

New practice guidelines on risk stratification and management of portal hypertension: towards a personalized multidisciplinary approach

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The American Association for the Study of Liver Diseases (AASLD) has recently released the practice guidance on portal hypertension (PH) and varices in cirrhosis, offering a comprehensive framework for management of PH in chronic liver disease (1). By emphasizing early intervention with non-selective beta-blockers (NSBBs), particularly carvedilol, the guidance aims to prevent disease decompensation, enhance survival rates, and improve patient quality of life. Although there are some minor pragmatic differences, the AASLD goals align with those of the Baveno VII Consensus (2) on the relevance and use of non-invasive tests in the field of PH. AASLD and Baveno VII both recognize the critical importance of stratifying the risk of decompensation in patients with compensated advanced chronic liver disease (cACLD) using noninvasive diagnostic methods. Clinically significant portal hypertension (CSPH) is identified as the main driver of decompensation risk. Although the hepatic venous pressure gradient (HVPG) measurement is the gold standard for diagnosing CSPH, its invasiveness limits widespread use (3). Therefore, both guidelines recommend utilizing liver

stiffness measurement (LSM) via transient elastography (TE) in combination with platelet counts to diagnose CSPH.

According to AASLD and the Baveno VII "rule of five", patients are at significant risk (>60%) for CSPH with LSM values greater than 25 kPa, or in those with LSM between 20 and 25 kPa accompanied by platelet counts below 150×10°/L, or LSM between 15 and 20 kPa with platelet counts under 110×10°/L. While any of these combinations can be used to diagnose CSPH according to AASLD, Baveno VII suggests to use only LSM above 25 kPa to rule-in CSPH (4). Indeed, LSM values between 15 and 25 kPa are considered indeterminate, a "gray zone", representing 40–60% of cACLD patients who would require further testing through HVPG and/or endoscopy.

To reduce diagnostic uncertainty, Baveno VII incorporates spleen stiffness measurement (SSM) into the diagnostic algorithm, suggesting that values <21 kPa rule out CSPH and values >50 kPa rule in CSPH. In fact, SSM has become increasingly valuable as a non-invasive method (4). Studies show that SSM improves diagnostic accuracy in

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identifying CSPH when combined with LSM and platelet count (5), leading to a significant reduction in the number of patients in the gray zone and, most importantly, to a significant reduction of the number of decompensation events in the gray zone of the Baveno VII. These data were confirmed in a recent individual patient data meta-analysis (6), as SSM-based algorithms showed a positive predictive value (PPV) and negative predictive value (NPV) above 90% for accurately classifying CSPH, highlighting SSM's potential in confirming or excluding CSPH and reducing diagnostic uncertainty. Differently from Baveno VII criteria, AASLD's guidance is more restrained regarding SSM integration, due to the high technical failure rates and the validation on only patients with viral etiology.

Technological advancements have addressed previous technical issues with SSM. The development of a new spleen-dedicated TE module (SSM 100 Hz) has overcome the problem of a ceiling threshold of 75 kPa and has led to a significant reduction of the technical failure rate from more than 20% to less than 5–10% (7). This technique was recently validated in a prospective multicentric population with contemporary etiologies, including metabolic-associated steatotic liver disease (MASLD), showing high feasibility and reliability, with SSM-based model achieving a higher area under the curve (AUC) than the ANTICIPATE NASH model (8).

Both AASLD and Baveno VII acknowledge that an SSM value of ≤40–46 kPa can rule out the presence of varices needing treatment (VNT) in patients who would otherwise require screening endoscopy per Baveno VI criteria (9) (LSM ≥20 kPa, platelets <150 K/mm³) (10). This could potentially spare an additional 20–25% of endoscopies for variceal detection, reducing patient burden and healthcare costs (10). Given the high burden of PH complications, innovative non-invasive methods are fundamental to enhance risk stratification via CSPH diagnosis, advancing personalized care for patients with liver disease. Novel evidence show that SSM is a valuable tool that should be integrated in diagnostic algorithms.

A significant paradigm shift in the AASLD guidance is the proactive use of NSBBs to prevent decompensation. AASLD, adopting the insights given by the PREDESCI trial (11), and in line with the Baveno VII consensus, recommends NSBB therapy in patients with CSPH to portal pressure and prevent complications such as ascites. The AASLD's recommendation aligns with studies indicating that early NSBB intervention can significantly lower decompensation rates and improve survival outcomes (12).

Additionally, respiratory infections remain the most common bacterial complications in acute variceal bleeding (AVB) patients, occurring early after admission and often associated with invasive procedures like nasogastric tube placement and orotracheal intubation (13). These infections significantly worsen prognosis, particularly in patients with liver failure, highlighting the need to minimize unnecessary invasive interventions. Despite current antibiotic prophylaxis protocols, nearly 20% of patients develop infections, with high rates of antibiotic resistance (13). This emphasizes the pressing need to revise strategies and tailor prophylaxis to high-risk patients.

Another fundamental topic addressed by the guidelines is the role pre-emptive transjugular intrahepatic portosystemic shunt (TIPS) in selected patients, specifically patients with Child-Turcotte-Pugh (CTP) class B score >7 with active bleeding on endoscopy (despite vasoactive drugs) and CTP class C score 10-13. This is the main novelty in variceal bleeding management and the evidence supporting this indication is strong (14), but data on feasibility and implementation in clinical practice are limited. The indication to insert a TIPS should always be contextualized to a specific patient and the disease burden (age, frailty, co-morbidities, heart failure, hepatocellular carcinoma presence, portal vein thrombosis, transplantation candidate etc.). Moreover, logistic and organizational barriers should be taken into account when introducing this practice changing indication.

The prevention of bleeding and rebleeding in gastric and ectopic varices is a difficult topic in the management of PH, since data from trials are extremely limited. NSBBs remain the mainstay to reduce bleeding risk, while controversary on the role of TIPS, cyanoacrylate injection and balloon-occluded retrograde transvenous obliteration is present among hepatologists (15). The combination of TIPS and/or embolization according to local expertise, patient's anatomy, and characteristics should be the best approach to find a balance between reducing rebleeding risk, worsening portal pressure and liver function, other than decreasing the incidence of hepatic encephalopathy at follow-up. Therefore, at the moment, a multidisciplinary approach and discussion at a case-by-case level, is fundamental to appropriately manage this condition.

In conclusion, the new AASLD guidelines on managing PH and varices in cirrhosis emphasize early intervention and non-invasive diagnostic methods to improve patient outcomes. The guidelines fully adopt the insights on the early use of NSBBs, particularly carvedilol, to prevent

disease progression, enhance survival and improving the quality of life for patients. For diagnosing clinically significant PH, the guidelines highlight the use of LSM and platelet counts. While the AASLD is cautious about incorporating SSM due to technical challenges, advancements in technology have improved its reliability. The guidelines also address the importance of infections in patients with AVB, suggesting a need for revised treatment strategies. Additionally, they recommend the use of pre-emptive TIPS for high-risk patients, though its implementation in real-life clinical practice is work in progress at the moment. Overall, a personalized multidisciplinary approach to managing PH and varices, is recommended to enhance patient care and outcomes.

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