Spleen Stiffness: The "New Kid on the Block" in the Diagnosis of Clinical Significant Portal Hypertension

Measurement of hepatic venous pressure gradient (HVPG) is considered as the "gold standard" in the evaluation of portal hypertension (PH) in patients with liver cirrhosis.[1] However, it involves performing an invasive test not available in most centers.

Clinically significant portal hypertension (CSPH) (HVPG ≥ 10 mmHg) is considered the cutoff point from which clinical complications such as ascites may appear.[1] Liver stiffness measurement (LSM) has been able to detect patients with CSPH.[2] Indeed, the last Baveno VII consensus determined that with a LSM cut-off of 25 KPa we could assume the presence of CSPH and with LSM ≤ 15 kPa & platelet count ≥ 150 x 109/L we could rule-out CSPH in most etiologies.[3]

Even so, there is still a grey area in which LSM is not entirely useful for the diagnosis of CSPH. Spleen stiffness measurement (SSM) can capture dynamic component of portal hypertension. Passive congestion of the spleen leads to an increase in size and stiffness of this organ, aggravated by an increased splenic arterial flow. Previous studies have detected good correlation between SSM and HVPG (r = 0.885, $P = 0.0001$).[4–6] Thus, more high-quality prospective studies are required to evaluate the role of SSM in predicting portal hypertension.

On the other hand, considering specifically SSM measured by Fibroscan® most studies have used de 50 Hz probe which was initially designed for performing LSM (maximal value of 75 kPa for LSM). Recently, the novel spleen probe (100 Hz) has been introduced and allows to measure SSM values up to 100 kPa. However, there are few studies in the literature evaluating the correlation between SSM and HVPG with this new probe and its ability to predict CSPH. Similarly, it is necessary to determine which are the best cut-off points to detect CSPH with this new probe. The recent evidence suggests that it complements the information and improves the performance of LSM, both in the prediction of high-risk varices and in the stratification of the risk of decompensation and development of hepatocellular carcinoma.[7–9] Besides, it has a potential use even in the evaluation of the therapeutic response.[10]

Finally, current guidelines suggest SSM could be used as an additional measure to LSM that could improve risk stratification for high-risk varices and CSPH.[11]

In this issue, Lantinga *et al.* propose to determine the SSM cut-off value to identify the presence of probable CSPH in a cohort of patients with liver diseases and to identify factors associated with SSM failure in real-world practice.

This study includes 185 patients with potential intrinsic liver disease, successful SSM and LSM were obtained in 118. Mean age was 53 and 53% were male. Main etiology of liver disease was viral hepatitis, 31% had liver cirrhosis and 38% had previously diagnosed signs of portal hypertension.

Applicability was moderate (70%) for SSM and high (97.7%) for LSM. Stefanescu *et al.* and Rigamonti *et al.*[12,13] have reported higher success rates for SSM. Probably this is because this cohort includes a small proportion of patients with splenomegaly (21%). Previously commented studies have shown that the absence of splenomegaly significantly decreases the reproducibility of the measurement.[12,13] Indeed, in this study the multivariate analysis showed that the only factor related with SSM failure was spleen size (odds ratio [OR] 0.66 increment per cm, 95% CI 0.52–0.82, $P < 0.001$).

To note, body mass index was not associated with SSM failure in this study. Overweigh slightly but not significantly reduced the reproducibility of the technique in the study of Rigamonti *et al.*[13] We believe that more studies are ongoing to clarify this fact and to assess the need of an XL 100 Hz probe in the overweight population.

In the global population included in the study median SSM was 23.8 kPa. In patients without liver cirrhosis, median SSM was 17.7 kPa, very similar with normal values reported in the study of Rigamonti *et al.* that were on average 16.1 KPa (14–18K).[13] In patients with liver cirrhosis, median SSM was 46.7 kPa [34.8–60.6 kPa], very similar also than previously reported results with the 50 Hz probe.[14]

The prevalence of CSPH considering clinical, ultrasound and LSM signs was 41%. As expected patients with CSPH had more advanced liver disease. There was a positive correlation between SSM and the presence of probable CSPH, (rpb = 0.61, n = 118, $P < 0.001$). The optimal cut-off value for spleen stiffness to detect probable CSPH in the total group of patients was > 26.5 kPa with high sensitivity and specificity. In patients with LSM ≥ 10 KPa the cut-off value was higher as 41.5 kPa with high sensitivity and specificity. Authors didn't find differences in the performance of LSM and SSM for detecting CSPH but they didn't combine them to detect CSPH. Previous reported cut-off values to detect CSPH are higher,[4,15,16] probably because were only including patients with advanced liver

Abbreviations: cACLD: Compensated advanced chronic liver disease; CSPH: Clinical significant portal hypertension; HVPG: Hepatic venous pressure gradient; LSM: Liver stiffness measurement; SSM: Spleen stiffness measurement

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disease. In fact, the cut-off point obtained in the population with LSM ≥ 10 KPa is more consistent with previously published studies.[4,15–17] In patients without advanced liver disease SSM is a tool of dubious utility except in very selected cases. Nevertheless, more prospective studies with the novel probe (100 Hz) are needed to evaluate the ability of SSM to predict CSPH in the compensated advanced chronic liver disease (cACLD) and to evaluate and establish the role of SSM in the algorithm of noninvasive evaluation of portal hypertension. Besides, more studies are needed to validate its usefulness considering different etiologies the or ethnicities.

It is specially necessary to assess its applicability in patients with fatty metabolic liver disease due to its increased prevalence and the implicit limitations of noninvasive techniques due to overweight. Moreover, long-term prospective studies that allow us to determinate the prognosis of liver disease with this new probe are essential.

It is very clear that we have "a new kid on the block" in the noninvasive diagnosis of CSPH that improves the performance of LSM in these patients. The spread of this technology should impact positively in the evaluation of CSPH in all patients with advanced liver disease.

Editorial

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