

## EDITORIAL

## Bedside spleen stiffness measurement can be reliably performed in most cases: High applicability and reproducibility using a specific 100-Hz module on vibration-controlled transient elastography

Splenomegaly is a hallmark 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, regardless of the cause leading to the increase in portal pressure. Given the well-known limitations of liver stiffness measurement (LSM),<sup>[1]</sup> spleen stiffness measurement (SSM) using the standard liver 50-Hz module on vibration controlled transient elastography (FibroScan; Echosens) was first proposed by Stefanescu et al. in 2011<sup>[2]</sup> as a potential additional noninvasive tool (NIT) to assess the presence/absence of high-risk varices. Since the first publication, several other authors have tested SSM, showing that it correlates hepatic venous pressure gradient (HVPG) with the size of esophageal varices and with liver-related events in patients with compensated advanced chronic liver disease (cACLD).<sup>[3]</sup> In addition, and contrary to LSM changes, SSM changes correlate with changes in the HVPG on nonselective beta-blockers<sup>[4]</sup> and with changes in portal pressure gradient after TIPS.<sup>[5]</sup> Furthermore, SSM has been tested in patients with vascular liver disease<sup>[6]</sup> and myeloproliferative neoplasms (MPNs), and has proven to correlate with the presence of high-risk varices in the first, and with bone marrow fibrosis in the latter.<sup>[7]</sup> Data in these settings were generated with the standard 50-Hz module.

The observation that SSM might complement LSM to refine noninvasive stratification of risk of clinically significant portal hypertension, high-risk varices and clinical decompensation, and that it might mirror the portal pressure response to drug therapy, has led to increasing interest in this NIT.<sup>[3]</sup> The recent Baveno VII Consensus workshop on portal hypertension suggested considering using this parameter in the setting of viral cACLD to improve the performance of LSM in ruling out and ruling in portal hypertension.<sup>[8]</sup> Nonetheless, most available data on SSM are based on measurement using the liver-specific module, and as such, SSM

had to be considered an off-label method. In addition, given the anatomic characteristics of the spleen, which is a much stiffer organ as compared with the liver, SSM using the standard 50-Hz LSM module leads to measurements facing the ceiling effect (maximal value of 75 kPa for LSM). Finally, and importantly, SSM using the standard 50-Hz liver module fails in 10%–27% of cases and is almost invariably not applicable to normal size spleens.

A novel spleen-dedicated module (SSM@100 Hz), allowing measuring values up to 100 kPa, was recently introduced in the market, but data on its applicability and reproducibility were limited to one prospective study up until now.<sup>[9]</sup>

The study by Rigamonti et al.<sup>[10]</sup> overcomes this limitation by presenting data on the applicability and intra-observer and interobserver reproducibility of SSM@100 Hz in a real-life, large, bicentric cohort of patients, encompassing 1680 SSM evaluations.

The study included 297 patients with chronic liver disease (CLD), of whom about 30% had cirrhosis, 63 patients with chronic myeloproliferative neoplasms (MPNs), and 60 healthy volunteers, all of whom with normal-sized spleens. An important piece of information provided by the study regards normal values of SSM@100 Hz, which was on average 16.1 kPa, ranging from 14 to 18 kPa, which is significantly lower than that reported previously with the 50-Hz liver standard module. This information is key for the interpretation of future results.

Applicability was very high (>95% in all groups), and technical failure only occurred in 3.2% of the cases (all observed in patients with normal spleen size). This is in line with (and even smaller) than the results on failure rate provided by Stefanescu et al. in the first experience published with SSM@100 Hz in patients with cACLD (7.5%).<sup>[9]</sup> Median time for examination was 50 s, and reproducibility and interobserver agreement were overall over 90% both in patients with CLD and MPNs.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2022 The Author. *Hepatology Communications* published by Wiley Periodicals LLC on behalf of American Association for the Study of Liver Diseases.

Absence of splenomegaly significantly decreased the reproducibility and interobserver agreement of SSM in all groups; operators should be aware of this aspect and interpret results carefully in not enlarged spleens. In addition, being overweight insignificantly and moderately reduced reproducibility of SSM. This result is not surprising, as SSM@100 Hz is currently available only for the M probe, and likely only patients with an acceptably low skin-to-capsule distance were included. On the other hand, it underlines that studies in patients with obesity, in whom one expects a further increase in the variability of measurement due to a deeper located spleen, are needed. This is particularly important given the ongoing discussion regarding a potential pre-sinusoidal component of portal hypertension in patients with cACLD due to NAFLD,<sup>[11]</sup> which would not be reflected by LSM. Therefore, in this population, a SSM@100 Hz for the XL probe would be a useful development.

As for the etiology of liver disease, only 10% of the included patients had NAFLD as a cause of their liver disease; however, as stated previously, the study likely did not include obese subjects, as SSM@100 Hz is not available for the XL probe. On the other hand, 55% of the included patients had an autoimmune or cholestatic cause. LSM can be used to assess portal hypertension in this population, but SSM could provide additional data given the well-known presence of a pre-sinusoidal component of portal hypertension in this setting; future studies might focus on this aspect.

The results of the present study are helpful in setting up future studies on the several unmet needs on SSM@100 Hz. The best cutoffs for clinically significant portal hypertension, high-risk varices, prediction of clinical decompensation, and prediction of treatment response in cACLD remain to be identified and validated. Although the road to full validation is still long and will require comparison with LSM, the very short examination time, excellent applicability, and high reproducibility of this NIT proven in the study of Rigamonti et al.<sup>[10]</sup> opens the door for testing this parameter as a potential surrogate of outcomes in hepatology and potentially beyond hepatology.

## CONFLICT OF INTEREST

Nothing to report.

Annalisa Berzigotti 

*Department of Visceral Surgery and Medicine,  
Inselspital, Bern University Hospital, University  
of Bern, Bern, Switzerland*

## Correspondence

Annalisa Berzigotti, Department of Visceral  
Surgery and Medicine, Inselspital,  
Bern University Hospital, University of Bern,  
Switzerland, BHH D115, Freiburgstrasse 10,  
Bern 3010, Switzerland.  
Email: [annalisa.berzigotti@insel.ch](mailto:annalisa.berzigotti@insel.ch)

## ORCID

Annalisa Berzigotti  <https://orcid.org/0000-0003-4562-9016>

## REFERENCES

- Berzigotti A. Non-invasive evaluation of portal hypertension using ultrasound elastography. *J Hepatol.* 2017;67:399–411.
- Stefanescu H, Grigorescu M, Lupsor M, Procopet B, Maniu A, Badea R. Spleen stiffness measurement using Fibroscan for the noninvasive assessment of esophageal varices in liver cirrhosis patients. *J Gastroenterol Hepatol.* 2011;26:164–70.
- Reiberger T. The value of liver and spleen stiffness for evaluation of portal hypertension in compensated cirrhosis. *Hepatol Commun.* 2022;6:950–64.
- Marasco G, Dajti E, Ravaioli F, Alemanni LV, Capuano F, Gjini K, et al. Spleen stiffness measurement for assessing the response to beta-blockers therapy for high-risk esophageal varices patients. *Hepatol Int.* 2020;14:850–7.
- Jansen C, Moller P, Meyer C, Kolbe CC, Bogs C, Pohlmann A, et al. Increase in liver stiffness after transjugular intrahepatic portosystemic shunt is associated with inflammation and predicts mortality. *Hepatology.* 2018;67:1472–84.
- Sharma P, Mishra SR, Kumar M, Sharma BC, Sarin SK. Liver and spleen stiffness in patients with extrahepatic portal vein obstruction. *Radiology.* 2012;263:893–9.
- Iurlo A, Cattaneo D, Giunta M, Gianelli U, Consonni D, Fraquelli M, et al. Transient elastography spleen stiffness measurements in primary myelofibrosis patients: a pilot study in a single Centre. *Br J Haematol.* 2015;170:890–2.
- de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C, Baveno VII. Baveno VII—renewing consensus in portal hypertension. *J Hepatol.* 2022;76:959–74.
- Stefanescu H, Marasco G, Cales P, Fraquelli M, Rosselli M, Ganne-Carrie N, et al. A novel spleen-dedicated stiffness measurement by FibroScan(R) improves the screening of high-risk oesophageal varices. *Liver Int.* 2020;40:175–85.
- Rigamonti C, Cittone MG, Manfredi G, Sorge A, Moia RM, Patriarca A, et al. High reproducibility of spleen stiffness measurement by vibration-controlled transient elastography with a spleen-dedicated module. *Hepatol Commun.* 2022; in press.
- Baffy G, Bosch J. Overlooked subclinical portal hypertension in non-cirrhotic NAFLD: is it real and how to measure it? *J Hepatol.* 2022;76:458–63.