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INVITED COMMENTARY

Spleen Stiffness Measurement in Metabolic Dysfunction-Associated Steatotic Liver Disease—Value Added or Work in Progress?

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Abbreviations

MASLD	Metabolic dysfunction-associated steatotic liver disease
CSPH	Clinically significant portal hypertension
HVPG	Hepatic portal venous gradient
LSM	Liver stiffness measurement
TE	Transient elastography
NIT	Noninvasive test
cACLD	Compensated advanced chronic liver disease
SSM	Spleen stiffness measurement
NPV	Negative predictive value
PPV	Positive predictive value

Metabolic dysfunction-associated steatotic liver disease (MASLD), defined as hepatic steatosis associated with the metabolic syndrome, is of increasing global prevalence and importance due to its many consequent morbidities. MASLD is characterized by several clinical milestones that predict prognosis. Compared with patients with none—mild liver fibrosis (F0-2), those with advanced fibrosis (≥ F3) or cirrhosis (F4) have a progressively higher risk of liver-related complications [1]. Once cirrhosis develops, the presence of clinically significant portal hypertension [CSPH; i.e., hepatic portal venous gradient (HVPG) ≥ 10 mmHg] is associated with morbid complications such as esophageal varices, variceal bleeding, and ascites [2]. Thus, determining the disease stage has important implications for management, including informing decisions on when to initiate liver-directed pharmacotherapy (based on liver fibrosis stage), initiate hepatocellular carcinoma surveillance (based on the development of cirrhosis), and performing variceal screening (based on development of portal hypertension) [3].

In hepatology, a field with strong histology-centric roots, the validation of liver stiffness measurement (LSM) determined by transient elastography (TE) as a noninvasive test (NIT) to estimate liver fibrosis was a major paradigm shift in the management of chronic liver disorders [4]. Yet, it is often difficult in clinical practice to precisely determine where a patient is along the continuum of liver fibrosis. The term "compensated advanced chronic liver disease" (cACLD) is therefore used to describe the disease spectrum ranging from advanced fibrosis to compensated cirrhosis [5]. The Baveno VII consensus guidelines proposed thresholds of LSM ≤ 15 kPa plus platelet count ≥ 150×10^9/L to exclude clinically significant portal hypertension (CSPH) in patients with cACLD with sensitivity and negative predictive value (NPV) of > 90%. Furthermore, LSM ≥ 25 kPa was sufficient by itself to diagnose CSPH, defining a high-risk group of patients at risk for endoscopically identified signs of portal hypertension [5]. Importantly, these guidelines suggest that these cutoff values need validation in patients with MASLD and obesity, in whom the positive predictive value (PPV) for CSPH was only 62%, highlighting the need to define MASLD-specific thresholds to guide management decisions [6].

An extension of the concept of TE-determined LSM is noninvasive assessment of CSPH to predict esophageal

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Table 1 Potential clinical utility of spleen stiffness measurement in risk stratification of patients with MASLD for cirrhosis, clinically significant portal hypertension, and risk of esophageal varices

Liver stiffness measurement (kPa)	Spleen stiffness measurement (kPa)	Interpretation of risk
< 10	N/A	Rule out cACLD[a]
10–25	< 21	Rule out CSPH[a]
Any (or nondiagnostic)	> 21	High risk for cirrhosis, CSPH and EV
Any (or nondiagnostic)	> 40	Suspect high-risk EV

kPa kilopascal, *N/A* not applicable, *cACLD* compensated advanced chronic liver disease, *CSPH* clinically significant portal hypertension, *EV* esophageal varices, *MASLD* metabolic dysfunction-associated steatotic liver disease

[a]Endoscopy can be deferred

varices in patients with cACLD using spleen stiffness measurement (SSM), [7] based on the frequent occurrence of splenomegaly and hypersplenism in patients with CSPH. Thus, measuring SSM with TE in addition to LSM offers an additional noninvasive risk stratification tool useful for identifying patients who should benefit from endoscopic variceal screening. Though for patients with viral hepatitis and lean [Body Mass Index < 25 kg/m^2] MASLD, cutoff values of SSM < 21 kPa to rule out, and > 50 kPa to rule in CSPH, and SSM ≤ 40 kPa to rule out high-risk varices have been proposed, [5] these cutoff values have not been defined in patients with MASLD and obesity.

In this issue of *Digestive Diseases and Sciences*, Williams et al. move the field a step closer to using SSM for risk stratification of patients with MASLD and cACLD for the presence of varices [8]. They included in their study patients with MASLD who underwent simultaneous LSM and SSM; 47% of the cohort underwent endoscopy within a year to determine the presence of varices. The most important finding from this study is the validation of the previously proposed SSM cutoff of < 40 kPa as a negative predictor of high-risk varices (NPV 100%,) and SSM > 40 kPa with 100% sensitivity for identifying esophageal varices. Thus, clinicians can use the same SSM values proposed for viral hepatitis for managing patients with MASLD. Furthermore, the authors also validated the SSM ≥ 21 kPa cutoff value for detecting cirrhosis (88% PPV) and with > 96% sensitivity for cirrhosis and esophageal varices.

Yet, this study also highlights several technical and logistical challenges to the application of SSM to routine clinical practice. This study utilized a newer version of Fibroscan that is not yet widely available outside of specialized tertiary care centers. A further limitation of the current technology is the need to first identify the location of the spleen in the left upper quadrant of the abdomen with a standard ultrasound probe and then switch to measuring SSM with the M probe. This process can fail to obtain adequate SSM readings if the spleen cannot be located with the probe, which occurs more commonly when the spleen is not enlarged. A feature of the Fibroscan device called SmartExam® helps the operator obtain valid LSM readings, although this feature is not yet available for SSM. The most important limitation of SSM is that an XL+ probe that can measure SSM at greater depth in patients with truncal obesity or high body mass index is not yet available. Indeed, the authors found a high failure rate of SSM examination in almost one in five patients, which is a significant current limitation of the technology. Furthermore, practitioners seeking to incorporate SSM in clinical care need to factor in the additional cost of the equipment and special training required to perform the test.

The study by Williams et al. raises the question as to where SSM fits into the ever-expanding armamentarium of NITs for risk stratification of MASLD? For clinicians who already have the newer Fibroscan device, combining both LSM and SSM in the same examination for all patients with MASLD may provide additional diagnostic data to assist with management of patients with MASLD (Table 1). As with TE-determined LSM, obtaining SSM is safe, well tolerated, and adds only a few minutes to total testing time. Since for patients with LSM < 10 kPa, which has a high NPV for cACLD, determining SSM is unlikely to provide additional risk stratification, suggesting that SSM measurements could be deferred in such patients. Yet, for patients with LSM 10–15 kPa, in whom cACLD may be possible, or 15–25 kPa, who may have cirrhosis with or without CSPH, SSM may provide additional prognostic information regarding CSPH using the SSM cutoff < 21 kPa, providing additional support for deferral of endoscopy in some patients. For patients with MASLD and obesity in whom LSM > 25 kPa has low PPV for CSPH, SSM may again provide additional risk stratification for the presence of esophageal varices.

This study also raises several questions that will need to be addressed by future research. Portal hypertension is a dynamic process that can improve with treatment of the underlying liver disease etiology and/or by nonselective beta-blockers. With the impending availability of approved treatments for MASLD and metabolic dysfunction-associated steatohepatitis (MASH), it would be interesting to determine the impact of treatment on SSM values as a surrogate for improvement in portal hypertension. The question of

whether the rate of increase in SSM over time may identify the high-risk patients with impending decompensation also deserves attention in future studies. To further validate SSM cutoff with robust data, rigorously performed prospective studies are also needed that include patients with MASLD in whom endoscopy and SSM are performed on the same day. Finally, future studies should compare the diagnostic performance of SSM with other NITs for CSPH, such as the ANTICIPATE model (incorporating LSM, platelet count, and BMI) and the FIB-4+ model (incorporating Fibrosis-4 index and albumin) [9].

In conclusion, SSM, another NIT that improves risk stratification of patients with MASLD, is a useful adjunct to LSM. Although SSM technology is still evolving with several technological- and patient-related limitations remaining, it may be used in clinical practice to help prioritize patients suspected of having MASLD-related cACLD for endoscopic screening for esophageal varices.

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