eGastroenterology

Spleen stiffness measurement as a non-invasive assessment in patients with portal hypertension

Xiaoming Xu,[1] Jiacheng Liu,[2] Yixuan Zhu,[3] Fajuan Rui,[1] Chao Wu,[1,2,3,4] Jie Li[1,2,3,4]

To cite: Xu X, Liu J, Zhu Y, *et al*. Spleen stiffness measurement as a non-invasive assessment in patients with portal hypertension. *eGastroenterology* 2024;**0**:e100031. doi:10.1136/egastro-2023-100031

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/egastro-2023-100031).

Received 19 September 2023
Accepted 30 November 2023

[1]Department of Infectious Diseases, Nanjing Drum Tower Hospital Clinical College of Nanjing University of Chinese Medicine, Nanjing, Jiangsu, China
[2]Department of Infectious Diseases, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing, Jiangsu, China
[3]Department of Infectious Diseases, Nanjing Drum Tower Hospital Clinical College of Nanjing Medical University, Nanjing, Jiangsu, China
[4]Institute of Viruses and Infectious Diseases, Nanjing University, Nanjing, Jiangsu, China

Correspondence to
Jie Li; lijier@nju.edu.cn

ABSTRACT

For patients with advanced chronic liver disease who are in a compensated state, the development of portal hypertension (PHT) can lead to a heightened risk of hepatic decompensation and mortality. This underscores the importance of timely and appropriate treatment to manage the condition and prevent further complications. The current gold standard procedure for determining PHT is the hepatic venous pressure gradient, but its invasiveness limits its usage in clinical practice and larger trials of novel agents. The current clinical demand for accurate, validated and non-invasive methods to assess the severity of PHT remains unmet. One potential non-invasive option is tissue elastography, which examines the elastic behaviour of tissue after a force has been applied. This method involves quantifying alterations in the biomechanical properties of the liver or spleen in patients with cirrhosis. Available methods are various, including transient elastography, shear wave elastography, acoustic radiation force impulse and magnetic resonance elastography. Importantly, the measurement of spleen stiffness appears to outperform liver stiffness as a direct and dynamic indicator of portal pressure, offering the potential to monitor PHT and evaluate improvements in PHT as a marker for clinical outcomes.

INTRODUCTION

Portal hypertension (PHT) is characterised by an abnormal elevation in the pressure difference between the portal vein and hepatic venous system.[1] It is the primary cause of the development of main complications observed in cirrhosis patients, such as variceal haemorrhage, ascites and hepatic encephalopathy, causing a high risk of mortality and morbidity. About one million deaths worldwide annually are attributable to cirrhosis, which can be a consequence of hepatitis B or C infection, alcohol misuse, non-alcoholic fatty liver disease, autoimmune liver disease and drug-related liver disease. Compared with the general population, patients with compensated cirrhosis have a fivefold increased risk of mortality, while patients with decompensated cirrhosis have a 10-fold increased risk. The overall survival rates for individuals with compensated cirrhosis are reported to be 87% at 1 year and 67% at 5 years, while the survival rates for individuals with decompensated cirrhosis are 75% at 1 year and 45% at 5 years.[2] The increased mortality risk and varying survival rates associated with compensated and decompensated cirrhosis underscore the importance of proactive management and comprehensive care for patients with this condition.

A conundrum for patients with cirrhosis and PHT remains the diagnosis during the development phase. The Baveno VI consensus guidelines[3] recommended hepatic venous pressure gradient (HVPG) as the reference standard in clinical practice. HVPG values >5 mm Hg determine PHT, and HVPG values ≥10 mm Hg correspond to the presence of clinically significant portal hypertension (CSPH).[4] Moreover, severe PHT often complicates life-threatening upper gastrointestinal bleeding when HVPG values increase above 12 mm Hg. HVPG plays a crucial role in diagnosis and prognosis of PHT; however, the invasiveness, expense and limited feasibility hinder its widespread application in clinical routine.[5] Such limitations have resulted in the advancement of non-invasive tools for assessing severity of PHT and predicting decompensation events. Among these, liver stiffness measurement (LSM) has gradually imposed itself as a widely accepted method used in the clinical evaluation of patients with PHT. However, the accuracy of its performances can be affected by certain confounding factors, such as inflammation of liver cells, liver congestion and cholestasis. Finally, increasing attempts have been made to evaluate the accuracy of spleen stiffness (SS) measurement (SSM) and establish the optimal SSM values for rule-in and rule-out PHT. More recently, SSM has been demonstrated by several elastography techniques.[6–10] Herein, we aim to provide a brief overview of the advantages and disadvantages of using SSM for the diagnosis of PHT as well as the supporting evidence.

SS MEASUREMENT

Notable technical progress has taken place in elastography, which is used to detect changes in the elasticity of the spleen, as an emerging non-invasive approach, and the superficial location of the spleen allows the possibility to obtain reliable outcomes. There are four main different types of elastography, for example, transient elastography (TE), shear wave elastography (SWE), acoustic radiation force impulse (ARFI) and magnetic resonance elastography (MRE).[11] Owing to the fact that the spleen has intrinsic elastic properties,[12] SS evaluation with elastography requires determination of normal reference interval for healthy individuals. Table 1 provides a detailed information of different techniques that are currently available for SSM and measurements in healthy subjects.[13–33]

Transient elastography

As a quantitative ultrasound-based method, TE has been validated for the diagnosis of the liver disease development in diverse populations.[34] FibroScan 630 Expert is a highly innovative device that can be applied on both LSM @50 Hz and SSM @100 Hz, approved by The United States Food and Drug Administration to facilitate routine application for detection, surveillance and prioritisation for treatment.[35] It only comes with an M probe dedicated to SSM, the technical successful rate is lower in patients with large body habitus and ascites.[36]

Shear wave elastography

There are two different techniques implemented on the basis of using high-intensity ultrasound waves, both of which can combine imaging with elastography and generally summarised under the term SWE: point SWE (p-SWE) and two-dimensional SWE (2D-SWE). SWE is integrated into high-end ultrasound devices, guiding the examiner to choose a region of interest with a high frame-rate B-mode image and can generate waves deeply within the tissue, offering the advantage of measuring stiffness even in patients with ascites.[37]

Acoustic radiation force impulse

As an effective sonographic imaging modality, ARFI can generate localised push pulses in the measuring site within the visual field. A strong wave is produced and radiates outwards from the point of stimulation, which reflects the velocity of the shear wave in a quantitative manner.[38 39]

Magnetic resonance elastography

More recently, extensive utilisation of MRE has received substantial attention for mapping the viscoelastic properties of tissues. The MRE-assessed SS has shown strong correlation with HVPG, hence indicating promising value of MRE in patients with PHT.[40 41] Despite all that, the expense, the inability of the spot measurement as well as the requirement for professional operation and formal interpretation by a radiologist restrains its clinical applicability for SS determination.

Of note, there are limitations and situations in clinical practice where SSM may not work effectively. In cases of splenic infarct, where there is an area of ischaemic necrosis in the spleen, the stiffness measurements may not accurately reflect the overall SS due to the presence of localised tissue damage. This can potentially lead to misleading results. Additionally, in the presence of splenic vein thrombosis, which is the blockage of the splenic vein by a blood clot, the blood flow in the spleen may be disrupted. This can affect the reliability of SSM, as the altered blood flow dynamics can influence the overall stiffness of the spleen.

CLINICAL APPLICATIONS OF SSM

Role in cirrhotic PHT

Predicting the presence of CSPH

SSM has been proposed as a helpful surveillance tool for the prediction of PHT and the presence of oesophageal varices (OVs) in cirrhotic patients. Table 2 shows original studies assessing the predictive performance of SSM for the detection of PHT and its progression.[6 13 36 42–49] In 2018, a meta-analysis showed the excellent accuracy of SSM in diagnosing CSPH (area under the receiver operating characteristic curve (AUROC)=0.92).[50] According to Baveno VII recommendation, TE-SSM <21 kPa and >50 kPa can be used to rule out and rule in CSPH, respectively, in patients with viral hepatitis-related compensated advanced chronic liver disease (cACLD). A recent meta-analysis included 17 studies confirmed the effectiveness of the Baveno VII algorithm in diagnosing PHT. However, it may have limitations as half of the patients had indeterminate results. Incorporating SSM into the algorithm-improved accuracy and correctly identified more patients with PHT.[51] Also, it is important to note that the validation of the best cut-off is needed, via TE @100 Hz, p-SWE and 2D-SWE.

Considering the recent finding, it is reasonable to consider that utilising composite scores or diagnostic algorithms that incorporate both SSM and LSM could potentially improve the accuracy of PHT prediction. Jansen *et al*[52] found that the patients with a 2D-SWE-LSM ≥16 kPa had a high risk of having CSPH. They elaborated an algorithm combining LSM and SSM to detect CSPH with a high accuracy of prediction. 2D-SWE-SSM of <26.6 kPa was able to rule out CSPH in patients with a 2D-SWE-LSM <16 kPa, while ≥26.6 kPa ruled in CSPH (98.6% sensitivity, 70.3% specificity). The authors optimise the prediction model in further study, 2D-SWE-LSM >38 kPa as well as 2D-SWE-LSM ≤38 kPa and 2D-SWE-SSM >27.9 kPa sequentially can improve the prediction power of confirming the presence of CSPH (100% sensitivity, 60% specificity).

As evidence has accumulated,[53–57] SSM appears to be a superior biomarker of PHT to LSM. Consensually, it was found that SSM and the full range of HVPG values were strongly correlated, as demonstrated in the influential paper by Colecchia *et al*.[46] This may result from the fact

Table 1 SSM in healthy subjects

Elastography technique		Machine name	Study participants	Number of healthy volunteers	Age	Gender(M/F)	SS	Reference
Transient elastography		FibroScan	Adults	17	28 (25–33)	5/12	17.8 kPa (6.9–42.08)	13
		FibroScan	Adults	50	28.6±8.5 (16–50)	30/20	16.0±3.0 kPa (10.5–19.8)	14
		FibroScan	Adults	40	26.98±5.16	N/A	19.41±3.63 kPa	15
Shear wave elastography	SWE	SuperSonic Imagine SA	Adults	59	36 (21–80)	25/34	16.6±2.5 kPa	16
		SuperSonic Imagine SA	Adults	171	40.6±10.8	68/103	17.3±2.6 kPa (8.05–24.9)	17
		G4 xMATRIX iU22	Children	146	7.47±3.39 (2–15)	100/46	6.1±3.6 kPa (0.8–20.4)	18
		Aplio 500 Platinum	Children	37	11.6±4.9 (0.5–18)	19/18	16.8 kPa (1.6–22.8)	19
	p-SWE	Philips Affiniti 70	Adults	100	46±18 (18–87)	49/51	18.14±3.08 kPa (12.66–24.88)	20
		Siemens Acuson S2000	Adults	92	42.6±12.0	67/25	From 2.39±0.34 m/s to 2.49±0.42 m/s	21
		Siemens Acuson S2000	Children	38	8.07±0.72	17/21	2.59±0.14 m/s	22
	2D-SWE	Logiq E9 XDclear	Adults	65	41.25±13.77 (18–87)	31/34	13.82±2.91 kPa	23
Acoustic radiation force impulse		Siemens Acuson S2000	Adults	16	34 (24–56)	7/9	2.16 m/s (1.99–2.26)	24
		Siemens Acuson S2000	Adults	25	32.3 (22.1–63.0)	11/14	2.46±0.35 m/s (breath hold after expiration) vs 2.66±0.36 m/s (deep inspiration)	25
		Siemens Acuson S2000	Adults	15	N/A	N/A	2.04±0.28 m/s	26
		Siemens Acuson S2000	Adults	33	N/A	N/A	2.2±0.31 m/s (1.6–3.3)	27
		Siemens Acuson S2000	Adults	20	32.9±9 (18–50)	11/9	2.27±0.35 m/s (1.57–2.83)	28
		Siemens Acuson S2000	Children	202	8.1±4.7	92/110	2.25±0.028 m/s	29
		Siemens Acuson S3000	Children	102	6±5.1 (8–17)	32/70	2.43±0.31 m/s	30
		Siemens Acuson S3000	Children	24	10.5 (5.2, 15.0)	12/12	2.53 m/s	31
Magnetic resonance elastography		Signa HDx	Adults	16	37±9 (28–56)	9/7	3.565±0.586 kPa (2.353–4.442)	32
		Signa HDx	Adults	12	37 (25–82)	9/3	3.6±0.3 kPa	32

2D-SWE, two-dimensional shear wave elastography; F, female; M, male; N/A, not applicable; p-SWE, point shear wave elastography; SS, spleen stiffness; SSM, spleen stiffness measurement; SWE, shear wave elastography.

Table 2 Performance of SSM in the diagnosis of CSPH and OVs

Author and year	Study type	Aetiology	Population	Elastography technique (Machine)	Outcome	Cut-off values	Performance	AUROC
Colecchia *et al* 2012[46]	Prospective	HCV	100	TE (FibroScan)	CSPH	Rule-in: ≥52.2 kPa Rule-out: < 40 kPa	SE: 76.9%; Sp: 97.1% SE: 98.5%; Sp: 74.3%	0.941
Takuma *et al* 2013[47]	Prospective	Mixed (HBV, HCV, alcohol, other)	62	ARFI (Siemens Acuson S2000)	CSPH	3.1 m/s	Accuracy: 80.0%; SE: 97.1%; Sp: 57.7%; PPV:75.0%; NPV: 93.7%	0.943
Zykus *et al* 2015[48]	Prospective	Mixed (HCV, Alcoholic liver disease, Cryptogenic liver disease, other)	107	TE (FibroScan)	CSPH	50.7 kPa	Accuracy: 77.7%; SE: 78.1%; Sp: 77.1%; PPV:86.2%; NPV: 65.8%	0.846
Stefanescu *et al* 2020[36]	Prospective	Mixed (HBV, HCV, alcohol, other)	260	TE (FibroScan 630 Expert：SSM@100 Hz)	CSPH	34.15 kPa	Accuracy: 85%	0.811
Stefanescu *et al* 2011[13]	Prospective	Mixed (HCV, alcohol)	191	TE (FibroScan)	OVs	46.4 kPa	Accuracy: 80.45%; SE: 83.56%; Sp: 71.43%; PPV:93.8%; NPV: 45.5%	0.781
Colecchia *et al* 2012[46]	Prospective	HCV	100	TE (FibroScan)	OVs	Rule-in: ≥55.0 kPa Rule-out: < 41.3 kPa	SE: 71.7%; Sp: 95.7% SE: 98.1%; Sp: 66.0%	0.966
Sharma *et al* 2013[49]	Prospective	Mixed (HBV, HCV, alcohol, cryptogenic)	174	TE (FibroScan)	OVs	40.8 kPa	SE: 94%; Sp: 76%; PPV:91%; NPV: 84%	0.898
Giuffrè *et al* 2020[45]	Prospective	Mixed (Viral, Alcohol abuse, others)	210	p-SWE (Philips Affiniti 70)	OVs	31 kPa	Accuracy: 76%; SE: 100%; Sp: 60%; PPV:62%; NPV: 100%	N/A
Mnif *et al* 2021[43]	Prospective	HBV	84	TE (FibroScan)	OVs	33.1 kPa	SE: 72.2%; Sp: 77.1%; PPV:51%; NPV: 63%	0.795
Hirooka *et al* 2021[44]	Retrospective	Mixed (HBV, HCV)	349	TE (FibroScan)	HRV	45 kPa	SE: 92.1%; Sp: 64.6%; PPV:47.3%; NPV: 95.9%	0.854
Tanaka *et al* 2021[6]	Prospective	Mixed (HBV, HCV)	292	TE (FibroScan)	HRV	46.4 kPa	Accuracy: 80.45%; SE: 92.3%; Sp: 72.4%; PPV:53.3%; NPV: 74.5%	0.88
Nagai *et al* 2022[42]	Prospective	Mixed (HBV, HCV, alcohol, NAFLD, IPH, other)	123	TE (FibroScan 630 Expert：SSM@100 Hz)	HRV	43.8 kPa	SE: 93.3%; Sp: 82.0%; PPV:70.0%; NPV: 96.4%	0.941

ARFI, acoustic radiation force impulse; AUROC, area under the receiver operating characteristic curve; CSPH, clinically significant portal hypertension; HBV, hepatitis B virus; HCV, hepatitis C virus; HRV, high-risk varices; IPH, idiopathic portal hypertension; NAFLD, non-alcoholic fatty liver disease; NPV, negative predictive value; OVs, oesophageal varices; PPV, positive predictive value; p-SWE, point shear wave elastography; SE, sensitivity; Sp, specificity; SSM, spleen stiffness measurement; TE, transient elastography.

that the SS is not affected by the primary aetiology agents of PHT. It is worth mentioning that SS increasement may occur earlier in patients with hepatitis B or C virus infections than liver stiffness, even when liver fibrosis remains absent.[58] Therefore, these studies justify the proposal to use SS as a more dynamic parameter for the prediction of PHT with high diagnostic performance.

Detecting oesophageal varices and avoiding esophagogastroduodenoscopies

Manatsathit *et al*[56] recently carried out a meta-analysis that compared SSM and LSM in detection of OVs. SSM also showed better performance than LSM (sensitivity: 90% vs 85%, specificity: 73% vs 64%, AUROC: 0.90 vs 0.82). Another meta-analysis including about 3952 patients from 32 studies, highlighted that SSM could be used as a preliminary screening technique to eliminate the possibility of high-risk varices (HRV) with the combined sensitivity and negative predictive value (NPV) reaching 0.87 and 0.88, respectively, thereby avoiding unnecessary esophagogastroduodenoscopies (EGDs).[59] In fact, a fairly low percentage (<5%) of patients with compensated cirrhosis develop varices needing treatment (VNT).[60] One prospective study proved that SSM may be applicable in identifying VNT. The optimal cut-off values of SSM by 2D-SWE and p-SWE were 13.2 kPa (AUROC=0.84) and 2.91 m/s (AUROC=0.90), respectively.[61] While the postulation of Baveno VI criteria (LSM <20 kPa and platelet count >150×10^9/L) have been validated in clinical practice, there still were many attempts made to improve the rate of saving EGDs. A new combination of SSM (cut-off ≤46 kPa, assessed by TE) with Baveno VI is a reliable option. The model was found to safely spare 43.8% of EGDs in the internal validation cohort, while missing less than 5% of HRV. In the prospective external validation cohort, the model would have safely spared 37.4% of EGDs, compared with only 16.5% with Baveno VI criteria alone, and no HRV would have been missed,[62] as proved to be efficient also by Wang *et al*.[63] A recent study also showed that using an SSM @100 Hz cut-off of ≤41.3 kPa (FibroScan 630 Expert) along with Baveno VI criteria can help avoid a significant number of EGDs when ruling out HRV.[36]

Estimating treatment response for CSPH

Furthermore, SSM may have major utility in monitoring response and stratifying risk following therapy on PHT. First, with the broad administration of non-selective beta-blockers (NSBB) to prevent variceal bleeding and prophylaxis failure in all patients with CSPH, the acute or chronic response to NSBB has not yet been sufficiently evaluated. Kim *et al*[64] demonstrated that the only significant predictor of haemodynamic response was dynamic changes in SSM, with a goal of reducing it by 10% or more from baseline or to 12 mm Hg or less, and there was evidence concerning its superiority over LSM in cirrhotic patients with OVs. Similarly, in another study,[65] Δ SSM ≥10% after NSBB initiation presented commendable accuracy in identifying HVPG responders (AUROC=0.973). In addition, an SSM of ≥74 KPa, as evaluated by TE, has been reported by Elba Llop *et al* that it had excellent performance on predicting poor acute response (100%

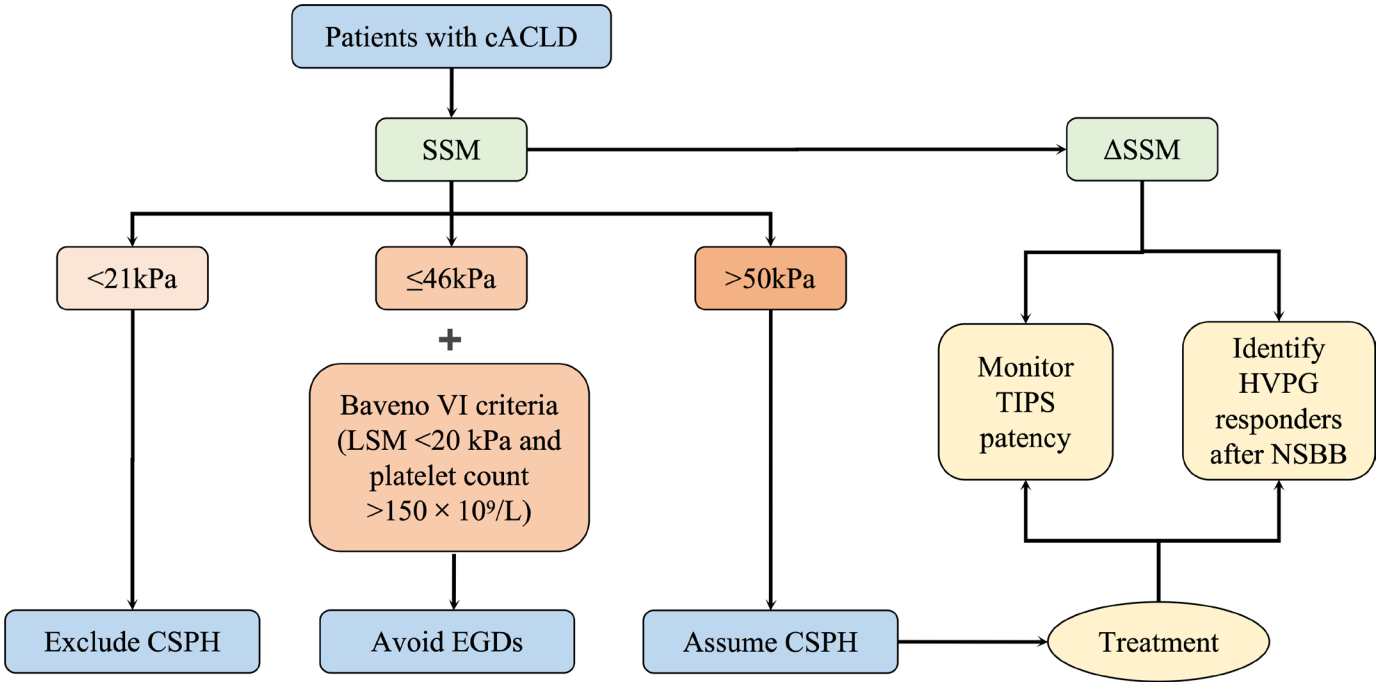

Figure 1 The suggested approach for the management of patients with compensated advanced chronic liver disease. cACLD, compensated advanced chronic liver disease; CSPH, clinically significant portal hypertension; EGDs, esophagogastroduodenoscopies; HVPG, hepatic venous pressure gradient; LSM, liver stiffness measurement; NSBB, non-selective beta-blockers; SSM, spleen stiffness measurement; TIPS, transjugular intrahepatic portosystemic shunt.

sensitivity, 60% specificity and 100% NPV) and poor chronic response (87% sensitivity, 71% specificity and 71% NPV) to beta-blockers.[66] Second, one effective way to reduce portal pressures is through transjugular intrahepatic portosystemic shunt (TIPS) intervention. An increasing body of studies[57 67–71] suggested that changes in portal pressure gradient before and after TIPS were positively correlated with SSM. However, there was little to no correlation found between LSM and these changes. The SSM value of 3.60 m/s has been proposed as the cut-off value to predict survival.[72] It is notable that increased SSM value can be an independent prognostic factor of survival after TIPS, playing a vital role in non-invasively monitoring TIPS patency and determining TIPS dysfunction.[72–75] Third, after liver transplantation, SSM decreases significantly when PHT resolves.[76 77] According to preliminary results,[78] SSM may have value for early prognosis after liver transplantation and follow-up of liver dysfunction. However, the study sample size is limited and additional research is encouraged. A suggested approach for fibrosis assessing and managing PHT in individuals with cACLD using SSM is outlined in figure 1.

Role in non-cirrhotic PHT

SSM also has emerging roles in those with non-cirrhotic portal hypertension (NCPH), for example, hepatosplenic schistosomiasis,[79] extrahepatic portal vein obstruction,[80–84] Budd-Chiari syndrome,[85] biliary atresia,[86–89] idiopathic PHT,[90] Gaucher disease,[91] etc. Together, these studies indicate that SSM is an accurate predictor of NCPH, particularly in the extrahepatic portal vein obstruction subgroup. On the other hand, data show that LSM and platelet count are not effective indicators for evaluating the risk of HRV in NCPH,[92] thus SSM could offer a chance to assess, stratify risks and monitor therapy response in patients with NCPH.

CONCLUSION

Considering the performance of SSM in several clinical scenarios, it may be reasonable to propose SSM as a screening method for identifying PHT in patients with cACLD. Confirmation of the results from preliminary studies is eagerly anticipated, along with optimisation of the accuracy of CSPH diagnosis. This could increase the number of safely spared screening endoscopies, presenting potential for clinical application in the characterisation of PHT. The use of SSM to monitor response to NSBB or TIPS and to predict prognosis after such treatments is promising and warrants further exploration through future prospective studies.

Contributors XX, JLiu: study concept and design, XX, JLiu, YZ: acquisition of data. XX, YZ and FR: drafting of the manuscript, JLi and CW critical revision of the manuscript for important intellectual content. All authors have made a significant contribution to this study and have approved the final manuscript.

Funding The work was supported in part by a grant from the National Natural Science Fund (Number 81970545;82170609), Natural Science Foundation of Shandong Province (Major Project) (Number ZR2020KH006) and Ji'nan Science and Technology Development Project (Number 2020190790).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Sanyal AJ, Bosch J, Blei A, *et al*. Portal hypertension and its complications. *Gastroenterology* 2008;134:1715–28.
2 Devarbhavi H, Asrani SK, Arab JP, *et al*. Global burden of liver disease: 2023 update. *J Hepatol* 2023;79:516–37.
3 de Franchis R. Expanding consensus in portal hypertension: report of the Baveno VI consensus workshop: Stratifying risk and individualizing care for portal hypertension. *J Hepatol* 2015;63:743–52.
4 de Franchis R, Bosch J, Garcia-Tsao G, *et al*. Renewing consensus in portal hypertension. *J Hepatol* 2022;76:959–74.
5 Leung JC-F, Loong TC-W, Pang J, *et al*. Invasive and non-invasive assessment of portal hypertension. *Hepatol Int* 2018;12(Suppl 1):44–55.
6 Tanaka T, Hirooka M, Koizumi Y, *et al*. Development of a method for measuring spleen stiffness by transient elastography using a new device and ultrasound-fusion method. *PLoS One* 2021;16:e0246315.
7 Fofiu R, Bende F, Popescu A, *et al*. Spleen and liver stiffness for predicting high-risk varices in patients with compensated liver cirrhosis. *Ultrasound Med Biol* 2021;47:76–83.
8 Liu Y, Tan H, Zhang X, *et al*. Prediction of high-risk esophageal varices in patients with chronic liver disease with point and 2d shear wave elastography: a systematic review and meta-analysis. *Eur Radiol* 2022;32:4616–27.
9 Fierbinteanu-Braticevici C, Tribus L, Peagu R, *et al*. Spleen stiffness as predictor of esophageal varices in cirrhosis of different etiologies. *Sci Rep* 2019;9:16190.
10 Abe H, Midorikawa Y, Matsumoto N, *et al*. Prediction of esophageal varices by liver and spleen MR elastography. *Eur Radiol* 2019;29:6611–9.
11 Mladenovic A, Vuppalanchi R, Desai AP. A primer to the diagnostic and clinical utility of spleen stiffness measurement in patients with chronic liver disease. Clin Liver Dis 2022;19:124–30.
12 Gibiino G, Garcovich M, Ainora ME, *et al*. Spleen ultrasound elastography: state of the art and future directions - a systematic review. *Eur Rev Med Pharmacol Sci* 2019;23:4368–81.
13 Stefanescu H, Grigorescu M, Lupsor M, *et al*. Spleen stiffness measurement using fibroscan for the noninvasive assessment of esophageal varices in liver cirrhosis patients. *J Gastroenterol Hepatol* 2011;26:164–70.
14 Sharma P, Mishra SR, Kumar M, *et al*. Liver and spleen stiffness in patients with extrahepatic portal vein obstruction. *Radiology* 2012;263:893–9.
15 Rewisha EA, Elsabaawy MM, Alsebaey A, *et al*. Evaluation of the role of liver and splenic transient elastography in chronic hepatitis C related fibrosis. *J Liver Disease Transplant* 2016;05.
16 Pawluś A, Inglot MS, Szymańska K, *et al*. Shear wave elastography of the spleen: evaluation of spleen stiffness in healthy volunteers. *Abdom Radiol* 2016;41:2169–74.

17 Leung VY, Shen J, Wong VW, *et al*. Quantitative elastography of liver fibrosis and spleen stiffness in chronic hepatitis B carriers: comparison of shear-wave elastography and transient elastography with liver biopsy correlation. *Radiology* 2013;269:910–8.
18 Bhatia A, Bhatia H, Saxena AK, *et al*. Shear wave elastography of the spleen using elastography point quantification: stiffness values in healthy children. *Abdom Radiol* 2022;47:2128–34.
19 Çalişkan E, Atay G, Kara M, *et al*. Comparative evaluation of liver, spleen, and kidney stiffness in HIV-monoinfected pediatric patients via shear wave elastography. *Turk J Med Sci* 2019;49:899–906.
20 Giuffrè M, Macor D, Masutti F, *et al*. Evaluation of spleen stiffness in healthy volunteers using point shear wave elastography. Ann Hepatol 2019;18:736–41.
21 Ferraioli G, Tinelli C, Lissandrin R, *et al*. Ultrasound point shear wave elastography assessment of liver and spleen stiffness: effect of training on repeatability of measurements. *Eur Radiol* 2014;24:1283–9.
22 Burak Özkan M, Bilgici MC, Eren E, *et al*. Diagnostic accuracy of point shear wave elastography in the detection of portal hypertension in pediatric patients. *Diagn Interv Imaging* 2018;99:151–6.
23 Albayrak E, Server S. The relationship of spleen stiffness value measured by shear wave elastography with age, gender, and spleen size in healthy volunteers. *J Med Ultrasonics* 2019;46:195–9.
24 Takuma Y, Nouso K, Morimoto Y, *et al*. Measurement of spleen stiffness by acoustic radiation force impulse imaging identifies cirrhotic patients with esophageal varices. *Gastroenterology* 2013;144:92–101.
25 Karlas T, Lindner F, Tröltzsch M, *et al*. Assessment of spleen stiffness using acoustic radiation force impulse imaging (ARFI): definition of examination standards and impact of breathing maneuvers. *Ultraschall Med* 2014;35:38–43.
26 Bota S, Sporea I, Sirli R, *et al*. Spleen assessment by acoustic radiation force impulse elastography (ARFI) for prediction of liver cirrhosis and portal hypertension. *Med Ultrason* 2010;12:213–7.
27 Cabassa P, Ravanelli M, Rossini A, *et al*. Acoustic radiation force impulse quantification of spleen elasticity for assessing liver fibrosis. *Abdom Imaging* 2015;40:738–44.
28 Grgurevic I, Cikara I, Horvat J, *et al*. Noninvasive assessment of liver fibrosis with acoustic radiation force impulse imaging: increased liver and splenic stiffness in patients with liver fibrosis and cirrhosis. *Ultraschall Med* 2011;32:160–6.
29 Lee MJ, Kim MJ, Han KH, *et al*. Age-related changes in liver, kidney, and spleen stiffness in healthy children measured with acoustic radiation force impulse imaging. *Eur J Radiol* 2013;82:e290–4.
30 Hanquinet S, Habre C, Laurent M, *et al*. Acoustic radiation force impulse imaging: normal values of spleen stiffness in healthy children. *Pediatr Radiol* 2021;51:1873–8.
31 Hartung EA, Wen J, Poznick L, *et al*. Ultrasound elastography to quantify liver disease severity in autosomal recessive polycystic kidney disease. *J Pediatr* 2019;209:107–15.
32 Mannelli L, Godfrey E, Joubert I, *et al*. MR elastography: spleen stiffness measurements in healthy volunteers--preliminary experience. Am J Roentgenol 2010;195:387–92.
33 Talwalkar JA, Yin M, Venkatesh S, *et al*. Feasibility of in vivo MR elastographic splenic stiffness measurements in the assessment of portal hypertension. *AJR Am J Roentgenol* 2009;193:122–7.
34 Uzlová N, Mejzlíková N, Fraňková S, *et al*. Transient elastography - role in the assessment of the liver disease development. *Vnitr Lek* 2018;64:916–22.
35 Bastard C, Miette V, Calès P, *et al*. A novel Fibroscan examination dedicated to spleen stiffness measurement. *Ultrasound Med Biol* 2018;44:1616–26.
36 Stefanescu H, Marasco G, Calès P, *et al*. A novel spleen-dedicated stiffness measurement by Fibroscan® improves the screening of high-risk oesophageal varices. *Liver Int* 2020;40:175–85.
37 Roccarina D, Rosselli M, Genesca J, *et al*. Elastography methods for the non-invasive assessment of portal hypertension. *Expert Rev Gastroenterol Hepatol* 2018;12:155–64.
38 Bota S, Sporea I, Şirli R, *et al*. Can ARFI elastography predict the presence of significant esophageal varices in newly diagnosed cirrhotic patients Ann Hepatol 2012;11:519–25.
39 Zhang Y, Mao DF, Zhang MW, *et al*. Clinical value of liver and spleen shear wave velocity in predicting the prognosis of patients with portal hypertension. *WJG* 2017;23:8044–52.
40 Kennedy P, Stocker D, Carbonell G, *et al*. MR elastography outperforms shear wave elastography for the diagnosis of clinically significant portal hypertension. *Eur Radiol* 2022;32:8339–49.
41 Singh R, Wilson MP, Katlariwala P, *et al*. Accuracy of liver and spleen stiffness on magnetic resonance elastography for detecting portal hypertension: a systematic review and meta-analysis. *Eur J Gastroenterol Hepatol* 2021;32:237–45.
42 Nagai K, Ogawa Y, Kobayashi T, *et al*. Gastroesophageal varices evaluation using spleen-dedicated stiffness measurement by vibration-controlled transient elastography. *JGH Open* 2022;6:11–9.
43 Mnif L, Hachicha S, Abid F, *et al*. Role of splenic and hepatic stiffness in predicting esophageal varices. *Tunis Med* 2021;99:544–51.
44 Hirooka M, Tanaka T, Koizumi Y, *et al*. Accurate reflection of hepatic venous pressure gradient by spleen stiffness measurement in patients with low controlled attenuation parameter values. *JGH Open* 2021;5:1172–8.
45 Giuffrè M, Macor D, Masutti F, *et al*. Spleen stiffness probability index (SSPI): a simple and accurate method to detect esophageal varices in patients with compensated liver cirrhosis. Ann Hepatol 2020;19:53–61.
46 Colecchia A, Montrone L, Scaioli E, *et al*. Measurement of spleen stiffness to evaluate portal hypertension and the presence of esophageal varices in patients with HCV-related cirrhosis. *Gastroenterology* 2012;143:646–54.
47 Takuma Y, Nouso K, Morimoto Y, *et al*. Portal hypertension in patients with liver cirrhosis: diagnostic accuracy of spleen stiffness. *Radiology* 2016;279:609–19.
48 Zykus R, Jonaitis L, Petrenkienė V, *et al*. Liver and spleen transient elastography predicts portal hypertension in patients with chronic liver disease: a prospective cohort study. *BMC Gastroenterol* 2015;15:183.
49 Sharma P, Kirnake V, Tyagi P, *et al*. Spleen stiffness in patients with cirrhosis in predicting esophageal varices. *Am J Gastroenterol* 2013;108:1101–7.
50 Song J, Huang J, Huang H, *et al*. Performance of spleen stiffness measurement in prediction of clinical significant portal hypertension: a meta-analysis. *Clin Res Hepatol Gastroenterol* 2018;42:216–26.
51 Dajti E, Ravaioli F, Zykus R, *et al*. Accuracy of spleen stiffness measurement for the diagnosis of clinically significant portal hypertension in patients with compensated advanced chronic liver disease: a systematic review and individual patient data meta-analysis. Lancet Gastroenterol Hepato 2023;8:816–28.
52 Jansen C, Bogs C, Verlinden W, *et al*. Algorithm to rule out clinically significant portal hypertension combining shear-wave elastography of liver and spleen: a prospective multicentre study. *Gut* 2016;65:1057–8.
53 Ma X, Wang L, Wu H, *et al*. Spleen stiffness is superior to liver stiffness for predicting esophageal varices in chronic liver disease: a meta-analysis. *PLoS ONE* 2016;11:e0165786.
54 Dajti E, Marasco G, Ravaioli F, *et al*. Risk of hepatocellular carcinoma after HCV eradication: determining the role of portal hypertension by measuring spleen stiffness. *JHEP Rep* 2021;3:100289.
55 Ravaioli F, Colecchia A, Dajti E, *et al*. Spleen stiffness mirrors changes in portal hypertension after successful interferon-free therapy in chronic-hepatitis C virus patients. *World J Hepatol* 2018;10:731–42.
56 Manatsathit W, Samant H, Kapur S, *et al*. Accuracy of liver stiffness, spleen stiffness, and LS-spleen diameter to platelet ratio score in detection of esophageal varices: systemic review and meta-analysis. *J Gastroenterol Hepatol* 2018;33:1696–706.
57 De Santis A, Nardelli S, Bassanelli C, *et al*. Modification of splenic stiffness on acoustic radiation force impulse parallels the variation of portal pressure induced by transjugular intrahepatic portosystemic shunt. *J Gastroenterol Hepatol* 2018;33:704–9.
58 Pawluś A, Inglot M, Chabowski M, *et al*. Shear wave elastography (SWE) of the spleen in patients with hepatitis B and C but without significant liver fibrosis. *Br J Radiol* 2016;89:20160423.
59 Piscaglia F, Salvatore V, Mulazzani L, *et al*. Ultrasound shear wave elastography for liver disease. A critical appraisal of the many actors on the stage. *Ultraschall Med* 2016;37:1–5.
60 Ding NS, Nguyen T, Iser DM, *et al*. Liver stiffness plus platelet count can be used to exclude high-risk oesophageal varices. *Liver Int* 2016;36:240–5.
61 Fofiu R, Bende F, Lupușoru R, *et al*. Spleen stiffness for predicting varices needing treatment: comparison between two different elastography techniques (point vs. 2d-SWE). *Can J Gastroenterol Hepatol* 2021;2021:6622726.
62 Colecchia A, Ravaioli F, Marasco G, *et al*. A combined model based on spleen stiffness measurement and Baveno VI criteria to rule out high-risk varices in advanced chronic liver disease. *J Hepatol* 2018;69:308–17.
63 Wang H, Wen B, Chang X, *et al*. Baveno VI criteria and spleen stiffness measurement rule out high-risk varices in virally suppressed HBV-related cirrhosis. *J Hepatol* 2021;74:584–92.
64 Kim HY, So YH, Kim W, *et al*. Non-invasive response prediction in prophylactic carvedilol therapy for cirrhotic patients with esophageal varices. *J Hepatol* 2019;70:412–22.

65 Marasco G, Dajti E, Ravaioli F, *et al*. Spleen stiffness measurement for assessing the response to B-blockers therapy for high-risk esophageal varices patients. *Hepatol Int* 2020;14:850–7.
66 Llop E, Perelló C, Fontanilla T, *et al*. Spleen transient elastography and damping index identify a subgroup of patients without an acute or chronic response to beta-blockers. *Front Med (Lausanne)* 2022;9:900073.
67 Giunta M, La Mura V, Conti CB, *et al*. The role of spleen and liver elastography and color-Doppler ultrasound in the assessment of transjugular intrahepatic portosystemic shunt function. Ultrasound Med Biol 2020;46:1641–50.
68 Buechter M, Manka P, Theysohn JM, *et al*. Spleen stiffness is positively correlated with HVPG and decreases significantly after TIPS implantation. *Dig Liver Dis* 2018;50:54–60.
69 Tomita H, Fuchimoto Y, Ohkuma K, *et al*. Spleen stiffness measurements by acoustic radiation force impulse imaging after living donor liver transplantation in children: a potential quantitative index for venous complications. *Pediatr Radiol* 2015;45:658–66.
70 Novelli PM, Cho K, Rubin JM. Sonographic assessment of spleen stiffness before and after transjugular Intrahepatic portosystemic shunt placement with or without concurrent embolization of portal systemic collateral veins in patients with cirrhosis and portal hypertension: a feasibility study. *J Ultrasound Med* 2015;34:443–9.
71 Attia D, Rodt T, Marquardt S, *et al*. Shear wave elastography prior to transjugular intrahepatic portosystemic shunt may predict the decrease in hepatic vein pressure gradient. *Abdom Radiol (NY)* 2019;44:1127–34.
72 Zhu H, Guo H, Yin X, *et al*. Spleen stiffness predicts survival after transjugular intrahepatic portosystemic shunt in cirrhotic patients. *Biomed Res Int* 2020;2020:3860390.
73 Han H, Yang J, Jin W-K, *et al*. Diagnostic value of conventional ultrasound and shear wave elastography in detecting transjugular intrahepatic portosystemic shunt dysfunction. *Acta Radiol* 2021;62:1575–82.
74 Gao J, Zheng X, Zheng Y-Y, *et al*. Shear wave elastography of the spleen for monitoring transjugular intrahepatic portosystemic shunt function: a pilot study. *J Ultrasound Med* 2016;35:951–8.
75 Ran H-T, Ye X-P, Zheng Y-Y, *et al*. Spleen stiffness and splenoportal venous flow: assessment before and after transjugular intrahepatic portosystemic shunt placement. *J Ultrasound Med* 2013;32:221–8.
76 Chin JL, Chan G, Ryan JD, *et al*. Spleen stiffness can non-Invasively assess resolution of portal hypertension after liver transplantation. *Liver Int* 2015;35:518–23.
77 Goldschmidt I, Brauch C, Poynard T, *et al*. Spleen stiffness measurement by transient elastography to diagnose portal hypertension in children. *J Pediatr Gastroenterol Nutr* 2014;59:197–203.
78 Bayramov N, Yilmaz S, Salahova S, *et al*. Liver graft and spleen elastography after living liver transplantation: our first results. Transplant Proc 2019;51:2446–50.
79 Nardelli MJ, Veiga Z da S, Faria LC, *et al*. Noninvasive predictors of esophageal varices in patients with hepatosplenic schistosomiasis mansoni. *Acta Trop* 2022;226:106283.
80 Yuldashev RZ, Aliev MM, Shokhaydarov SI, *et al*. Spleen stiffness measurement as a non-invasive test to evaluate and monitor portal hypertension in children with extrahepatic portal vein obstruction. *Pediatr Surg Int* 2020;36:637–41.
81 Vadlapudi SS, Jagadisan B, Ananthkrishnan R, *et al*. Splenic stiffness and platelet count to predict Varices needing treatment in pediatric extrahepatic portal vein obstruction. *Indian J Gastroenterol* 2020;39:576–83.
82 Kumar A, Lal SB, Bhatia A, *et al*. Role of noninvasive tools for prediction of clinically evident portal hypertension in children. *Eur J Gastroenterol Hepatol* 2020;32:931–7.
83 Madhusudhan KS, Kilambi RShalimar*et al*. Evaluation of splenic stiffness in patients of extrahepatic portal vein obstruction using 2D shear wave elastography: comparison with intra-operative portal pressure. *J Clin Exp Hepatol* 2018;8:250–5.
84 Madhusudhan KS, Kilambi RShalimar*et al*. Measurement of splenic stiffness by 2D-shear wave elastography in patients with extrahepatic portal vein obstruction. *Br J Radiol* 2018;91:20180401.
85 Dajti E, Ravaioli F, Colecchia A, *et al*. Liver and spleen stiffness measurements for assessment of portal hypertension severity in patients with Budd Chiari syndrome. *Can J Gastroenterol Hepatol* 2019;2019:1673197.
86 Tomita H, Ohkuma K, Masugi Y, *et al*. Diagnosing native liver fibrosis and esophageal varices using liver and spleen stiffness measurements in biliary atresia: a pilot study. *Pediatr Radiol* 2016;46:1409–17.
87 Uchida H, Sakamoto S, Kobayashi M, *et al*. The degree of spleen stiffness measured on acoustic radiation force impulse elastography predicts the severity of portal hypertension in patients with biliary atresia after portoenterostomy. J Pediatr Surg 2015;50:559–64.
88 Yoon H, Shin HJ, Kim MJ, *et al*. Predicting gastroesophageal varices through spleen magnetic resonance elastography in pediatric liver fibrosis. *WJG* 2019;25:367–77.
89 Yokoyama S, Ishigami M, Honda T, *et al*. Spleen stiffness by 2-D shear wave elastography is the most accurate predictor of high-risk esophagogastric varices in children with biliary atresia. *Hepatol Res* 2019;49:1162–8.
90 Furuichi Y, Moriyasu F, Taira J, *et al*. Noninvasive diagnostic method for idiopathic portal hypertension based on measurements of liver and spleen stiffness by ARFI elastography. *J Gastroenterol* 2013;48:1061–8.
91 Webb M, Zimran A, Dinur T, *et al*. Are transient and shear wave elastography useful tools in Gaucher disease? Blood Cells Mol Dis 2018;68:143–7.
92 Cunningham ME, Parastandeh-Chehr G, Cerocchi O, *et al*. Noninvasive predictors of high-risk varices in patients with non-cirrhotic portal hypertension. *Can J Gastroenterol Hepatol* 2019;2019:1808797.