



## Brief Report

## Spleen stiffness can be employed to assess the efficacy of spontaneous portosystemic shunts in relieving portal hypertension

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## ABSTRACT

**Introduction:** Spleen stiffness (SS) has been found to mirror dynamic changes in portal pressure after transjugular intrahepatic portosystemic shunt (TIPS) placement. However, there is no data available regarding SS in patients with spontaneous portosystemic shunting (SPSS), especially in regards to prediction of hepatic decompensation.

**Methods:** We retrospectively selected patients with confirmed SPSS and esophageal varices (EVs) at endoscopic examination, and recorded any decompensating event (i.e., variceal hemorrhage, overt hepatic encephalopathy, refractory ascites, spontaneous bacterial peritonitis, hepatorenal syndrome) in the first twelve months following liver and spleen elastography.

**Results:** The patients who presented decompensating events showed lower platelet count (94.5 vs. 121.5 g/L,  $p < 0.001$ ), higher SS (44 vs. 30 kPa,  $p < 0.001$ ), higher probability of EVs according to SS (77 vs. 2%,  $p < 0.001$ ), and higher spleen diameter (14 vs. 12 cm,  $p = 0.043$ ). They also showed a higher prevalence of splenorenal shunts (66.7 vs. 31.2%), and a significantly wider SPSS major diameter (14.5 vs. 8 mm,  $p < 0.001$ ).

**Conclusion:** SS could predict SPSS efficacy in relieving portal pressure, and could predict decompensating events in patients with SPSS.

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## 1. Introduction

Portal Hypertension (PH), defined as a portal pressure  $>10$ – $12$  mmHg, is a common and critical complication of liver cirrhosis, which defines the transition to a stage of liver disease characterized by a significant reduced life expectancy and quality of life. [1] Generally, PH is associated with increased risk of esophageal varices, (EVs) and decompensating events (such as ascites, variceal haemorrhage, and hepatic encephalopathy) [2]. Therefore, appropriate PH quantification is crucial and spleen elastography seems to address this unmet clinical need. Despite its proven correlation with the invasive gold standard of hepatic venous pressure gradient (HVPG) [3], spleen stiffness (SS) has been found to mirror dynamic changes in portal pressure after transjugular intrahepatic portosystemic shunt (TIPS) placement [4,5].

This led us to investigate the role of SS in the parapsychological version of TIPS (i.e., spontaneous portosystemic shunts, SPSS). In particular, we aimed to determine if SS could have predicted the efficacy of SPSS in relieving portal pressure, especially considering the fact that a group of patients with esophageal varices (EVs) and without current non-selective beta-blockers (NSBB) administration were not correctly classified by the spleen stiffness probability index, a mathematical device that we had previously developed in a sample of 210 cirrhotic patients [6]. In detail, this index provides a given probability of having EVs based on the individual value of SS, which could also be employed as a non-invasive surrogate of clinically significant portal hypertension (CSPH). Surprisingly, in this group of patients the SS was either low or comparable to those of healthy individuals [7,8] despite the presence of EVs at endoscopy. Of notice all presented SPSS.

## 2. Methods

Spleen and Liver Stiffness as well as the laboratory tests reported in Table 1 were performed, as per the standard clinical

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**Table 1**  
Patients were stratified in two groups according to the development of decompensating events in two groups. Variable are presented as absolute number (relative percentage) or median (Quartile 1; Quartile 3). Intergroup differences were assessed through Mann-Whitney U test for numerical variables and Chi-Square Test for ordinal variable. SPSS: spontaneous portosystemic shunt; AST (aspartate aminotransferase); ALT (alanine aminotransferase); ALP (alkaline phosphatase); LS (liver stiffness); SS (spleen stiffness); EVs (esophageal varices).

	Total n = 52	Patients without Decompensating Events n = 22	Patients with Decompensating Events N = 30	Significance
Gender, Male (%)	30 (57.7)	14 (63.6)	16 (53.3)	NS
Age, years	65 (62;68)	65.5 (63;69)	64.5 (62;67)	NS
Etiology, N (%)	29 (55.8) 23 (44.2)	15 (68.2) 7 (31.8)	14 (46.7) 16 (53.3)	
Alcohol Abuse				
Viral Hepatitis				
Type of SPSS, N (%)	25 (48.1) 27 (51.9)	15 (68.2) 7 (31.2)	10 (33.3) 20 (66.7)	P = 0.013 Cramer's Phi = 0.345
Paraumbilical Splenorenal				
AST (IU/L)	27 (23;29.5)	28.5 (24.25;31.75)	26 (23;28.75)	NS
ALT (IU/L)	22 (20;24)	21.5 (19.25;23.5)	22 (20;30.75)	NS
GGT (IU/L)	27 (26;39)	27 (23.75;36.75)	27.5 (26;39)	NS
ALP (IU/L)	82 (80;91)	81.5 (80;90)	82 (80; 97.75)	NS
Total Bilirubin (mg/dL)	2 (1.75;2.20)	1.95 (1.60; 2.20)	2.04 (1.70; 2.32)	NS
Albumin (g/dL)	3.2 (2.9;3.4)	3.4 (3;3.6)	3.3 (2.9;3.6)	NS
Platelet (g/L)	110 (92.75;121)	121.5 (115.75;123.75)	94.5 (78.25;100)	P < 0.001
LS (kPa)	42 (40;46)	40.5 (32.5;43)	45 (40.25;47.75)	p = 0.003
Probability of EVs according to LS (%)	74 (73;75)	73 (69;74)	75 (74;77)	P = 0.006
SS (kPa)	39.5 (30;45)	30 (26.5;32.75)	44 (41.25;55)	p < 0.001
Probability of EVs according to SS (%)	56 (4;81)	2 (0.5;11)	77 (66;94)	p < 0.001
SPSS Diameter (mm)	8 (11;16)	8 (7;10)	14.5 (10.25;19)	p < 0.001
Spleen Diameter (cm)	13 (12;15)	12 (12;14)	14 (12;16)	p = 0.043

cal practice, on patients who were evaluated by the Liver Clinic between January 2018 and December 2018. The methodology behind elastography measurement was already explained in detail elsewhere [6,8,9].

We retrospectively selected patients with confirmed SPSS and EVs at endoscopic examination, and recorded any decompensating event (i.e., variceal hemorrhage, overt hepatic encephalopathy, refractory ascites, spontaneous bacterial peritonitis, hepatorenal syndrome) in the first twelve months following elastography examination.

### 3. Results

Patients were stratified in two groups based on the development of decompensating events; their characteristics are reported in Table 1. Patients were predominantly male (57.5%), with a median age of 65 (62; 68) years. The etiology of liver disease was alcohol abuse in 55.8% of patients and virus-related in 44.2% of patients. The patients who presented decompensating events showed lower platelet count (94.5 vs. 121.5 g/L,  $p < 0.001$ ), higher SS (44 vs. 30 kPa,  $p < 0.001$ ), higher probability of EVs according to SS (77 vs. 2%,  $p < 0.001$ ), and higher spleen diameter (14 vs. 12 cm,  $p = 0.043$ ). They also showed a higher prevalence of splenorenal shunts (66.7 vs. 31.2%), and a significantly wider SPSS major diameter (14.5 vs. 8 mm,  $p < 0.001$ ).

### 4. Discussion

The importance of these findings resides in the fact that SPSS can be interpreted as a physiological attempt of the human body to decompress the portal venous system. Unfortunately, SPSS often does not allow adequate reduction of portal pressure, which can present elevated value despite the presence of massive SPSS [10]. What if we could employ a simple and non-invasive method to check if SPSS are effectively accomplishing their purpose of reducing the portal pressure? The answer to this question yields high relevance (given the fact that SPSS are relatively common in liver cirrhosis and that the clinical evolution of cirrhotic patients is extremely variable) and could find a possible answer in SS, especially because SS has already been reported to predict hepatic decompensation [11].

These results, albeit interesting, must be taken with caution due to the relatively low numerosity of the sample size and the possible limitations related to selection bias. While waiting for the essential external validation, we strongly believe that SS may be valuable in the everyday clinical evaluation of cirrhotic patients.

### Authors' contributions

M.G., G.B., C.A., F.M., C.T. and L.S.C. were involved in the conceptualization and supervision of the current work. M.G., C.A., F.M., L.S.C. were involved in patients' investigation and data collection. M.G. and L.S.C. performed formal statistical analysis. M.G., G.B., C.A.,

F.M., C.T. and L.S.C. were involved in the writing the original draft and approving the final version of the manuscript.

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#### Conflict of interest

The authors have no conflicts of interest to declare.

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