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The Power of Share Wave Elastography in Evaluating Portal Hypertension Signs in Children

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Abstract

Objective: We wanted to investigate the value of spleen elastography and liver elastography values measured by shear wave elastography and some parameters such as spleen size and spleen ratio in detecting the presence and grade of esophageal varices.

Methods: The patient group included 43 patients diagnosed with portal hypertension and 63 healthy children. Spleen elastography and liver elastography were evaluated by shear wave elastography in patients who had screening gastroscopy for esophageal varices, and these patients were compared with healthy controls.

Results: Both the liver elastography and spleen elastography values were significantly higher in portal hypertension patients than controls. The mean liver elastography and spleen elastography values were higher in the variceal hemorrhage group than in the varices non-hemorrhage group. The spleen ratio measured by ultrasonography and spleen elastography values were weakly correlated, while the mean liver elastography and spleen elastography values were higher in the esophageal varices group than in the non-varices group. The spleen elastography values and the liver elastography values are both higher in the presence of esophageal varices. For spleen elastography values of >30 kPa was the cutoff value for the detection of the esophageal varices. The spleen elastography values of >37 kPa was the cutoff for the detection of the esophageal varices hemorrhage. There is no significant correlation with the esophageal varices grade.

Conclusions: We realized that the liver and spleen elastography values are changing with the presence of portal hypertension, esophageal varices, and variceal hemorrhage. But we could not find a significant correlation with the esophageal varices grade and liver elastography or spleen elastography values. Further studies are needed to determine the cutoff points for spleen elastography to indicate hemorrhage.

Keywords: Children, esophageal varices, shear wave elastography (SWE), portal hypertension (PHT)

Introduction

Esophageal varices (EV) are an important manifestation of portal hypertension (PHT) that develops over time in children with chronic liver disease. The risk of EV hemorrhage increases depending on the underlying disease as well as the duration of the disease, and the mortality rate is as high as 5%-20%.[1] The risk of EV hemorrhage increases cirrhosis, while this rate increases to 38% at the 5-year follow-up of the patients.[2] During patient follow-up, invasive procedures such as gastroscopy are performed repeatedly to detect the presence and progression of EV. Many non-invasive methods have been investigated for their efficacy in determining the presence of EV and the risk of complications in the detection of the presence of PHT in adult patient groups. These include spleen size, platelet count, platelet count-to-spleen size *Z*-score,[3,4] fibrotest that serologically assesses liver fibrosis,[5] and liver stiffness (LS)[6,7] and spleen stiffness (SS)[8] assessed by transient elastography (TE) or acoustic radiation force impulse (ARFI) sonoelastography. In children, in turn, the liver elastography (LE) value measured by ARFI imaging[9] and shear wave elastography (SWE)[10] was shown to be valuable in demonstrating liver fibrosis. In children, liver fibrosis and PHT markers were compared with SS measured by TE.[11]

Gastroscopy is performed at regular intervals to assess the signs of PHT and follow up on the varices that develop during the course of the disease in children. Developing non-invasive methods is important to reduce the number of gastroscopic procedures. There are not enough studies on this subject in children. Several variables were examined in adults, and among these, spleen elasticity was found to have a high accuracy rate in reflecting the presence and grade of EV.[4,6,7,11] In our study, we wanted to investigate the value of LS and SS values measured by SWE and some parameters such as spleen size and spleen ratio in detecting the presence and grade of EV.

Methods

The patient group included 43 patients diagnosed with PHT, who were followed up in the İstanbul University, Cerrahpasa Medical Faculty, Pediatric Gastroenterology Outpatient Clinic between 2000 and 2014. The patients were aged from 10 months to 19.5 years. The research protocol was initiated after approval by the İstanbul University-Cerrahpaşa ethic committee (Date:

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February 10, 2015, Number: 83045 809/6 04.01 /02-4 1287). The legal guardians of all patients included in the study provided their consent stating voluntary participation in the study. Children diagnosed with PHT and scheduled for gastroscopy to screen varices were included in the patient group. Study exclusion criteria were the presence of ascites, non-compliance of the patient during the procedure, and previous splenectomy and/or portosystemic shunt surgery, which would affect the accuracy of the procedure. Patients who received sclerotherapy, band ligation, and transjugular intrahepatic portosystemic shunt were excluded from the study.

All patients were examined, and clinical and laboratory data were recorded. Liver and spleen sizes of all patients were measured by ultrasonography (USG). The spleen size was assessed by Doppler USG and the signs of PHT by measuring the portal vein diameter and flow velocity and splenic vein diameter and flow velocity. The spleen size measured by USG and the longitudinal coronal extension of the spleen were evaluated. The longitudinal spleen size was determined according to the patient's age and sex and proportioned to the normal spleen size to establish the spleen ratio. Patients scheduled for gastroscopy to screen varices were included in the patient group, and LS and SS were measured simultaneously by SWE. It was ensured that there was no longer than 3 months between elastography and gastroscopy. Also, blood tests were performed for platelet count, aspartate aminotransferase, alanine aminotransferase, and prothrombin time. The control group consisted of children who presented to the pediatric outpatient clinic of our hospital without any chronic diseases and who had blood tests and abdominal USG for other reasons, which were normal. A total of 64 healthy children were included in the study. The same laboratory tests were performed for healthy controls. Liver USG, LE, and spleen elastography (SE) were performed.

Shear wave elastography was performed using the Aixplorer ultrasound system (SuperSonic Imagine SA, Aix-en-Provence, France) with a convex broadband probe (SC6-1). The average of 3 measurements on the right lobe of the liver, 2 measurements on the left lobe of the liver, and 3 measurements on the spleen were calculated. The spleen size was measured longitudinally with gray-scale ultrasound. The presence or absence of splenorenal shunts and perigastric collaterals was assessed with color Doppler USG. Portal vein patency, diameter, and flow velocity, and splenic vein diameter and flow velocity were examined by Doppler USG in all patients. Hepatic vein patency, presence of cavernous transformation, and collateral formation in perisplenic, perigastric, and paraumbilical regions were examined. Coronal vein patency and splenorenal shunts were investigated.

In the statistical analysis, the study variables were summarized as mean and SD and as median and interquartile range where appropriate. The normality of distribution for continuous variables was confirmed with the Shapiro–Wilk test. For comparison of continuous variables between 2 groups, the Student's *t*-test or the Mann–Whitney *U*-test was used depending on whether the statistical hypotheses were fulfilled or not. To evaluate the correlations between the spleen size measured by USG and elastography values, the Spearman correlation coefficient was used. For comparison of more than 2 groups, 1-way analysis of variance or Kruskal–Wallis test was used depending on whether the statistical hypotheses were fulfilled or not. For normally distributed data, regarding the homogeneity of variances, Tukey and Games–Howell tests were used for multiple comparisons of groups. For non-normally distributed data, Mann–Whitney *U*-test was used for multiple comparisons of groups. A receiver operator characteristic (ROC) curve analysis was performed in order to identify the optimal cutoff point of elastography values (liver and spleen) to predict hemorrhage. All analyses were performed using IBM Statistical Package for Social Sciences Statistics version 20.0 statistical software package (IBM Corp.; Armonk, NY, USA). The statistical level of significance for all tests was considered to be .05.

Results

A total number of 43 patients diagnosed with PHT, including 22 boys and 21 girls, and 63 healthy controls were included in the study. The mean age of the patients was 7.7 years (10 months-19.5 years). The most common diagnosis was operated biliary atresia in the patient group with PHT. There were 10 cases diagnosed with operated biliary atresia, 6 cases with autoimmune hepatitis, 3 cases with congenital hepatic fibrosis, 3 cases with progressive familial intrahepatic cholestasis, 1 case with portal vein thrombosis, and 1 case with Wilson's disease. The cause of PHT in other patients could not be fully identified. When the study patients were evaluated according to esophageal varices, there were 18 patients without esophageal varices, 10 patients with grade 1 varices, 7 patients with grade 2 varices, and 8 patients with grade 3 varices. There were 38 patients without variceal hemorrhage and 5 patients with variceal hemorrhage. While 30 patients did not

Figure 1. Liver shear wave elastography value in a control group patient (7.4 kPa).

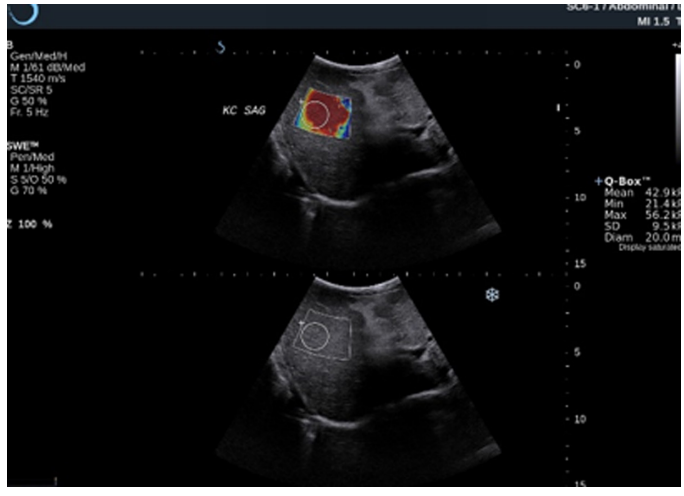

Figure 2. Liver shear wave elastography value in a patient with portal hypertension (42.9 kPa).

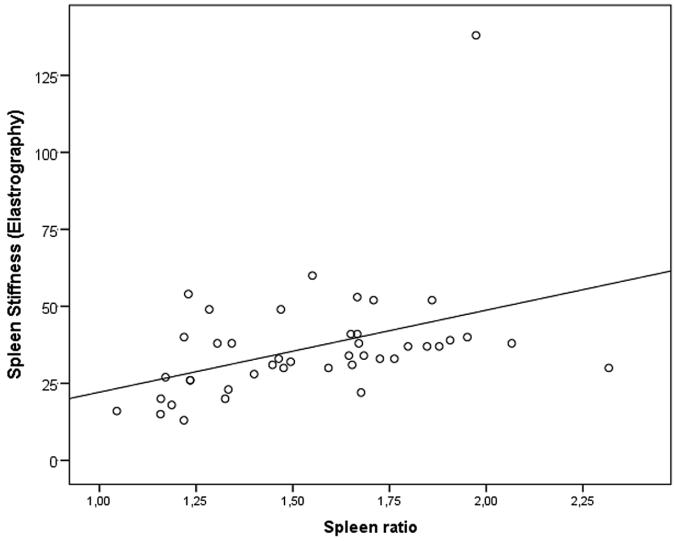

Figure 3. A weak correlation was found between the spleen ratio and spleen elastography value.

have portal hypertensive gastropathy (PHG), 12 patients had PHG (Figures 1 and 2).

In PHT, the spleen size measured by USG and the SS measured by elastography values of the patients were weakly correlated (r = 0.347, P = .023). The spleen ratio measured by USG and SE values was weakly correlated (r = 0.402, P = .008) (Figure 3).

The mean LE value was significantly higher in patients with PHT (25.4 kPa) than the control group (8 kPa) (P < .001). There was no significant difference between the elastography values of the right and left liver lobes (Table 1).

There was no significant difference in reflecting the presence of varices between the elastography values of the right and left liver lobes, while the mean LE value was 27.9 kPa in the varices group and 21.9 kPa in the non-varices group (P = .037). The SE values were higher in the varices group than in the non-varices group (P = .006) (Table 2). The SE values and the LE values are both higher in the presence of EV (Figure 4).

The area under the curve (AUC) measured by ROC analysis of the success of the detection of varices by SE is 0.747 (95% CI: 0.578-0.915). For SE values of >30 kPa in the presence of varices, the SE had a sensitivity of 84% and a specificity of 61%. The AUC measured by ROC analysis of the success of the detection of variceal hemorrhage by SE is 0.824 (95% CI: 0.673-0.974). For SE values of >37 kPa in the presence of variceal hemorrhage, the SE had a sensitivity of 80% and a specificity of 66%. The SE and LE value increases with the presence of variceal hemorrhage. The SE value was 62.98 kPa in the presence of variceal hemorrhage and 33.2 kPa in patients without variceal hemorrhage (P = .016) (Table 3).

The SE value increased significantly with increasing spleen ratios. The SE value was 28.2 kPa when the spleen ratio was

Table 1. Liver Elastography Measurements of the Portal Hypertensive Group and the Control Group

	PHT (n = 43)	CG (n = 63)	*P*
BMI, mean ± SD	17.1 ± 3.1	18.6 ± 3.3	**.026**
Liver elastography, mean ± SD	25.4 ± 22.0	8.0 ± 1.9	**<.001**
Median (IQR)	21 (11)	8 (2)	
Right lobe, mean ± SD	26.7 ± 26.8	7.9 ± 2.4	**<.001**
Median (IQR)	22 (12)	8 (2)	
Left lobe, mean ± SD	24.1 ± 18.7	8.3 ± 1.9	**<.001**
Median (IQR)	18 (13)	8 (2)	

BMI, body mass index; CG, control group; IQR, interquartile range; PHT, portal hypertension; SD, standard deviation.
The statistical level of significance for all tests was considered to be .05. The bold values are statistically significant.

Table 2. The Mean Liver and Spleen Elastography Value According to the Presence and Absence of Varices

	Varices Group (n = 25)	Non-varices Group (n = 18)	*P*
Age, mean ± SD	7.1 ± 4.7	8.5 ± 5.3	.351
Sex, male/female	14/11	8/10	.455
BMI, mean ± SD	17.2 ± 3.3	17.1 ± 3.0	.951
Liver elastography, mean ± SD	27.9 ± 21.4	21.9 ± 23.0	**.037**
Median (IQR)	22 (12)	15.5 (15.3)	
Right lobe, mean ± SD	28.5 ± 25.6	24.2 ± 28.9	**.042**
Median (IQR)	22 (8)	15 (16)	
Left lobe, mean ± SD	27.3 ± 18.9	19.6 ± 18.0	**.014**
Median (IQR)	22 (13.5)	13.5 (12.5)	
Spleen USG, mean ± SD	14.0 ± 3.1	12.6 ± 3.3	.116
Spleen ratio, mean ± SD	1.63 ± 0.23	1.42 ± 0.32	**.013**
Spleen elastography, mean ± SD	41.9 ± 21.5	29.4 ± 13.1	**.006**

BMI, body mass index; IQR, interquartile range; USG, ultrasonography. The statistical level of significance for all tests was considered to be .05. The bold values are statistically significant.

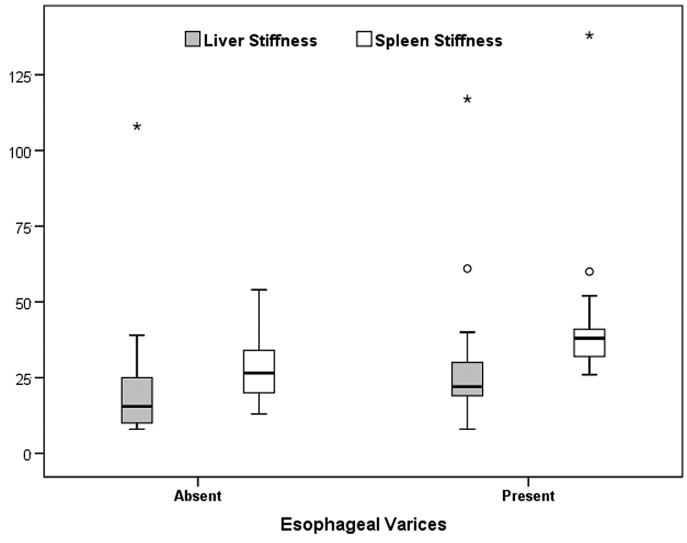

Figure 4. Liver and spleen stiffness measurements with the absence or presence of the esophageal varices.

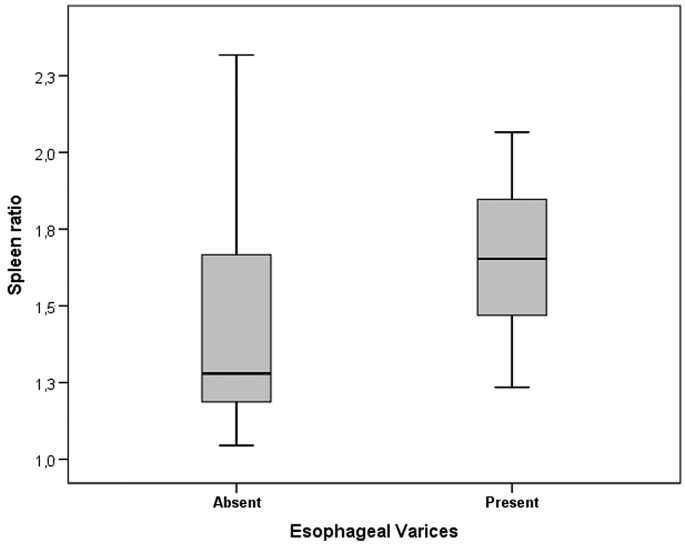

Figure 5. The spleen ratio correlation with the absence or presence of the esophageal varices.

1-1.3 (15 patients), 35.9 kPa when the spleen ratio was 1.4-1.7 (18 patients), and 47.1 kPa when the spleen ratio was >1.7 (10 patients). The spleen ratio was 1.51 in the absence of variceal hemorrhage and 1.85 in patients with variceal hemorrhage. The spleen ratio was high in the presence of variceal hemorrhage.

When evaluated according to the grade of varices, the SE value and the spleen ratio were found to increase as the grade of varices increased. The SE value was 29.4 kPa in patients without varices, as compared with 37.3 kPa in the presence of grade 1 varices, 38.9 kPa in the presence of grade 2 varices, and 50.3 kPa in the patients with grade 3 varices (P = .08). The spleen ratio was 1.42 in patients without varices, while it increased with increasing grades of varices. The spleen ratio was 1.57 in patients with grade 1 varices and 1.66 in patients with grade 2 varices and increased to 1.7 in patients with grade 3 varices (P = .07).

Table 3. The Liver and Spleen Elastography Value According to the Presence of Variceal Hemorrhage

	Variceal Hemorrhage Group (n = 5)	Non-variceal Hemorrhage Group (n = 38)	*P*
Liver elastography, mean ± SD	44.2 ± 40.9	22.9 ± 17.8	**.032**
Median (IQR)	28 (8)	19.5 (12)	
Right lobe, mean ± SD	48.6 ± 53.4	23.8 ± 20.8	.071
Median (IQR)	26 (5)	20.5 (14)	
Left lobe, mean ± SD	40.2 ± 28.4	22 ± 16.4	**.016**
Median (IQR)	28 (13)	17 (11)	
Spleen USG, mean ± SD	17.2 ± 3.6	12.9 ± 2.9	**.004**
Spleen size *N* length, mean ± SD	9.4 ± 1.5	8.7 ± 1.2	.211
Spleen ratio, mean ± SD	1.85 ± 0.23	1.51 ± 0.28	**.011**
Spleen elastography, mean ± SD	62.8 ± 42.6	33.2 ± 11.1	**.016**
Median (IQR)	33 (13)	49 (14)	

IQR, interquartile range; USG, ultrasonography.
The statistical level of significance for all tests was considered to be .05. The bold values are statistically significant.

Discussion

Portal hypertension-related complications are an important cause of mortality in children, and therefore several studies have been conducted on early diagnosis. Elastography has been a guiding method to avoid gastroscopy in assessing the risk of variceal hemorrhage and the grade of varices. Further studies are required regarding the validity of SWE in determining the signs and complications of PHT in children. In the presence of liver disease, the measurement of hepatic venous pressure gradient (HVPG), which is the most important diagnostic finding to clinically assess the presence of PHT, and LE, which is measured by SWE, were found to be valuable in detecting the presence of EV.[12] Despite being very important data for the prediction of PHT complications in the pediatric patient group,[13] the use of HVPG assessment is limited because it is invasive, contains ionizing radiation, and requires anesthesia. Therefore, EV is usually diagnosed by gastroscopy.[14] Our study performed simultaneous liver and SE by SWE to assess the presence of EV, risk of hemorrhage, and grade of varices in pediatric patients. Hepatic venous pressure gradient was not evaluated due to its invasiveness. We measured and assessed portal vein PV flow velocity and diameter and splenic vein SV flow velocity and diameter for establishing a diagnosis. Pediatric studies showed that SE and LE by TE and ARFI imaging without HVPG measurement were effective in demonstrating EV.[13,15]

The TE technique was found to be valuable in detecting the presence of varices requiring invasive procedures in an adult patient group.[16] Many adult studies showed that LE by SWE was helpful in diagnosing clinically significant PHT.[17] Our study observed that SE measured by 2-dimesnional (2D) mode[18] was as significant as LE in the assessment of PHT findings. A previous study found that the elastography value measured in segment 8 of the liver of the patients was more significant than the LE value measured in segment 1.[19] We, in turn, compared the right and left liver lobe elastography values. The mean right lobe elastography value was 26.7 kPa, while the left lobe elastography value was 24.1 kPa, with no significant difference between the values. In demonstrating the presence of EV in patients, the mean SE values were found to be significantly higher compared to the mean LE values.[4]

The SE assessment by the 2D SWE technique was considered more difficult in achieving reliable results because of the obstruction of the image by colonic gas due to the location of the spleen and the heterogeneous tissue of the spleen.[18] Some studies found that spleen elasticity measured by the 2D SWE technique was more diagnostically valuable and successful in reflecting the HVPG when compared to liver elasticity.[9,20] Further studies are required to assess the elasticity of the liver and spleen by 2D SWE for the detection of PHT signs in patients with chronic liver disease.

The study evaluated parameters such as platelet count, platelet count-to-spleen length *Z*-score, and albumin and established a significant difference between patients with and without varices.[21] The patients' spleen size and spleen ratio measured by USG and the SE values were significantly correlated.[11] The spleen ratio was calculated by proportioning the longitudinal spleen size measured by USG to the normal values determined according to the patient's age and sex.[22] The spleen ratio was correlated with SE and the

grade of varices. A significant correlation was found between the portal vein flow velocity and SE.

The mean SE value was 36.6 kPa in patients with PHT and 18.12 kPa in the control group. The mean SE was significantly higher in the PHT patients than in the control group ($P < .001$). When evaluated independently of the PHT etiology and according to the presence/absence of cirrhosis, the SE value was higher compared to the control group.[23] The mean LE value was 26.7 kPa in the right lobe and 24.1 kPa in the left lobe in PHT patients and 7.86 kPa in the control group. The right lobe/left lobe elastography values were significantly higher in PHT patients than in the control group ($P < .001$).

The mean LE value was 25.4 kPa in patients with PHT and 8.0 kPa in the control group. The mean LE was significantly higher in the PHT patients than in the control group ($P < .001$). The mean LE value was 27.9 kPa in the varices group and 21.9 kPa in the non-varices group. The SE value was 41.92 kPa in patients with varices compared with 29.4 kPa in those without varices.

Our study established that both LE and SE values were valuable in demonstrating the presence/absence of varices. It was also found valuable in showing the grade of varices in cases of higher grades. As determined in some studies,[6,11] SS measured by TE was found to be valuable in detecting the grade of varices. Wang et al[7] established that the LE value measured by TE was poor in detecting the grade of varices but significant in demonstrating the presence of varices. Our study, in turn, found that not only LE but also SE was valuable in detecting the presence of varices and high-grade varices.[7] In a meta-analysis, the SE value was found to indicate the presence of EV and the presence of treatment-requiring varices as much as LE.[24]

The mean LE value was 44.2 kPa in the presence of variceal hemorrhage and 22.9 kPa in patients without variceal hemorrhage. For LE values of >22.2 kPa in the presence of hemorrhage, the LE had a sensitivity of 100.0% and a specificity of 65.8% in detecting hemorrhage. In 2015 a study mentioned that TE values of 10-15 kPa and >15 kPa were suggestive of probable and chronic compensated liver disease, respectively. The same guidelines indicated that a platelet count of > 150 000 and a TE value of <20 kPa were significant in detecting the presence of varices that would require intervention.[25] The SE value (62.8 kPa) was significantly higher in patients with variceal hemorrhage. The SE value was 33.2 kPa in patients without variceal hemorrhage. In the presence of variceal hemorrhage, the SE value was significantly higher and the spleen ratio was also proportional. For SE values >30 kPa in the presence of hemorrhage, the SE had a sensitivity of 84% and a specificity of 61%. In a study with 99 pediatric patients, it was found that hemorrhage was not observed in patients with an SE value of <60 kPa.[11] In our study, the SE value was 62.8 kPa in the presence of variceal hemorrhage and 33.20 kPa in patients without variceal hemorrhage.

The main limitation of our study is the small number of the patients.

Conclusion

In our study, we found that not only LE but also SE was valuable in detecting the presence of varices and high-grade varices. The patients' spleen size and spleen ratio measured by USG and the SE values were significantly correlated. Further studies involving more patients are needed to determine the cutoff points for SE to indicate hemorrhage. Different mean values should be used for liver and spleen as elastography values. As seen in our study, SE values (in kPa) are usually higher. Normal LE and SE values should be established individually for all ages and sexes.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul University-Cerrahpaşa (Date: February 10, 2015, Number: 83045 809/6 04.01 /02-4 1287).

Informed Consent: The legal guardians of all patients included in the study provided their consent stating voluntary participation in the study.

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Author Contributions: Concept – D.G.T., Ö.F.B., F.Ç.Ç.; Design – D.G.T., Ö.F.B., F.Ç.Ç., T.E., T.K.; Supervision – M.C., Ö.F.B.; Materials – İ.A.; Data Collection and/or Processing – H.A.C., İ.A.; Analysis and/or Interpretation – M.C., H.A.C.; Literature Review – İ.A., G.Ç.Ç., T.E., T.K.; Writing – D.G.T., T.E.; Critical Review – F.Ç.Ç., T.E., T.K.

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