Evaluation of Spleen Stiffness Using Point Shear Wave Elastography in Healthy Individuals

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Abstract

Aim: Sonoelastography is a non-invasive imaging method used to evaluate the mechanical properties of any tissue. The clinical value of method, the usage of which is increasingly prevailing, is gradually increasing and on account of having newly entered the application field, it is becoming a potential in the research area. Shear wave (SW) propagates faster in stiffer and lower elastic tissues. Studies on liver fibrosis musculoskeletal, breast, prostate, testis, and thyroid nodules accept this principle. In this study, aimed to determine the average values using the point shear wave elastography (pSWE) technique in normal healthy individuals and to determine the relationship of these values with age, gender, body mass index (BMI), and the spleen dimensions.

Method: In 2019, patients who had visited the internal medicine service and those who have been directed to this clinics for grayscale ultrasound (US) for various reasons are voluntarily included in the study. The research was carried out consecutively on the same day by two specialist doctors who had 10 and 15 years of experience in ultrasonography and 3-year experience in elastography.

Results: 39 (39%) of the 100 patients who participated in the study were men, and 61 (61%) were women. And the ages varied between 32-75 years (y) (54,5±9,5). The average spleen stiffness was found to be 89,2±43,3 kilopascal (kPa) (14,2-152,3) by the first observer and 89,4±41,1 kPa (14,4-151,1) by the second observer.

Conclusion: To facilitate the common clinical usage and to evaluate the change in the stiffness of the spleen in different patients, first of all, it is required to determine the normal values of the stiffness of the spleen in healthy individuals using sonoelastography. In this study, the average spleen parenchyma stiffness was detected as higher than in previous studies. The values obtained in this study can be used to function as a

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comparison to determine the spleen stiffness. They can be used as referential to examine the different spleen pathologies in the clinical environments that use Esaote myLab device and pSWE method.

Keywords: Spleen, stiffness, point shear wave elastography.

Sağlıklı Bireylerde Dalak Sertliğinin Point Shear Wave Elastografi ile Değerlendirilmesi

Öz

Amaç: Sonoelastografi, dokunun mekanik özelliklerini değerlendirmede kullanılan noninvaziv bir görüntüleme yöntemidir. Kullanımı giderek yaygınlaşan bu yöntemin klinik değeri giderek artmakta olup bazı cihazların uygulama alanına yeni girmiş olması nedeniyle araştırma alanında potansiyel oluşturmaktadır. Daha sert ve elastisitesi daha düşük dokularda kayma dalgası daha hızlı yayılmaktadır. Karaciğer fibrozu, kas-iskelet sistemi, meme, prostat, testis ve tiroid nodülleri üzerine yapılan çalışmalar bu prensibi kabul etmektedir. Bu çalışmada normal sağlıklı bireylerde dalak sertliğini pSWE tekniği kullanılarak kantitatif olarak değerlendirerek ortalama değerleri saptamayı ve bu değerlerin yaş, cinsiyet, vücut kitle indeksi ve dalak boyutları ile ilişkisini saptamayı amaçlanmıştır.

Yöntem: 2019 yılında Dahiliye kliniğine başvuran, farklı nedenlerle rutin gri skala US için Radyoloji kliniğine yönlendirilen hastalardan gönüllü olan bireyler çalışmaya dahil edilmiştir. Araştırma, US alanında 10 ve 15 yıllık, elastografi alanında ise 3 yıllık deneyime sahip iki uzman doktor tarafından aynı gün içinde ardışık olarak gerçekleştirilmiştir.

Bulgular: Çalışmaya dahil 100 hastanın 39'u (39%) erkek, 61'i (61%) kadın olup yaşları 32-75 (54,5±9,5) arasında değişmekte idi. Ortalama dalak sertliğini birinci araştırmacı 89,2±43,3 kPa (14,2-152,3), ikinci araştırmacı 89,4±41,1 kPa (14,4-151,1) olarak saptamıştır.

Sonuç: Yaygın klinik kullanımını kolaylaştırmak için ve farklı hastalıklarda dalak sertliği değişikliklerinin değerlendirilebilmesi için öncelikle sağlıklı bireylerde sonoelastografi ile dalak sertliğinin normal değerlerinin belirlenmesi gerekmektedir. Bu çalışmada sağlıklı bireylerde ortalama dalak parankim sertliği diğer çalışmalara göre yüksek olarak tespit edilmiştir. Bu çalışmada elde ettiğimiz değerlerin Esaote myLab9 cihazı ve pSWE yöntemi kullanan klinik ortamlarda dalak sertliğini belirlemek için bir karşılaştırma işlevi görebileceğine, farklı dalak patolojilerinin incelenmesinde referans değerler olarak kullanılabileceğini düşünülmektedir.

Anahtar Kelimeler: Dalak, sertlik, nokta kayma dalgası elastografi.

Introduction

Sonoelastography is a non-invasive imaging method used to evaluate mechanical properties of any tissue. It is considered as the sonographic equivalent of palpation. Unlike palpation, after the power is applied in sonoelastography, the degree of the softness and stiffness of the tissue can be measured qualitatively and quantitatively. The clinical value of this method, the usage of which is increasingly prevailing, is gradually increasing and on account of having newly entered the

application field, it is becoming a potential in the research area. According to the shape of the force applied to the tissue in sonoelastography, there are two basic methods. The first is Strain Elastography (SE). In this method, force is used to the tissue in the form of push-pull with probe. The force related deformation that is formed over time in the tissue and the stiffness and elasticity maps of the tissue are created. In the second method, which is Shear Wave Elastography (SWE), the deformation of the tissue is created with the collimated and fortified ultrasound waves called Acoustic Radiation Force Impulse (ARFI)[1]. SWE is measured with the principle of measuring the speed of shear waves that is created with the pushing pulse that is moving perpendicular and towards the scanning axis. The obtained speed in"meters/second" or the quantitative values converted to"kilopascal" enable us to perform quantitative measuring concerning tissue elasticity[2]. It is denoted that the propagation velocity of these waves towards the transverse is directly proportional to the stiffness of the tissue. What is discussed here is the measurement of the speed on a small anatomical area of the shear waves created towards transverse by sending just one ARFI wave on Point SWE. In the second technic which is 2D-SWE, multiple ARFI waves are sent successively or uninterruptedly to a bigger area. Then, shear Wave speed measurements are done from the multiple points of that area. In the 2D-SWE technic, while the speed measurement that is to say the elasticity map of that area can be shown qualitatively with a special colthis scale, and also quantitative values can be obtained with 'region of interest (ROI)' measurements taken from different focuses of the same area[2]. Shear wave is expanded faster at the stiffer and lower elastic tissues[3]. In other words, after applying the force, pathological tissue hardly changes its place compared to healthier tissue. The studies were done on liver fibrosis, musculoskeletal system, breast, prostate, testicle, and thyroid nodules accept that principal[4-8]. The evaluation of spleen stiffness has attracted many researchers' attention in recent years. In some researches, sonoelastography is used to evaluate how the spleen stiffness differs in different diseases and it is shown that spleen elastography is potentially useful in showing the risk of esophageal varicosis development in patients having liver cirrhosis[9]. However, the spleen elastography studies done on healthy individuals who don't have any viral infection, hematologic disease, or chronic liver disease are very few thus much more data is required in that area. In this study, aimed to determine the average values using the point SWE technique to quantitatively evaluate spleen stiffness in healthy individuals and its relation with age, sex, BMI, and spleen dimensions.

Material and Methods

In 2019, patients who had visited the internal medicine service and those who have been directed to the Radiology clinic for grayscale ultrasound (US) for various reasons are voluntarily included in the study. Chronic liver disease, portal hypertension symptoms, hematological diseases

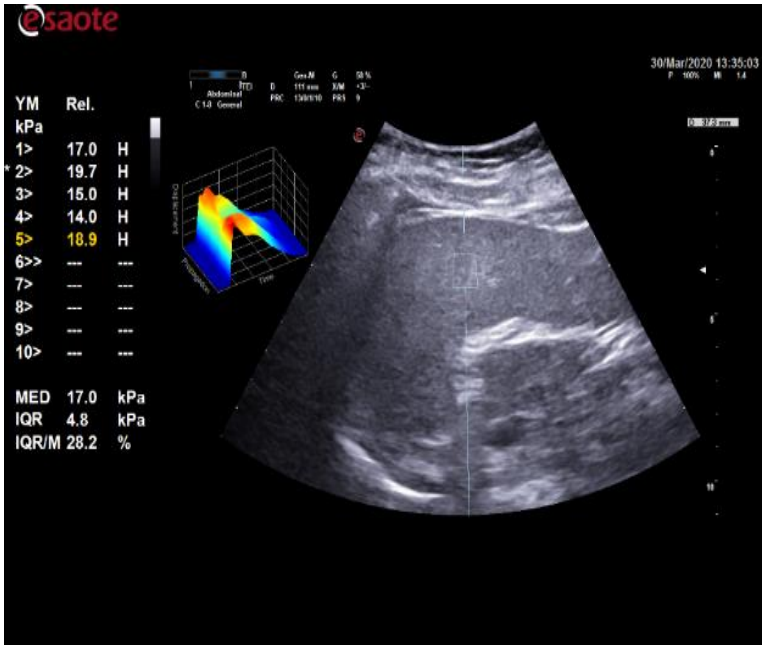
(leukemia, lymphoma, hereditary hematological anemia), or patients with a malignancy history have been excluded from the study.

Received approval from the ethical committee of Health Sciences University İstanbul Haseki Training and Research Hospital (Date: 11.12.2019, Decision Number: 2019-47). After having all the participants read the detailed information forms and got their consent, the research started. The participants were notified that there would be a US examination after 6-8 hunger before starting the research. For this research, ultrasonography and elastography examination were performed with the Esaote MyLab9 US device available in the Radiology Clinic of this hospital, using a convex probe in the 3-5mHz frequency range. The age, height, and weight of the subject in the study group were recorded. BMI value was calculated with kg/m^2 formula and according to World Health Organization, criteria were classified**.** B-mode ultrasonography was done with the patients in the right lateral decubitus position and a probe was placed in intercostal space and told the patients to hold their breath when they were normally breathing. The longitudinal dimension of the spleen was measured. Then point SWE was done. The sample box was placed to >10mm deeper than the capsule, five measurements were done at the areas far away from the vascular structures, and the obtained kPa values were recorded as averages (Figure. 1). The IQR/M values lower than 0.30 were accepted as reliable. The research was carried out consecutively in the same day by two specialist doctors who had 10 and 15 years of experience in ultrasonography and 3-year experience in elastography.

Statistics

SPPS 15.0 for Windows program was used for statistical analysis. Descriptive analysis; number and percentage were given for categorical variables and average, standard deviation, minimum and maximum were given for numeric variables. Since the normal range condition could not be provided, the comparing of the numeric variables in two independent groups was done with Mann Whitney U test. Since parametrical test conditions could not be established, the analysis of more than two groups were done with Kruskal-Wallis test. Because of the parametrical test conditions could not be established, the inter-numeric variation relations were done with Spearman Correlation Analysis. The harmony of the interobserver evaluation was examined with Reliability Analysis. The statistical alpha significance level was accepted as $p<0,05$.

Figure 1. In the spleen parenchyma, the ROI was placed approximately 1 cm deep and parallel to the capsule. The Propagation Map graph is of high quality and five measurements were made. IQR/M values below 30% are considered reliable.



Results

A total of 100 patients participated to the study 61 females (61%) and 39 males (39%) were included in the study. Ages varied between 32-75 y (54,5±9,5). 43% of patients were 50-59 y group. The mean BMI was 30,2±4.6 (18.6-44.2). The mean spleen size was 98,7±19,4 mm (38-182) (Table 1).

Table 1. Distribution of volunteers by gender, body mass index groups and spleen size

		Mean±SD (Min-Max)
Age		54,5±9,5 (32-75)
Gender	Male	39%
	Female	61%
BMI		30,2±4.6 (18,6-44,2)
	18,5-24,9 (normal weight)	10%
	25-29,9 (overweight)	43%
	30-39,9 (obese class I-II)	42%

	≥40 (obese class III)	5%
Spleen size		98,7±19,4 (38-182)
	<130 mm	95%
	≥ 130 mm	5%

The average pSWE values of spleen as determined by the first and second researchers were 89,2±43,3 kPa and 89,4±41,1 kPa, respectively. The ICC (95% CI) was 0,969 (0,955-0,979), which was excellent (Table 2).

Table 2. Mean spleen stiffness values obtained by the first and second observers; and ICC

				1. researcher vs. 2. researcher	
		researcher 1	**researcher 2**	**p(r) #**	**ICC (95% CI) ***
Mean		89,2	89,4	<0,001 (0,954)	0,969 (0,955-0,979)
SD		43,3	41,1		
95% CI	**Min**	80,6	81,2		
	Max	97,8	97,6		
Minimum		14,2	14,4		
Maximum		152,3	151,1		
Median		94,6	94,5		

The mean pSWE values of spleen determined by age groups are shown in Table 3. The mean pSWE values of the spleen were highest in the 6th decade. Both researchers determined 96,4±42.2 kPa and 96,7±39,8 kPa values, respectively, in the 6th decade. However, no statistically significant difference was found between the mean spleen pSWE values in all decades for both researchers (p values 0,714 and 0.473). ICC (95% CI) was excellent, 0,884; 0,975; 0,976; 0,969 and 0,970 in all decades, respectively.

Table 3. Spleen mean pSWE values in the age groups

		researcher 1		**researcher 2**	
		Mean±SD	Min-Max (Median)	Mean±SD	Min-Max (Median)
Age groups	30-39 y	83,7±41,3	32,1-135,3 (81,35)	76,4±29,5	37,6-112,4 (82,2)
	40-49 y	81,2±46,3	18,3-143,7 (73,3)	81,6±44,8	14,5-134,6 (89,6)
	50-59 y	96,4±42,2	14,2-152,3 (105,6)	96,7±39,8	22,8-151,1 (111,7)
	60-69 y	87,4±42,9	15,4-144,1 (93,2)	88,6±42,2	14,4-147,7 (93,3)
	70-79 y	78,1±49,4	32,5-141,9 (55,25)	80,9±46,0	29,5-147,5 (67,5)
	p	0,714		0,473	

The mean pSWE values of spleen determined by two researchers by patient gender are shown in Table 4. The mean pSWE values of the spleen determined by the first and second researchers were 92,7±41,9 kPa and 92,8±40,5 kPa in women, and 83,8±45,2 kPa and 84,2±42,1 kPa in men. Although both researchers found higher values in women, no statistically significant difference was found in the mean spleen pSWE values between the gender (p values 0,373 and 0,321, respectively). The ICC (95% CI) was 0,982 in men and 0,960 in women which was excellent.

Table 4. Spleen mean pSWE values by gender

	Male		**Female**		
	Mean±SD	Min-Max (Median)	Mean±SD	Min-Max (Median)	p
observer 1	83,8±45,2	14,2-144,8 (76,7)	92,7±41,9	18,6-152,3 (99,2)	0,373
observer 2	84,2±42,1	14,5-151,1 (87,7)	92,8±40,5	14,4-147,7 (98,7)	0,321

The mean pSWE values of spleen determined by two researchers by patient BMI are shown in Table 5. Considering the average pSWE values of the spleen according to BMI, the first and second researchers found 117,8±47,3 kPa in those with the highest BMI≥40 (obese class III). No statistically significant difference was found in the mean spleen pSWE values according to BMI for both researchers (p values 0,175 and 0,166, respectively). The ICC (95% Cl) was excellent in all BMI groups.

Table 5. Spleen mean pSWE values by BMI

		researcher 1		**researcher 2**	
		Mean±SD	Min-Max (Median)	Mean±SD	Min-Max (Median)
BMI	18,5-24,9 (normal)	107,5±45,4	34,8-144,8 (130,95)	106,0±46,7	28,4-143,9 (129,15)
	25-29,9 (overweight)	84,1±46,4	14,2-143,9 (82,5)	84,4±42,9	14,4-151,1 (90,1)
	30-34,9 obese class I	86,4±38,7	18,3-152,3 (93,3)	86,9±36,9	14,5-147,5 (87,35)
	35-39,9 obese class II	87,4±36,1	41,8-140,8 (82,55)	90,1±33,9	33,2-141,2 (93,3)
	≥40: obese class III	117,8±47,3	33,6-145 (134,4)	117,8±47,3	24,4-141,4 (135,1)
	p	0,175		0,166	

Considering the mean pSWE values according to spleen size, the values determined by the first and second researchers were 88,7±43,5 kPa and 89,0±41,6 kPa in those with normal size, and 98,2±40,7 and 97,9±32,9 kPa in those with enlarged spleen. Although an increase was observed in pSWE values with increasing spleen size, no statistically significant difference was found in mean pSWE values according to spleen size for both researchers (p values 0,591 and 0,782).

Discussion

In many studies conducted with the sonoelastography method, the clinical application of which has been increasing day by day, the assumption that pathological tissue is harder and less elastic than healthy tissue has been taken into account[9]. Being relatively a new noninvasive method and enabling us to evaluate the stiffness of the tissue qualitatively and quantitatively, it seems that this method has taken the place of palpation which has been a part of physical examination for centuries. To facilitate the common clinical usage and to evaluate the change in the stiffness of the spleen in different patients, first of all, it is required to determine the normal values of the stiffness of the spleen of healthy individuals using sonoelastography.

In this study, the first researcher determined the average spleen stiffness as 89,2±43,3 kPa (14,2-152,3) and the second researcher as 89,4±41,1 kPa (14,4-151,1). A few investigators have tried to determine spleen stiffness values in healthy individuals. In table 6, a few of these studies are shown. The elastography method used, the elastography device and the spleen stiffness values are given**.** In their studies Leung et al. reported that the average spleen stiffness as 17,3±2,6 kPa and, Pawlus et al., as 16,6±2,5 kPa[8,4]. In their study that they evaluated the soft tissues with SWE, Arda et al reported the stiffness of the spleen as 2,9±1,8 kPa (1-10 kPa)[7]. Pawlus et al. and Leung et al., found the average spleen stiffness values to be similar in their study using the Aixplorer device

(Aixplorer Ultrasound System, Supersonic Imagine SA, France) and the 2D-SWE method. However, in the study of Arda et al., using the same device and method, lower values were obtained. In this study, it is thought that the reason why the values of the stiffness of the spleen were much higher than in the other studies could be the result of using the point SWE method. Mauro Giuffré et al. reported that in their studies they had used Philips Affinity and pSWE methods to evaluate the stiffness of the spleen of the healthy individuals and obtained 18,1±3,08 kPa values[10]. The reason why obtained higher values in this studies lead us to think that the difference may be resulted from the device even though the elastography method is the same. In published studies, it was reported that with ARFI based technics, the normal spleen stiffness values varied between 20,5kPa and 24,4kPa[11-,13]. As is known, ultrasound and elastography examinations are user-dependent methods. However, it is thought that different findings may be obtained depending on the patient's subcutaneous fat tissue thickness and unequal inspiration. It is thought that studies should be conducted by the same researcher with different devices and methods in the same patient group in order to evaluate these differences and make a comparative evaluation.

When compared according to the age with 5th, 6th and 7th decades the spleen stiffness at the 4th and 8th decades were detected as high, statistically, no significant difference was detected between the age groups. In Pawlus' study the healthy volunteers were grouped into two. For the group below 45 years of age, the average spleen stiffness was determined as 16,5±2,4 kPa and as 16,8±2,6 for the group above 45 years of age. It was statistically reported that, no significant difference for spleen stiffness was determined among these two groups[8]

Table 6. Several studies show spleen stiffness values in healthy individuals using different elastographic techniques and devices

	Elastography technique	Device	Number of patients	Spleen stiffness
Pawlus et al., 2016	2D SWE (convex transducer with a frequency range 1–6 MHz)	Aixplorer device (Aixplorer Ultrasound System, SuperSonic Imagine SA, France)	59	16,6±2,5 kPa
Leung et al., 2013	2D SWE (convex transducer with a frequency range 1–6 MHz)	Aixplorer device (Aixplorer Ultrasound System, SuperSonic Imagine SA, France)	171	17,3±2,6 kPa
Arda et al., 2011	2D SWE (convex transducer with a frequency 3 MHz)	Aixplorer device (Aixplorer Ultrasound System, SuperSonic Imagine SA, France)	127	2,9 ± 1,8 kPa

Mauro Giuffré et al., 2019	Point SWE (convex transducer with a frequency 1-5 MHz)	Philips Affiniti 70, ElastPQ evaluation protocol.	100	18,1±3,08 kPa
Albayrak et al., 2019	2D SWE (convex transducer with a frequency range 1–6 MHz)	Logiq E9 XDclear, GE Healthcare, Milwauke,	65	13,82± 2,91 kPa

In the literature, there are some other publications, which did not detect any relation between age and spleen stiffness, that support this studies[10]. However, increased spleen stiffness on deep breaths in adults has been confirmed[14]. All the subjects participating in this study were told to breathe while breathing normally, no deep breath was held**.**

In this study, two researchers determined the spleen stiffness in women as 92,7±41,9kPa and 92,8±40,5kPa and in men as 83,8±45,2kPa and 84,2±42,1kPa, respectively. Higher values were determined in women than in men, but statistically, no significant difference related to gender was determined. In their studies, Guiffré et al. determined the stiffness in women as 16,71±3,32kPa and in men as 17,73±2,91kPa and reported that statistically there was not any significant difference between spleen stiffness and gender[10]. Similarly, in their 2011 study Arda et al. determined the average value of the spleen stiffness in men as 3,1±1,9kPa and in women as 2,9±1,8kPa. They reported that statistically there were no significant difference between gender and spleen stiffness[7]. Unlike this study, these two studies detected slightly higher values in men compared to women but statistically, this was not found meaningful. Yet, Kassym et al., by using ARFI in their study that they evaluated the relation between the rate of the spleen stiffness values of healthy individuals and their age, gender, spleen dimensions, ethnicity and obesity, similar to this study, they determined that the spleen stiffness was higher in women than men but differently from this study, these higher values were found statistically meaningful[15]. It was estimated that this difference resulted from the number of the population which was more than this study population.

The healthy volunteers in this study divided into 5 groups according to the BMI. The researchers determined the spleen stiffness of the group above 40 BMI as 117,8±47,3 and 114,9±50,7kPa respectively, slightly higher than the other groups. But there was not found statistically any significant difference between spleen stiffness and BMI. It has been thought that in extremely obese patients, fat may accumulate in the spleen as in the liver and the elasticity of the fat cells trapped in the capsule may decrease. Since only five percent of the subjects included in this study were extremely obese, it is thought that studies with larger extremely obese population should be

conducted in order to confirm this hypothesis. In their study published in 2019, Albayrak et al reported that they did not find any relation between BMI and spleen stiffness[16].

In this study, the researcher determined the spleen stiffness of individuals whose spleen dimensions were less than 130 mm as 88,7±43,5 and 89,0±41,6kPa and of individuals whose spleen dimensions were higher than 130mm as 98,2±40,7 and 97,9±32,9. In individuals whose spleen dimensions were high, the spleen stiffness values were higher but this did not show statistically any significant difference. Similar to this study there are also other studies reporting that did not detect any relation between spleen stiffness and dimensions[8,11,15,16]. In their studies, Guiffré et al reported that they looked at the average spleen stiffness according to the spleen bipolar diameter and spleen area. While they did not detect statistically any significant difference between spleen stiffness and spleen bipolar diameter, they also detected the values as 18,44±3,75kPa in individuals whose spleen area was lower than 37,40cm^2 and as 16,13±2,46kPa in individuals whose spleen area was above it[10].

In this study, the average spleen stiffness was measured by two researchers and with ICC 0.969 it was perfect. ICC was also perfect for age, gender, spleen dimensions and BMI groups. The researchers showed that the values would fluctuate approximately 12% based on the difference of measurements of the different manufacturers, devices and the observers[10]. In his study Pawlus reported that the replicability of the measurement results were good but were not ideal[8]. In this study showed that the method and perfect ICC values were replicable and reliable in measuring the spleen stiffness by using pSWE method.

The major limitation of this study was the low number of the healthy volunteers and the lack of a similar study that was done with the same device and same elastography method. The other limitation was that this results were compared to the results taken from different devices and methods.

Conclusions

Compared to other studies, in this study the average spleen parenchyma stiffness was detected as higher. As in the studies mentioned above, it can be estimated that systems could provide different referral measurement values that used the same methods but produced by different companies. At the same time, it was shown that there was a difference between the stiffness values detected by 2D-SWE and pSWE methods. The spleen stiffness can be detected quantitatively with SWE. The spleen stiffness does not affected by age, gender, spleen dimention and BMI. Believed that the values obtained in this study can be used to function as a comparison to determine the spleen stiffnes and can be used as referential to examine the different spleen pathologies in clinical environment that use Esaote myLab device and pSWE method. It is necessary to do much more

studies with large patient series to compare the stiffness values of the normal and pathological tissues to determine the diagnostic role of the spleen stiffness.

In order to conduct the study, approval was obtained from the Ethics Committee of Health Sciences University İstanbul Haseki Training and Research Hospital (Date: 11.12.2019, Desicion Number: 2019-47). Before the application, the participants were informed about the study and their verbal and written consents were obtained.

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