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Original Research Article

SPLEEN STIFFNESS MEASUREMENT USING ACOUSTIC RADIATION FORCE IMPULSE (ARFI) FOR THE ASSESSMENT OF ESOPHAGEAL VARICES IN CHRONIC LIVER PARENCHYMAL DISEASE

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ABSTRACT

Background: Acoustic radiation force impulse elastography is a noninvasive and reliable method for assessing liver and spleen stiffness, which aids in predicting variceal severity. This study aimed to determine the effectiveness of measuring spleen stiffness (SSM) using ARFI in the diagnosis of oesophageal varices (EV). **Materials and Methods:** This prospective observational study included 50 patients at MIOT Hospital, Chennai, from December 2020 to August 2021. Patient data, cause of cirrhosis, and laboratory values were collected, and MELD scores were calculated. All patients underwent upper GI endoscopy for variceal grading. B-mode ultrasound measured liver size, spleen size, portal vein diameter, and velocity. ARFI elastography was performed after 12-hour fasting, with liver stiffness measured in the right lobe and spleen stiffness across multiple regions; mean ARFI values were used for the analysis. **Results:** Of the patients, 50% had EV, with Grade III being the most common. Patients with EV had significantly lower platelet counts (82,600/µL vs. 134,960/µL, p=0.001), lower PSR (555.24 vs. 981.72, p=0.001), and higher spleen ARFI values (3.30 vs. 2.98 m/sec, p=0.001). Spleen ARFI ≥3.135 m/sec showed strong agreement with EV presence (p=0.001), while ≥3.265 m/sec was significantly associated with high-grade varices (p=0.001). ROC analysis showed excellent diagnostic performance of spleen ARFI for detecting EV (AUC=0.903) and high-grade EV (AUC=0.935), with diagnostic accuracies of 88% and 92%, respectively. In contrast, liver ARFI had poor discriminatory value (AUC=0.553, accuracy 56%). **Conclusion:** Splenic stiffness measured using ARFI demonstrated superior sensitivity, specificity, and diagnostic accuracy compared to liver stiffness in detecting EV. Cut-off values of ≥3.135 m/s and ≥3.265 m/s effectively identified the presence of varices and differentiated high-grade from low-grade varices, respectively.

INTRODUCTION

Every year, liver disease causes approximately 2 million deaths worldwide, with 50% attributed to cirrhosis complications and the remaining 50% to viral hepatitis and hepatocellular carcinoma.[1] Cirrhosis represents the final stage of chronic liver disease and is broadly classified into two prognostic stages: compensated and decompensated.[2] Median survival significantly decreases once the disease enters the decompensated phase.[3] Based on the severity of decompensation, the 1-year mortality rate in cirrhosis ranges from 1% to 57%.[4] Histologically, cirrhosis is characterised by hepatocyte degeneration, necrosis, fibrous tissue replacement, and regenerative nodule formation.[2] These pathological changes cause increased resistance to hepatic blood flow, leading to portal hypertension.[5] Approximately 70% of the increase in portal pressure is attributed to structural changes, and 30% to functional abnormalities.[4]

Portal hypertension is further exacerbated by splanchnic vasodilation and increased portal inflow resulting from hyperdynamic circulation. When portal pressure surpasses a critical threshold,

portosystemic collaterals develop, with gastroesophageal varices (GEV) being the most significant.[6] These varices can enlarge and rupture, becoming a major source of morbidity and mortality in patients with cirrhosis. Annually, approximately 5% of cirrhotic individuals develop oesophageal varices (EV), with 10–20% of small varices progressing to large varices each year. The 2-year risk of bleeding after EV diagnosis is approximately 20–30%, and mortality can reach 25–50% within the first week following variceal rupture. Therefore, early identification and screening of EV in cirrhotic patients is critical to prevent severe complications.[7]
Esophagogastroduodenoscopy (EGD) is the gold standard for variceal detection.[8] However, EGD has limitations, including invasiveness, cost, requirement for anaesthesia, limited accessibility, and the need for skilled personnel.[9] Additionally, many patients may not have varices or require prophylactic treatment, leading to unnecessary procedures. This has driven the need for reliable, non-invasive alternatives for varices vein detection. Various markers, such as spleen size, platelet count, portal vein diameter, fibro tests, and elastography, have been evaluated, but their diagnostic accuracy remains suboptimal.[8]
Ultrasound elastography (USE) is a promising technique for assessing the stiffness of tissues.[10] It operates on the principle that pathological tissues are stiffer than healthy tissues, similar to manual palpation.[11] USE offers benefits such as bedside applicability, lower costs, and wide availability.[10] One of its advanced forms, Acoustic Radiation Force Impulse (ARFI) elastography, uses focused acoustic pulses to generate shear waves and measure tissue stiffness.[12] It is non-invasive, reproducible, quick, and user-friendly.[13] In cirrhosis and portal hypertension, liver stiffness increases due to fibrosis, and splenic stiffness also increases due to venous congestion and splenic hyperplasia.[11] Both liver stiffness (LS) and splenic stiffness (SS) can be quantified using ARFI to help assess cirrhosis severity and predict the presence of oesophageal varices (EV).[14]
The Paquet classification grades EV from I to IV based on size and risk, with Grades III and IV considered high-risk due to the risk of rupture. Studies have emphasised a strong correlation between increasing spleen stiffness and higher Paquet grades. As varices progress in severity, splenic stiffness increases, supporting the use of spleen ARFI not only for variceal detection but also for non-invasive grading, making it a practical alternative to endoscopy in patients with cirrhosis.[15]
Despite several studies evaluating the diagnostic accuracy of splenic and liver ARFI against EGD for detecting EV, no clear consensus exists. This study aimed to determine the effectiveness of measuring spleen stiffness (SSM) using ARFI in diagnosing EV and grading varices using ARFI values of the spleen as high and low grades in patients with chronic liver parenchymal disease.

Objectives

This study aimed to evaluate the diagnostic utility of SSM using ARFI in chronic liver parenchymal disease by determining its sensitivity, specificity, predictive value, diagnostic accuracy, and optimal cutoff values through ROC curve analysis for diagnosing oesophageal varices and differentiating between high- and low-grade varices.

MATERIALS AND METHODS

This prospective observational study was conducted on 50 patients diagnosed with chronic liver parenchymal disease and undergoing treatment in the Department of Gastroenterology and Hepatology at MIOT Hospital, Chennai, from December 2020 to August 2021. Before initiating the study, it was approved by the Institutional Ethics Committee. Written informed consent was obtained before patient enrolment.

Inclusion Criteria

Patients aged > 18 years with clinical/radiological features of chronic liver parenchymal disease who underwent screening EGD for the detection of EV were included.

Exclusion Criteria

Patients with focal liver/spleen lesions, those who did not undergo screening EGD, those currently receiving treatment with beta-blockers, those with portal vein thrombosis or extrahepatic portal vein obstruction, pregnant women, those with acute variceal bleeding, terminally ill patients, those with mental illness, those who did not provide consent, and those who underwent endoscopic variceal ligation/sclerotherapy in the past were excluded.

Methods

Age, aetiology of cirrhosis, and recent biochemical parameters (serum bilirubin, INR, creatinine, and platelet count within the last 7 days) were recorded from the patient records. The MELD score was calculated using a standard formula to assess disease severity. All patients underwent Esophagogastroduodenoscopy (EGD) the gold standard for diagnosing EV, and were classified according to the Paquet grading system. After undergoing upper gastrointestinal endoscopy, all participants were classified according to the Paquet classification system for EV. Based on this, the varices were classified into 0-5 grades, where grade 0 indicated the absence of varices and grade 5 indicated large varices. Ultrasonography using a Siemens Acuson S2000 with a 6C1(1.5 – 6MHz) transducer recorded the liver size (midclavicular line), spleen size (maximum cephalo – caudal length), portal vein diameter (at porta hepatis), and maximum portal vein velocity. Following a 12-hour fast, ARFI elastography was performed using the same system.
Liver ARFI was performed in the left lateral position using an intercostal approach. The region of interest (10 mm depth and 5 mm width) was placed >1 cm

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below the liver capsule, and five readings were taken from segments V–VIII. The mean of the 20 values was used for liver stiffness measurement. Spleen ARFI was performed in the right lateral position, sampling from nine splenic regions using the breath-hold technique. Ten valid readings were obtained, and the mean value was used for the spleen stiffness analysis. In patients with morbid obesity or massive ascites, ARFI was limited to the accessible splenic regions.

Statistical Analysis

The collected data were entered into Microsoft Excel Office 360 to create a master chart, which was then imported into IBM SPSS version 23.0 for analysis. Descriptive statistics were expressed as frequencies and percentages for categorical variables and mean ± standard deviation for continuous variables. ROC curves were used to determine the cutoff values, and diagnostic metrics such as sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated. Kappa statistics were used to assess the agreement between splenic ARFI and EGD in diagnosing EV.

RESULTS

Among the 50 patients, the most common age group was 41–50 years, comprising 16 patients (32%), followed by 14 patients (28%) aged 51–60 years, 12 patients (24%) aged ≤40 years, and 8 patients (16%) aged >60 years. The majority was male, accounting for 41 patients (82%), while only 9 were female (18%). Regarding aetiology, alcohol-related liver disease was the predominant cause, seen in 42 patients (84%), followed by non-alcoholic fatty liver disease in 6 patients (12%) and autoimmune liver disease in 2 patients (4%). Based on MELD scores, 35 patients (70%) had a score ≥25, 7 (14%) had scores between 10–18 and another 7 (14%) between 19 and 24, and only 1 (2%) had a MELD score ≤10. EV were present in only 25 patients (50%), with Grade III varices being the most common, observed in 12 patients (24%), followed by Grade I in 6 (12%), Grade II in 5 (10%), and Grade IV in 2 (4%).

The mean platelet count was 108,780 ± 38,944/µL. The mean spleen size was 143.24 ± 19.51 mm. The mean platelet spleen ratio was 768.48 ± 281.64. The mean liver size was 140.02 ± 18.68 mm in length. The mean portal vein diameter averaged 12.28 ± 2.06 mm. The mean portal vein velocity was 19.76 ± 5.78 cm/s. The mean spleen ARFI value was 3.66 ± 3.14 m/s. The mean liver ARFI was 2.94 ± 0.67 m/s. [Table 1]

Table 1: Mean Values of haematological and ultrasonographic parameters

Variables	Mean ± SD
Platelet count (per µL of blood)	108780 ± 38944.38
Spleen size (mm)	143.24 ± 19.51
Platelet spleen ratio	768.48 ± 281.64
Liver size (mm)	140.02 ± 18.68
Portal vein diameter (mm)	12.28 ± 2.06
Portal vein velocity (cm/sec)	19.76 ± 5.78
Spleen ARFI (m/sec)	3.66 ± 3.14
Liver ARFI (m/sec)	2.94 ± 0.67

Patients with high-grade oesophageal varices were older (49.64 ± 10.38 vs. 44.36 ± 8.25 years, p=0.182) and had lower platelet counts (72,071 ± 27,107 vs. 96,000 ± 42,925/µL, p=0.102). Alcohol was the most common aetiology in both groups; however, autoimmune disease and NAFLD were observed only in the high-grade group, with no significant association (p=0.262). The liver size was smaller in patients with high-grade EV (137.00 ± 16.97 vs. 149.55 ± 19.12 mm, p=0.096), and the platelet spleen ratio was lower (481.07 ± 200.40 vs. 649.64 ± 221.19, p=0.058). Spleen ARFI values were significantly higher in patients with high-grade EV (3.39 ± 0.16 vs. 3.17 ± 0.09 m/sec, p=0.001). The MELD scores (p=0.916), portal vein diameter (p=0.530), portal vein flow velocity (p=0.711), spleen size (p=0.318), and liver ARFI (p=0.571) showed no significant differences between the two groups.[Table 2]

Table 2: Comparison of clinical and ultrasound parameters between low and high-grade EV

Predictors		Low-grade EV	High-grade EV	P value
Age (in years)		44.36 ± 8.25	49.64 ± 10.38	0.182
Platelet count		96000 ± 42925	72071 ± 27107	0.102
Sex	Male	11 (100%)	10 (71.4%)	0.053
	Female	0	4 (28.6%)	
Aetiology	Alcohol	11 (100%)	11 (78.6%)	0.262
	Auto immune	0	1 (7.1%)	
	NAFLD	0	2 (14.3%)	
Liver size		149.55 ± 19.12	137.00 ± 16.97	0.096
PSR		649.64 ± 221.19	481.07 ± 200.40	0.058
Spleen ARFI		3.17 ± 0.09	3.39 ± 0.16	0.001
MELD		29.45 ± 10 .05	29.86 ± 8. 81	0.916

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PVD	12.09 ± 2.46	12.64 ± 1.86	0.53
PV flow velocity	19.40 ± 8.66	18.31 ± 5.81	0.711
Spleen size	143.82 ± 24.93	152.36 ± 16.84	0.318
Liver ARFI	3.07 ± 0.61	2.91 ± 0.73	0.571

Patients with EV were younger (47.32 ± 9.69 vs. 52.12 ± 12.40 years, p=0.134) and had higher MELD scores (29.68 ± 9.17 vs. 25.64 ± 6.56, p=0.08), although these differences were not significant. Platelet count was significantly lower in patients with varices (82,600 ± 36,231 vs. 134,960 ± 18,864/µL, p=0.001). Other parameters, such as sex distribution (p=0.713), aetiology (p=0.683), portal vein diameter (p=0.685), portal vein velocity (p=0.242), liver size (p=0.349), spleen size (p=0.051), and liver ARFI (p=0.623), were similar in both groups and were not significant. The platelet spleen ratio was lower in those with varices (555.24 ± 222.33 vs. 981.72 ± 133.38, p=0.001). Liver ARFI values were similar between the groups (2.98 ± 0.67 vs. 2.89 ± 0.68 m/sec, p=0.623).

A spleen ARFI value ≥3.135 m/sec was strongly associated with the presence of EV, being observed in 92% of patients with varices and only 16% of those without EV (kappa = 0.76, p = 0.001). In contrast, liver ARFI ≥2.425 m/sec was present in 80% of patients with varices and 68% without EV (kappa = 0.12, p = 0.333).

A spleen ARFI value ≥3.265 m/sec showed strong diagnostic agreement with the presence of high-grade EV, being present in 92.9% of high-grade cases and only 9.1% of low-grade cases. In contrast, a value <3.265 m/sec was found in 90.9% of low-grade and only 7.1% of high-grade varices (kappa = 0.838, p = 0.001).[Table 3]

Table 3: Comparison of key parameters between patients with and without EV

Predictors		EV		P value
		Present	Absent	
Age (in years)		47.32 ± 9.69	52.12 ± 12.40	0.134
MELD		29.68 ± 9.17	25.64 ± 6.56	0.08
Platelet count		82600 ± 36231	134960 ± 18864	0.001
Sex	Male	21 (84%)	20 (80%)	0.713
	Female	4 (16%)	5 (20%)	
Aetiology	Alcohol	22 (88%)	20 (80%)	0.683
	Autoimmune	1 (4%)	1 (4%)	
	NAFLD	2 (8%)	4 (16%)	
Portal vein diameter (mm)		12.40 ± 2.12	12.16 ± 2.03	0.685
Portal vein velocity (cm/sec)		18.79 ± 7.06	20.72 ± 4.05	0.242
Platelet spleen ratio (PSR)		555.24 ± 222.33	981.72 ± 133.38	0.001
Liver ARFI (m/sec)		2.98 ± 0.67	2.89 ± 0.68	0.623
Platelet count (per µL of blood)		82600 ± 36231.89	134960 ± 18864.61	0.001
Liver size (mm)		142.52 ± 18.67	137.52 ± 18.72	0.349
Spleen size (mm)		148.60 ± 20.78	137.88 ± 16.90	0.051
Spleen ARFI (m/sec)		3.30 ± 0.18	2.98 ± 0.18	0.001
Liver ARFI	≥ 2. 425	20 (80%)	17 (68%)	0.333
	< 2. 425	5 (20%)	8 (32%)	
Spleen ARFI	≥ 3. 135	23 (92%)	4 (16%)	0.001
	< 3. 135	2 (8%)	21 (84%)	
High-grade EV with spleen ARFI	≥ 3. 265	13 (92.9%)	1 (9.1%)	0.001
	< 3. 265	1 (7.1%)	10 (90.9%)	

Table 4: Evaluation parameters of liver ARFI for the diagnosis of EV

Evaluation Parameter	Liver ARFI	Spleen ARFI	Spleen ARFI (high-grade EV)
Sensitivity (%)	80	92	92.86
Specificity (%)	32	84	90.91
Positive Predictive Value (%)	54.05	85.19	92.86
Negative Predictive Value (%)	61.54	91.3	90.91
Accuracy (%)	56	88	92

The area under the curve for using liver ARFI to diagnose EV was 0.553 (95% CI: 0.391–0.714), with a standard error of 0.082 and a p-value of 0.522. The cutoff value was 2.425 m/s. [Figure 1]

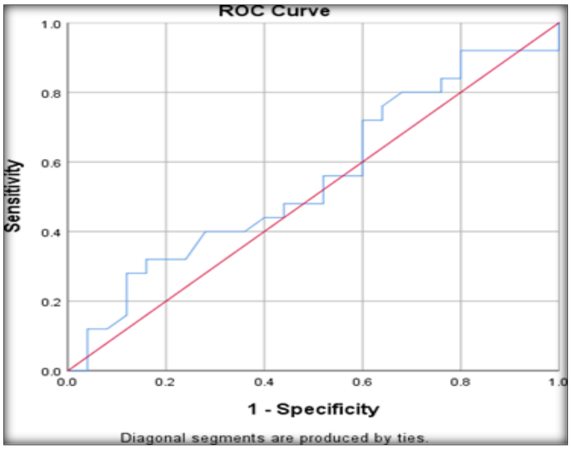

Figure 1: ROC of liver ARFI for diagnosing EV

The area under the curve for spleen ARFI in diagnosing EV was 0.903 (95% CI: 0.808–0.998), with a standard error of 0.049 and $p < 0.001$. A cutoff value of 3.135 m/s was identified. [Figure 2]

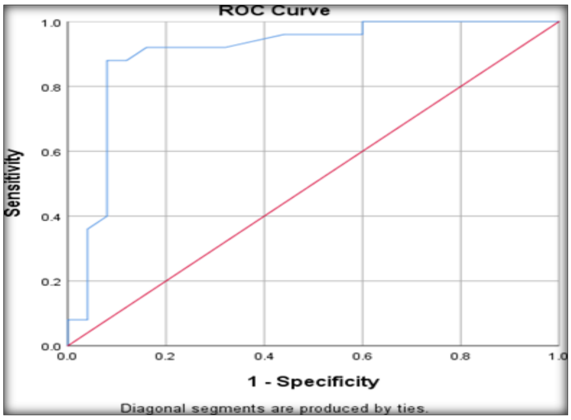

Figure 3: Comparing mean SBP between groups

Figure 2: ROC curve of spleen ARFI for diagnosing EV.

The area under the curve for spleen ARFI in diagnosing high-grade oesophageal varices was 0.935 (95% CI: 0.811–1.0), with a standard error of 0.063 and a p-value of < 0.001. The cutoff value for diagnosing high-grade EV was 3.265 m/s (Figure 3).

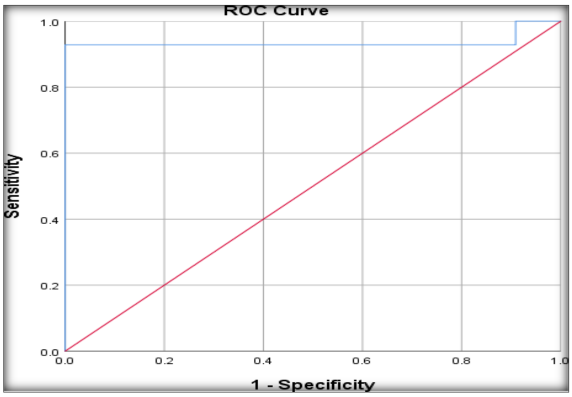

Figure 3: ROC for spleen ARFI to diagnose high-grade EV

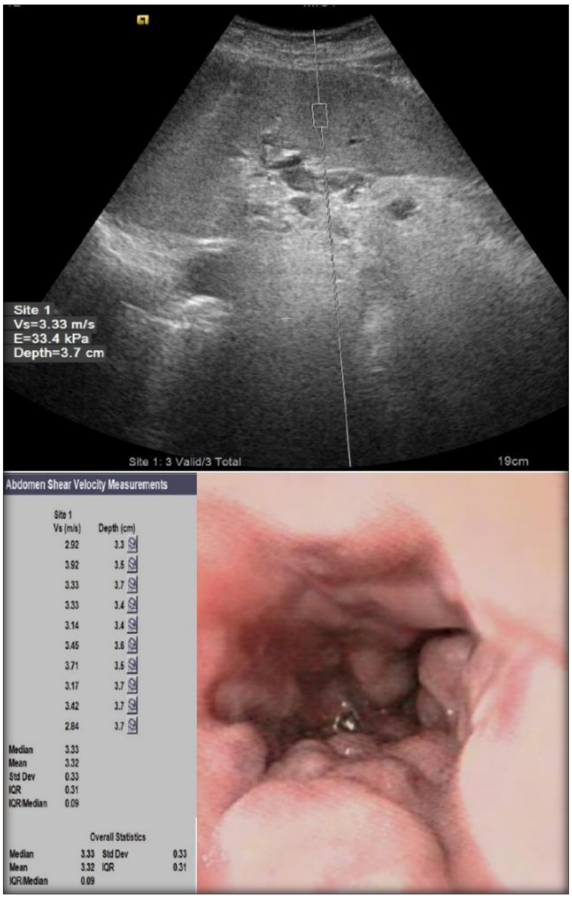

Figure 4: Chronic liver disease with ROI in spleen's intermediate segment

DISCUSSION

In our study, demographics, cirrhosis aetiology, and MELD scores were similar between the groups. No significant differences were observed in the liver size, portal vein diameter, portal vein velocity, spleen size, or liver ARFI. However, significant differences were noted in the platelet count, platelet spleen ratio, and spleen ARFI values. The mean platelet count among those with EV was significantly lower (82600 ± 36231.89/μL) than that among those without EV (134960 ± 18864.61/μL). This aligns with findings by Baig et al. (2008), where the platelet count was 90,500 in patients with EV, whereas those without EV had a platelet count of 156,000.[16] Giannini et al. (2006) reported significantly lower platelet counts (83.6%) among patients with varices.[17]

In the present study, the platelet spleen ratio was also significantly different. Among those with EV, the mean ratio was 555.24 ± 222.33, while it was 981.72 ± 133.38 among those without EV. This aligns with the findings of Giannini et al. (2006), who reported a platelet spleen ratio of 86%.[17] Baig et al. (2008) had the findings where the patients with EV had 702 (140-1065), whereas patients without EV had 1300 (388-5650).[16]

In our study, spleen ARFI values were significantly elevated in patients with EV (3.30 ± 0.18 m/s) compared to those without (2.98 ± 0.18 m/s), with a

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p-value of < 0.05. This was in concordance with studies by Kim et al. (2015), who reported spleen ARFI values of 3.58 ± 0.47 m/s in EV-positive and 3.02 ± 0.49 m/s in EV-negative patients.18 Similar observations were made by Mori et al. (2020), confirming that spleen ARFI increases with the presence of varices.[19]

In the present study, the spleen ARFI AUC was excellent at 0.903 (95% CI 0.808–0.998), with a cutoff of 3.135 m/s; sensitivity was 92% and specificity 84% for diagnosing EV. These findings align with Peagu et al. (2019), who found an AUC of 0.872 (95% CI: 0.799 to 0.944) and a cut-off of 2.89 m/s for diagnosing EV, with a sensitivity of 91.4% and specificity of 67.7%.[13] Similarly, Rizzo et al. (2013) reported an AUC of 0.959 (95% CI: 0.91 to 1), with a cut-off of 3.1 m/s and sensitivity and specificity of 96% and 88%, respectively. Their PPV and NPV were 90% and 96%, respectively.[9] Takuma et al. (2013), in 340 cirrhotic patients, found spleen ARFI sensitivity of 98.5% for any varices and 98.9% for high-risk EV.[20] Together, these studies highlight the diagnostic capacity of spleen ARFI in detecting EV in cirrhotic patients.

In our study, with a cutoff of 3.265 m/s, spleen ARFI distinguished high-grade EV with an AUC of 0.935, sensitivity of 92.9%, and specificity of 90.9%. These findings align with those of Maheswaran et al. (2019), who reported a cutoff of >3.29 m/s for high-grade varices, with an AUC of 0.874, sensitivity of 85%, and specificity of 100%.[11] Kim et al. (2015) showed that increasing stiffness up to 3.85 m/s was associated with severity. Their optimal threshold for identifying high-grade varices was 3.40 m/s.[18]

Liver ARFI had poor diagnostic utility (AUC 0.553), with a cutoff of 2.425 m/s yielding a sensitivity of 80% but a specificity of only 32%. Bota et al. (2012) reported an AUROC of 0.596, with a sensitivity of 93.4% but a specificity as low as 28.9% for predicting ≥ grade-2 EV using liver ARFI.[21] This high false-positive rate limits the use of liver ARFI as a diagnostic tool, although its sensitivity suggests its potential use as a screening modality.

Limitations: This study was limited by a small sample size and single-centre design, which may affect the generalizability of the results. Intra- and inter-observer variability for ARFI measurements was not evaluated. Long-term follow-up to assess changes in spleen stiffness after treatment was also not performed.

CONCLUSION

Based on the study results, splenic stiffness obtained using the ARFI method could act as a valid, non-invasive diagnostic tool for EV. A splenic stiffness of ≥ 3.135 m/s was identified as the cutoff in the present study for diagnosing EV among those with chronic liver parenchymal disease. A splenic stiffness of ≥ 3.265 m/s was identified as the cutoff for differentiating high-grade EV from low-grade EV. Splenic stiffness measured using ARFI, when compared with liver stiffness, was found to have higher sensitivity, specificity, and diagnostic accuracy for diagnosing EV among those with chronic liver disease. Splenic ARFI could also act as a valid tool in differentiating high-grade EV from low-grade EV.

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