Cirrhosis Management: Utilization and Optimizing Non-Invasive Tests in Portal Hypertension

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Cirrhosis, characterized by advanced scarring of the liver due to chronic liver disease, remains a major global health issue and is the leading cause of liver-related mortality worldwide. According to the Institute for Health Metrics and Evaluation (IHME), cirrhosis was the fourth leading cause of death in Indonesia in 2021. At Cipto Mangunkusumo Hospital, the 90-day mortality rate for hospitalized cirrhosis patients was 42.2%. Furthermore, hepatitis B infection was the most common etiology, accounting for 33.6%, which differs from Western countries, where non-alcoholic fatty liver disease (NAFLD) and alcohol-related liver disease are the most common etiologies.[1-3]

The burden of cirrhosis arises not only from its high mortality rate but also from significant socioeconomic implications. In Indonesia, cirrhosis is recognized as a catastrophic disease associated with high healthcare expenditures, primarily driven by frequent hospital admissions due to complications. Patients with cirrhosis experience a lower health-related quality of life compared to the general population, largely due to its complications and end-stage cancer symptoms (including pain, nausea, and depression). Therefore, comprehensive and effective management of cirrhosis is essential.[3,4]

Decompensated cirrhosis has a mortality rate five times higher than that of compensated cirrhosis, highlighting the need for early identification and prevention of disease progression. The transition from compensated to decompensated cirrhosis is primarily driven by portal hypertension, resulting from architectural distortion that increases hepatic vascular resistance. Portal hypertension (PH) is defined as an increase in portal venous pressure greater than 5 mmHg, while values of 10 mmHg or more indicate clinically significant portal hypertension (CSPH), which is associated with decompensation risks, including esophageal varices, hepatic encephalopathy, and ascites. Thus, early diagnosis of CSPH is crucial for improving patient care and preventing liver decompensation.[5,6]

Traditionally, the gold standard for diagnosing portal hypertension has been the direct measurement of the hepatic venous pressure gradient (HVPG) via hepatic venous catheterization, an invasive procedure with inherent risks. However, this procedure is limited to specialized centers, which are few in Indonesia. Recently, there has been growing interest in non-invasive techniques for evaluating portal hypertension, which could either replace or complement invasive methods. Non-invasive assessments are vital for identifying CSPH patients who require further evaluation or referral to a hepatologist and can also help rule out CSPH to avoid unnecessary examinations.[5]

Non-invasive assessments of portal hypertension can be blood-based or imaging-based. Blood-based tests may include single

serum biomarkers or composite scores. Single serum biomarkers consist of platelet count, alanine transaminase (ALT), aspartate transaminase (AST), albumin, gamma-glutamyl transferase (GGT), bilirubin, and international normalized ratio (INR), while composite scores include FIB-4, the index for liver fibrosis, and APRI. Single serum tests alone have limited predictive value and should be combined with other assessments. For instance, platelet count and FIB-4 alone have areas under the receiver operating characteristic curve (AUROC) of 0.72 and 0.75, respectively, in predicting CSPH. In contrast, the combination of FIB-4 and liver stiffness measurement (LSM) shows improved performance with an AUROC of 0.82. Recently, Rabiee et al. introduced a new scoring system, FIB-4+, which combines FIB-4 and albumin. This score is particularly useful when transient elastography (TE) is not accessible and has shown an area under the curve (AUC) of 0.8 in predicting CSPH.[5,7-9]

Compared to blood-based tests, certain imaging-based tests exhibit better predictive performance for CSPH. The most common and widely used imaging technique is LSM by transient elastography (TE). Most guidelines recommend LSM by TE and platelet count as validated non-invasive methods to rule in and rule out CSPH. Baveno VII and the American Association for the Study of Liver Diseases (AASLD) suggest using LSM < 15 kPa and platelets > 150,000/mm³ to exclude CSPH. CSPH can be identified using three criteria: (1) LSM > 25 kPa, (2) LSM between 20 and 25 kPa with platelets < 150,000/mm³, or (3) LSM between 15 and 20 kPa with a platelet count < 110,000/mm³. The latest method is spleen stiffness measurement (SSM), which is considered a good parameter for CSPH due to increased splenic vein pressure during portal hypertension. Baveno VII also endorses SSM by TE for CSPH due to viral hepatitis, using SSM < 21 kPa and > 50 kPa to rule out and rule in CSPH, respectively. In addition to identifying CSPH, esophageal varices should be detected early in cirrhotic patients. Both LSM and SSM can be utilized to screen patients who should undergo endoscopic evaluation. The Baveno VII criteria recommend LSM ≥ 20 kPa or a platelet count ≤ 150,000/mm³ to select patients for endoscopy, while SSM ≤ 40 kPa can identify those at low risk for high-risk varices.[6,9]

In this issue, Nababan et al. validated the use of SSM for screening high-risk esophageal varices using a 100 Hz spleen-dedicated TE probe. Their study recommends employing dual cut-offs to rule out (SSM < 20 kPa) or rule in (SSM > 70 kPa) the presence of high-risk varices in cirrhotic patients. Compared to the Baveno VII criteria, which uses a single cut-off (SSM < 40 kPa), these dual cut-offs demonstrate better performance. Specifically, the SSM cut-off value of 20 kPa had a sensitivity of 98.1% with a negative predictive value (NPV) of 87.5%, while the cut-off value of 70 kPa had a specificity of 82.4% with a positive predictive value (PPV) of 81.3%. In contrast, SSM with a cut-off value of 40 kPa had a sensitivity of 86.5%, specificity of 55.9%, PPV of 75%, and NPV of 73.1%. This promising result is particularly beneficial for identifying appropriate candidates for endoscopy, especially in Indonesia, where the availability of endoscopy centers is limited.[11]

In conclusion, non-invasive tests can effectively predict CSPH and esophagus varices, though they should be combined to enhance their predictive value. It is important to acknowledge the limitations of non-invasive tests. Currently, LSM by TE combined with platelet count remains the best non-invasive method for evaluating CSPH.

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