ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 11 | November - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ROLE OF SHEARWAVE ELASTOGRAPHY IN PATIENTS WITH SPLENOMEGALY

Radiology

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ABSTRACT

Background: Splenomegaly is a common clinical finding that can arise from various underlying conditions, including hematologic, vascular, neoplastic, infectious, and immunologic disorders. Accurate identification of the etiology is crucial for effective management. This study aimed to evaluate the reproducibility of spleen stiffness measurements using point shear wave elastography (pSWE) during the initial detection of splenomegaly, regardless of whether it was identified incidentally or through clinical evaluation. **Material & Methods:** A cross-sectional study was conducted in the Department of Radiodiagnosis at SAIMS & PG Institute, Indore, involving 50 patients with splenomegaly and 50 healthy controls. Spleen stiffness measurements were obtained using pSWE, and the underlying causes of splenomegaly were categorized into three main groups: hepatoportal, myeloproliferative, and infectious. Statistical analysis included the Spearman correlation test to assess the relationship between spleen volume and elasticity. **Results:** The study revealed statistically significant differences in splenic parenchymal elasticity among the groups: the hepatoportal group had a shear wave velocity of 3.26 ± 0.35 m/s, the myeloproliferative group measured 2.95 ± 0.32 m/s, the infectious disease group recorded 2.44 ± 0.20 m/s, and the control group showed 2.14 ± 0.18 m/s (P = 0.001). The intraclass correlation coefficients (ICCs) for shear wave velocity were 71.0% between hepatoportal and myeloproliferative causes, 99.5% between hepatoportal and infectious causes, and 83.1% between myeloproliferative and infectious causes. Spleen volumes were also significantly different across groups, with measurements of 64.06 ± 9.44 cm² for hepatoportal causes, 78.14 ± 17.42 cm² for myeloproliferative disorders, 51.55 ± 7.11 cm² for infectious diseases, and 26.72 ± 6.51 cm² for controls (P = 0.001). These findings underscore the potential of point shear wave elastography (pSWE) for effectively differentiating between various causes of splenomegaly based on elasticity and volume. **Conclusion:** This study supports the use of pSWE as a non-invasive tool for assessing spleen stiffness in patients with splenomegaly. The findings suggest that increased spleen stiffness correlates with splenic enlargement, highlighting the potential of pSWE in improving the evaluation and monitoring of splenic disorders. Future multi-center studies are recommended to further validate these results.

KEYWORDS

Shear wave elastography, spleen stiffness, splenomegaly, ultrasound elastography.

INTRODUCTION

The spleen is a vital organ in the immune system, responsible for removing aged or damaged red blood cells from circulation. In adults, its average dimensions, as assessed via ultrasound, are typically under 13 cm in length and 5 cm in thickness. [1]

Splenomegaly is a common clinical challenge, often requiring careful differentiation between primary spleen disorders and those in which spleen enlargement is secondary to hepatic or systemic conditions. The wide range of potential causes, many of which are secondary in nature, complicates diagnosis. Symptoms, signs, and test results are frequently nonspecific and can be associated with both benign, infectious, and malignant conditions, leading to extensive diagnostic evaluation across multiple medical specialties.[2]

Splenomegaly can arise from both physiological conditions, such as recovery from blood loss or pregnancy, and various pathological processes, including infections and chronic illnesses. The causes of splenomegaly are typically categorized into three main groups: hematological disorders (e.g., myeloproliferative disorders, leukemia, lymphoma, and hemolytic conditions), hepatic diseases (e.g., cirrhosis, portal hypertension, portal vein thrombosis, and malignancies), and infections (e.g., malaria, typhoid fever, cytomegalovirus, and acute mononucleosis). Accurately identifying the underlying cause of splenomegaly is essential for effective treatment, which is primarily aimed at addressing the root issue. [3,4]
Elastography is an innovative, non-invasive diagnostic technique used to assess the stiffness (elasticity) of soft tissues, based on the principle that diseased tissues are generally stiffer and less elastic than healthy ones. This method is particularly valuable because elasticity changes rapidly in pathologically altered tissues compared to other characteristics [5,6]. The primary elastographic techniques include magnetic resonance elastography (MRE), two-dimensional shear wave elastography (2D-SWE), point shear wave elastography (pSWE), and transient elastography (TE). TE utilizes a 3.5-MHz ultrasonic transducer and a low-amplitude vibrator to generate low-frequency shear waves, allowing for the assessment of tissue stiffness through wave velocity measurements. In contrast, pSWE employs ultrasound tracking beams to create shear waves within a defined region of interest, while 2D-SWE uses focused ultrasound beams to generate a radiation force that measures shear waves in real time, producing a two-dimensional color map of tissue elasticity [7]. In shear-wave elastography, stiffness values result from the elastic return forces acting on the tissue in response to a shear force. By measuring the velocity of these shear waves, the technique provides insights into the mechanical properties of tissues, revealing that certain conditions lead to increased tissue hardness; higher shear wave velocities indicate stiffer tissues. [8]

The purpose of this study was to assess the reproducibility of spleen stiffness measurements during the initial detection of splenomegaly, regardless of whether it was discovered incidentally or through clinical evaluation. The goal was to determine the underlying cause of splenomegaly while reducing unnecessary investigations and alleviating patient anxiety.

MATERIAL AND METHODS

After obtaining approval from the institutional ethical committee, this cross-sectional study was conducted in the Department of Radiodiagnosis at SAIMS & PG Institute in Indore. and included two groups: a Study group comprising 50 patients with splenomegaly (defined as a spleen length >13 cm) and a Control group comprised of 50 healthy individuals without a history of significant alcohol consumption or any systemic or metabolic diseases affecting the spleen. Prior to participation, all individuals provided written informed consent after being fully briefed on the study protocol.

Inclusion And Exclusion Criteria

- Participants had to be over 18 years old;
- For the case group, patients referred to the radiology department with splenomegaly, defined as a maximum spleen length greater than 13 cm on ultrasound; and
- For the control group, healthy individuals without a history of significant alcohol consumption (less than 30 g/day for men and less than 20 g/day for women), or any systemic, metabolic, or other spleen-affecting diseases.

Exclusion Criteria

- Non-consenting patients
- Patients who were unable to hold their breath in a neutral position;

- Patients who had gross ascites;
- Pregnant patients; and
- Patients who had a splenic mass were excluded.

Methodology

The ultrasound examinations were conducted using a General Electric company LOGIQ E9, LOGIQ F8 machine using the 7.5-15 MHz frequency probe. B-mode and elastographic examinations were performed without having any knowledge about the patient's history and laboratory and imaging findings, and the obtained data were recorded.

The splenic shear wave velocity (SWV) values were analyzed after identifying the underlying pathologies responsible for splenomegaly, which were categorized into three primary groups: hepatoportal, myeloproliferative, and infectious causes.

- Splenomegaly due to portal hypertension was diagnosed based on clinical features, along with evidence of splenic vein dilation or associated varices.
- The myeloproliferative disorders were identified through microscopic examination of peripheral blood and bone marrow samples.
- In cases of splenomegaly caused by infectious diseases, diagnosis relied on serological testing. For instance, brucellosis was confirmed with significant titers of ≥1/160 in the standard tube agglutination test. Infectious mononucleosis was diagnosed through elevated levels of VCA-IgM and VCA-IgG antibodies, while IgG anti-EBNA results were negative. Tuberculosis diagnosis was made using culture and polymerase chain reaction analysis, and typhoid fever was confirmed through culture and significant titers of ≥1/200 in the Gruber-Widal test. Additionally, the diagnosis of infectious causes was supported by clinical indicators such as increased fever and elevated white blood cell counts, while excluding hepatoportal and myeloproliferative disorders.

The following procedure was followed for Shear wave elastography:

1. Spleen size was calculated in the form of a cross-sectional spleen area in the US images by using the following formula: the cross-section area (cm^2) = longest diameter (cm) x shortest diameter (cm), and a diagnosis of splenomegaly was made if the area was 40 cm^2 or greater. [9]
2. Point shear wave elastography (pSWE) imaging was performed using a curvilinear probe.
3. Patients were scanned in the right lateral decubitus position with their left arm extended away from the body.
4. Participants were instructed to hold their breath in a neutral position during the scan.
5. Spleen stiffness was measured at a depth of 1 to 2 cm below the splenic capsule using pSWE.
6. The region of interest (ROI) was selected to exclude any visible blood vessels.
7. Stiffness was measured at three locations: the upper pole, hilum, and lower pole of the spleen, using both intercostal and subcostal approaches.
8. Three measurements were taken at each location.
9. Median values were calculated for each individual by averaging nine successful measurements and were expressed in kilopascals (kPa).

Statistical Analysis

Data were entered into Microsoft Excel 10.0 and analysis was performed using IBM SPSS Statistics for Windows, Version 22.0. Categorical variables were presented as frequencies and proportions, while continuous variables were described using the mean (SD) and the median (IQR). Spleen stiffness data followed a normal distribution. The Spearman correlation test was utilized to assess the relationship between spleen volume and splenic elasticity across all groups with detected splenomegaly, as well as in the control group. A p-value of <0.05 was considered statistically significant.

RESULTS

The study comprised 100 subjects, categorized based on their pathologies: 17 individuals with hepatoportal diseases (specifically cirrhosis), 19 with myeloproliferative disorders (which included 7 patients with chronic myeloid leukemia, 4 with Hodgkin lymphoma, 3 with acute lymphocytic leukemia, 3 with chronic lymphocytic leukemia, and 2 with thalassemia), and 14 with infectious diseases (consisting of 6 patients with brucellosis, 3 with infectious mononucleosis, 3 with tuberculosis, and 2 with typhoid). Additionally, there were 50 normal patients included in the study.

The study included 100 participants divided into two groups: 50 diagnosed with splenomegaly (cases) and 50 with normal spleen size (controls). The splenomegaly group had an age range of 27 to 60 years, with a mean age of 43.25 years (±9.32 years). The control group consisted of individuals aged 23 to 66 years, with a mean age of 38.75 years (±10.15 years). The median age was 43 years for the cases and 42 years for the controls, indicating that the splenomegaly cases had a slightly higher mean age compared to the controls.

In terms of sex distribution, the splenomegaly group comprised 23 females (46%) and 27 males (54%). The control group had an equal distribution, with 25 females (50%) and 25 males (50%). Overall, the study population included 48 females (48%) and 52 males (52%).

Table 1. Demographic Characteristics of the study participants

Statistics	Study group (N=50)			Controls (N=50)
	Hepatoportal Diseases (N=17)	Myeloproliferative Diseases (N=19)	Infectious Diseases (N=14)	
Sex (Male/female)	11/6	12/7	4/10	25/25
Age, mean ± SD, years	44.55 ± 9.72	46.25 ± 9.55	41.75 ± 9.22	38.75 ±10.15
Spleen Size, median (SD), cm^2	67.1 ± 9.71	86.2 ± 18.20	50.2 ± 7.32	27.0 ± 6.5
Spleen stiffness, median (SD), m/s	3.26 ± 0.35	2.95 ± 0.32	2.44 ± 0.20	2.14 ± 0.18

The elastographic evaluation of splenic parenchymal elasticity revealed significant differences between various disease groups. The highest elasticity was observed in the hepatoportal disease group (3.26 ± 0.35 m/s), followed by the myeloproliferative disease group (2.95 ± 0.32 m/s), infectious disease group (2.44 ± 0.20 m/s), and the control group (2.14 ± 0.18 m/s). These variations were statistically significant (P = 0.001), indicating that splenic elasticity measurements can effectively differentiate between different pathological conditions, making it a valuable tool in diagnosing and assessing disease severity.

The study utilized receiver operating characteristic (ROC) curves to differentiate between various causes of splenic abnormalities using shear wave velocity (SWV) measurements. For distinguishing hepatoportal from myeloproliferative causes, a SWV cutoff of >3.10 m/s yielded a sensitivity of 68.2% and specificity of 71.2%, with an intraclass correlation coefficient (ICC) of 71.0%. For differentiating hepatoportal from infectious causes, a cutoff of >2.77 m/s showed a sensitivity of 94.2% and specificity of 100%, with an ICC of 99.5%. Lastly, a cutoff of >2.75 m/s differentiated myeloproliferative from infectious causes with a sensitivity of 85.2% and specificity of 89.1%, and an ICC of 83.1%. (Figure 1 A-C)

Table 2. Receiver operating characteristic (ROC) curves for distinguishing between different causes of splenic abnormalities based on shear wave velocity (SWV) measurements

	SWV Cut off	Sensitivity	Specificity	Intraclass correlation coefficient (ICC)
Hepatoportal Diseases from myeloproliferative	>3.10 m/s	68.2 %	71.2 %	71.0%
Hepatoportal from infectious causes	>2.77 m/s	94.2 %	100 %	99.5%
Myeloproliferative from infectious causes	>2.75 m/s	85.2 %	89.1 %	83.1%

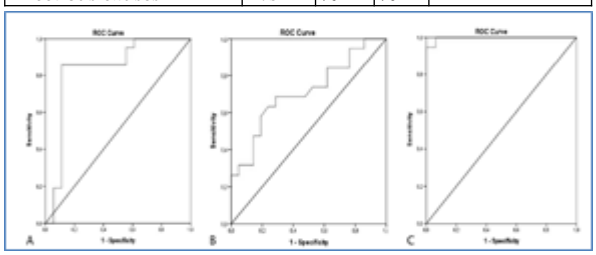

Figure 1 presents the receiver operating characteristic (ROC) curves for distinguishing between different causes of splenic abnormalities based on shear wave velocity (SWV) measurements: A: Hepatoportal causes from myeloproliferative causes; B: Hepatoportal causes from infective causes; C: Myeloproliferative causes from infective causes.

Additionally, spleen volumes across the groups—64.06 cm² (hepatoportal), 78.14 cm² (myeloproliferative), 51.55 cm² (infective), and 26.72 cm² (control)—were significantly different (P = 0.001). These findings highlight the efficacy of SWV measurements and spleen volume in distinguishing between various splenic disease etiologies.

In assessing the relationship between splenic elasticity and spleen volume across different disease groups and the control group, the Spearman correlation test showed a significant positive correlation of 0.687 (P = 0.001) in the hepatoportal disease group and a moderate positive correlation of 0.451 (P = 0.040) in the myeloproliferative disease group. In contrast, weak negative correlations were found in the infective patient group (−0.148, P = 0.584) and the control group (−0.119, P = 0.649), indicating no meaningful relationship in these groups. (Figure 2A-D)

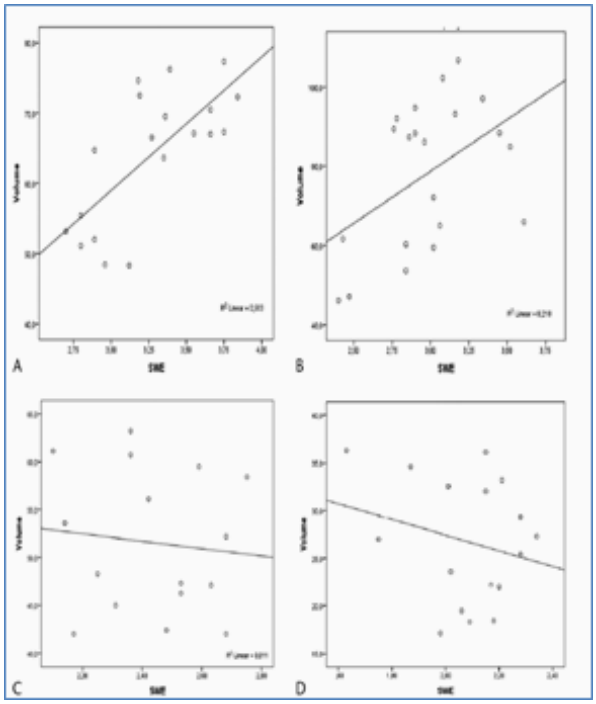

Figure 2. Correlation Between Splenic Elasticity and Spleen Volume Across Disease and Control Groups showed that the Spearman correlation test results were found to be 0.687 (P = 0.001) in the hepatoportal disease group (A), 0.451 (P = 0.040) in the myeloproliferative disease group (B), −0.148 (P = 0.584) in the infective patient group (C), and −0.119 (P = 0.649) in the control group (D).

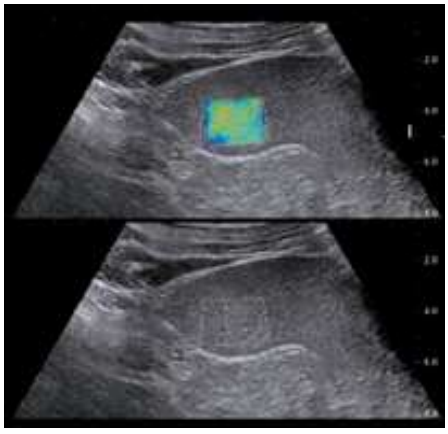

Figure 3. Elastography of a normal spleen at upper pole

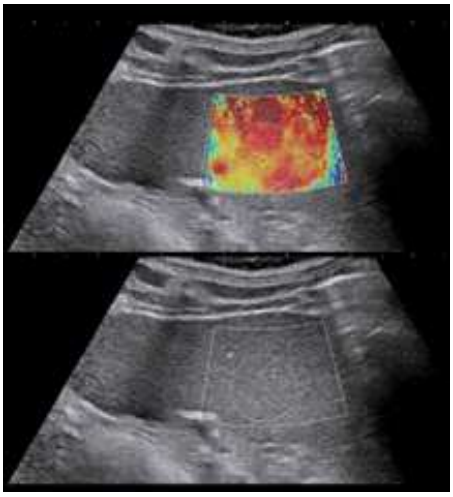

Figure 4. Elastography of spleen in a patient with splenomegaly due to portal hypertension at interpolar region

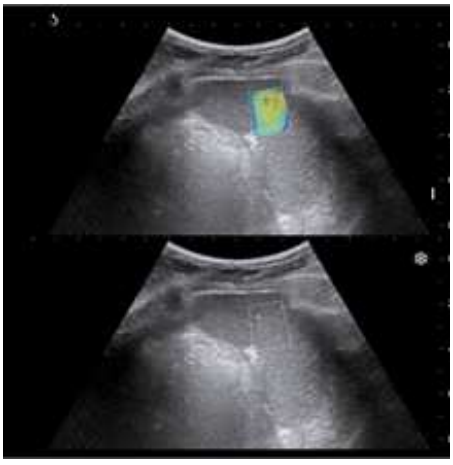

Figure 5. Elastography of a normal spleen at interpolar region

DISCUSSION

Splenomegaly can result from various causes, including hematologic, vascular, neoplastic, infectious, and immunologic disorders, as well as storage diseases. It is important to recognize that splenomegaly is not a specific diagnosis but rather a common pathological finding that suggests an underlying splenic disorder. Accurate differentiation among these causes is essential for appropriate management. A study by O'Reilly RA [10] classified splenomegaly causes into six diagnostic groups: hepatic diseases (36%), hematologic disorders (35%), infectious diseases (16%), inflammatory conditions (5%), primary splenic disorders (4%), and other causes (3%).

The mechanisms causing splenomegaly are not fully understood. However, in hepatic diseases, it is often linked to congestion from increased blood flow, pulp hyperplasia, and fibrosis [11,12]. In hematologic disorders, splenomegaly arises from increased spleen size and blood flow, elevated red blood cell counts, red pulp enlargement, and reticular component expansion [13]. Furthermore, chronic systemic infections, viral illnesses, and immune-mediated disorders can cause splenomegaly through follicular hyperplasia [14]. Ultrasonography is a cost-effective and reliable method for diagnosing splenomegaly; however, it falls short in determining the underlying cause of the condition. In contrast, elastography can aid in identifying the etiology of splenomegaly in patients. [15] Enlarged spleens exhibit varying densities due to factors such as tissue hyperplasia, fibrosis, and splenic congestion. By quantifying these mechanical properties, elastography provides valuable insights into the causes of splenomegaly. [16] Studies by Batur et al. (2019) [2] and Yalçın K et al. (2020) [17] have sought to differentiate the three primary categories of splenomegaly—hepatoportal, myeloproliferative, and infectious—based on measurements of splenic stiffness, thereby enhancing diagnostic accuracy.

Our study demonstrated that patients with splenomegaly exhibited

significantly higher mean spleen stiffness values compared to individuals with a normal spleen size. Specifically, the mean spleen stiffness was measured at 3.27 ± 0.36 m/s for cirrhotic patients, 2.95 ± 0.32 m/s for those with myeloproliferative disorders, and 2.44 ± 0.20 m/s for patients with infectious diseases, contrasting with a mean stiffness of 2.14 ± 0.18 m/s in individuals without splenomegaly ($p = 0.003$). These results align with the findings of Cho et al. (2018) [18], who reported mean spleen stiffness values of 35.1 ± 14.4 kPa for splenomegaly patients compared to 23.7 ± 8.7 kPa for those without splenomegaly ($p < 0.001$). The discrepancies between our study and Cho et al. may stem from differences in patient demographics and the elastography methods employed.

Further in our research, the mean spleen stiffness in cirrhotic patients was found to be 3.27 ± 0.36 m/s, which is comparable to the 3.24 ± 0.44 m/s reported by Ye et al. [19] and slightly higher than the 3.10 ± 0.55 m/s documented in the study by Bota et al.[20] Among patients with myeloproliferative disorders, we recorded a mean spleen stiffness of 2.98 ± 0.33 m/s, which is significantly lower than the 4.30 m/s (55.6 kPa) reported by Fraquelli et al. [13] Additionally, the spleen stiffness in patients with splenomegaly due to infectious diseases was measured at 2.44 ± 0.21 m/s, consistent with findings from the study by Batur A et al. [2] Overall, these findings suggest that elastography may serve as an essential tool in distinguishing between the three primary disease groups contributing to the development of splenomegaly. Nonetheless, this similarity in findings reinforces the reliability of pSWE as a diagnostic tool for assessing spleen stiffness.

The study by Batur et al. (2019) [2] corroborates our findings, demonstrating significantly higher spleen stiffness in patients with splenomegaly compared to those without, with a reported p-value of 0.001. This alignment between our results and theirs reinforces the consistency and reliability of spleen stiffness measurements in clinical settings. The agreement underscores the potential of point shear wave elastography (pSWE) as a valuable non-invasive diagnostic tool for assessing splenic disorders.

In cases of splenomegaly, significant increases in both spleen volume and shear wave velocity (SWV) values are noted in the hepatoportal and myeloproliferative groups. However, when comparing these two groups, spleen stiffness did not correlate with the increase in volume. This finding suggests that congestion and fibrosis are key factors in the development of hepatoportal splenomegaly.[21] In the myeloproliferative group, fibrosis limits spleen growth while increasing tissue stiffness due to its dense structure. Although this group has the largest spleen size, its SWV values are lower than those of the hepatoportal group, as cellular proliferation does not provide the same degree of tissue stiffness as fibrosis. Additionally, in cases of splenomegaly due to infections, the expected increase in spleen stiffness was not observed, likely due to cellular damage from vasodilation and inflammation, even with a rise in inflammatory cell count. [22,23]

The studies on shear wave elastography (SWE) of the spleen emphasize its significant clinical potential. Karagiannakis et al. (2019) [24] demonstrated that 2D-SWE could effectively exclude high-risk varices in patients with liver cirrhosis, potentially reducing the need for upper gastrointestinal endoscopy. Hirooka et al. (2022) [25] revealed a strong correlation between splenic shear wave speed and hepatic venous pressure gradient, identifying it as a valuable marker for predicting high-risk varices in patients with chronic liver disease. Collectively, these findings indicate that SWE of the spleen can enhance diagnostic accuracy, minimize invasive procedures, and provide critical insights into disease etiology and progression.

Our study faced several limitations. Firstly, it was conducted at a single center, which may have introduced selection bias. Additionally, the small sample size limited the generalizability of the findings to the broader population. Lastly, all measurements were performed by a single radiologist, and the study did not assess inter-observer agreement, which could impact the reliability of the results.

CONCLUSION

Splenomegaly can result from various causes, including hematologic, vascular, neoplastic, infectious, immunologic disorders, and storage diseases. Accurately distinguishing between these underlying pathologies is essential, as each condition requires specific management strategies. Although the precise pathogenic mechanisms remain poorly understood, variations in tissue composition associated with splenomegaly can be influenced by the underlying etiology. These changes in the mechanical properties of the spleen can be effectively measured using elastography, which provides valuable insights into the processes contributing to splenic enlargement.

This study demonstrates that point shear wave elastography (pSWE) is an effective, non-invasive tool for assessing spleen stiffness. The elevated spleen stiffness observed in patients with splenomegaly highlights the diagnostic potential of pSWE. Moreover, a positive correlation was found between spleen diameter and stiffness, suggesting that increased stiffness may accompany splenic enlargement. To further substantiate these findings, multi-center studies are recommended. In conclusion, pSWE shows significant promise for enhancing the evaluation and monitoring of splenic disorders, paving the way for improved patient management.

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