification system will lead to incorrect conclusions that the treatment was invalid. Therefore, histological subclassification of cirrhosis with adequate discrimination power is essential. The reproducibility of Laennec scoring system in histological subclassification of cirrhosis was demonstrated with a Kappa value of 0.83 for the interobserver agreement. Therefore, histological subclassification of cirrhosis on the basis of septal thickness appears to be feasible with simplicity and high reproducibility, but more validations are still needed. Prof. Baik summarized that further histological subclassification of cirrhosis is needed since heterogeneity exists within the grade of cirrhosis; a modification of METAVIR fibrosis stage 4 using Laennec scoring system was recommended as F4A, F4B and F4C; Laennec scoring system is correlated with clinical stages of liver cirrhosis, CSPH and liver-related morbidity and mortality. He added that in a systematic

review and meta-analysis, higher scores of Laennec scoring system indicated increased clinical stages of cirrhosis and Child-Pugh/MELD scores. Two open-labeled researches showed that Laennec scoring system was useful in evaluation of the efficacy of anti-fibrosis treatment. At last, Prof. Baik suggested that the histology of cirrhosis should be further subdivided into different levels based on severity.

Recent progress in CEUS for portal hypertension assessment

Cosmas R. A. Lesmana (Medistra Hospital, Jakarta, Indonesia) presented the development course of non-invasive diagnostic techniques related to liver histology for the prediction of portal hypertension, involving non-invasive formula (APRI), Fibrotest, TE, FibroScan, Acoustic Radiation Force Impulse (ARFI) and Doppler ultrasound. The evolution of the ultrasonic technology was featured by the development of a series of devices and parameters including transabdominal ultrasound, Doppler ultrasound, portal vein diameter, and portal vein velocity. Despite the great progress in recent years, he pointed out that the application of non-invasive ultrasound technology with reliability and accuracy is currently blocked by problems in real practice regarding training curriculum, operator skills and experience, contrast injection (including cost and availability), availability of other non-invasive tools and the impact in clinical practice despite the usual common practice guideline. Prof. Lesmana concluded that as the progression of innovative ultrasonic technology being continuously made, the requirement of invasive test used for accurately predicting the degree and development of portal hypertension will be reduced in the future. However, high volume clinical trials performed in experienced centers will be required for the validation and meanwhile, the training, cost and hospital investment will become major issues.

Transjugular intrahepatic portosystemic shunt (TIPS) for portal vein thrombosis (PVT) in cirrhotic patients with variceal bleeding

Guohong Han (Xijing Hospital of Digestive Diseases, Fourth Military Medical University, Xi'an, China) discussed the role of TIPS for PVT in cirrhotic patients with variceal bleeding and compared the treatment effect to that of the anticoagulation. The degree of PVT includes partial PVT, complete PVT, and fibrotic cord. Decreased portal blood flow velocity and increased flow volume in the largest

collateral vessel both contribute to the development of PVT. He mentioned that PVT was proved to have no impact on the natural history of cirrhosis and most PVT in the study was nonocclusive. However, data showed that PVT was an independent risk predictor for varices bleeding, failure for endoscopy to control bleeding and recurrent bleeding; and it is correlated with a higher 6-week mortality. There is doubt about the impact of PVT for the prognosis of patients with cirrhosis and so far no specific recommendation has been proposed for treatment of PVT in cirrhotic patients with recurrent variceal bleeding. Anticoagulation is often effective for partial PVT with complete recanalization in 40–75% of patients while the efficacy decreases in complete PVT. As for the case of TIPS for PVT in cirrhosis, a success rate for placement of 75–100% was described and the degree of PVT greatly affected the technical success. Besides, Prof. Han suggested that successful TIPS insertion was capable of decreasing the risk of recurrent bleeding in cirrhotic patients with variceal bleeding. Extensive superior mesenteric vein thrombosis was responsible for shunt dysfunction in 21–28% patients. In addition, whether the pre-existing PVT could affect the outcome of TIPS remained unclear. After comparing the advantage and disadvantage of the two therapeutic options, Prof. Han hypothesized that TIPS may be better than conservative therapy for variceal rebleeding and should be considered in cirrhotic patients with nontumoral PVT. Finally, he concluded that natural history of PVT in cirrhosis and the clinical impact of recanalization are unclear and further studies are necessary to identify the role of TIPS in preventing variceal bleeding for selected cirrhotic patients with PVT.

Diagnostic value of virtual HVPG and radiomic HVPG for portal hypertension

On behalf of the Chinese Portal Hypertension Noninvasive Diagnosis Study (CHESS) Group, Xiaolong Qi (Nanfeng Hospital, Southern Medical University, Guangzhou, China) presented two potential novel techniques for noninvasively diagnosis of portal hypertension: Virtual hepatic venous pressure gradient (*v*HVPG) and Radiomic hepatic venous pressure gradient (*r*HVPG). Inspired by an article published in *JAMA* in 2012 about the noninvasive parameter FFR_{CT} , which was used to diagnose coronary artery ischemia, Prof. Qi's team started to investigate the possibility of combing the anatomic methods with the functional methods for noninvasive diagnosis of portal hypertension. Thus, he

proposed *v*HVPG based on CTA and Doppler ultrasound and presented the preliminary result of their multicenter diagnosis performance trial, the CHESS-01 trial at the meeting. As expected, *v*HVPG demonstrated higher diagnostic performance for CSPH and better capability of predicting the risk of variceal bleeding (HVPG >12 mmHg) compared to other indexes including FibroScan, HVPG_{CT} score, Portal diameter, AAR, APRI, and FIB-4. Prof. Qi said that the CHESS-01 trial is ongoing and larger population should be enrolled and more data is needed before *v*HVPG is considered as a validated surrogate method for invasive HVPG. Besides, Prof. Qi and his colleagues are getting down to cooperating with medical instrument company (SIUI) to develop portable devices for detecting the *v*HVPG. Prof. Qi also proposed the concept of *r*HVPG, which aims to diagnose portal hypertension noninvasively and monitor the patients' portal pressure during the therapy and follow-up by extracting the imaging feature that is invisible to naked eyes.

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Footnote

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