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ORIGINAL ARTICLE

Role of Spleen Stiffness Measurement by 2D-Shear Wave Elastography in Ruling Out the Presence of High-Risk Varices in Cirrhotic Patients

Dimitrios S. Karagiannakis[1] · Theodoros Voulgaris[1] · Evgenia Koureta[1] · Elissavet Chloupi[1] · George V. Papatheodoridis[1] · John Vlachogiannakos[1]

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Abstract

Background and Aim To evaluate if spleen stiffness measurement (SSM) can rule out the presence of high-risk varices in patients with cirrhosis, avoiding an upper gastrointestinal endoscopy (UGE).

Methods We enrolled 71 cirrhotic patients irrespective of liver disease's etiology. 2D shear wave elastography (SWE) of spleen and UGE was performed. High-risk varices (HRV) were defined as esophageal varices ≥ 5 mm and/or red spots and any gastric varices.

Results Esophageal varices were documented in 37 (52.1%) and HRV in 25 (35.2%) patients. SSM was not technically feasible in 7/71 patients (9.8%). From the remaining 64 patients, when those with cholestatic liver disease were excluded ($n = 17$), SSM < 35.8 kPa was found to exclude well the existence of HRV offering an AUROC of 0.854 ($p < 0.001$), sensitivity 88.9%, negative predictive value (NPV) 91.3%, specificity 72.4%, and positive predictive value (PPV) 66.7%. Only 2/47 patients (4.3%) were misclassified, and 23 (48.9%) could avoid endoscopy. In the total cohort of 64 patients, SSM < 33.7 kPa was found to exclude well the presence of HRV offering AUROC 0.792 ($p < 0.001$), sensitivity 91.7%, specificity 60%, NPV 92.3%, and PPV 57.9%. The misclassification rate was 3.1% (2/64), while 26/64 (40.6%) could avoid endoscopy.

Conclusions 2D-SWE of spleen is a reliable method for ruling out the presence of HRV in cirrhotic patients. If larger studies confirm our results, a large number of endoscopies could be avoided.

Keywords Spleen stiffness · Variceal bleeding · Cirrhosis · Portal hypertension

Abbreviations

HVPG	Hepatic venous pressure gradient
CSPH	Clinically significant portal hypertension
GEV	Gastroesophageal varices
HRV	High-risk varices
UGE	Upper gastrointestinal endoscopy
LSM	Liver stiffness measurements
TE	Transient elastography
SSM	Spleen stiffness measurement
SWE	Shear wave elastography
HCC	Hepatocellular carcinoma
TIPS	Transjugular intrahepatic portosystemic shunt
INR	International normalized ratio
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
MELD	Model for end stage liver disease
SD	Standard deviation
AUROC	Area under receiving operating characteristic
PPV	Positive predictive value
NPV	Negative predictive value
ARFI	Acoustic radiation force impulse imaging

✉ Dimitrios S. Karagiannakis
d_karagiannakis@hotmail.com

Theodoros Voulgaris
thvoulgaris87@gmail.com

Evgenia Koureta
j.koureta@gmail.com

Elissavet Chloupi
chloupiel@yahoo.gr

George V. Papatheodoridis
gepapath@med.uoa.gr

John Vlachogiannakos
jvlachog@hotmail.com

[1] Academic Department of Gastroenterology, Laiko General Hospital, Medical School of National, Kapodistrian University of Athens, 17 Aghiou Thoma, 11527 Athens, Greece

Introduction

Portal hypertension is a major complication of liver cirrhosis, as it predisposes to the development of serious clinical manifestations and contributes to patients' mortality [1]. Hepatic venous pressure gradient (HVPG) is considered the reference standard method to ascertain the presence of clinically significant portal hypertension (CSPH) [2], defined as levels of HVPG above the threshold of 10 mmHg. CSPH has been associated with the development of gastroesophageal varices (GEV) and an increased risk of clinical decompensation with the appearance of ascites, hepatic encephalopathy, and variceal bleeding [3–7].

Variceal bleeding is one of the most serious complications of liver cirrhosis, as its estimated mortality is around 15% [8]. The risk of variceal bleeding mostly depends on the size of GEV and can be reduced with appropriate medical or endoscopic treatment, applied principally in high-risk varices (HRV) defined by the presence of large varices or hemorrhagic stigmata irrespective of size [9]. Upper gastrointestinal endoscopy (UGE) is the gold standard method for the diagnosis of varices, but a large proportion of cirrhotic patients do not present HRV, making endoscopy a non-ideal screening test, as it is an invasive procedure associated with significant costs and patient's discomfort [10].

Liver stiffness measurements (LSM) using transient elastography (TE) are an easy, noninvasive method that has been extensively studied and found to correlate with HVPG and the presence of GEV [11–14]. Unfortunately, a dedicated device is required for the accomplishment of TE, whereas the rate of failure or unreliable measurements are not unremarkable ranging from 14 to 19% [15]. Moreover, the correlation between LSM and HVPG has been found not to be linear for HVPG levels > 12 mmHg, whereas no association between LSM and the size of GEV has been clearly documented [16–19]. For that reason, several parameters, such as spleen diameter, portal vein diameter, platelet counts, and many combinations of them, have been proposed in order to improve the accuracy of LSM using TE for the prediction of GEV [20–24]. The last Baveno consensus (Baveno VI) suggested that the combination of LSM < 20 kPa by TE and platelet count > 150,000/mm^3 could help to avoid endoscopy in advanced compensated cirrhotic patients, as the possibility of having HRV is very low (< 5%) when these criteria are fulfilled [9]. Initially, the Baveno VI criteria were applied only to patients with viral cirrhosis. Recently, those criteria have been validated in patients with cirrhosis of viral etiology, as well as in patients with alcoholic and nonalcoholic fatty liver disease, but not in patients with cholestatic liver diseases. Additionally, major limitation remains that only 20–30% of patients fulfill these criteria and could avoid endoscopy [25–29].

Spleen stiffness measurement (SSM) by TE has been proposed as a useful tool for the prediction of CSPH and the presence of GEV [30–32]. SSM by using two-dimensional real-time shear wave elastography (2D-SWE), a technique that has been developed more recently, seems to have higher success rates than TE [33, 34]. Furthermore, SSM by using 2D-SWE has been found to correlate well with HVPG [34–36].

Therefore, the aim of our study was to investigate the accuracy of SSM assessed by 2D-SWE for prediction of absence of HRV in comparison with other approaches.

Materials and Methods

Patient Population

Over a period of 12 months (05/2017–04/2018), all cirrhotic patients aged from 18 to 75 years who attended our outpatient liver clinics were considered eligible for inclusion in the study regardless of the etiology and severity of liver disease. The diagnosis of cirrhosis was based on clinical, laboratory findings, and imaging studies, or on liver histology. All patients had LSM by 2D-SWE ≥ 10 kPa. We excluded patients with splenectomy, porto-splenic vein thrombosis, non-cirrhotic portal hypertension, hepatocellular carcinoma (HCC), history of transjugular intrahepatic portosystemic shunt (TIPS), bacterial infection, alcoholic hepatitis, a previous episode of variceal bleeding and/or band ligation, or current use of non-selective *b*-blockers.

The study protocol was approved by the Ethics Committee of Laiko General Hospital of Athens, Greece. A written consent was obtained from each patient with respect to all ethical guidelines issued by the 2000 revision (Edinburgh) of the 1975 Declaration of Helsinki.

Clinical and Laboratory Data

Routine blood tests, including platelet count, prothrombin time, serum albumin, serum creatinine, international normalized ratio (INR), serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), and bilirubin were measured. The severity of liver disease was determined by the Child–Pugh score and the model for end stage liver disease (MELD) score calculated according to the UNOS formula [37].

Endoscopy

A screening upper gastrointestinal endoscopy was performed by two expert gastroenterologists (> 2000 endoscopies each of them) in all patients in order to establish the relationship between noninvasive methods and the

presence of GEV. A flexible EVIS EXERA video gastroscope (Olympus Europa Medical Systems, Hamburg, Germany) was used. HRV were considered to be present in case of esophageal varices ≥ 5 mm, varices with red spots irrespective of size, or any gastric varices. The procedure was carried out up to 60 min after 2D-SWE, and the operators had no any information about the results of 2D-SWE.

Two-Dimensional SWE

All patients underwent LSM and SSM by 2D-SWE performed by a single experienced operator (more than 500 exams) in fasting patients (fast for a minimum of 2 h). The Aixplorer ultrasound system (Supersonic Imagine S.A., Aix-en-Provence, France) with an abdominal 3.5 MHz curved array probe was used as recommended [38]. 2D-SWE measurements were performed blindly to the endoscopic findings just before endoscopy.

LSM were carried out on the right lobe of the liver through the intercostal spaces with the patient in the supine position and the right arm maximally abducted, during breath hold, avoiding deep inspiration prior to the breath hold. The 2D-SWE region of interest (ROI) was placed in an area of parenchyma free of large vessels and bile ducts, avoiding liver capsule, avoiding artifactual areas (reverberation, noisy areas from rib shadowing and also avoiding positioning the *Q* box on the edges of the elastogram. The measurement depth from the liver capsule was between 20 and 55 mm, at a region of liver parenchyma > 6 cm. The examiners aimed for a measurement angle close to 0° (region of interest at the centre of the transducer surface) [39]. LSM were based on the updated 2017 EFSUMB guidelines and recommendations of liver ultrasound elastography [40].

SSM were performed in the supine position with the left arm in maximum abduction and by placing the probe in the left intercostal spaces. ROI was placed between the central region and the lower pole, in a position near the abdominal wall via an intercostal approach. The examiners aimed for an equal distance from spleen capsule at both sites [39].

LSM and SSM were considered reliable when there is (1) temporal stability of the selected liver or spleen area for at least 3 s before measurement; (2) two-dimensional quality confirmed by a homogenous color in the region of interest; (3) *Q* box of at least 15 mm. Liver or spleen stiffness failure was defined as either no signal obtained or failure to obtain a reliable 2D-SWE measurement, i.e., no temporal or spatial stability and/or *Q* box < 15 mm [41, 42]. Ten reliable LSM and 10 reliable SSM were obtained from each patient, and the mean values were, respectively, calculated. The standard deviation (SD) was < 20% of the mean value of LSM and SSM, respectively.

Statistical Analysis

Statistical analysis was done by using SPSS (SPSS software; SPSS Inc, Chicago, IL, USA). Quantitative variables were compared with Student's *t* test or Mann–Whitney test for normally distributed and non-normally distributed variables, respectively. Qualitative variables were compared with Chi-squared test or Fisher's exact test, as appropriate. The relationship between parameters was done by using the Spearman's correlation coefficient. The area under the receiving operating characteristic (AUROC) curves for SSM predictability as well as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) was calculated. The *c*-statistics of AUROC curves were provided with their 95% confidence intervals. Diagnostic accuracy was considered to be poor in case of a *c*-statistic < 0.65, moderate in case of a *c*-statistic 0.65–0.75, good in case of a *c*-statistic 0.76–0.85 and excellent in case of a *c*-statistic > 0.85. The optimal cutoff was selected from the AUROCs curves as the point which provided the maximum sum of sensitivity and specificity. All tests were two sided, and *p* values < 0.05 were considered to be significant.

Results

Over the study period, 73 consecutive cirrhotic patients were identified. Two patients were excluded because of previous splenectomy. Of the 71 included patients, 36 (50.7%) were males and their mean age was 60 ± 14 years old. The cause of cirrhosis was chronic viral hepatitis in 23 (32.4%), alcoholic or nonalcoholic fatty liver disease in 31 (43.6%) and cholestatic liver disease in 17 patients (23.9%). Fifty-three patients (74.6%) had child class A, and 18 (25.4%) had child class B (score 7) cirrhosis. None of the patients had history of decompensated disease (presence of ascites, hepatic encephalopathy, or history of variceal bleeding). Thirty-seven patients (52.1%) had GEV, and 25 (35.2%) patients had HRV. Forty-six patients (64.8%) had splenomegaly (long axis of spleen > 13 cm). The mean spleen diameter was 13.8 ± 2.8 cm. The diameter of portal vein was estimated in 62 patients, and 27 (42.5%) of these 62 cases had portal vein diameter > 1.3 cm. The mean portal vein diameter was 1.3 ± 0.3 cm.

2D-SWE of spleen was not technically feasible in 7/71 (9.8%) patients because of small spleen size. Patients' demographics are presented in Table 1.

Differences Between Patients With or Without HRV

Patients with HRV compared to those without HRV had more frequently platelet counts less than 150,000/mm^3 and significantly lower mean platelet count (Table 2). No statistically

Table 1 Characteristics of the study population

Parameter	Values
Gender	
Males	36 (50.7%)
Females	35 (49.3%)
Age (years)[a]	60 ± 14
Etiology	
HBV	8 (11.3%)
HCV	15 (21.1%)
NAFLD	17 (23.9%)
ALD	14 (19.7%)
Cholestatic	17 (23.9%)
Esophageal varices	
Yes	37 (52.1%)
No	34 (47.9%)
HRV	25 (35.2%)
No HRV	46 (64.8%)
Child–Pugh score	6.0 ± 1.2
Child–Pugh class	A: 53/71 (74.6%)
	B: 18/71 (25.4%)
Mean MELD score	11.4 ± 3.4
Liver stiffness (kPa)	23.2 ± 9.2 (9.9–45.1)
Spleen stiffness (kPa)	35.1 ± 8.9 (11.1–57.6)
Bilirubin (mg/dl)	1.5 ± 1.4
Albumin (g/l)	3.8 ± 0.7
PLTs × 10^6/mm^3	121 ± 52
Hb (g/dl)	12.5 ± 1.9
AST (IU/ml)	49 ± 32 (13–153)
ALT (IU/ml)	45 ± 42 (8–228)
Creatinine (mg/dl)	1.2 ± 1.6 (0.4–10.2)
INR	1.3 ± 0.2 (0.96–1.8)

HBV hepatitis B virus, *HCV* hepatitis C virus, *NAFLD* nonalcoholic fatty liver disease, *ALD* alcoholic liver disease, *PLTs* platelets

[a]Values are expressed as mean ± SD

significant differences were found between these two groups regarding the mean values of LSM. Moreover, the proportion of patients with LSM > 20 kPa, the cutoff proposed by Baveno VI, did not differ significantly between cases with HRV (56%) or no HRV (40%) ($p = 0.22$).

Patients with HRV had significantly longer mean diameter of spleen, larger mean portal vein diameter, and higher values of SSM. INR, albumin levels, bilirubin levels, and MELD score were not statistically different between the two groups (Table 2).

Table 2 Patients' characteristics in relation to the presence of high-risk varices (HRV)

Parameter	HRV	Non-HRV	*p* value
Age (years)[a]	58 ± 17	60 ± 12	0.607
Platelets (10^3/mm^3)	95 ± 42	136 ± 51	0.003
Platelets < 150 × 10^3/mm^3	22/24 (91.7%)	27/44 (61.4%)	0.010
Albumin (gr/dl)	3.7 ± 0.6	3.8 ± 0.7	0.770
INR	1.3 ± 0.2	1.2 ± 0.2	0.947
Bilirubin (mg/dl)	2 ± 2.1	1.3 ± 0.8	0.058
MELD score	12 ± 4	11 ± 3	0.278
Spleen diameter (cm)	14.9 ± 2.4	13.2 ± 2.9	0.011
Spleen > 13 cm	20/25 (80%)	26/46 (56.5%)	0.069
Portal vein diameter (cm)	14.9 ± 2.4	13.2 ± 2.9	0.006
Portal vein diameter > 1.3 cm	14/22 (63.6%)	13/40 (32.5%)	0.031
LSM (kPa)	25.9 ± 9.6	21.7 ± 8.8	0.069
SSM (kPa)	39.5 ± 7.6	32.4 ± 8.6	0.001

INR international normalized ratio, *LSM* liver stiffness measurement, *SSM* spleen stiffness measurement

[a]Values are expressed as mean ± SD

Diagnostic Performance of Different Noninvasive Methods in Predicting the Absence of HRV

LSM

LSM alone was found to have poor predictability for the detection of patients without HRV (AUROC, *c*-statistic: 0.628, $p = 0.077$). Slightly better results, with just moderate predictability, were observed when patients with cholestatic diseases were excluded (AUROC, *c*-statistic: 0.660, $p = 0.054$).

In the subgroup of 54/71 patients (i.e., excluding those with cholestatic liver disease, $n = 17$), the absence of HRV was found in 100% (8/8) of patients who fulfilled and 58.7% (27/46) of patients who did not fulfill the Baveno VI criteria by using 2D-SWE ($p = 0.04$). For the absence of HRV, the strict application of Baveno VI criteria offered specificity of 22.9%, sensitivity of 100%, PPV of 41.3%, and NPV of 100%. According to these criteria, none of patients (0/19) with HRV was misclassified, whereas eight out of 54 patients (14.8%) could spear UGE (Table 3).

In the total cohort of 71 patients, the absence of HRV did not differ in cases who fulfilled and those who did not fulfill the Baveno VI criteria by using 2D-SWE (60.3% vs. 83.3%, $p = 0.191$).

SSM

SSM estimation was feasible in 64/71 patients (7 had small spleen size), offering good predictability for the absence of HRV (AUROC, *c*-statistic: 0.792, $p < 0.001$) (Fig. 1). SSM

Table 3 Reliability of methods predicting the absence of high-risk varices (HRV)

Method	Spared UGE	HRV misclassification	Se	Sp	NPV	PPV
Patients with non-cholestatic liver disease						
LSM (cutoff value 27.5 kPa)	61.1% (33/54)	14.8% (8/54)	57.9% (11/19)	71.4% (25/35)	75.8% (25/33)	52.4% (11/21)
Baveno VI criteria	14.8% (8/54)	0% (0/19)	100% (19/19)	22.9% (8/27)	100% (8/8)	41.3% (19/46)
SSM (cutoff value 35.8 kPa)	48.9% (23/47)	4.3% (2/47)	88.9% (16/18)	72.4% (21/29)	91.3% (21/23)	66.7% (16/24)
Method	Spared UGE	HRV missing	Se	Sp	NPV	PPV
All patients						
LSM (cutoff value 22.5 kPa)	51.4% (36/70)	14.3% (10/70)	60% (15/25)	57.8% (26/45)	72.2% (26/36)	44.1% (15/34)
Baveno VI criteria	17.1% (12/70)	2.9% (2/70)	92% (23/25)	22.2% (10/45)	83.3% (10/12)	39.7% (23/58)
SSM (cutoff value 33.7 kPa)	40.6% (26/64)	3.1% (2/64)	91.7% (22/24)	60% (24/40)	92.3% (24/26)	57.9% (22/38)

LSM liver stiffness measurement, *SSM* spleen stiffness measurement, *UGE* upper gastrointestinal endoscopy, *AUROC* area under receiving operator characteristic, *Se* sensitivity, *Sp* specificity, *NPV* negative predictive value, *PPV* positive predictive value

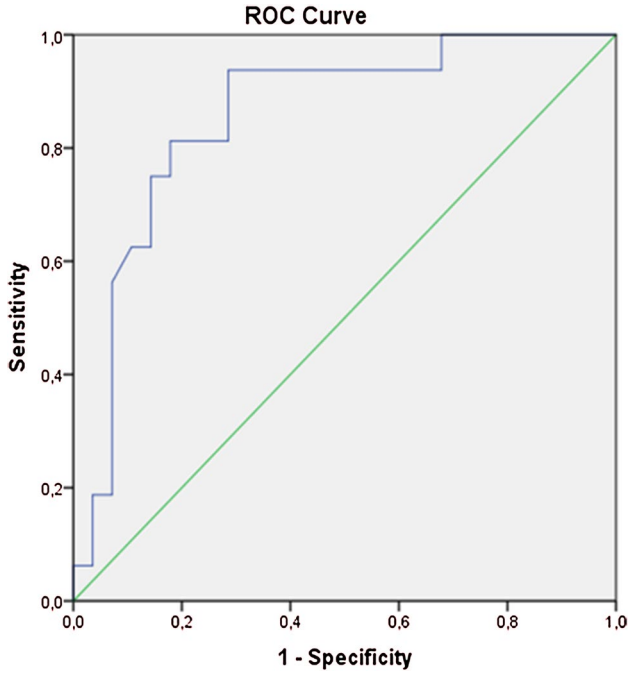

Fig. 1 AUROC curve from SSM in the total cohort of patients

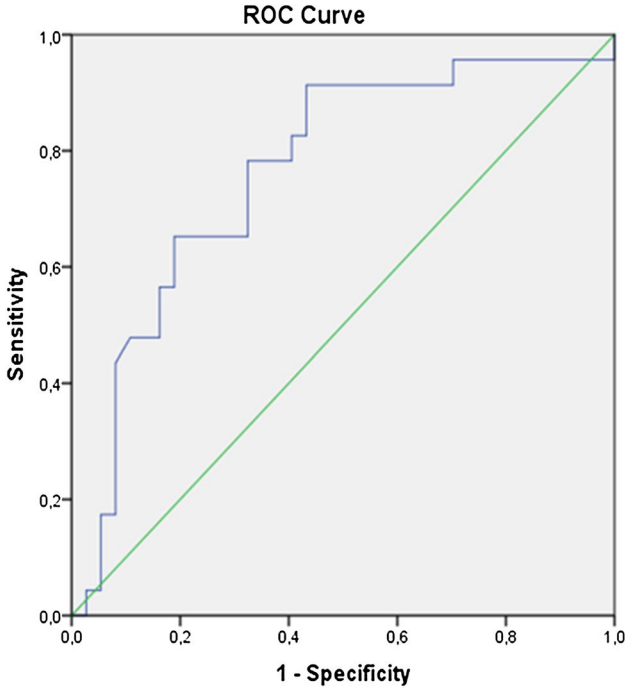

Fig. 2 AUROC curve from SSM when patients with cholestatic liver diseases were excluded

value < 33.7 kPa had sensitivity 91.7%, specificity 60%, NPV 92.3%, and PPV 57.9% for the diagnosis of absence of HRV. The misclassification rate was 3.1% (2 out of 64 patients). Using this cutoff value, 26 (40.6%) out of 64 patients would avoid UGE (Table 3).

After the exclusion of patients with cholestatic liver disease, the predictability of SSM for the absence of HRV became excellent (AUROC, *c*-statistic: 0.854, $p < 0.001$) (Fig. 2). A new cutoff value of 35.8 kPa had sensitivity 88.9%, NPV 91.3%, specificity 72.4%, and PPV 66.7% in this setting. Only two (4.3%) out of 47 patients with SSM < 35.8 kPa had HRV and were therefore misclassified. With this cutoff value, 23 of 47 patients (48.9%) could avoid UGE (Table 3). The addition of LSM or Baveno VI criteria to the SSM did not improve SSM's predicting ability (data not shown).

Discussion

We studied the role of SSM by using 2D-SWE as an alternative tool for the prediction of cirrhotic patients not having HRV and thus not needing UGE. We preferred the use of 2D-SWE instead of TE, as in a recent study of Elkrief et al.

[34], 2D-SWE was found to be superior to TE for the assessment of both liver and spleen stiffness.

In our cohort of patients, SSM was more accurate than the LSM and the Baveno VI criteria in order to predict the absence of HRV and this accuracy was independent of the etiology of liver disease. Specifically, LSM alone was found inadequate to predict the absence of HRV. This is somewhat expected as LSM seems to correlate well with portal hypertension only at the early stages of cirrhosis [13, 14], where the main factor influencing the portal pressure is fibrosis [43]. However, at the later stages of liver cirrhosis, where the portal pressure does not only depend on fibrosis, but also on the increased portal vein inflow due to splanchnic vasodilation and hyperdynamic circulation [44, 45], the correlation between LSM and portal hypertension seems to be insignificant.

These pathophysiological aspects have been supported by the results of several recent studies. In particular, Vizzuti et al. [16] investigated 61 HCV infected cirrhotics and found that the relationship between LSM and portal hypertension was strong mainly for HVPG values up to 10–12 mmHg, while the linear regression analysis was suboptimal for HVPG values > 12 mmHg. In the same study, although a positive correlation between LSM and the presence of GEV was revealed, no correlation between LSM and GEV's size was detected. Subsequently, Bureau et al. [17] using a cutoff value of 21 kPa accurately predicted the presence of CSPH in 92% of cirrhotic patients, independently of the etiology, but once again, no association between LSM and the size of GEV was found. Two recent studies including 326 and 502 cirrhotic patients confirmed the above results, as they also showed that LSM values greater than 21.6 kPa and 18 kPa, respectively, correlated with the presence of HVPG > 10 mmHg, with this relationship not to be linear in higher HVPG values [18, 19].

Because changes in splenic density due to tissue's hyperplasia, congestion, and fibrosis may better reflect the hyperdynamic component of portal hypertension [46], the Baveno VI group adopted the combination of LSM by TE with the platelets counts (the latter as an indicator of hypersplenism). It was found that the advanced compensated cirrhotic patients with LSM < 20 kPa and platelets > 150,000/mm^3 had a low probability of presenting HRV (< 5%). However, only 20% of patients were found to fulfill these criteria and thus to avoid UGE [9, 25–29, 47, 48]. Similar results were provided after the implementation of these criteria to our group of patients. To date, the Baveno VI criteria have been validated in patients with cirrhosis due to viral hepatitis, or alcoholic and nonalcoholic fatty liver disease [9, 25–29]. That is why we first assessed the effectiveness of these criteria in our patients, excluding those with cholestatic liver disease. We found that the Baveno VI criteria could predict well the absence of HRV with 0% misclassification rate. However, only 14.8% of patients could fulfill these criteria and thus skip UGE. Furthermore, when these criteria were performed in the total cohort of our patients including cholestatic liver disease, they were found not to be suitable for ruling out patients with HRV, as the absence of HRV did not differ significantly between patients who fulfilled and those who did not fulfill the Baveno VI criteria ($p = 0.191$).

In our study, SSM was more accurate than the Baveno VI criteria in predicting patients not having HRV. In the subgroup of non-cholestatic liver diseases, patients with SSM < 35.8 kPa had 88.9% probability of not having HRV and almost 50% of unnecessary UGE could be speared with an acceptable misclassification rate of 4.3%. Importantly, these impressive findings were also validated even when patients with cholestatic liver disease were included, as cases with SSM < 33.7 kPa had 91.7% probability of not having HRV. Forty percent of patients had SSM below this cutoff value and could avoid UGE, while the misclassification rate was remained low (3%).

Our results are in agreement with other already published data regarding the importance of SSM in the evaluation of cirrhotic patients, but with some meaningful differences [49–56]. Hirooka et al. studied 60 patients with chronic liver damage and measured the liver and spleen elasticity with real-time tissue elastography. They estimated the HVPG and observed a strong correlation between SSM and HVPG ($r = 0.854$, $p < 0.0001$). However, they did not investigate the role of SSM as a predictor of the presence of HRV [49]. Fraqueli et al. investigated the feasibility and reproducibility of SSM by TE and its correlation with the severity of liver fibrosis in patients with chronic liver hepatitis. They also studied the efficacy of SSM in predicting cirrhotic patients with GEV, but the results are difficult to be characterized as efficient enough, since only 26 patients with cirrhosis were included and just 11 of them had GEV [51]. Stefanescu et al. investigated the significance of SSM on identifying patients with GEV. They found that a SSM cutoff value of 40.8 kPa could predict GEV with sensitivity of 94% and diagnostic accuracy of 89%. Additionally, SSM was higher in bleeders than in non-bleeders (58 vs. 50 kPa, $p = 0.001$) as well as in patients with large than small varices (56 vs. 49 kPa, $p = 0.001$). However, this study used TE and not 2D-SWE for the estimation of spleen stiffness, and furthermore, only patients with HCV and alcoholic cirrhosis were included [52]. Three more recent studies identified the capability of SSM in excluding patients with GEV or HRV. Two of them used TE for the assessment of SSM [53, 54], and one applied the acoustic radiation force impulse imaging (ARFI) [56].

In concluding, our data showed for the first time the ability of SSM by 2D-SWE to detect those cirrhotic patients at low risk for HRV, regardless of the etiology of liver disease. If our results are confirmed by larger clinical trials, SSM by 2D-SWE could be used alone as a reliable, easily performed,

noninvasive technique for the prediction of the absence of HRV. This could prevent undesired events of portal hypertension, while it would improve the quality of life of patients by saving unnecessary endoscopies.

Compliance with ethical standards

Conflict of interest All the authors have no financial or other conflict of interest to declare concerning this manuscript.

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