



Editorial

The cutoff of transient elastography for the evaluation of portal hypertension should be different according to the etiology?

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Portal hypertension (PH) is a major consequence of liver tissue fibrogenesis¹ that results in serious complications such as variceal bleeding, ascites, and hepatic encephalopathy among patients with liver cirrhosis.² Hence, PH is responsible for significant morbidity and mortality, particularly among patients with decompensated cirrhosis.^{3,4} The hepatic venous pressure gradient (HVPG), the gradient between wedged (i.e., balloon-occluded) and free hepatic venous pressure, is considered the reference standard for assessing the degree of PH. Thus, clinically significant PH, usually defined as an HVPG of ≥ 10 mmHg, is associated with the formation of esophageal varices and with a poor prognosis.⁵⁻⁸ However, the routine assessment of HVPG in the clinical setting is limited by its invasiveness and the need for expertise and specialized equipment such as an angio-intervention unit. Thus, alternative approaches with acceptable diagnostic performance are needed for clinicians to noninvasively assess PH in patients with cirrhosis.

Recently, accumulating evidence has suggested that liver stiffness (LS) assessed using transient elastography (TE) can adequately reflect the findings of HVPG, indicating that it is a useful modality for evaluating PH and the resultant cirrhotic complications.⁹⁻¹⁵ However, TE is not sufficiently accurate to replace HVPG due to its insufficient sensitivity and specificity.¹⁶ Furthermore, TE has limitations for clinical application because of the wide range of cutoff values (range, 13.9–21.5 kPa) and variability in performance among studies (area under the receiver operating characteristic curve, 0.76–0.85).^{10,17,18} Recently, Ryu et al.¹⁹ evaluated the correlation between LS, LS to platelet ratio (LPR), LS–spleen diameter-to-platelet ratio score (LSPS), and HVPG according to the etiology of cirrhosis (alcoholic cirrhosis vs. viral cirrhosis).

According to the Baveno VI recommendations, an LS cutoff of 21 kPa can be used to confirm the presence of clinically significant PH.^{11,20} However, most evidence to support this recommendation was based on studies that had recruited patients with viral cirrhosis. Ryu et al.¹⁹ reported a higher LS value in patients with alcoholic cirrhosis than in those with viral cirrhosis (43.5. vs. 32.0 kPa,

Abbreviations:

HVPG, hepatic venous pressure gradient; LPR, liver stiffness to platelet ratio; LS, liver stiffness; LSPS, liver stiffness–spleen diameter-to-platelet ratio score; PH, portal hypertension; PPV, positive predictive value; TE, transient elastography

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$P < 0.001$), whereas there were no significant differences in the LPR or LSPS between the two groups. Ryu et al.¹⁹ also suggested an LS cutoff value of 32.2 kPa with a positive predictive value (PPV) of 94.5% to predict an HVPG ≥ 10 mmHg and an LS cutoff value of 36.6 kPa with a PPV of 91.0% to predict an HVPG > 12 mmHg. However, there are several considerations when interpreting these results.

First, while the hypothesis that the higher the LS value, the worse the prognosis might be generally reasonable, the association between the LS value and fibrotic burden might be non-linear. Furthermore, the correlation between the LS value and the risk of PH-related complications might be even more nonlinear, given that LS is primarily a fibrosis-marker and not a hemodynamic parameter. In a similar context, the measurement of spleen stiffness by ultrasound seemed to at least partially overcome the limitations associated with the LS value in the evaluation of PH.²¹ In contrast, Ryu et al.¹⁹ showed that the addition of spleen diameter and/or platelet count did not improve the predictive performance compared to that of the LS value alone. Thus, further studies to evaluate the role of other ancillary methods based on laboratory, ultrasonography, and other markers are required. Second, the prognostic performance of alcoholic cirrhosis-specific LS cutoffs should be validated in further studies in which the cumulative risk of PH-related complications, such as variceal hemorrhage, hepatorenal syndrome, hepatic encephalopathy, and hospital admission for other PH-related complications, should be assessed using longitudinal follow-up. Lastly, Ryu et al.¹⁹ suggested several hypotheses explaining their observation: the difference in the spatial distribution of fibrosis, with perisinusoidal fibrosis being more frequent, and concomitant necro-inflammation with steatosis in alcoholic cirrhosis. However, the exact mechanism underlying the increase in LS, the degree of increment in the LS value, and the way to adjust for such microscopic milieus in alcoholic cirrhosis remain to be determined.

In conclusion, a relatively higher LS value should be applied to predict clinically significant PH in patients with alcoholic cirrhosis than in patients with viral cirrhosis. However, since the severity of PH is more dependent on the amount of portal blood inflow and peripheral hemodynamic changes than on the stiffness of the hepatic parenchyma, further studies on ways to assess PH non-invasively are required.

Conflicts of Interest

The author has no conflicts to disclose.

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