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Editorial

Baveno VII criteria to predict decompensation in compensated advanced chronic liver disease: Still some shades of grey

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For over six decades, hepatic venous pressure gradient (HVPG) has been the established method to assess accurately portal pressure in patients with cirrhosis¹⁻³ and the best predictor of decompensation in compensated patients.⁴ Given its invasive nature and reduced accessibility in most centers, HVPG is limited in its widespread applicability. The appearance of noninvasive tests (NITs), most notably, transient elastography,⁵ catapulted these methods from diagnostic and staging tools to prognostic markers for the evaluation of portal hypertension. In the previous Baveno VI, NIT criteria were defined to stratify patients with high-risk varices, sparing endoscopies.⁶ The most recent Baveno VII took the role of NITs in patients with clinically significant portal hypertension (CSPH) one step further by defining cut-offs for the presence of CSPH and prognosis, risk stratification and indication for start of beta-blocker therapy.⁷

In a recent issue of *Clinical and Molecular Hepatology*, Wong et al.⁸ reported, in a retrospective cohort study, that one-third of compensated advanced chronic liver disease (cACLD)

patients fulfilled the non-invasive criteria of CSPH defined in the Baveno VII Consensus Workshop.⁷ These criteria had yet to be evaluated to predict the risk of decompensation, making this a very timely study. The authors found that, although the noninvasive assessment of CSPH predicts first liver decompensation (variceal bleeding, clinically overt ascites and overt hepatic encephalopathy), and the need for non-selective beta-blocker (NSBB) in cACLD patients, for patients in the category “probable CSPH” these criteria were suboptimal to predict decompensation in cACLD patients. Over three-fourths of the patients included in this multicentre study had treated hepatitis B or C-associated cACLD. In this study, the Baveno VII criteria to define CSPH (liver stiffness measurement [LSM] ≥ 25 kPa) and exclude it (LSM < 15 kPa and platelet count [PLT] $\geq 150 \times 10^9/L$) were used.⁷ Grey zones were classified into two groups: (high – LSM between 20–25 kPa and PLT $< 150 \times 10^9/L$, or LSM between 15–20 kPa and PLT $< 110 \times 10^9/L$, or low – defined as the remaining patients within the grey zone).⁷ Within a median follow-up of 40 months (30–52), among the 1,159 cACLD patients, 7.2% developed a first decompensation (ascites, variceal bleeding or hepatic encephalopathy), 5.8% hepatocellular carcinoma and 4.4%

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died. Decision curve analysis to assess various screening strategies to stratify patients for NSBB to prevent decompensation showed treating definite CSPH (LSM ≥ 25 kPa) as a superior strategy was to “treating probable CSPH” and “treating any varices” to initiate NSBB. The number needed to treat was 27 and 50, at treatment thresholds of 5% and 10%, respectively.⁸

The Baveno VII consensus cut-offs were based on previous studies, such as the ANTICIPATE study which showed that using NITs, namely LSM combined with PLT showed an excellent discriminative value (AUC, 0.85) in patients with Child-Pugh A compensated cirrhosis.⁹ A subsequent study including more patients with non-alcoholic steatohepatitis (NASH) demonstrated that a LSM ≥ 25 kPa is sufficient to rule in CSPH in most aetiologies, including nonobese patients with NASH, but not in obese patients with NASH.¹⁰ The “rule of five” for LSM, at 5–10–15–20–25 kPa, is a tool to stratify the risk of liver-related events, and LSM alone or in combination with PLT, was presented at the recent Baveno VII meeting, and can be used to rule-in and rule-out cACLD and CSPH, as well as to rule-out high-risk varices.⁷ During the preparation for the Baveno VII consensus, an individual patient data meta-analysis was performed in patients with cACLD after hepatitis C virus (HCV) eradication, with paired HVPG and LSM, and recently published.¹¹ Regarding the association between NITs and HVPG, a stronger correlation between LSM and HVPG was observed after HCV cure than in patients with active HCV infection, and similar for PLT and HVPG.¹¹ Furthermore, LSM/PLT ratio for CSPH was comparable or tended to be even better after HCV cure compared to pre-treatment (AUC 0.753 vs. 0.800 for PLT, 0.831 vs. 0.837 for LSM, and 0.871 vs. 0.884 for both).¹¹ The authors applied these criteria for LSM and PLT to predict decompensation in a validation cohort of cACLD patients. The 3-year decompensation risk was 0% in patients who met the LSM < 12 kPa and PLT > 150 g/L criteria. In patients with LSM ≥ 25 kPa, the 3-year decompensation risk was 9.6%. Among the 40.7% between these cut-offs, only 1.3% developed a decompensation.¹¹

There are several limitations of the study by Wong et al.⁸ Among these, are the variability in patients’ characteristics and clinical practices across the different institutions, the ret-

rospective nature of the study introduces particularly information bias, not accounting for missing information in patients’ records. As the authors mentioned over 75% of the patients included had treated viral cACLD, the applicability of these criteria for patients with other aetiologies remains unclear. In this study, the non-viral aetiology, such as alcohol- or metabolic-related, was identified as one driving factor of liver decompensation, which is unsurprising. The study leaves questions regarding the role “active versus treated disease”, regarding the applicability of the Baveno VII criteria.

The study by Wong et al.⁸ has highlighted the need to better stratify the 40–50% of cACLD patients that belong to the “grey zone” of LSM 15–25 kPa for CSPH according to the Baveno VII criteria. In fact, pilot data from a recent retrospective study, using an algorithm combining spleen stiffness measurement (cut-off $>/< 40$ kPa) with the latest rule in and rule out CSPH criteria (LSM ≤ 15 kPa + PLT ≥ 150 g/L to rule out CSPH and LSM > 25 kPa to rule in CSPH), reduced the grey zone from 40–60% to 7–15%. All first decompensation events occurred in the “rule-in” zone of the model including spleen stiffness measurement.¹² Besides combining with other tools to refine the patients at risk, these criteria require validation in patients with nonviral causes for cACLD, particularly in obese NASH patients, where LSM is not as accurate.¹⁰ Additionally, the role cofactors, such as obesity and diabetes, play in disease progression and LSMs values is a matter of further investigation. Apart from expanding NITs in different aetiologies,¹³ there is a need for further validate NITs other than transient elastography in cACLD. Another point to explore is the validation of the use of deltas of LSM alone or in combination with other NITs, such as Fibrosis-4 index, and which reduction in stiffness, constitutes an improvement with clinical significance. Recent data has shown that a percentage drop in stiffness, 10% or 20%, can help predict liver-related events.^{14,15} Until date, very few studies have analysed the use of NITs alone or in combination with other markers, to evaluate response to beta-blocker therapy.^{16,17} Despite the grey areas that remain, the recent Baveno VII criteria have sent the ball rolling to expand the role of NITs in the clinical management of patients, solidifying their crucial role in patients with cACLD.

Abbreviations:

cACLD, compensated advanced chronic liver disease; CSPH, clinically significant portal hypertension; HCV, hepatitis C virus; HVPG, hepatic venous pressure gradient; LSM, liver stiffness measurement; NASH, non-alcoholic steatohepatitis; NIT, noninvasive test; NSBB, non-selective beta-blocker; PLT, platelet count

Conflicts of Interest

The author has no conflicts to disclose.

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