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ORIGINAL ARTICLE

The relationship of spleen stiffness value measured by shear wave elastography with age, gender, and spleen size in healthy volunteers

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Abstract

Purpose The aim of this study is to evaluate spleen stiffness values with shear wave elastography (SWE) quantitatively in healthy adults and investigate the relationship of spleen stiffness with age, gender, and spleen size.

Methods This study included 65 healthy individuals. Spleen stiffness measurement was obtained with 2 dimensional (2-D) SWE method from the middle portion of spleen and calculated in kilopascals by taking the average of three valid measurements. Longitudinal and transverse spleen sizes were measured. The relationship of spleen stiffness with age, gender, and spleen size was investigated. The association between spleen size and age and gender was also evaluated.

Results The mean spleen stiffness value was 13.82 ± 2.91 kPa, and the spleen stiffness was not affected by age, gender, or spleen size. Longitudinal spleen size was significantly lower in females than that in males. Moreover, there was a significant negative correlation between longitudinal spleen size and age ($r = 0.247$, $p = 0.048$).

Conclusion Spleen stiffness can be quantitatively measured by 2-D SWE, and the spleen stiffness is not affected by age, gender, and spleen size. The values obtained in this study can be used as normal base values in examination of different spleen pathologies.

Keywords Spleen · Shear wave elastography · Ultrasonography

Introduction

The spleen is the largest lymphoid organ in the human body and plays a critical role in immune system functions. The spleen is responsible for Ig M, T lymphocytes, B lymphocytes, and plasma cells production. Furthermore, the spleen serves as a primer reservoir for platelets, helps in destroying malformed or damaged red blood cells, and extramedullary hematopoiesis. The spleen consists of highly detailed tissue and cell structures and is anatomically connected to the liver via the portal vein system. As a result of this connection, all diseases affecting portal vein blood flow will affect the spleen and spleen flexibility. Thus, spleen parenchyma stiffness measurement is important in patients with chronic liver disease [1–3].

Shear wave elastography (SWE) is a noninvasive method that provides both qualitative and quantitative measurement of tissue stiffness. In SWE, transducer applies localized acoustic radiation force to a tissue in a selected investigation area, and the excited tissue emits shear waves reflecting the degree of its elasticity [4]. There are three basic SWE techniques today, i.e., transient elastography (TE), acoustic radiation force impulse (ARFI), and 2-dimensional (2-D) SWE [5, 6]. SWE is currently used for the evaluation of large number of tissues and organs pathologies, especially liver [5, 7, 8]. The quantitative values obtained in SWE can be influenced by the technique used and the transducer which can lead to variances in results [6]. It requires a large number of studies involving different techniques and obtaining normal reference values in order to be able to understand the physiology or pathological conditions of an organ [3]. There are many studies that have evaluated spleens with SWE. However, most studies have focused on assessment of spleen elasticity in chronic liver disease, portal hypertension,

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and esophageal varices [3, 9–18]; on the other hand, there are only few studies that determined the elasticity of normal spleen parenchyma [19–22]. The aim of this study is to evaluate spleen elasticity values with SWE quantitatively in healthy adults and investigate the relationship of spleen elasticity with age, gender, height, weight, body mass index (BMI) and spleen size.

Materials and methods

Patients

The study is approved by the clinical research ethics committee. Healthy volunteers without chronic liver disease, portal hypertension, portal vein or bile duct dilatation, autoimmune or hematologic disease, massive splenomegaly, focal splenic lesion, or another disease history or doubt were included in the study. The height and weight of the subjects in the study group were recorded. BMI value was calculated with kg/m^2 formula, and those in the normal group according to the World Health Organization criteria were included in the study. The spleen sizes and spleen elasticity values of the patients were measured. The relationship of spleen elasticity values with age, gender, weight, height, BMI and spleen size was investigated. All subjects enrolled in the study were fasting for at least 8 h.

2-D SWE measurements

SWE measurements were performed by a radiologist with at least 5 years elastography experience. SWE measurements were conducted with Logiq E9 XDclear, GE Healthcare, Milwauke; WI ultrasonography device using C1-6-D XDclear 1–6 MHz convex probe.

SWE measurements were performed in the supine position, during normal breathing (neither the maximum inspiration nor the maximum expiration), while the left arm was at maximum abduction, and from the left intercostal space. A rectangular box was placed at the middle portion of spleen, so it did not contain vessels. The SWE images were obtained in the form of homogeneous color coding filling inside the rectangle. The spleen parenchyma stiffness was calculated in kilopascals by placing a region of interest (ROI) drawn in the largest possible diameter into the rectangular box (Fig. 1). The measurements were validated as follows: (1) artifacts (spots, pixelization, and lack of a signal) occupying less than one-third of the elastographic map; (2) no sharp transition from soft (blue) to hard (red) elastographic areas; and (3) greater than two-thirds of the elastographic map with homogeneous coloring or a gradual color transition [8, 9]. Three valid measurements were conducted and the average of these three measurements was accepted as the mean spleen stiffness value. Patients who were not co-operative or their spleen parenchyma was too small for measurement were not included in the study.

Spleen size measurement

After SWE measurements, spleen sizes were measured. The spleen sizes were measured by the same radiologist performing SWE measurements with 15 years of experience in gray scale ultrasonographic examination with Logiq E9 XDclear, GE Healthcare, Milwauke; WI ultrasonography device on transverse and longitudinal plane using C1-6-D XDclear 1–6 MHz convex probe. The measurements were performed in the supine position with the left arm at maximum abduction, and the patient deeply breathing, from the section where the spleen was completely on the examination plane. The longitudinal diameter was measured between the lowest and the highest points of the spleen at the level of

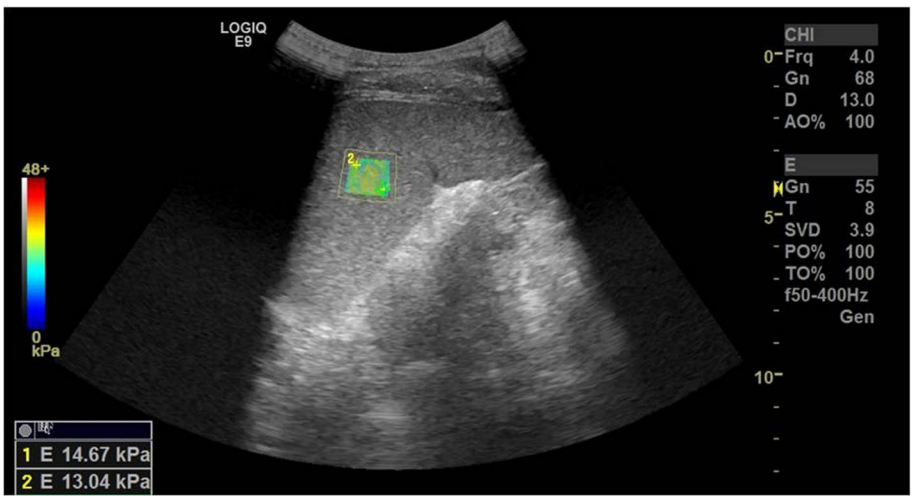

Fig. 1 2-D SWE measurement obtained by placing ROI from the middle part of the spleen

the hilus on the coronal plane. The transverse diameter was obtained by measuring the distance between the hilus and spleen dome.

Statistical analysis

Descriptive analyses were carried out with the purpose of giving information about the general characteristics of working groups. Mean ± standard deviation for continuous variables and number, percentage for categorical variables are used. Two independent sample *t* tests or one-way analysis of variances were used to compare the normal-distribution continuous data between/among groups. Pearson correlation coefficient is used for correlation between continuous variables. *p* values below 0.05 were considered statistically significant. Statistical analysis was performed using commercial software (IBM SPSS Statistics 19, SPSS Inc., an IBM Co., Somers, NY, USA).

Results

A total of 65 healthy individuals, 34 females (52.3%) and 31 males (47.7%), were included in the study. The mean age, spleen dimensions, and spleen stiffness are shown in Table 1.

Table 2 shows the spleen sizes and distribution of spleen stiffness values according to gender. Spleen stiffness was not different between gender. However, longitudinal spleen sizes were significantly lower in females when compared to males ($p = 0.026$).

The relationship of the mean spleen stiffness value and spleen sizes with age was evaluated based on age range. First, the individuals were divided into two groups: Those older than or equal to 40 years and those younger than 40 years (Table 3). However, no difference was found in terms of numerical variables (Table 3). Secondly, all individuals were divided into three different age groups: under 25 years, between 25 and 40 years, and over 40 years. No difference was found in terms of spleen stiffness value in this classification too (Table 4). Interestingly, subjects under 25 years of age had significantly higher longitudinal spleen size when compared to individuals older than 40 years (Table 4).

According to Pearson correlation coefficient, no significant correlation was found between spleen stiffness value and age ($r = -0.068$, $p = 0.592$), longitudinal spleen size ($r = 0.238$, $p = 0.057$), transverse spleen size ($r = 0.176$, $p = 0.160$), height ($r = 0.098$, $p = 0.438$), weight ($r = 0.050$, $p = 0.692$) and BMI ($r = -0.055$, $p = 0.666$). However, a significant weak negative correlation was found between longitudinal spleen size and age ($r = 0.247$, $p = 0.048$).

Table 1 General distribution of quantitative variables

	Mean	Standard deviation	Minimum	Maximum
Age (year)	41.25	13.77	18	67
Longitudinal diamater (mm)	100.83	14.78	67.24	132.26
Transverse diamater (mm)	44.35	6.99	29.30	61.10
Spleen stiffness (kPa)	13.82	2.91	6.27	20.06
Height (cm)	166.71	7.76	151	183
Weight (kg)	63.69	7.19	50	80
BMI (kg/m^2)	22.88	1.88	18.59	24.82

BMI body mass index

Table 2 Distribution of variables by gender

	Female	Male	*p*
Age (year)	41.56 ± 11.63	40.9 ± 15.99	0.850
Longitudinal diamater (mm)	96.95 ± 15.2	105.08 ± 13.27	0.026
Transverse diamater (mm)	43.14 ± 7.15	45.68 ± 6.67	0.145
Spleen stiffness (kPa)	13.57 ± 3.38	14.1 ± 2.3	0.463
Height (cm)	163.03 ± 6.02	170.74 ± 7.52	< 0.001
Weight (kg)	61.74 ± 5.74	65.84 ± 8.06	0.020
BMI (kg/m^2)	23.22 ± 1.69	22.51 ± 2.04	0.129

Independent samples *t* test was used

BMI body mass index

Discussion

The evaluation of the spleen parenchyma with SWE has been discussed in a small number of studies with variant elastography techniques. Pawluś et al. showed a mean spleen stiffness of 16.6 ± 2.5 kPa as measured with 2-D SWE and no relationship between stiffness value, age, gender, and

Table 3 Distribution of variables by age (classification 1)

	Age		*p*
	< 40	≥ 40	
Longitudinal diamater (mm)	104.55 ± 13.31	98.5 ± 15.32	0.109
Transverse diamater (mm)	45.1 ± 6.67	43.88 ± 7.23	0.501
Spleen stiffness (kPa)	13.95 ± 2.5	13.74 ± 3.16	0.776
Heights	168.56 ± 8.47	165.55 ± 7.16	0.129
Weights	63.72 ± 8.03	63.68 ± 6.73	0.981
BMI	22.42 ± 2.24	23.18 ± 1.58	0.116

Independent samples *t* test was used

BMI body mass index

Table 4 Distribution of variables by age (classification 2)

	Age			*p*
	< 25	25–40	> 40	
Longitudinal diamater (mm)	110.62 ± 12.43[a]	100.85 ± 11.9[ab]	97.98 ± 15.55[b]	0.042
Transverse diamater (mm)	47.18 ± 6.88[a]	43.97 ± 6.1[a]	43.69 ± 7.33[a]	0.340
Spleen stiffness (kPa)	14.33 ± 2.58[a]	13.56 ± 2.44[a]	13.78 ± 3.21[a]	0.797
Heights	170.36 ± 7.85[a]	167.56 ± 8.64[a]	165.29 ± 7.14[a]	0.142
Weights	63.73 ± 5.61[a]	64.13 ± 9.71[a]	63.5 ± 6.53[a]	0.959
BMI	22.02 ± 2.15[a]	22.74 ± 2.23[a]	23.2 ± 1.58[a]	0.178

One-way ANOVA test was used. (ab) Different superscripts (a, b) in the same row indicate statistically significant difference

spleen size similar [19]. Leung et al. evaluated liver and spleen elasticity values in liver fibrosis and healthy individuals using TE and 2-D SWE technique. They found that the spleen stiffness value of the healthy group as 17.3 ± 2.6 kPa using SWE [18]. Our study showed a mean spleen stiffness value of 13.82 ± 2.91 kPa which is very close to the others. The small difference might be due to the use of different brand elastography devices. Arda et al. assessed different soft tissues including spleen using 2-D SWE technique and found no relationship of spleen elasticity values with age and gender [20]. The mean spleen stiffness value in their study was 2.9 ± 1.8 kPa, which differs significantly from published values [18, 19]. Gallotti et al. examined upper abdominal organs of healthy individuals with ARFI method and found spleen elasticity value of 2.44 m/s [21]. Kassym et al. evaluated the proportion of liver and spleen stiffness values of healthy subjects using ARFI and their relationship with age, gender, spleen and liver sizes, ethnicity, and obesity. Interestingly, the proportion was higher in females when compared to males but no significant difference in terms of other parameters [22]. In their study, Kassym et al. evaluated the relationship between BMI and the ratio of liver and spleen elasticity value and they did not find a significant relationship between these two parameters. In our opinion, our study is the first study investigating the relationship between spleen elasticity values and height, weight and BMI values. In our study, we did not find a relationship between spleen elasticity values and height, weight and BMI values.

It has been emphasized that spleen elasticity values could be affected by physiological conditions [23, 24]. For example, calorie intake was reported to affect spleen stiffness. It is shown that evaluation within 3 h after meal may inadvertently lead to a diagnosis of higher stage liver fibrosis [23]. In our study, spleen elasticity was measured after 8 h of fasting. Karlas et al. emphasized that deep inspiration increases spleen stiffness value; therefore, they suggested standards to perform spleen stiffness measurements [24]. Based on these reports, we measured spleen stiffness during normal breathing.

We also evaluated the relationship between spleen sizes and age and gender in this study. Our findings that spleen longitudinal size decreased with age are consistent with the literature [25–27]. Moreover, we found longitudinal spleen size is lower in females as compared to males coherent with the literature too [25–29].

Our study has limitations. First, the measurements were performed by a single radiologist and intra-observer and inter-observer agreement rates were not evaluated. However, previous study has emphasized that intra-observer and inter-observer agreement rates are excellent in evaluating spleen elasticity with 2-D SWE [17]. Second, the number of individuals was relatively small. More extensive studies involving more patient populations may be conducted in the future.

Conclusions

Spleen parenchyma elasticity can be quantitatively measured by 2-D SWE, and the spleen stiffness value is not affected by age, gender, and spleen size. The values obtained in this study can be used as normal base values in examination of different spleen pathologies.

Compliance with ethical standards

Conflict of interest Eda Albayrak, Sadık Server declare that they have no conflict of interest.

Ethical statement All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from all patients for being included in the study.

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