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Shear wave elastography prior to transjugular intrahepatic portosystemic shunt may predict the decrease in hepatic vein pressure gradient

Dina Attia,[1,2] Thomas Rodt,[3] Steffen Marquardt,[3] Jan Hinrichs,[3] Bernhard C. Meyer,[3] Michael Gebel,[1] Frank Wacker,[3] Michael P. Manns,[1] and Andrej Potthoff[1]

[1]Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Carl-Neuberg-Str. 1, 30625 Hannover, Germany
[2]Department of Gastroenterology, Hepatology and Endemic Medicine, Faculty of Medicine, Beni-Suef University, Mokbel Street, Beni-Suef 62511, Egypt
[3]Department of Diagnostic and Interventional Radiology, Hannover Medical School, Carl-Neuberg-Str. 1, 30625 Hannover, Germany

Abstract

Background: Transjugular intrahepatic portosystemic shunt (TIPS) is a procedure used to treat portal hypertension complications. Our aim was to evaluate liver and spleen stiffness measurement (LSM and SSM, respectively) changes using acoustic radiation force impulse imaging (ARFI) in comparison to Child–Pugh scores for predicting hepatic venous pressure gradient (HVPG) decreases after TIPS implantation.
Methods: This prospective study included 31 consecutive clinically significant portal hypertension patients with TIPS indication. All patients received LSM and SSM before TIPS, at baseline, 2 days (follow-up 1) and 6 weeks (follow-up 2) post-implantation. HVPG was performed during the TIPS procedure.
Results: The mean decrease in HVPG after TIPS was 63%. LSM and SSM decreased significantly between baseline and follow-up 2 ($p < 0.001$ and $p < 0.001$, respectively). At baseline, follow-up 1 and follow-up 2, significant correlations were detected between mean SSM and mean HVPG ($p = 0.026$; $p = 0.018$; $p = 0.002$, respectively). HVPG decreased to ≤ 10 mmHg in 61% of patients for which LSM, SSM, and Child–Pugh score were predictors ($p = 0.033$, $p = 0.002$ and $p = 0.030$, respectively). The area under the curve (AUC) for LSM, SSM, and Child–Pugh was 0.88, 0.90, and 0.84, respectively, with close sensitivity and specificity. SSM had the highest diagnostic accuracy for predicting an HVPG decrease to ≤ 10 mmHg in comparison to LSM and Child–Pugh score.
Conclusion: Spleen stiffness is superior to liver stiffness and Child–Pugh score as a non-invasive surveillance tool for evaluating patients with clinically significant portal hypertension (HVPG ≥ 10 mmHg) prior to TIPS.

Key words: ARFI—Acoustic radiation force impulse imaging elastography—TIPS—Transjugular intrahepatic portosystemic shunt—Spleen stiffness—Liver stiffness

Abbreviations

TIPS	Transjugular intrahepatic portosystemic shunt
LSM	Liver stiffness measurement
SSM	Spleen stiffness measurement
ARFI	Acoustic radiation force impulse imaging
HVPG	Hepatic venous pressure gradient
AUC	Area under the curve
TE	Transient elastography
CSPH	Clinical significant portal hypertension
FU	Follow-up
PVV	Portal vein velocity
Tmax	Maximal flow velocity
DEGUM	Deutsche Gesellschaft für Ultraschall in der Medizin (German Association for ultrasound in medicine
ROI	Region of interest
MELD	Model of end-stage liver disease

Correspondence to: Dina Attia; *email:* dinaattia14@yahoo.com

The development of portal hypertension and decompensated liver cirrhosis is associated with reduced 2-year survival if the primary etiology is not radically treated [1]. Transjugular intrahepatic portosystemic shunt is a standard treatment option when pharmacological and endoscopic interventions fail [2, 3]. TIPS results in a reduction in complications including refractory ascites, haematemesis, hepatic hydrothorax, and hepatorenal syndrome [4] and prevents re-bleeding [5]. TIPS improves patient quality of life and subsequently results in improved survival rates [6]. The best response is obtained after reducing the hepatic venous pressure gradient (HVPG) to 8–10 mmHg, which reduces the risk of complications and hepatocellular carcinoma [7]. The Child–Pugh score is a predictor of survival after TIPS insertion. This score has been shown to improve after TIPS [8–12]. A model for end-stage liver disease (MELD) score > 18 predicts increased 3-month mortality after TIPS insertion [13]. Transient elastography (TE) is a non-invasive imaging modality that can identify patients with compensated advanced chronic liver disease (cACLD) from those with clinically significant portal hypertension (CSPH, HVPG ≥ 10 mmHg) [14]. Spleen stiffness measurement (SSM) has shown a better correlation with portal hypertension than liver stiffness measurement (LSM) [15]. Another non-invasive imaging procedure is ARFI elastography. Analogous to TE, SSM by ARFI correlates better with portal hypertension than LSM [16]. Different studies have shown that SSM correlates with portal vein pressure and can be used in addition to color Doppler to investigate TIPS function [17–20].

However, there is a lack of studies into the role of LSM and SSM in predicting a decrease of HVPG to ≤ 10 mmHg after TIPS. The aim of this small prospective study was to evaluate LSM and SSM changes using ARFI elastography in comparison to Child–Pugh score for predicting the HVPG decrease after TIPS implantation.

Patients and methods

Study cohort

This study was performed in compliance with the Declaration of Helsinki and with the approval of the local ethics committee. Ultimately, 31 patients (mean age 59 ± 12 years; 65% males) had baseline ARFI measurements prior to TIPS implantation and were enrolled in this prospective study between May 2012 and April 2015 at the Hannover Medical School, Hannover, Germany. Written informed consent was obtained from all patients. All patients received ARFI stiffness measurements of the liver (LSM) and the spleen (SSM), Doppler, duplex flow of the portal vein, and its branches 1 day before TIPS insertion (Baseline, BL), 2 days (FU1) and 6 weeks (FU2) after TIPS. Patients with clinically significant portal hypertension (HVPG > 10 mmHg) and indicated for TIPS (refractory ascites (39%), refractory bleeding (16%), refractory ascites and bleeding (19%), hepatorenal syndrome (16%), and hepatic hydrothorax (10%)) were included in the study. Patients with contraindication to TIPS insertion or in which TIPS was not feasible (severe liver failure, right-sided heart failure, hepatic encephalopathy, portal hypertension, portopulmonary, and hepatopulmonary hypertension) were excluded from the study. After enrolment, six patients were excluded from the study, TIPS failed in one patient (3%), and five patients had Budd–Chiari syndrome. Patients were also classified according to the Child–Pugh score as follows:

Points	Bilirubin (mg/dL)	Albumin (g/dL)	INR	Ascites	Hepatic encephalopathy
+ 1	< 2	> 3.5	< 1.7	No	No
+ 2	2–3	2.8–3.5	1.7–2.2	Mild	Grade 1–2
+ 3	> 3	< 2.8	> 2.2	Moderate to severe	Grade 3–4

Liver cirrhosis is classified into classes A, B, and C according to this scoring system [8].

Points	Class	1-Year survival (%)	2-Year survival (%)
(5–6)	Class A	100	85
(7–9)	Class B	80	60
(10–15)	Class C	45	35

Laboratory parameters

Serum platelet count, international normalization ratio (IRN), bilirubin, albumin, and creatinine parameters were recorded at baseline, at follow-up 1 (FU1) and follow-up 2 (FU2).

Ultrasound examinations

All patients were evaluated using abdominal and neck ultrasonography, which included evaluation of the patency of the right internal jugular vein. The convex probe (C4-1, 1–4 MHz) and the linear probe (VL9-4, 4–9 MHz) (Siemens Acuson S2000, Munich, Germany) were used. The sonographic signs of liver cirrhosis including liver surface irregularity, vein irregularity, angle of inferior border greater than 45°, splenomegaly (defined as a longitudinal diameter ≥ 13 cm), homogeneity of parenchyma, and signs of portal hypertension (dilatation of the portal vein ≥ 13 mm, reduction of portal vein velocity < 13 cm/s, dilatation of the splenic vein and superior mesenteric vein ≥ 11 mm, splenomegaly > 12 cm, increased resistive index of the hepatic artery > 0.78, and presence of portosystemic shunts) were evaluated according to EFSUMB recommendations [21].

Duplex sonography included portal vein flow velocity (PVV) [normal range 20–40 cm/s] (PV_{max} and PV_{min}) at

baseline, FU1, and FU2. PV time-averaged maximal flow velocity (T_{max}) and PV flow volume (normal range 12–20 L/s) were automatically calculated. Before TIPS implantation, PVV was measured at the hilum of PV, while the direction of flow and patency were evaluated in the right and left branches using intercostal and subcostal approaches. After TIPS implantation, the PVV was measured within 2 cm of TIPS insertion in the proximal, middle, and distal thirds and direction of flow in PV branches. Measurements were determined after an overnight fast, mid-inspiration, and angle $< 60°$. Signs of TIPS malfunction included reversal of hepatofugal to hepatopetal flow in portal branches, development or recurrence of ascites, increase or decrease in shunt velocity > 50 cm/s compared to a previous examination, shunt Vmax < 90 cm/s or > 190 cm/s [22–26]. The sonographer was blinded to the results of the HVPG in the follow-up.

Liver and spleen stiffness measurements using ARFI elastography

ARFI elastography was performed during the ultrasound examination before TIPS implantation and at FU1 and FU2. ARFI was conducted using a conventional ultrasonographic system (Siemens ACUSON S2000 Virtual TouchTM Tissue Quantification; Siemens, Munich, Germany) with a standard broadband 4–1 MHz curved probe. ARFI transmits very short acoustic high-intensity impulses with a fixed frequency (2.67 MHz), which induce local tissue excitation at the region of interest through local tissue displacement. The displaced tissue responds by propagating shear waves away from the region of excitation. The propagation velocity of the shear waves is measured by ultrasonographic waves, with the tissue stiffness correlating to the propagation velocity [27, 28]. The measurements were performed after an overnight fast and while patients held their breath, but without deep inspiration. DEGUM-certified physicians performed all measurements. The region of interest (ROI) (location of measurement) was placed through an intercostal approach. For LSM, the ROI was placed at the right hepatic lobe, segment 8, at an insertion depth of at least 1–2 cm below the liver and spleen capsules [29]. For SSM, the ROI was placed between the central region and the lower pole of the spleen in a position near the abdominal wall [30]. Patients were examined in the supine position with both arms maximally abducted. Care was taken to minimize the pressure exerted with the transducer. At least 10 successful measurements were performed in each patient. Results are expressed in meters per second (m/s). No specific quality criteria are recommended yet. However, success rate was calculated at least 60% of the ten valid acquisitions and an interquartile range $< 30\%$ of the mean value (IQR/M) was defined as eligible for the study. Mean values of the ARFI measurement were used.

TIPS implantation

TIPS insertion (Viatorr, Gore Medical, nominal stent graft diameter 10 mm) was previously discussed. Portal vein and central venous pressures were measured before and after TIPS; the calculated pressure gradient difference was used to evaluate the technical success of the procedure (portosystemic pressure gradient $<$ 12 mmHg).

Statistical analysis

Statistical analyses were performed using SPSS 22.0 (SPSS, Chicago, IL). A p value less than 0.05 was considered statistically significant. Quantitative variables are expressed as mean ± standard deviation. The statistical significance of intergroup differences before and after TIPS was evaluated using the Wilcoxon test, and a dot-plot distribution was used to display the difference between the LSM and SSM. For non-parametric data, Spearman's correlation coefficient was used. A MANOVA test for univariate and multivariate analyses was used to detect predictors of a decrease in HVPG to ≤ 10 mmHg from baseline. A ROC curve was used to predict the diagnostic performance and accuracy of SSM, LSM, and Child–Pugh score—predicting a decrease in HVPG to ≤ 10 mmHg from baseline. Sensitivity, specificity, the positive and negative likelihood ratios (PLR and NLR, respectively), and odds ratios were also calculated.

Results

A total of 31 patients with clinically significant portal hypertension and TIPS indication were enrolled in this study. The majority of patients had alcoholic liver cirrhosis (16, 52%), followed by cryptogenic cirrhosis (9, 29%) and virus-related liver cirrhosis (6, 19%). Child–Pugh B (23, 77%) was the predominant score, while A and C were 3 (10%) and 5 (17%), respectively. Similarly, a model of end-stage liver disease (MELD) score of 10–19 (16, 53%) was the highest among patients, while MELD < 10 and > 20 were 9 (30%) and 6 (20%), respectively. HVPG decreased to < 12 mmHg after TIPS in 27/31 (87%) patients and < 10 mmHg in 26/31 (84%) patients. Four patients had HVPG decrease of less than 20% from baseline.

Significant decline in LSM and SSM after TIPS insertion

After TIPS implantation, LSM and SSM showed a significantly rapid and sustained decrease in all patients (Table 1). The mean decrease in SSM at FU1 (15%) and FU2 (23%) was higher than LSM at FU1 (10%) and FU2 (17%). An overall decrease was observed from baseline to FU2 in LSM ($p < 0.001$) and SSM ($p < 0.001$).

Table 1. Changes in laboratory, haemodynamic, clinical, and duplex parameters after TIPS implantation in all patients

	BL Before TIPS	After TIPS	FU1	*p* value BL vs. FU1	FU2	*p* value FU1 vs. FU2	*p* value BL vs. FU2
Laboratory parameters							
PLT ($\times 10^3/\mu L$)	120 ± 67		113 ± 73	0.446	109 ± 54	0.819	0.327
INR	1.4 ± 0.4		1.4 ± 0.3	0.564	1.5 ± 0.4	0.581	0.029***
Bilirubin (μmol/L)	22 ± 16		49 ± 54	0.003*	45 ± 54	0.597	0.023***
Albumin (g/dL)	28 ± 7		25 ± 8	0.132	23 ± 10	0.933	0.094
Creatinine (μmol/L)	152 ± 168		129 ± 125	0.029*	120 ± 72	0.324	0.368
Haemodynamic parameters							
PP (mmHg)	38 ± 8	31 ± 10		< 0.001*	–	–	–
CVP (mmHg)	19 ± 6	25 ± 7		< 0.001*	–	–	–
HVPG (mmHg)	20 ± 6	8 ± 4		< 0.001*	–	–	–
Duplex parameters							
Portal vein							
Flow volume (L/s)	0.9 ± 0.8		2.8 ± 4.6	0.001*	2.3 ± 1.6	0.681	< 0.001***
V_{max} (cm/s)	22 ± 9		47 ± 20	< 0.001*	45 ± 16	0.509	< 0.001***
T_{max} (cm/s)	15 ± 7		38 ± 19	< 0.001*	37 ± 15	0.305	< 0.001***
TIPS V_{max}							
Proximal third (cm/s)	–		138 ± 60	–	123 ± 46	0.657	–
Middle third (cm/s)	–		146 ± 49	–	122 ± 52	0.397	–
Distal third (cm/s)	–		141 ± 41	–	123 ± 43	0.264	–
Clinical parameters							
Spleen size (cm)	13.9 ± 6.1		14.6 ± 5.0	0.001*	12.4 ± 4.1	< 0.001**	0.002***
Ascites grading (0/1/2/3)	2/14/9/6		3/9/14/5	0.694	10/7/10/4	0.219	0.087
Child–Pugh score	6.46 ± 1.19		6.86 ± 1.89	0.152	6.90 ± 1.66	0.247	0.389
ARFI elastography							
LSM (m/s)	3.15 ± 0.62		2.92 ± 0.69	0.008*	2.67 ± 0.60	0.019**	< 0.001***
SSM (m/s)	3.79 ± 0.37		3.21 ± 0.39	< 0.001*	2.91 ± 0.38	0.001**	< 0.001***

This table shows a significant worsening of bilirubin and a rapid improvement in creatinine between baseline (BL) and FU1. For the hemodynamic parameters, an immediate decrease in HVPG and portal pressure is detected. The PV flow volume, T_{max}, and V_{max} show an immediate increase after stent implantation

INR, international normalization ratio; PLT, platelet count; PP, portal pressure; CVP, central venous pressure; HVPG, hepatic venous pressure gradient; V_{max}, maximum velocity; T_{max}, time-average maximal velocity; TIPS, transjugular intrahepatic portosystemic shunt; μmol/L, micromoles per liter; L/s, liters per second; cm/s, centimeters per second; FU, follow-up

*p values refer to signficant values obtained before and after TIPS at FU1; **p values refer to signficant values obtained between FU1 and FU2; ***p values refer to signficant values obtained before and after TIPS at FU2

Improvement in HVPG and the duplex parameters after TIPS implantation

After TIPS insertion, significant decreases in HPVG and portal pressure, as well as a significant increase in central venous pressure ($p < 0.001$, $p < 0.001$ and $p < 0.001$, respectively), were detected (Table 1). The mean HVPG decrease was 63% from baseline. A rapid and significant rise in PV flow volume, PVV_{max}, and Tmax were observed at FU1 ($p = 0.001$, $p < 0.001$ and $p < 0.001$, respectively) and were stable throughout the follow-up period, indicating sufficient TIPS function (Table 1). At FU1, the mean Vmax in the middle third of the TIPS was 146 ± 49 cm/s and remained stable throughout, which indicated sufficient TIPS function and the absence of stenosis (Table 1).

Worsening of the laboratory parameters

A significantly rapid rise in bilirubin was detected after TIPS insertion ($p = 0.003$). A rapid and significant decrease in creatinine ($p = 0.029$), and delayed prolongation of INR ($p = 0.029$) were also detected. Finally, a gradual non-significant decrease in platelet count was also observed (Table 1).

Table 2. Correlation between HVPG and LSM and SSM at baseline, FU1, and FU2

	HVPG baseline	Decrease of HVPG FU1
LSM baseline	$R = 0.151$, $p = 0.418$	$R = -0.014$, $p = 0.942$
Decrease LSM FU1	$R = 0.014$, $p = 0.940$	$R = 0.120$, $p = 0.521$
Decrease LSM FU2	$R = 0.211$, $p = 0.255$	$R = 0.131$, $p = 0.483$
SSM baseline	$R = 0.398$, $p = 0.026$*	$R = 0.131$, $p = 0.482$
Decrease of SSM FU1	$R = 0.254$, $p = 0.183$	$R = 0.436$, $p = 0.018$*
Decrease of SSM FU2	$R = 0.341$, $p = 0.082$	$R = 0.575$, $p = 0.002$*

This table shows that HVPG correlated with SSM at the baseline and the decrease HVPG after TIPS insertion correlated with the decrease of SSM at FU1 and FU 2

HVPG, hepatic venous pressure gradient, LSM, liver stiffness measurement; SSM, spleen stiffness measurement, FU, follow-up

*p values refer to positive correlation before and after TIPS

Table 3. Changes in hemodynamic parameters and liver and spleen stiffness according to the underlying liver disease

	BL Before TIPS	After TIPS	FU1	*p* value BL vs. FU1	FU2	*p* value FU1 vs. FU2	*p* value BL vs. FU2
Alcoholic cirrhosis							
Hemodynamic parameters							
PP (mmHg)	38 ± 7	30 ± 7		< 0.001*	–	–	
CVP (mmHg)	18 ± 5	22 ± 7		< 0.001*	–	–	
HVPG (mmHg)	20 ± 5	8 ± 4		< 0.001*	–	–	
ARFI elastography							
LSM S8 (m/s)	3.26 ± 0.52		3.09 ± 0.54	0.046*	2.92 ± 0.42	0.121	0.020***
LSM S6 (m/s)	3.39 ± 0.47		3.20 ± 0.61	0.074	2.77 ± 0.82	0.109	0.003***
SSM (m/s)	3.54 ± 0.46		3.19 ± 0.46	0.008*	3.19 ± 0.36	0.109	0.004***
Cryptogenic cirrhosis							
Hemodynamic parameters							
PP (mmHg)	38 ± 11	29 ± 15*		0.004*			
CVP (mmHg)	23 ± 5	31 ± 5*		0.003*			
HVPG (mmHg)	19 ± 7	6 ± 2*		0.001*			
ARFI elastography							
LSM S8 (m/s)	2.70 ± 0.65		2.39 ± 0.67	0.214	2.24 ± 0.70	0.051	0.015***
LSM S6 (m/s)	2.72 ± 0.63		2.55 ± 0.70	0.441	2,34 ± 0.70	0.214	0.138
SSM (m/s)	3.48 ± 0.65		3.28 ± 0.34	0.051	2.99 ± 0.33	0.008**	0.008***
Virus-related cirrhosis							
Hemodynamic parameters							
PP (mmHg)	39 ± 6	35 ± 6		0.130*			
CVP (mmHg)	21 ± 6	26 ± 7		0.003*			
HVPG (mmHg)	20 ± 7	9 ± 5		0.005*			
ARFI elastography							
LSM S8 (m/s)	3.25 ± 0.47		3.14 ± 0.86	0.739	2.95 ± 0.36	0.249	0.028***
LSM S6 (m/s)	3.21 ± 0.41		3.01 ± 0.86	0.463	2.13 ± 1.69	0.686	0.138
SSM (m/s)	3.43 ± 0.56		3.24 ± 0.25	0.249	3.06 ± 0.55	0.046**	0.046***

A continuous decrease in LSM and SSM was observed in all patients at the end of the follow-up period. Patients with alcoholic liver cirrhosis showed an early decrease in LSM and SSM; patients with cryptogenic liver cirrhosis and virus-related liver cirrhosis showed only a delayed decrease in SSM
PP, portal pressure; CVP, central venous pressure; HVPG, hepatic venous pressure gradient; BL, baseline; FU, follow-up; LSM, liver stiffness measurement; SSM, spleen stiffness measurement; ARFI, acoustic radiation force impulse imaging
**p* values refer to significant values obtained before vs. immediately after TIPS; ***p* values refer to signficant values obtained between FU1 and FU2; ****p* values refer to signficant values obtained before and after TIPS at FU2

Table 4. Uni- and multivariate analyses of factors for predicting an HVPG decrease to ≤ 10 mmHg after TIPS insertion

	Univariate *p* value	Odds Ratio	Multivariate *p* value	Odds Ratio
Age	0.097	0.381	0.113	0.353
Gender	0.652	0.073	0.757	0.065
Child–Pugh score	0.029*	0.716	0.030*	0.597
MELD score	1.000	0.050	1.000	0.050
Platelets	< 0.001*	1.000	0.826	0.055
LSM	0.028*	0.611	0.033*	0.583
SSM	0.019*	1.000	0.002*	0.907

This table shows that lower Child–Pugh score, LSM, and SSM values are factors predicting a decrease of HVPG to ≤ 10 mmHg after TIPS insertion
MELD, model end-stage liver disease; LSM, liver stiffness measurement; SSM, spleen stiffness measurement
**p* values refer to significant values in the uni- and multivariate analysis

Clinical improvement after TIPS implantation

Regression of ascites at FU2 was detected in 52% of patients (n = 16/31). Reduction in splenic size was observed in 70% of patients (n = 21/30, p = 0.002) (Table 1).

HVPG improvement was associated with a decrease in SSM

At baseline, HVPG correlated with SSM (r = 0.398, p = 0.026), but no correlation was detected with LSM. The decrease in HVPG from baseline correlated positively with SSM decrease from baseline at FU1 (r = 0.436, p = 0.018) and SSM decrease at FU2 (r = 0.575, p = 0.002) but not the decrease of LSM. No correlation was observed between portal vein pressure or inferior vena cava pressure and SSM or LSM at baseline or after TIPS insertion (Table 2).

Aetiological behavioral differences in LSM and SSM after TIPS implantation

After TIPS insertion, an overall decrease in LSM and SSM was detected in different aetiologies (Table 3). Pa-

Table 5. Diagnostic accuracy of LSM, SSM, and Child–Pugh score for predicting an HVPG decrease to ≤ 10 mmHg after TIPS insertion

	Cut-off	AUC 95% CI	Sen 95% CI	Sp 95% CI	PPV 95% CI	NPV 95% CI	+ LR 95% CI	− LR 95% CI	DOR 95% CI
HVPG ≤ 10 mmHg									
SSM	≤ 4.09 m/s	0.90 (0.73–1.00)	80 (28–99.5)	96 (82–99.9)	80 (35.7–96.6)	96.4 (82.4–99.4)	22.4 (3.11–161.3)	(0.21) (0.04–1.20)	108 (5.57–2092.7)
LSM	≤ 3.60 m/s	0.88 (0.74–1.00)	80 (28.4–99.5)	90 (73.5–97.9)	57.1 (29.5–80.7)	96.4 (82.3–99.4)	8 (2.51–25.5)	0.22 (0.04–1.26)	36 (2.97–436.4)
Child–Pugh	≤ 6.5	0.84 (0.70–0.98)	100 (39.8–100)	79 (61.1–91)	36.4 (22.8–52.5)	100 –	4.71 (2.44–9.1)	0.00 –	31.8 (1.53–659.6)

This table shows that SSM, LSM, and Child–Pugh score at baseline are able to predict an HVPG decrease to below 10 mmHg after TIPS insertion with closer AUC, sensitivity and specificity; however, the diagnostic odds ratio is highest in SSM
HVPG, hepatic vein pressure gradient; SSM, spleen stiffness measurement; LSM, liver stiffness measurement; AUC, area under the curve; Sen, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value; + LR, positive likelihood ratio; − LR, negative likelihood ratio; DOR, diagnostic odds ratio

tients with alcoholic liver cirrhosis showed a rapid reduction in both LSM and SSM, which paralleled the HVPG decrease after TIPS insertion. A delayed decrease subsequently followed until the end of follow-up (Table 3). Interestingly, patients with cryptogenic liver cirrhosis and virus-related liver cirrhosis showed only a delayed decrease in LSM and SSM with significant SSM reduction between FU1 and FU2.

Prediction of HVPG decrease to ≤ 10 mmHg after TIPS insertion

HVPG decreased below 10 mmHg in 84% of patients after TIPS. The univariate and multivariate analyses revealed that lower LSM and SSM values and Child–Pugh score at baseline are predictive of a decrease in HVPG to ≤ 10 mmHg after TIPS insertion ($p = 0.033$, $p = 0.002$ and $p = 0.030$, respectively) (Table 4).

Diagnostic accuracy of SSM, LSM, and Child–Pugh score

Patients with baseline SSM ≤ 4.09 m/s, LSM ≤ 3.60 m/s , and Child–Pugh score ≤ 6.5 showed an HVPG decrease to ≤ 10 mmHg after TIPS insertion with AUC of 0.90, 0.88, and 0.84, respectively, and with close sensitivity and specificity. However, the diagnostic accuracy (odds ratio) was highest with SSM (Table 5; Fig. 1).

Complications after TIPS insertion

Three patients developed complications (8%). One 67-year-old male patient with alcoholic liver cirrhosis etiology and hepatorenal syndrome died due to acute liver failure after TIPS implantation. The second, a 44-year-old male patient, had severe uncontrolled bleeding from oesophageal varices after TIPS. The third patient was a 70-year-old female who developed grade IV hepatic encephalopathy.

Discussion

This prospective observational study reveals that spleen stiffness can non-invasively identify patients with CSPH who will derive most benefit from TIPS insertion. Liver and spleen stiffness decreased continuously after TIPS insertion. This decrease began within the first few days and continued for 6 weeks. Interestingly, spleen stiffness correlated best with HVPG at baseline and with the dynamic decrease in HVPG after TIPS insertion, while liver stiffness and the Child–Pugh score did not correlate. Data from the current study show that liver and spleen stiffness and Child–Pugh score at baseline are predictive of an HVPG reduction to ≤ 10 mmHg after TIPS insertion. Patients with SSM ≤ 4.09 m/s at baseline showed an HVPG reduction to ≤ 10 mmHg with a consequent decrease in risk of developing complications. While baseline LSM ≤ 3.60 m/s and Child–Pugh score ≤ 6.5 showed slightly lower AUC than SSM in predicting the HVPG decrease to ≤ 10 mmHg, the diagnostic accuracy of SSM was the highest. This is consistent with other studies [31]. Despite liver stiffness decreasing significantly after TIPS insertion in all patients, HVPG showed no significant correlation with liver stiffness at either baseline or at any follow-up. This is in agreement with a recent study [17]. However, this is not in line with published data, which show that TIPS insertion is associated with an immediate parallel reduction in HVPG and liver stiffness [32]. This can be explained by multifactorial causes. All patients had significant cirrhosis, which would have delayed the significant changes after TIPS insertion. Another factor was the worsening of liver function after TIPS insertion (especially bilirubin), which might also explain the delayed significant decrease in liver stiffness in accordance with the HVPG reduction. Our observations are consistent with previous studies that indicate spleen stiffness to be the best predictor of portal hypertension when compared to liver stiffness, to correlate best with HVPG before management, and to have a dynamic decrease after treatment [33]. In addition, our data are consistent with a recent study indicating the

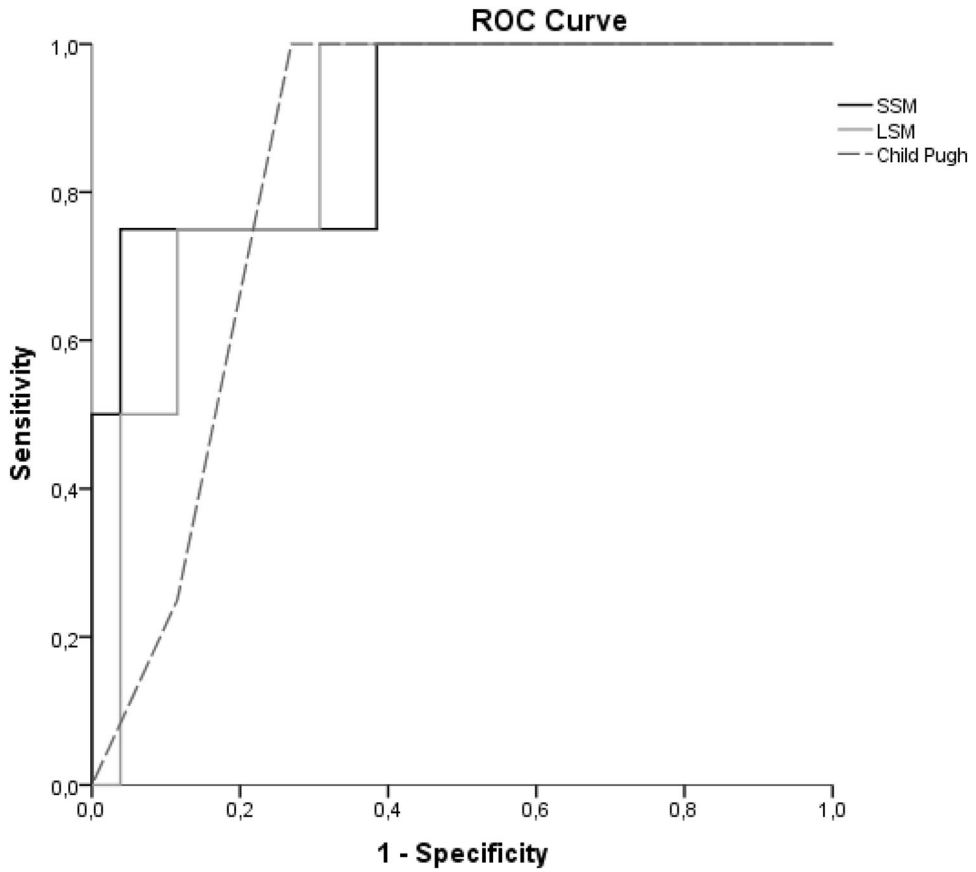

Fig. 1. Receiver operator curve (ROC) predicting decrease of HVPG ≤ 10 mmHg after TIPS insertion by LSM, SSM , and Child–Pugh. SSM has the highest AUC in comparison to LSM and Child–Pugh score in predicting HVPG ≤ 10 mmHg after TIPS insertion. LSM, liver stiffness measurement; SSM, spleen stiffness measurement; HVPG, hepatic vein pressure gradient; ROC, receiver operating curve.

importance of SSM use in TIPS surveillance in patients with chronic liver disease [33]. In contrast, one study showed that LSM and SSM could not predict TIPS outcome and could only be used in monitoring its function [34].

Studies have shown that portal hypertension is composed of two components. The first is a static component secondary to the intrahepatic resistance, which can only be modified by removal of the causative factor (abstinence, HCV treatment) [35, 36]. The second is a dynamic and potentially reversible component, which involves a vasoregulation imbalance between increased vasoconstrictors of hepatic vasculature and a decrease in vasodilation in the systemic circulation. Similarly, liver stiffness is affected by the static component (liver fibrosis) and the dynamic component [35]. Therefore, reduction in the portal pressure resulted in a decrease in the dynamic component of liver stiffness, but the appearance was somewhat delayed because the static component was aggravated (patients where Child B in 77% of cases). This also explains why the decrease in portal pressure did not correlate with the liver stiffness reduction. Moreover, the decrease appeared rapidly in the alcoholic patients (abstinence before treatment) due to removal of the causative agent, which was not the case in viral-related cases or cryptogenic cirrhosis. That was not the case for spleen stiffness, which is only affected by the dynamic component of the portal pressure and therefore correlated with HVPG at baseline and continuously after the HPVG reduction at the follow-up period up to 6 weeks. Although studies have shown the MR elastography is an excellent and sensitive tool in assessing the change in the two components of liver stiffness in comparison to portal pressure change [35, 37, 38], the technique is expensive and not readily available in every center.

The current study has some limitations. The number of patients in this study was low, and the follow-up duration was too short to detect long-term complications and their effect on LSM and SSM.

Although liver and spleen stiffness, as well as Child–Pugh score prior to TIPS, can identify patients with an HVPG decrease to ≤ 10 mmHg after the procedure, spleen stiffness had the highest diagnostic accuracy. In the future, spleen stiffness measurements might represent

a non-invasive, reliable, cost-effective, and rapid bedside test to identify a patient's outcome after TIPS insertion.

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Compliance with ethical standards

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