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Can Location of Stiffness Measurement Impact Spleen 2-Dimensional Shear Wave Elastography Measurement?

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Abstract: Ultrasound-based spleen elastography is a promising surrogate to predict portal hypertension noninvasively. In contrast to defined standards for liver stiffness measurement, the standardized examination procedures for 2-dimensional (2D) shear wave elastography spleen elastography have not been established yet. The aim was to investigate the impact of location of stiffness measurement on 2D shear wave elastography spleen stiffness measurement (SSM). Patients with splenomegaly were enrolled. Both B-mode ultrasound and elastography of spleen were performed. For SSM, 3 regions were chosen for spleen measurement: lower pole region, central region, and the region between lower pole and center. Mean SSM value, success rate, and reliability predicators (standard deviation, standard deviation/mean, size of region of interest) were assessed. A total of 124 patients were included. For mean SSM value, there were no significant differences among 3 regions. Spleen stiffness measurement success rate in lower pole region, central region, and the region between them was 63.7% (79), 91.1% (113), and 78.2% (97), respectively. The success rate in the central region was significantly higher than that in the other 2 regions ($P < 0.05$). Reliability in the central region was also highest among the 3 regions. Location of stiffness measurement has a limited effect on SSM. Changing location of measurement will not influence mean stiffness value in spleen.

Key Words: spleen, ultrasonography, 2-dimensional shear wave elastography, portal hypertension

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Portal hypertension is a cause of complications of cirrhosis.[1] The prevalence of portal hypertension is probably more than 50% in patients with cirrhosis.[2,3] Clinically significant portal hypertension is defined as a hepatic venous pressure gradient of 10 mm Hg or greater, which contributes to gastroesophageal varices and increased risk of clinical decompensation.[4] However, measurement of the hepatic venous pressure gradient is an invasive method, which requires cares and training.[5] Recent research identified that spleen elastography based on ultrasound is a promising method to predict clinically significant portal hypertension and gastroesophageal varices noninvasively.[5,6] It has several benefits, including portability, cost-effectiveness, and zero radiation exposure and enables dynamic evaluation.[7–10] However, the diagnostic performance of spleen stiffness measurement (SSM) in these studies is different from each other.[6] This phenomenon may be caused by different procedures to measure the stiffness.[6] Meanwhile, the majority of these studies focus on transient elastography and point shear wave elastography (pSWE).[11,12] Unlike transient elastography and pSWE, real-time 2-dimensional shear wave elastography (2D-SWE) displays elastogram in real time. Meanwhile, 2D-SWE shows better success rate of in liver stiffness measurement (LSM).[13]

Some studies reported that location of LSM (left lobe or right lobe, even the different segment) influences the reliability of LSM.[14,15] For example, Ling et al[14] found that LSM in liver segment V shows lower variance than that in other segments. We hypothesize that there may also be an impact of location of stiffness measurement on SSM. There are rare studies investigating the impact of measurement location on SSM.[11,16] Meanwhile, in contrast to the standard procedure for LSM, the standardized examination procedures for 2D-SWE spleen elastography, which can improve the efficiency of clinical works and quality of related researches, have not been established yet.

The aim of this study was to investigate the impact of location of stiffness measurement on SSM. Spleen stiffness measurement value, success rate and reliability predicators were assessed.

MATERIAL AND METHODS

Patient Cohorts

All patients enrolled in this study gave their informed consent. The Biomedical Research Ethics Committee of West China Hospital, Sichuan University, approved this study. From January 2019 to May 2019, patients in our hospital with liver disease who underwent SSM and LSM were recruited. According to previous studies, spleen size affected success rate of SSM significantly.[12,17] Because the aim of the study was to investigate the impact on SSM of different spleen regions, we wanted to get successful SSM data in different regions of spleen. It was difficult to obtain successful SSM in patients with relatively small spleen, not to mention

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successfully measuring SSM in different locations. Therefore, we only enrolled patients with spleen longitudinal diameter of 12 cm or greater or patients with spleen perpendicular short diameter of 4 cm or greater.[18] The patients with small spleen (longitudinal diameter <12 cm in the meantime with perpendicular short diameter <4 cm) were excluded. Heights and weights were also recorded to calculate body mass index (BMI). A BMI of 25 kg/m^2 or greater was recognized as obese.

B-Mode Ultrasound Evaluation

Abdominal B-mode ultrasound examination and 2D-SWE examination were performed after fasting for at least 8 hours by 2 investigators. Before 2D-SWE examination, all included patients received B-mode liver and spleen ultrasound scanning. All the spleen ultrasound examinations (both B-mode and 2D-SWE) were measured with the left arm at maximum abduction. The spleen size (both longitudinal diameter and perpendicular short diameter) and abdominal wall thickness were examined by a 1- to 6-MHz transducer (Aixplorer US system). The spleen size was computed from a sectional area (S) of the spleen as S (in square centimeter) = 0.9 × *a* (in centimeter) × *b* (in centimeter), where "*a*" was the longitudinal diameter and "*b*" was the perpendicular short diameter.[19]

Two-Dimensional SWE Evaluation

For SSM, a trapezoidal color box was positioned greater than 2 cm below the capsule in an area without visible vessels in spleen parenchyma. All the measurement was taken in the supine or right lateral decubitus. The beam of ultrasound was as perpendicular as possible to the surface of the spleen. Three regions were chosen for spleen measurement: lower pole region, central region, and the region between lower pole and center. As shown in Figure 1, from spleen lower pole to center, spleen was divided into these 3 parts. The patients were asked to suspend breathing for several seconds after mild expiration. There was no widely accepted detailed rule to measure 2D-SWE spleen stiffness. Hence, we used the criteria similar to 2D-SWE LSM.[20] To get a successful SSM, the following criteria were required: (1) temporal stability of the selected spleen area for at least 3 seconds; (2) a homogenous color in the region of interest (ROI); and (3) a round ROI of at least 10 mm. Spleen stiffness measurement failure was defined as either no signal obtained or failure to obtain a

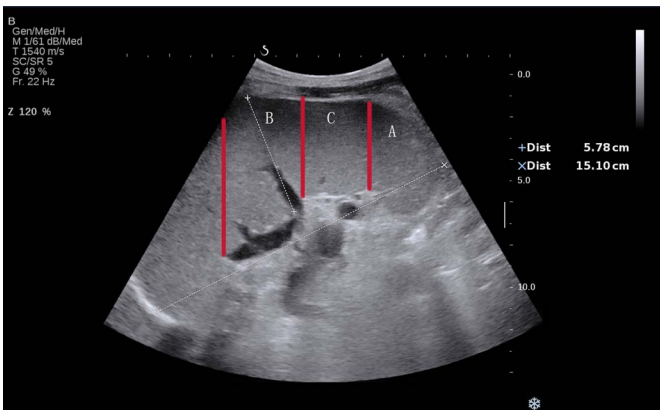

FIGURE 1. From spleen hilus to lower pole, the spleen was divided into 3 parts. A, The lower pole region. B, The central region. C, The region between lower pole and center.

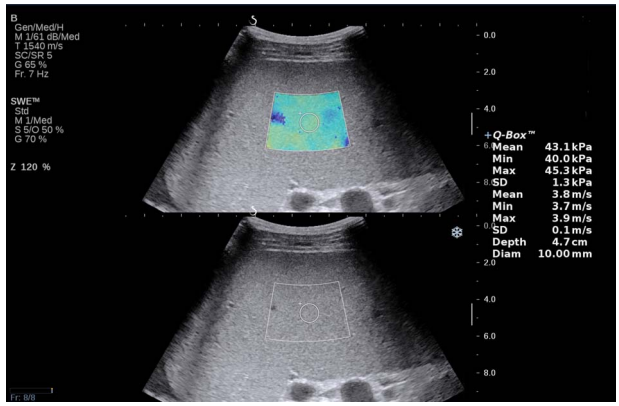

FIGURE 2. The figure showed a spleen 2D-SWE measurement. Mean SSM value and SD within a single ROI was displayed. To distinguish SD in a single ROI from SD calculated by several measurements, we recorded the former as "SD (in a single ROI)" and the latter as SD of 5 measurements.

measurement with no temporal stability and/or round ROI less than 10 mm. In each spleen region, 5 successful measurements were needed. For each measurement, SSM value, SD (in a single ROI), size of ROI, and depth of measurement were recorded for further analysis. As shown in Figure 2, each measurement value was shown with the mean stiffness value and the SD in a round ROI.[20] The success rate (= number of patients who got successful SSM / number of all the patients) and variable coefficient (= standard deviation (SD) of 5 measurement / mean SSM of 5 measurement) were also calculated.

For LSM, a same way as SSM was undertaken. A trapezoidal color box was positioned greater than 2 cm below the capsule in an area without visible vessels in right lobe of liver. A total of 3 measurements were needed for each patient. To get a successful LSM, the following criteria were required: (1) temporal stability of the selected spleen area for at least 3 seconds; (2) a homogenous color in the ROI; and (3) a round ROI of at least 10 mm. The mean value was used for further analysis.

Statistical Analysis

The summary statistics were shown as mean value with SD. For quantitative variables, the distribution of data was analyzed by the Shapiro-Wilk test. Normally distributed, independent samples, and paired groups were analyzed by *t* tests. The nonparametric Mann-Whitney *U* test was chosen to analyze independent parameters, which were not normally distributed. Categorical data were analyzed using the χ^2 test. All the *P* values were 2-sided, and the results were considered significant if a *P* value less than 0.05. SPSS 22.0 was used to analyze the data.

RESULT

Patient Characteristics

A total of 124 patients were enrolled in this study. The mean age was 54 ± 9 years and the mean BMI was 22.4 ± 3.2 kg/m^2. In all the patients, 91 patients (73%) were men and etiology of 81.4% patients was chronic hepatitis B. The characteristics of patients are shown in Table 1.

TABLE 1. Characteristics of the Patients

Male/female	91/33	
Age	54 ± 9 y	
Etiology	Chronic hepatitis B	101
	Alcoholic	8
	Others (chronic hepatitis C, fatty liver disease, etc)	15
BMI	22.4 ± 3.2	
Mean LSM	14.7 ± 8.0 kPa	
Longitudinal diameter	13.7 ± 2.6 cm	
Short diameter	5.1 ± 1.0 cm	
Spleen size	65.1 ± 24.7 cm^2	

Characteristics of B-Mode Ultrasound and 2D-SWE Measurement

Liver stiffness measurement was successfully obtained in 121 patients (98%). The mean LSM was 14.7 ± 8 kPa. The mean longitudinal diameter of spleen was 13.7 ± 2.6 cm and 89 patients had longitudinal diameter greater than 12 cm. The mean spleen size was 65.1 ± 24.7 cm^2 and 101 patients had spleen size greater than 45 cm^2.[19] The mean SSM value in lower pole region, central region, and the region between lower pole and center were 31.9, 33.3, and 32.2 kPa, respectively. Spleen stiffness measurement success rate in lower pole region, central region, and the region between lower pole and center were 63.7% (79), 91.1% (113) and 78.2% (97), respectively. The SSM value and size of ROI were normally distributed. The SSM characteristics in the 3 regions are shown in Table 2. Spleen stiffness measurement success rate in obese patients was lower than that in nonobese patients (99% vs 50%).

Impact of Location of Stiffness Measurement on SSM

The comparison of SSM in the 3 regions was shown in Table 3. For the patients who had got successful SSM in at least 2 regions, there was no significant difference among the 3 regions in the SSM value. Spleen stiffness measurement success rate in the central region was significantly higher than that of the other 2 regions ($P < 0.001$). The SD (in a single ROI) in lower pole region was significantly higher than that in the other 2 regions. As for SD of 5 measurements, variable coefficient, and size of ROI, the measurement in the center region showed best reliability. The depth of ROI did not show significant difference between the 3 regions.

The abdominal wall thickness in the lower pole region was thicker than that in the other 2 regions. Meanwhile, we also analyzed the relationship between success rate and abdominal wall thickness. In all the 3 regions, the abdominal wall thickness in the successful SSM group was thinner than that in the failed SSM group did (lower pole region, 1.67 vs 2.17 cm, $P < 0.001$; central region, 1.55 vs 1.90 cm, $P < 0.001$; region between them, 1.51 vs 1.80 cm, $P = 0.005$).

DISCUSSION

This study evaluated the effect of different locations on SSM in patients with spleen longitudinal diameter of 12 cm or greater or perpendicular short diameter of 4 cm or greater. We found that the location of measurement does not influence mean SSM value. However, success rate and reliability of measurement showed differences among the 3 locations.

Mean SSM value is one of important criteria to evaluate the impact of location of measurement on SSM. In our study, mean SSM value in the 3 regions were 31.9, 33.3, and 32.2 kPa, respectively. There were no significant differences among the 3 regions. In other words, mean SSM is independent upon the location of measurement in patients with splenomegaly. Therefore, if the operator fails in obtaining a "reliable" measurement in a region of the spleen, he/she can confidently choose another region knowing that there will be no change in stiffness value. To our knowledge, only one study reported the impact of measurement location on SSM.[16] Ferraioli et al[16] evaluated reproducibility of measurements of spleen stiffness at several locations by using pSWE. Spleen stiffness measurement in lower pole was higher than in center region (2.76 vs 2.48 m/s) in the research by Ferraioli et al.[16] The discrepancy between 2 studies may be caused by the different elastography method. The measurement times might be also a factor influencing results. According to the study by Ferraioli et al,[16] 2 measurements were taken in spleen. However, 10 measurements are recommended while using pSWE.[21] Two measurements might lead to misleading results of SSM.

According to the previous research focusing on LSM and SSM, the success rate of SSM is usually lower than that of LSM.[17,22,23] This is one of crucial reasons why we selected success rate as an important marker. In our study, the success rate of SSM in the lower pole region was the lowest one among all the 3 regions. One of the reasons to cause this result may be that it is hard to made ROI perpendicular to the surface of spleen in some cases. Interestingly, we also found that the abdominal wall thickness of lower pole region was the thickest. Meanwhile, in all the 3 regions, the abdominal wall thickness of successful SSM group was thinner than that of failed SSM group. Cho et al[17] also reported that the abdominal wall thickness is a predictor of successful SSM. Hence, we thought that the different

TABLE 2. Spleen Stiffness Measurement Characteristics in the 3 Regions

	Lower Pole	Center Region	Between Lower Pole and Center
Success rate	63.7% (79)	91.1% (113)	78.2% (97)
Mean SSM value	31.9 ± 15.1 kPa	33.3 ± 12.1 kPa	32.2 ± 13.3 kPa
SD (in a single ROI)	3.51 ± 1.8 kPa	2.52 ± 1.1 kPa	2.71 ± 1.3 kPa
SD of 5 measurements	4.0 ± 3.2 kPa	2.3 ± 1.0 kPa	3.2 ± 2.2 kPa
Variable coefficient	10.7% ± 2.9%	7.1% ± 1.4%	8.9% ± 1.9%
Size of ROI	10.9 ± 1.6 mm	14.7 ± 4.1 mm	11.5 ± 1.8 mm
Depth of ROI	3.7 ± 0.8 cm	3.8 ± 0.6 cm	3.6 ± 0.7 cm
Abdominal wall thickness	1.86 ± 0.5 cm	1.51 ± 0.4 cm	1.59 ± 0.4 cm

TABLE 3. Comparison Among the 3 Regions

	Lower Pole	Center Region	Between Lower Pole and Center	*P*
Successful rate	63.7%	91.1%		<0.001
		91.1%	78.2%	0.005
	63.7%		78.2%	0.018
Mean SSM value	31.9 kPa	31.8 kPa		0.9
		32.3 kPa	32.5 kPa	0.625
	31.5 kPa		31.4 kPa	0.823
SD (in a single ROI)	3.51 kPa	2.45 kPa		0.005
		2.54 kPa	2.69 kPa	0.34
	3.50 kPa		2.74 kPa	0.006
SD of 5 measurements	3.47 kPa	2.11 kPa		<0.001
		2.18 kPa	2.96 kPa	0.002
	3.47 kPa		2.61 kPa	0.008
Variable coefficient	10.8%		8.4%	0.005
		6.9%	8.9%	0.002
	10.7%	6.9%		<0.001
Size of ROI	10.9 mm	14.8 mm		0.01
		14.7 mm	11.6 mm	0.01
	10.9 mm		11.6 mm	0.6
Depth of ROI	3.7 cm	3.8 cm		0.5
		3.8 cm	3.7 cm	0.6
	3.7 cm		3.7 cm	0.5
Abdominal wall thickness*	1.86 cm	1.51 cm		<0.001
		1.51 cm	1.59 cm	0.35
	1.86 cm		1.59 cm	<0.001

*Abdominal wall thickness was measured in every patient even an SSM was failed. Other markers were only recorded only in patients who got successful corresponding SSM.

Paired-samples *t* test was used. Therefore, 2 different numbers was displayed on the same part.

abdominal wall thickness might be one of the reasons why the success rate of the lower pole region was different from the others. With increase of abdominal wall thickness, the echo signal of shear wave might be attenuated. As a result, the measurement of elastography is unstable or failed. The central region and the region between center and lower pole had similar abdominal wall thickness, but the central region had higher success rate. The cause leading to the discrepancy might be that the spleen parenchyma in center is more extensive than that in the region between center and lower pole.

In previous studies, markers of low variance were associated with reliable measurements.[20,22,24] Considering that there was no criterion evaluating the reliability of SSM, we used the method for liver as reference. Procopet et al[22] reported that LSM with the variable coefficient less than 10% was associated with high reliability diagnosing portal hypertension. In the report by Thiele et al,[20] high SD (in a single ROI) and large size of ROI in LSM increased the accuracy of a 2D-SWE measurement for correctly classifying liver cirrhosis. Therefore, SD (in a single ROI), variable coefficient, SD of 5 measurements (used to calculate variable coefficient), and size of ROI were chosen for the evaluation. For the patients who had successful SSM in at least 2 regions, SSM in the central region showed best performance in SD (in a single ROI), variable coefficient, and SD of 5 measurements. However, it is not clear whether different spleen regions could affect the diagnostic accuracy for portal hypertension.

Cho et al[17] and Procopet et al[22] reported that the success rates of SSM were 52.9% and 66%, respectively, which were lower than the results in this study. There might be 2 reasons. First, the aim of this study was to explore the influence of location of measurement on SSM. We only enrolled patients with longitudinal diameter of 12 cm or greater or short diameter of 4 cm or greater to improve the success rate of SSM. Several studies have revealed that spleen size is an important determinant of successful SSM.[12,17] Larger spleen longitudinal diameter improved success rate of SSM. Hence, it is reasonable that the success rate of SSM in this study was higher. Second, the average BMI in this study was 22.4 ± 3.2 kg/m^2, which was obviously lower than that in some previous studies (eg, BMI was 26.2 ± 4.2 kg/m^2 in the report by Procopet et al[22]). Lower BMI contributes to lower abdominal wall thickness.[25] The discrepancy of success rate might be the result from different abdominal wall thickness.

The limitations of the study are the following. First, the data of histology and endoscope were lacked. Therefore, we only compared mean SSM value, success rate of SSM, and reliability markers in the 3 regions. The comparison of the diagnostic accuracy is not performed. Second, the impact of the numbers of measurement on SSM is not evaluated. In this study, 5 times of SSM in each region were implemented. For LSM, 3 measurements suffice to obtain consistent results for the assessment of liver fibrosis and portal hypertension.[21] The number of measurements, which SSM required, is still unknown.

In conclusion, in patients with spleen longitudinal diameter of more than 12 cm or short diameter of more than 4 cm, the location of measurement has a limited effect on SSM. Mean SSM value is independent upon the location of measurement. Spleen stiffness measurement in the central region has the highest success rate with the smallest variance among the 3 regions. Meanwhile, SSM in the central region shows lowest variance. All the 3 regions are acceptable to measure spleen stiffness. If one region must be recommended, center region is most appropriate for SSM.

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