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EVALUATION OF SPLENIC STIFFNESS MEASUREMENT BY ACOUSTIC RADIATION FORCE IMPULSE IN PREDICTION OF HIGH-RISK ESOPHAGEAL VARICES.

Medical Gastroenterology

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ABSTRACT

Introduction: Gastroesophageal varices are one of the serious complication of liver cirrhosis, driven by portal hypertension and associated with significant morbidity and mortality. Early detection of high-risk varices is essential to prevent variceal hemorrhage. While, Hepatic venous pressure gradient (HVPG) is the gold standard method for estimating portal hypertension, invasive nature limits its widespread use and availability. Spleen stiffness measurement (SSM) by Acoustic Radiation Force Impulse (ARFI) imaging has emerged as a promising non-invasive alternative. This study evaluates the diagnostic accuracy of splenic stiffness measured by ARFI in predicting high-risk esophageal varices (HRV) in cirrhotic patients. **Methods:** A prospective observational study was conducted on 247 cirrhotic patients at a tertiary care hospital in Northern India. All patients underwent UGI endoscopy, Liver stiffness measurement (LSM) and Spleen stiffness measurement (SSM) via ARFI, and were evaluated for high-risk varices. **Results:** Out of 302 patients screened, 247 cirrhotic patients were enrolled (122 compensated, 125decompensated). High-risk esophageal varices (HRV) were detected in a significant proportion via upper gastrointestinal endoscopy. SSM by Acoustic Radiation Force Impulse (ARFI) imaging showed a strong correlation with variceal grade ($p < 0.001$), outperforming LSM in diagnostic accuracy. In the compensated cirrhosis subgroup (n=122), Spleen stiffness to spleen size to platelet ratio (SSPSR) and Spleen stiffness to platelet ratio (SPSR) outperformed liver and spleen stiffness alone. SSPR had an AUROC of 0.68, and SSPSR had an AUROC of 0.67. In contrast, liver ARFI showed minimal discrimination (AUROC 0.46). These findings emphasize the limited utility of liver stiffness in early-stage cirrhosis and support the mechanistic rationale for spleen based metrics, which more directly reflect portal hypertension and its hematologic consequences. **Conclusion:** This study demonstrates that spleen-based composite indices such as SSPR and SSPSR provide better predictive accuracy for high-risk varices than liver or spleen stiffness alone, especially in patients with compensated cirrhosis. Hence, SSM by ARFI is a reliable, non-invasive tool for identifying high-risk esophageal

KEYWORDS

Spleen stiffness measurement (SSM), Acoustic Radiation Force Impulse (ARFI) imaging, High-risk esophageal varices (HRV), and Spleen stiffness to platelet ratio (SSPR) and Spleen stiffness to spleen size to platelet ratio (SSPSR)

INTRODUCTION:

Gastroesophageal varices are a significant challenge that patients commonly face with cirrhosis [1]. This is one of the most serious complications of liver cirrhosis resulting from portal hypertension [2]. Variceal hemorrhage occurs in 10–15% of patients annually, depending on the size of the varices, the presence of red wale marks, and the severity of liver disease. In addition, acute variceal hemorrhage carries a significant risk of morbidity and mortality, with reported 6 week mortality rates of 15–25% [3]. Given the high prevalence of varices and the significant mortality rate associated with variceal hemorrhage, early diagnosis of clinically significant portal hypertension (≥10 mm Hg) and associated varices is of paramount importance in the management of compensated cirrhosis and in the prevention of liver-related morbidity and mortality [4], [5].

Variceal screening has been recommended routinely traditionally. High-risk varices are defined as medium to large varices, small varices with red wale marks or Child-Pugh class C disease [6].

Measurements of liver stiffness (LS) using transient elastography (TE) have proven their accuracy for diagnosing clinically significant portal hypertension [7]. Portal-hypertension causes splenic congestion, which leads to architectural changes in the splenic arteries and veins, resulting in fibrosis followed by an increase in spleen stiffness (SS). In addition, spleen stiffness measured via TE has been considered now a day as a promising method to assess portal hypertension. [8], [9].

However, measuring SS using TE requires additional ultrasound examination, and its measurement feasibility largely depends on the size of the spleen, which limits its wide applicability. Therefore, newer ultrasound-based elastography methods have emerged as important guidance for facilitating SS measurements, including point shear wave elastography such as acoustic radiation force impulse (ARFI) imaging, and 2-dimensional real-time shear wave elastography. These newer elastography methods have shown similar accuracy to TE for predicting portal hypertension [10], [11]. Various non-invasive methods of diagnosing esophageal varices (EV) have recently been proposed as the most promising one, the measurement of spleen stiffness (SSM). These techniques are also considered most accurate in predicting the existence of EVs in patients with cirrhosis with portal hypertension of viral and alcoholic etiology. TE is a valuable method to detect high-risk EVs, although it is limited by various other factors such as obesity and ascites [12].

With this background, this study is planned to assess the diagnostic accuracy of splenic stiffness (SS) by ARFI as a noninvasive modality to predict high-risk esophageal varices.

MATERIAL AND METHOD:

Objective

To assess the diagnostic accuracy of splenic stiffness measured by acoustic radiation force impulse technique in predicting high risk esophageal varices in patients with cirrhosis

Study Centre

The study was carried out in the department of Gastroenterology, Shri Ram Murti Smarak Medical college and Hospital, Bareilly, a tertiary care hospital in Northern India.

Study Population

Patients with cirrhosis either admitted as inpatient or attending the outpatient department.

Sample Size

Sample size (n) based on specificity = $Z2\ 1\text{-}\alpha/2 \times SP \times (1\text{-}\ SP) / L2\ (1\text{-}$ Prevalence)

- Where n = required sample size
- S P = anticipated specificity
- α = size of the critical region (1 – αis the confidence level)
- z 1-α/2 = standard normal deviate corresponding to the specified size of the critical region (α), and
- L = absolute precision desired on either side (half-width of the confidence interval) of sensitivity or specificity.

As per previous available literature the specificity of splenic stiffness by ARFI to detect high risk esophageal varices was 0.86, taking a 5% absolute precision and 95% confidence interval and adjusting for a 20% prevalence of high risk varices in patients with cirrhosis the estimated sample size was 232 (Non adjusted sample size 186) [12].

Duration Of Study
Study was conducted for a period of six months from 1st January 2026 to 30th June 2026.

Study Design
A single center prospective observational study.

Eligibility Criteria
Inclusion Criteria
All patients with liver cirrhosis above 18 years and below 80 years, regardless of cause of cirrhosis

Exclusion Criteria
1. Non-Cirrhotic Portal Hypertension
2. Active alcoholism (noncompliant to abstinence >3 months before enrollment)
3. Severe decompensated liver disease
4. End stage renal disease
5. Presence of Portal venous thrombosis
6. Coexistence of malignancies including Hepatocellular carcinoma (HCC)

METHODOLOGY
- All study participants had given their written informed consent to participate in the study. The present study was approved by the institutional ethical board (IEC/2026/01/35).
- Diagnosis of liver cirrhosis was made by a combination of clinical, biochemical (platelet count, international normalized ratio, prothrombin time, alanine aminotransferase [ALT], albumin, bilirubin), and radiographic imaging (Ultrasound or CT scan; Liver size and Characteristics). All diagnosed patients were evaluated with upper Gastrointestinal (GI) endoscopy and Spleen Elastography. The presence of high-risk esophageal varices on upper gastrointestinal endoscopicexamination were included in this study. High-risk varices were defined as medium large varices, small varices with red wale marks or Child-Pugh class C disease.
- All eligible patients were subjected to ARFI for spleen stiffness and liver stiffness at baseline.
- Those all patients were subjected to esophagogastroduodenoscopy for esophageal varices and compare the diagnostic accuracy of liver stiffness measurement assessed by ARFI against SSM for prediction of high-risk esophageal varices.

Patient Disposition
In the study period, 302 patients were screened for Cirrhosis of liver. 35 patients did not meet the eligibility criteria. Both the procedure of EGD and SS could not be done in 14 patients and 6 patients did not consent for study. 247 patients were enrolled in the study, among those 122 patients were in compensated cirrhosis group and 125 patients were in decompensated cirrhosis group.

Statistical Analysis
All the data obtained were analyzed by using SPSS/ MS – Excel software. Appropriate statistical test was applied whenever required at time of data analysis and $P<0.05$ were considered statistically significant for the study. Categorical percentage, continuous variable, Mean +/- SD and Median (Range) as per normality. Correlation between LSM and SSM were done Pearson/ Spearman correlation as per normality. Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value and Area under Curve were calculated. Paired values and SS values were calculated by Student t test.

RESULTS:

Table 1: Baseline demographic and liver disease characteristics of the overall cohort (N = 247)

Variables	Values
Age(years)	56.0[48.0–62.5]
Sex(Males%)	184(73.6%)
Sex(Females %)	63 (25.2%)
Compensated Cirrhosis(%)	122(48.8%)
Decompensated Cirrhosis(%)	125(50.0%)
PortalVeinDiameter(mm)	15.67±2.87
SSPR(ratio)	0.25[0.19–0.33]
SSPSR(ratio)	3.71[2.58–5.23]

SSPSR- Spleen stiffness to spleen size to platelet ratio, SSPR- Spleen stiffness to platelet.

Table 1 summarizes the baseline characteristics of 247 patients enrolled in the study, focusing on demographic details and cirrhosis status. Spleen stiffness to platelet ratio (SSPR) of 0.25 (IQR: 0.19–0.33), and spleen stiffness to spleen size ratio (SSPSR) of 3.71 (IQR: 2.58–5.23) which provides insight into the severity and progression of liver disease within the cohort.

Table 2: Baseline Laboratory parameters and elastography values of the overall cohort (N = 247)

Variables	Values
Haemoglobin(gm/dL)	11.04±1.78
Total Leucocyte Count(cells/mm³)	4600.0[3800.0–6000.0]
Bilirubin(mg/dL)	1.2[0.9–1.6]
Alanine amino transferase(U/L)	31.0[24.0–45.5]
Aspartate amino transferase(U/L)	47.0[36.0–67.5]
Splenic ARFI Mean(m/s)	3.02±0.47
Splenic ARFI(kPa)	27.18[22.28–33.87]
Liver ARFI(m/s)	2.62[2.26–3.06]
Liver ARFI(kPa)	20.59[15.26–28.18]

ARFI- Acoustic radiation force impulse.

Table 2 presents the baseline laboratory parameters and elastography measurements of the overall cohort of 247 patients. Hematological parameters revealed a median hemoglobin level of 11.1 g/dL, reflecting mild anemia, which is commonly observed in chronic liver disease. . Biochemical markers showed median bilirubin and direct bilirubin levels of 1.2 mg/dL and 0.4 mg/dL, respectively, suggesting mild cholestatic or hepatocellular dysfunction. ALT and AST levels were elevated, with median values of 33.0 U/L and 50.0 U/L, respectively, indicating hepatocellular injury. Elastography readings using ARFI revealed that splenic stiffness consistently averaged around 3.0 m/s, indicating significantly increased splenic stiffness associated with portal hypertension.

Table 3: Diagnostic Performance of Elastography and Clinical Indices for Predicting High-Risk Varices

Predictor	AUROC	Sensitivity	Specificity	F1 Score	OptimalCut-off
SSPR	0.70	74%	64%	0.63	0.25
SSPSR	0.72	66%	72%	0.62	4.04
SpleenARFI	0.58	87%	30%	0.57	22.2kPa
LiverARFI	0.52	99%	10%	0.56	10.4kPa

SSPSR- Spleen stiffness to spleen size to platelet ratio, SSPR- Spleen stiffness to platelet ratio, ARFI- Acoustic radiation force impulse.

Table 3 presents the diagnostic accuracy of various elastography-based and clinical indices in predicting high-risk varices in the overall cohort. Among the evaluated parameters, SSPSR (Splenic Stiffness to Platelet Spleen Ratio) demonstrated the highest AUROC of 0.72, indicating fair discriminative ability, with a sensitivity of 66%, specificity of 72%, and F1 score of 0.62 at an optimal cut-off of 4.04. SSPR (Splenic Stiffness to Platelet Ratio) followed closely with an AUROC of 0.70, sensitivity of 74%, and specificity of 64%, providing a good balance between sensitivity and specificity at a cut-off of 0.25.

On the other hand, Spleen ARFI showed a lower AUROC of 0.58, with high sensitivity (87%) but low specificity (30%), making it a sensitive but less specific marker for detecting high-risk varices. Liver ARFI had the lowest AUROC (0.52), with very high sensitivity (99%) but poor specificity (10%), suggesting limited usefulness as a standalone diagnostic tool in this setting.

Overall, SSPR and SSPSR emerged as more reliable predictors compared to ARFI values alone.

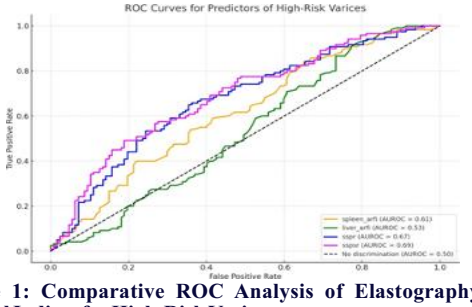

Figure 1: Comparative ROC Analysis of Elastography and Clinical Indices for High-Risk Varices

SSPSR- Spleen stiffness to spleen size to platelet ratio, SSPR- Spleen stiffness to platelet ratio, ARFI- Acoustic radiation force impulse.

In Figure 1, the ROC curve presented illustrates the diagnostic performance of four predictors—SSPR, SSPSR, spleen ARFI, and liver ARFI—for identifying high-risk varices in patients. The area under the ROC curve (AUROC) isused to assess the discriminative ability of each parameter:

- SSPSR (magenta curve) showed the highest diagnostic accuracy with an AUROC of 0.69, suggesting a fair ability to distinguish high-risk varices.
- SSPR (blue curve) followed closely with an AUROC of 0.67, indicating moderate diagnostic performance.
- Spleen ARFI (orange curve) had a lower AUROC of 0.61, suggesting limited but better-than-chance discrimination.
- Liver ARFI (green curve) demonstrated poor performance with an AUROC of 0.53, only marginally better than random chance (represented by the dashed black line with AUROC = 0.50).

In summary, SSPR and SSPSR outperformed elastography parameters, particularly liver ARFI, in predicting high-risk varices, indicating their potential as more reliable non-invasive markers.

Table 4: Diagnostic Accuracy of Combined SSPSR and SSPR Thresholds for High-Risk Varices

Rule	Sensitivity	Specificity	Accuracy	PPV	NPV	F1 Score
SSPSR	66%	72%	69.6%	57.7%	78.3%	0.62
SSPSR	73.6%	64%	67.6%	54.5%	80.6%	0.63

SSPSR- Spleen stiffness to spleen size to platelet ratio, SSPR-Spleen stiffness to platelet ratio.

Table 4 compares the diagnostic performance of SSPSR (≥ 4.04) alone and in combination with SSPR (≥ 0.25) for predicting high-risk varices. When SSPSR ≥ 4.04 was used as a single rule, it achieved a sensitivity of 66%, specificity of 72%, and an overall accuracy of 69.6%,with a positive predictive value (PPV) of 57.7%, negative predictive value (NPV) of 78.3%, and an F1 score of 0.62.

The combined rule, SSPSR ≥ 4.04 OR SSPR ≥ 0.25, demonstrated improved sensitivity (73.6%) at the expense of slightly lower specificity (64%). However, the overall diagnostic accuracy (67.6%) and F1 score (0.63) were comparable to the single SSPSR threshold. Notably, the combined approach provided a higher NPV (80.6%) than the single-parameter rule, suggesting better exclusion of non-high-risk cases.

Table 5: Diagnostic Performance of Non-Invasive Predictors for High-Risk Varices in Compensated Cirrhosis

Predictor	AUROC	Sensitivity	Specificity	F1 Score	Optimal Cutoff
SSPR	0.68	78%	68%	0.27	0.25
SSPSR	0.67	78%	59%	0.23	3.45
SpleenARFI	0.61	67%	63%	0.21	30.5kPa
LiverARFI	0.46	100%	11%	0.15	10.4kPa

SSPSR- Spleen stiffness to spleen size to platelet ratio, SSPR- Spleen stiffness to platelet ratio, ARFI- Acoustic radiation force impulse.

Table 5 presents a comparative evaluation of non-invasive predictors for identifying high-risk varices specifically within the compensated cirrhosis subgroup. Four predictors were assessed using AUROC, sensitivity, specificity, F1 score, and optimal cutoff values:

- SSPR demonstrated the highest diagnostic performance with an AUROC of 0.68, sensitivity of 78%, and specificity of 68% at a cutoff of 0.25, indicating a fair ability to detect high-risk varices with balanced accuracy.
- SSPSR followed closely with an AUROC of 0.67, maintaining the same sensitivity (78%) but with a slightly lower specificity (59%) at a cutoff of 3.45.
- Spleen ARFI had a moderate AUROC of 0.61, with sensitivity of 67% and specificity of 63% at an optimal cutoff of 30.5 kPa, suggesting limited discriminatory power.
- Liver ARFI performed poorly, with an AUROC of only 0.46, despite achieving 100% sensitivity, its specificity was just 11%, reflecting a high false-positive rate at the 10.4 kPa threshold.

Overall, SSPR and SSPSR showed better diagnostic accuracy than elastography -based parameters, particularly in patients with compensated cirrhosis.

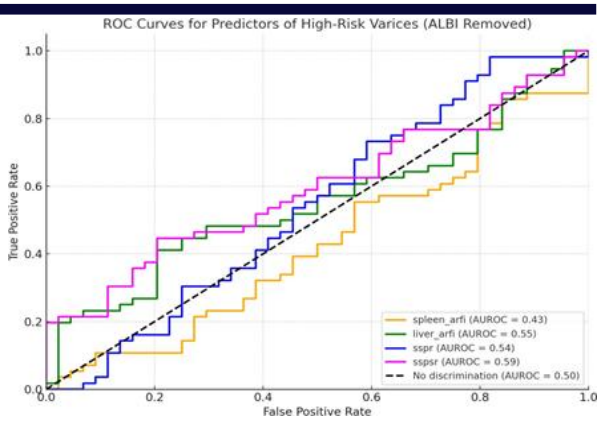

Figure 2: Comparative ROC Analysis of Elastography and Clinical Indices in Compensated Cirrhosis

SSPSR- Spleen stiffness to spleen size to platelet ratio, SSPR- Spleen stiffness to platelet ratio, ARFI- Acoustic radiation force impulse.

In Figure 2, The ROC curve illustrates the comparative diagnostic performance of four non-invasive predictors—Spleen ARFI, Liver ARFI, Spleen Stiffness to Platelet Ratio (SSPR), and Spleen Stiffness to Spleen Size Ratio (SSPSR)—for identifying high-risk varices. Among these, SSPSR showed the highest discriminatory power with an AUROC of 0.69, followed by SSPR (0.67), while Spleen ARFI and Liver ARFI demonstrated lower accuracy with AUROCs of 0.61 and 0.53, respectively. The reference line (AUROC = 0.50) is included for comparison. These findings suggest that combined clinical indices such as SSPR and SSPSR outperform standalone elastography measures in predicting high-risk varices.

DISCUSSION:

In this study, we systematically evaluated the performance of various non-invasive clinical and elastography predictors in identifying high-risk varices (HRV) in patients with chronic liver disease, with a particular focus on compensated cirrhosis.

Our cohort had a mean age of 55.3 years, with a male predominance (73.6%).

Nearly equal proportions had compensated and decompensated cirrhosis, allowing a meaningful analysis of the compensated subgroup. The high prevalence of HRV in our cohort (n=112, 45.3%) underscores the importance of refining screening tools to minimize unnecessary endoscopy, especially in resource-limited settings.

Non-invasive Predictors In The Overall Cohort

Among the variables evaluated, SSPR (AUROC 0.70) and SSPSR (AUROC 0.72) clearly outperformed both liver and spleen ARFI in predicting high risk varices (HRV). With an optimal cut off 0.25, SSPR achieved sensitivity of 74% and specificity of 64%, while SSPSR, at a threshold of 4.04, offered slightly improved specificity (72%) at the expense of sensitivity (66%). These findings are consistent with earlier reports by Kim et al.[4] and Shi et al.[7], who indicated that composite indices integrating spleen stiffness with platelet count or spleen size materially enhance diagnostic accuracy over single-parameter models.

Notably, liver ARFI demonstrated poor performance—AUROC 0.52—and spleen ARFI achieved only moderate discriminative ability (AUROC 0.58). These results are in line with the observations by Elkrief et al.[10], who also reported the limited utility of liver stiffness alone for HRV detection.

Multiple studies confirm that combining spleen stiffness, spleen size, and platelet count—either as ratios like LSPS or composite risk models—maximize diagnostic value. Berzigotti and colleagues [13] showed that LSPS (liver stiffness × spleen size/platelet count) achieved AUROCs >0.88 for CSPH and EV in compensated cirrhosis, validated across independent cohorts. Similarly, a point shear wave elastography study evaluating spleen stiffness alone paired with platelet count reported AUROC ~0.84–0.83 for portal hypertension and EV detection in mixed etiology populations. [14]

In our compensated cirrhosis subgroup, although the AUROCs of SSPR

(0.68) and SSPSR (0.67) were marginally lower than in the overall cohort, their F1 scores (0.27 and 0.23 respectively) reaffirmed their superior balance between sensitivity and specificity. In contrast, liver ARFI—despite a sensitivity of 100%—yielded only 11% specificity, rendering it clinically impractical dueto high false-positive rates. This pattern aligns with Abraldes et al.[15] and Marasco et al.[16], who reported that liver stiffness plateaus at moderate portal pressure levels and lacks discriminatory power in the early stage of the disease. The reproducibility of our optimal cutoffs (SSPR 0.25; SSPSR 4.04) supports consistent thresholds across diverse etiologies, including NAFLD and alcohol related liver disease, which comprised the majority in our cohort.

Taken together, our results affirm that composite indices such as SSPR and SSPSR, which integrate spleen stiffness with platelet count (and size), outperform standalone elastography measurements in predicting HRV in both overall and compensated cirrhotic cohorts. This aligns with mechanistic rationale and prior clinical evidence, and offers a practical, non-invasive tool to guide risk stratification and avoid unnecessary endoscopy.

Performance In Compensated Cirrhosis

In the compensated cirrhosis subgroup (n=122), the diagnostic performance of non-invasive indices such as SSPR and SSPSR remained consistently superior to that of conventional elastography measures. These findings are particularly relevant within the clinical framework proposed by the Baveno VII consensus[17], The compensated group in our study had lower CTP, MELD, and ALBI scores relative to the overall population, indicating better-preserved hepatic function. Despite this, a substantial proportion—nearly 40%—harboured high-risk varices (HRV).

Diagnostic Considerations

From a diagnostic performance standpoint, our findings highlight that neither liver nor spleen ARFI alone provide sufficient specificity to safely exclude high-risk varices (HRV) and there by a void unne-cessary endoscopy. Although liver ARFI demonstrated a high sensitivity of 99% at a threshold of 10.4 kPa, its specificity was markedly poor at just 10%, rendering it clinically untenable for risk stratification. Such a high rate of false positives could lead to unwarranted endoscopic procedures, undermining the goal of non-invasive triage. Spleen ARFI, while slightly better, still showed modest performance with an AUROC of 0.58 and specificity of only 30% at its optimal cutoff, which aligns with earlier reports by Elkrief et al.[10], who observed limited discriminatory value for spleen stiffness when used in isolation.

In contrast, composite indices such as the spleen stiffness-to-platelet ratio (SSPR) and spleen sizeto-platelet spleen stiffness ratio (SSPSR) offered a more favorable diagnostic profile. These indices achieved AUROC values of 0.70 and 0.72, respectively, with balanced sensitivity and specificity—74% and 64% for SSPR, and 66% and 72% for SSPSR. Notably, their F1 scores (0.63and 0.62) underscore their utility in optimizing the trade-off between false positives and false negatives. In our study, liver ARFI in the compensated group yielded an AUROC of only 0.46,highlighting its poor discriminative power in early portal hypertension. This finding is consistent with the pathophysiological model proposed by Marasco et al.[16] and Abraldes et al.[15], who noted that liver stiffness may plateau in the compensated phase, as structural remodeling of the hepatic parenchyma precedes significant increases in portal pressure.

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