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 Li1,2,3,4

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 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 can appear 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 guidelines3 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 sono graphic 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.\(^{4,13,36,42-49}\) 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 $\geq$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 $\geq 26.6$ 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 $\leq$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
States Food and Drug Administration to facilitate routine application of a highly innovative device that can be applied on both currently available for SSM and measurements in healthy individuals. Table 1 provides a summary of elastography techniques used in various studies.

### Table 1: SSM in healthy subjects

<table>
<thead>
<tr>
<th>Elastography technique</th>
<th>Machine name</th>
<th>Study participants</th>
<th>Number of healthy volunteers</th>
<th>Age (years)</th>
<th>Gender (M/F)</th>
<th>SS (kPa)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transient elastography</strong></td>
<td>FibroScan</td>
<td>Adults</td>
<td>17</td>
<td>28 (25–33)</td>
<td>5/12</td>
<td>17.8 ± 2.0 kPa</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>FibroScan</td>
<td>Adults</td>
<td>50</td>
<td>28.6 ± 8.5 (16–50)</td>
<td>30/20</td>
<td>16.0 ± 3.0 kPa</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>FibroScan</td>
<td>Adults</td>
<td>40</td>
<td>26.98 ± 5.16</td>
<td>N/A</td>
<td>19.41 ± 3.63 kPa</td>
<td>15</td>
</tr>
<tr>
<td><strong>Shear wave elastography</strong></td>
<td>SuperSonic Imagine SA</td>
<td>Adults</td>
<td>59</td>
<td>36 ± 21 (20–80)</td>
<td>25/34</td>
<td>16.6 ± 2.5 kPa</td>
<td>16</td>
</tr>
<tr>
<td><strong>SWE</strong></td>
<td>SuperSonic Imagine SA</td>
<td>Adults</td>
<td>171</td>
<td>46 ± 18 (18–87)</td>
<td>49/51</td>
<td>18.14 ± 3.08 kPa (12.66–24.88)</td>
<td>20</td>
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<tr>
<td></td>
<td>G4 xMATRIX iU22</td>
<td>Children</td>
<td>146</td>
<td>7.47 ± 3.39 (2–15)</td>
<td>100/46</td>
<td>6.1 ± 3.6 kPa (0.8–20.4)</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Apio 500 Platinum</td>
<td>Children</td>
<td>37</td>
<td>11.6 ± 4.9 (0.5–18)</td>
<td>19/18</td>
<td>16.8 ± 1.6 kPa (1.6–22.8)</td>
<td>19</td>
</tr>
<tr>
<td><strong>p-SWE</strong></td>
<td>Philips Affiniti 70</td>
<td>Adults</td>
<td>100</td>
<td>46 ± 18 (18–87)</td>
<td>49/51</td>
<td>18.14 ± 3.08 kPa (12.66–24.88)</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Siemens Acuson S2000</td>
<td>Adults</td>
<td>92</td>
<td>42.6 ± 12.0</td>
<td>67/25</td>
<td>2.49 ± 0.42 m/s (breath hold after expiration) vs 2.66 ± 0.36 m/s (deep inspiration)</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Siemens Acuson S2000</td>
<td>Children</td>
<td>38</td>
<td>8.07 ± 3.72</td>
<td>17/21</td>
<td>2.59 ± 0.14 m/s</td>
<td>22</td>
</tr>
<tr>
<td><strong>2D-SWE</strong></td>
<td>Logiq E9 XDefier</td>
<td>Adults</td>
<td>65</td>
<td>41.25 ± 13.77 (18–87)</td>
<td>31/34</td>
<td>13.82 ± 2.91 kPa</td>
<td>23</td>
</tr>
<tr>
<td><strong>Acoustic radiation force impulse</strong></td>
<td>Siemens Acuson S2000</td>
<td>Adults</td>
<td>16</td>
<td>34 (24–56)</td>
<td>7/9</td>
<td>2.16 m/s (1.99–2.26)</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Siemens Acuson S2000</td>
<td>Adults</td>
<td>25</td>
<td>32.3 ± 22.1 (63.0)</td>
<td>11/14</td>
<td>2.46 ± 0.35 m/s</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>Siemens Acuson S2000</td>
<td>Adults</td>
<td>15</td>
<td>N/A</td>
<td>N/A</td>
<td>2.04 ± 0.28 m/s (breath hold after expiration) vs 2.66 ± 0.36 m/s (deep inspiration)</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Siemens Acuson S2000</td>
<td>Adults</td>
<td>33</td>
<td>N/A</td>
<td>N/A</td>
<td>2.2 ± 0.31 m/s (1.6–3.3)</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Siemens Acuson S2000</td>
<td>Adults</td>
<td>20</td>
<td>32.9 ± 9 (18–50)</td>
<td>11/9</td>
<td>2.27 ± 0.35 m/s (1.57–2.83)</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Siemens Acuson S2000</td>
<td>Children</td>
<td>202</td>
<td>8.1 ± 4.7</td>
<td>92/110</td>
<td>2.25 ± 0.028 m/s</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>Siemens Acuson S3000</td>
<td>Children</td>
<td>102</td>
<td>6 ± 5.1 (8–17)</td>
<td>32/70</td>
<td>2.43 ± 0.31 m/s</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>Siemens Acuson S3000</td>
<td>Children</td>
<td>24</td>
<td>10.5 (5.2, 15.0)</td>
<td>12/12</td>
<td>2.53 m/s</td>
<td>31</td>
</tr>
<tr>
<td><strong>Magnetic resonance elastography</strong></td>
<td>Signa HDx</td>
<td>Adults</td>
<td>16</td>
<td>37 ± 9 (28–56)</td>
<td>9/7</td>
<td>3.56 ± 0.586 kPa (2.353–4.442)</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Signa HDx</td>
<td>Adults</td>
<td>12</td>
<td>37 (25–82)</td>
<td>9/3</td>
<td>3.6 ± 0.3 kPa</td>
<td>32</td>
</tr>
</tbody>
</table>

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

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

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. 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 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). In fact, a fairly low percentage (<5%) of patients with compensated cirrhosis develop varices needing treatment (VNT). 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. While the postulation of Baveno VI criteria (LSM ≤20 kPa and platelet count >150 x 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, as proved to be efficient also by Wang et al. 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.

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 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, SS increase by 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% of PHT patients).
sensitivity, 60% specificity and 100% NPV) and poor chronic response (87% sensitivity, 71% specificity and 71% NPV) to beta-blockers. Second, one effective way to reduce portal pressures is through transjugular intrahepatic portosystemic shunt (TIPS) intervention. An increasing body of studies 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 cutoff value to predict survival. 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. Third, after liver transplantation, SSM decreases significantly when PHT resolves. According to preliminary results, 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 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, extrahepatic portal vein obstruction, Budd-Chiari syndrome, biliary atresia, idiopathic PHT, Gaucher disease, 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, 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.

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Spleen Stiffness Measurement

- Transient elastography
- Shear wave elastography
- Acoustic radiation force impulse
- Magnetic resonance elastography

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