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Research

The Contribution of Point Shearwave Elastography to Diagnosis in Liver Steatosis, Is There a Threshold Value?

Hepatik Steatozda Point Shearwave Sonoelastografinin Tanıya Katkısının Değerlendirilmesi, Bir Eşik Değer Var mı?

Sevim Özdemir, Tuba Selçuk Can, Behice Kaniye Yılmaz, Rüştü Türkay

University of Health Sciences Turkey, Haseki Training and Research Hospital, Clinic of Radiology, Istanbul, Turkey

ABSTRACT

Objective: The reversible metabolic disorder called fatty liver is an acquired metabolic disorder that results in the collection of triglycerides in hepatocytes. When it turns into chronic, lobular inflammation occurs and the disease can derive to steatohepatitis, fibrosis, cirrhosis, portal hypertension, liver failure, and hepatocellular carcinoma. Chronic diseases of the liver is one of the important health problems today. This prospective study evaluates the contribution of point shearwave elastography (pSWE) to the diagnosis of hepatic steatosis, to determine the threshold value according to steatosis degrees.

Methods: A total of 140 patients who were referred to the radiology department for abdominal ultrasonography (USG) from the internal medicine outpatient clinic due to reasons such as cholesterol-triglyceride elevation, liver enzyme elevation, right upper quadrant pain, fatigue, weakness, hepatomegaly, between January-2019 and April-2020 were included in the study. US elastography was examined. Ten consecutive measurements were carried out, and the resulting median values in kPa were recorded. The interquartile range/median values below 30% were considered in the confidence interval.

Results: The ages of patients were between 32 and 79 (mean age: 55.2±9.2). Of the patients, 54 were male (38%) and 86 were female (62%). The cut-off pSWE values according to the degree of steatosis were (researcher 1/researcher 2) <101.05/<89, <18.2/<22.2 and <5.85/<6.55 respectively for grade 1,2 and 3 steatosis.

Conclusion: This prospective study determines the threshold values for pSWE method considering the steatosis grades in the liver steatosis using the Esaote MyLab9 ultrasound machine and pSWE technique. Our study showed that the pSWE is a reproducible, noninvasive, and easily accessible method for evaluating fatty liver disease. But, more studies are needed, including histopathological verifications.

Keywords: Nonalcoholic fatty liver disease, point shearwave elastography, steatosis

ÖZ

Amaç: Yağlı karaciğer adı verilen geri dönüşümlü bir metabolik hastalık, hepatositlerde trigliseridlerin birikmesiyle sonuçlanan edinilmiş bir metabolik bozukluktur. Kronik hale geldiğinde lobüler enflamasyon gelişir ve steatohepatit, fibrozis, siroz, portal hipertansiyon, karaciğer yetmezliği ve hepatosellüler karsinoma da dönüşebilir. Kronik karaciğer hastalığının nedenleri farklı olsa da prognoz benzerdir. Bu prospektif çalışma, kronikleştiğinde fibrozise dönüşebilen yağlı karaciğeri olan hastalarda yağlanma şiddetine göre karaciğerin point shearwave elastografi (pSWE) ile değerlendirilmesi ve cut-off değer belirlemeyi amaçlamaktadır.

Gereç ve Yöntem: Ocak 2019 ile Nisan 2020 tarihleri arasında, kolesterol-trigliserid yüksekliği, karaciğer enzim yüksekliği, sağ üst kadran ağrısı, yorgunluk, halsizlik, hepatomegali gibi nedenlerle dahiliye polikliniğinden batın ultrasonografisi (USG) için radyoloji bölümüne yönlendirilen 140 hasta çalışmaya dahil edildi. Dört saat açlık sonrasında, sol lateral dekübit pozisyonda karaciğer USG ve pSWE incelemeleri yapıldı. Her hastadan on pSWE ölçümü yapıldı. Çeyrekler açıklığı/medyan değerler %30'un altında olan değerler kabul edildi. Her hasta aynı gün içinde, ardışık olarak iki uzman doktor tarafından değerlendirildi.

Bulgular: Çalışmaya dahil 140 hastanın 54'ü (%38) erkek, 86'sı (%62) kadın olup yaşları 32-79 (55,2±9,2) arasında değişmekte idi. USG'de 32 hastada yağlanma saptanmadı, 38 hastada grade 1, 54 hastada grade 2 ve 16 hastada grade 3 yağlanma kaydedildi. Karaciğerdeki yağlanmanın derecesine göre her iki araştırmacının (araştırmacı 1/ araştırmacı 2) elde ettiği eşik pSWE değerleri evre 1,2 ve 3 steatoz için sırasıyla <101,05/<89, <18,2/<22,2 ve <5,85/6,55 idi.

Address for Correspondence: Sevim Özdemir, University of Health Sciences Turkey, Haseki Training and Research Hospital, Clinic of Radiology, Istanbul, Turkey
Phone: +90 212 414 20 01 E-mail: sevimozdemir76@yahoo.com ORCID ID: orcid.org/0000-0003-4270-6370

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Sonuç: Literatürde nonalkolik yağlı karaciğer hastalığında önemli bir prognostik faktör olan fibrozisin derecelendirmesine yönelik çok sayıda elastografi çalışması olmasına rağmen, karaciğer steatoz derecelerine göre pSWE değerleri gösteren çalışma bulunmamaktadır. Bu prospektif çalışma, Esaote MyLab9 US cihazı ve pSWE tekniği kullanılarak karaciğer steatozunda steatoz derecelerine göre eşik pSWE değerleri belirlemektedir. Çalışmamız pSWE'nin yağlı karaciğer hastalığının değerlendirilmesi için tekrarlanabilir, noninvaziv ve kolay erişilebilir bir yöntem olduğunu göstermiştir. Ancak histopatolojik doğrulamanın dahil edildiği daha fazla çalışmaya ihtiyaç vardır.

Anahtar Kelimeler: Nonalkolik yağlı karaciğer hastalığı, point shearwave elastografi, steatozis

INTRODUCTION

The reversible metabolic disorder called fatty liver is an acquired metabolic disorder that results in the collection of triglycerides in hepatocytes. When it turns into chronic, lobular inflammation occurs and the disease can derive to steatohepatitis, fibrosis, cirrhosis, portal hypertension, liver failure, and hepatocellular carcinoma (1,2). It's essential to diagnosis the steatosis of liver in early stage as these patients are much better used from treatment. In line with the growing obesity epidemic and increasing prevalence of type 2 diabetes mellitus, nonalcoholic fatty liver disease (NAFLD) appear as a leading public health problem in Turkey due to its higher obesity rates compared to the world in general (3). Chronic diseases of the liver is one of the important health problems today. Even though the causes of chronic diseases may be different, the prognosis is similar, thus, for a successful clinical management of chronic liver diseases accurate diagnosis and staging of liver fibrosis is a crucial step (4). Noninvasive, reproducible staging methods are particularly important for monitoring the disease and therapeutic response (5-8). Measures to prevent the formation of steatosis and steatohepatitis that are the first stages of the chronic liver disease, are important tasks.

NAFLD is the most probable cause of liver dysfunction in industrial countries because it's linked with obesity, insülin resistance and dyslipidemia and due to this fact it's recognized as hepatic manifestation of metabolic syndrome (9). Laboratory tests, imaging methods and biopsy are the diagnostic and monitoring possibilities for fatty liver disease and hepatic fibrosis. Ultrasound (US) is an effective method among imaging methods for diagnosis and follow-up (9).

However, liver biopsy is considered the gold standard for chronic liver disease diagnosis it's still an invasivechoise, which can lead to some complications. For this reason non-invasive methods are demanding to diagnose fibrosis (10). US used in conjunction with elastography has recently had a great benefit in the follow-up of such patients. Elastography is a method that quantifies liver fibrosis by measuring the propagation velocity of the US waves passing through the liver; as fibrosis progresses, the liver tissue get-stiffness and the waves propagate faster. It is possible to determine the wave propagation velocity and degree of stiffness, thus the stage of liver fibrosis (1). There are several types of US elastography, the major ones used for liver stiffness assessment are transient elastography, two-dimensional shearwave elastography (2D-SWE), and point shearwave elastography (pSWE) (1). Technical developments and availability of US elastography is still rising. Comparability and standardization of US elastography instruments manufactured by different companies are the most necessary and investigated areas in the evaluation of the follow-up and determination of the response to therapy in liver diseases. For this reason, it is obvious that standard threshold value determination in certain disease groups with SWE technology is a subject of interest.

This prospective study is conducted to evaluate the pSWE values of patients with hepatic steatosis. The primary outcome is to evaluate the contribution of pSWE to the diagnosis of hepatic steatosis, to determine the threshold value according to steatosis degrees. The secondary outcome is the evaluation the reproducibility of the examination.

METHODS

Patients who were referred to the Radiology department for abdominal ultrasonography (USG) from the internal medicine outpatient clinic due to reasons such as cholesterol-triglyceride elevation, liver enzyme elevation, right upper quadrant pain, fatigue, weakness, hepatomegaly, between January-2019 and April-2020 were included in the study. Patients with a known history of chronic liver disease, viral hepatitis, portal hypertension, malignancy, and chemoteraphy were excluded from the study.

Real-time QElaXto-pSWE was examined with 1-8 MHz multifrequency convex probe using the Esaote Mylab9 Digital USG (Italy, Esaote) device with QElaXto Pack software in the Radiology department.

The were examined by two expert radiologists with more than 10 years of USG and 2 years of elastography experience. After for hour fasting, liver US and elastography were examined by two researchers consecutively on the same day for each patient.

The grading of liver steatosis is done using some US findings such as liver brightness, contrast between the liver

and the kidney, US vision of the intrahepatic vessels, liver parenchyma and diaphragm (11). Steatosis was graded as follows: absent (grade 0) when the echotexture of the liver is normal; mild (grade 1), when the liver had higher echogenicity than the right renal cortex, with normal visualization of the diaphragm and of the portal vein wall; moderate (grade 2), a moderate increase in liver echogenicity with slightly impaired appearance of the portal vein wall and the diaphragm; severe (grade 3), marked increase in liver echogenicity with poor or no visualization of portal vein wall, diaphragm, and posterior part of the right liver lobe (11,12).

US elastography was examined by placing the probe in the intercostal space in the slight left lateral decubitis position and telling the patient to hold breath and remain still. The sampling box for pSWE was placed approximately 2 cm from the liver capsule, in the area away from vascular structures and ten consecutive measurements were carried out, and the resulting median values in kPa were recorded (Figure 1). The interquartile range/median values below 30% were considered in the confidence interval. These findings were evaluated to investigate the interobserver compliance.

This prospective study was conducted in accordance with the ethical standards of the local ethics committee on human experimentation and with the Helsinki Declaration of 1075, as revised in 2000 after getting approval from the University of Health Sciences Turkey, Haseki Training and Research Ethics Committee (decision no: 2019-54, date: 26.02.2020). Informed written consent was obtained from all volunteers.

Statistical Analysis

Power analysis was carried out by using the mean and standard deviation values obtained from the study by Suh et al. (13). The sample size for 90% power is calculated as 138 persons.

SPSS 15.0 for Windows program was used for statistical analysis. Descriptive statistics of evaluation results were given as numbers and percentage for categorical variables, and as mean and standard deviation, minimum and maximum for numerical variables. Comparison of numerical variables between two independent groups were carried out by using Mann-Whitney U test when normally distributed, analyzes of more than two independent groups were performed using the Kruskal-Wallis test when the parametric test conditions could not be fulfilled. Relationships between numerical variables were made using Spearman correlation analysis when parametric test conditions were not met. The statistical significance level of alpha was set as $p<0.05$. Receiver operating characteristic (ROC) curve analysis was used to calculate the cut-off value in the diagnosis and grading of liver steatosis.

RESULTS

The ages of 140 patients included in the study ranged from 32 to 79, the mean age was 55.2±9.2. Of the patients, 54 were male (38%) and 86 were female (62%). Sonografically, steatosis was not detected in 32 patients, mild steatosis was noted in 38 patients, moderate in 54 patients and severe steatosis in 16 patients.

Liver elasticity according to gender determined by both researchers are shown in Table 1. Liver elasticity according to body mass index (BMI) determined by both researchers are shown in Table 2.

The ROC curve of the shear modulus of the determining of the grade 1 liver steatosis is shown in Figure 2.

The ROC curve of the shear modulus of the determining of the grade 2 liver steatosis is shown in Figure 3.

The ROC curve of the shear modulus of the determining of the grade 3 liver steatosis is shown in Figure 4.

Liver mean p-SWE values in steatosis degrees of both researchers are shown in Table 3 and Intraclass Correlation Coefficient (ICC) values are shown in Table 4.

The cut-off pSWE values of grade 1-2 and 3 liver steatosis of both researchers are shown in Table 5.

DISCUSSION

NAFLD is the most common hepatic disease with an estimated one billion patients worldwide (14). NAFLD represents liver steatosis which means intracellular collection of lipids and may get worse and cause nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma (15). NAFLD is thought to be the hepatic manifestation of the metabolic syndrome, which comprises central obesity, hyperlipidemia, hyperglycemia, hypertension and insulin resistance that plays a key role (16). NASH can lead to progressive fibrosis, cirrhosis, and end-stage liver disease. NASH is becoming the most common indication for liver transplantation in Western Countries (17). Also, the degree of liver steatosis is linked to increased cardiovascular risk (18).

One of the biggest developments in the field of US recently is the widespread use of US elastography technology. It has started to take its place among the standard practices in many countries as a non-invasive preference in the evaluation and grading of fibrosis, which has great clinical importance,

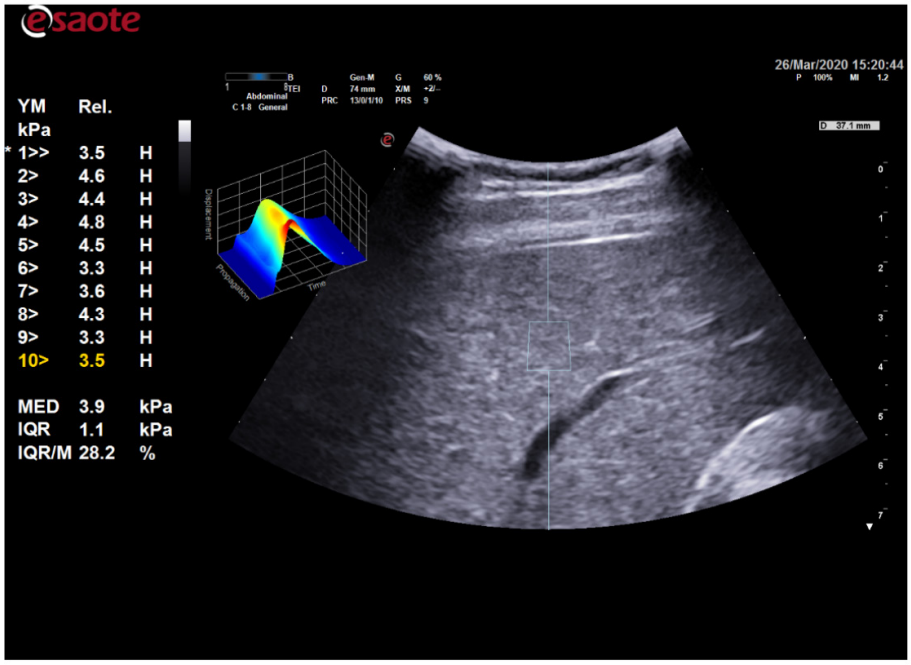

Figure 1. It was shown that the sample box was placed approximately 2 cm distal to the liver capsul, in the area away from vascular structures and ten consecutive measurements were carried out,and the resulting median values in kPa were recorded

especially in chronic parenchymal liver diseases. Currently, the method is being developed, practiced and popularized. In particular, the ability to standardize the versions of the technology offered by different imaging companies in a way that is comparable to each other is one of the most needed and areas being studied at the moment. If this is achieved, the US elastography method seems to be a candidate to become an indispensable component of relevant clinical practice applications. Conventional US is the most commonly employed diagnostic imaging method for the liver steatosis because it is easily accessible, well established, well tolerated, and cheap (19). In practice although US being the most widely used method to evaluate liver steatosis, on follow-up the severity of small alterations in steatosis this method has some difficulties. Thus, after therapeutic interventions of NAFLD patients US is not evaluated as the adequate method. To overpower the limitations of the US, computer-assisted quantitative US techniques are advanced for the follow-up assessment of liver steatosis (20). Other imaging techniques such as computerized tomography (CT), magnetic resonance imaging, magnetic resonance spectroscopy, have similar operating characteristics, but are more expensive, and CT involves radiation, therefore, their widespread use is limited (21). Due to such reasons and limitations, studies on US elastography are getting more popular. Most of the studies on liver elasticity in NAFLD in the literature were graded

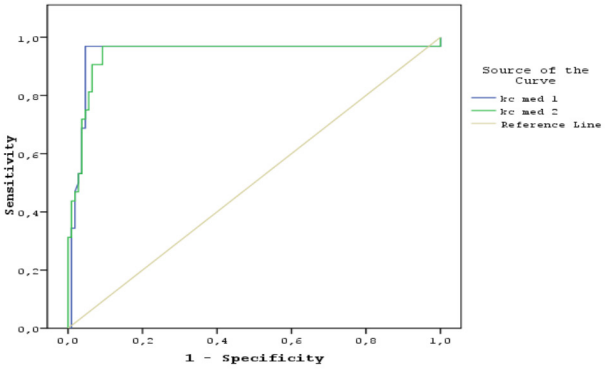

Figure 2. ROC curve of the shear modulus of the determining of the grade 1 liver steatosis
ROC: Receiver operating characteristic

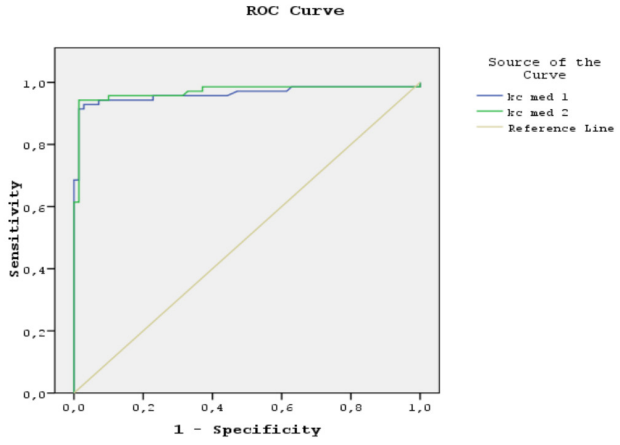

Figure 3. ROC curve of the shear modulus of the determining of the liver steatosis grade 2
ROC: Receiver operating characteristic

of liver fibrosis, which is important as a prognostic factor (22-24).

In the study by Özkan et al. (22), patients with NAFLD were evaluated with the pSWE and the median shearwave speed (SWS) value was reported to be approximately 1.56 m/s for the patients in the study. It has been reported that this SWS value is close to the low-grade histopathologic value and that patients with early stage NAFLD are likely to have histopathologic changes that do not cause significant tissue distortion, but this information should be evaluated by biopsy (22). In the Harris et al. (23) study, in the presence of steatosis, the Acoustic Radiation Force Impulse (ARFI) is very sensitive and accurate in detecting the higher stages of fibrosis, regardless of the severity of the steatosis. It tends to overestimate the fibrosis category in lower stages of fibrosis. This study it's reported that the presence of steatosis or its severity independently alters ARFI measurements are not shown. In our study, the cut-off pSWE values were determined according to the degree of steatosis in the liver and as the degree of liver steatosis increased the stiffness is decreased. Steatosis was evaluated only according to US findings and the histopathological evaluation was not performed. Therefore, it is inadequate to evaluate whether there are conditions that progress to steatohepatitis or fibrosis and its effect on the cut-off pSWE values we determined. A limitation of our study is that histopathological processes such as steatohepatitis or fibrosis were not excluded by biopsy after detecting steatosis with the US method.

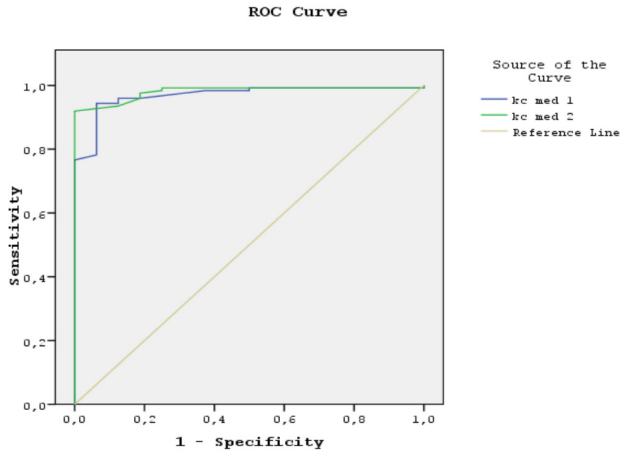

Figure 4. ROC characteristic curve of the shear modulus of the determining of the liver steatosis grade 3
ROC: Receiver operating characteristic

Also, according to the Ultrasound Liver Elastography Consensus Statement of the Society of Radiologists; it has been reported that depending on some published studies characterizing the Baveno VI consensus conference, the consensus panel proposes a vendor-neutral "rule of four" (5, 9, 13, 17 kPa) for the ARFI techniques for viral etiologies and NAFLD: Liver stiffness of 5 kPa (1.3 m/sec) or less has high probability of being normal; liver stiffness less than 9

Table 1. Liver elasticity according to gender determined by both researchers

	Gender				
	Male		Female		
	Mean ± SD	min-max (median)	Mean ± SD	min-max (median)	p
Researcher 1	46.9±51.3	4.4-137.6 (13.2)	55.4±52.8	0-144.5 (33)	0.879
Researcher 2	46.9±49.3	3.4-144.4 (12.8)	52.9±48.3	0-142.7 (35.85)	0.991

SD: Standard deviation, min: Minimum, max: Maximum

Table 2. Liver elasticity according to BMI determined by both researchers

		Researcher 1		Researcher 2	
		Mean ± SD	min-max (median)	Mean ± SD	min-max (median)
BMI	18.5-24.9	63.7±58.9	5.1-134.1 (47.45)	59.9±50.7	6.2-126.2 (67.2)
	25-29.9	39.7±47.5	3.1-142.3 (10.5)	40.0±46.0	3.4-142 (10.7)
	30-34.9	59.5±56.4	3.1-144.5 (33.9)	56.9±52.2	4.1-142.7 (35.15)
	35-39.9	70.1±42.9	0-131.7 (78.75)	67.1±41.2	0-144.4 (75.8)
	≥40:	43.8±46.4	4.6-129.5 (13.5)	42.8±43.7	5.3-116.9 (12.4)
	p	0.118		0.267	

SD: Standard deviation, min: Minimum, max: Maximum, BMI: Body mass index

Table 3. pSWE values according to liver steatosis grades determined by first and second researcher

		Researcher 1		Researcher 2	
	Grade	Mean ± SD	min-max (median)	Mean ± SD	min-max (median)
Liver steatosis	0	123.7±25.2	0-142.3 (131.75)	114.5±27.2	0-144.4 (113.35)
	1	71.4±34.9	6.2-144.5 (73.15)	72.6±29.1	8.5-131.4 (75.5)
	2	10.1±9.7	5.1-75.5 (7.7)	10.8±10.5	5.5-82.6 (8.4)
	3	4.8±1.2	3.1-7.5 (5.05)	5.1±0.9	3.4-6.4 (5.2)
	p	<0.001		<0.001	

SD: Standard deviation, min: Minimum, max: Maximum, pSWE: Point shearwave elastography

kPa (1.7 m/sec), in the absence of other known clinical signs, rules out compensated advanced chronic liver disease (cACLD); values between 9 kPa (1.7 m/sec) and 13 kPa (2.1 m/sec) are suggestive of cACLD but may need further test for confirmation; and values greater than 13 kPa (2.1 m/sec) are highly suggestive of cACLD (24). In this consensus, it has been shown that liver stiffness increases in case of cACLD development in NAFLD. In our study, liver stiffness in patients with normal liver was found to be quite high compared to values reported in the consensus. As the degree of steatosis increased, the stiffness decreased significantly. However, considering the chronicity of steatosis and the development of fibrosis in NAFLD, it does not mention a value related to liver stiffness in patients who are not chronic or have no clinical findings for cACLD, that is, only in the presence of steatosis. Whereas, in our study, we determined liver stiffness according to the degrees of fatty liver in the NAFLD without clinical findings suggestive of chronic liver disease.

In a study Sharma et al. (25), normal liver stiffness was measured in healthy people. In this study, elastography was performed on Philips iU22 and Affiniti70 US machines (Philips Healthcare, Best, The Netherlands), equipped with ElastPQ feature both using C5-1 probe, and reported as 4.48±0.78 kPa. In this study, it has been reported that, males have significantly higher liver elasticity compared to females, also, age, liver steatosis and BMI have no significant effect on liver elasticity. In the Huang et al. (26) study, they evaluated liver stiffness in 502 healthy subjects. SWE was performed using the Supersonic Imagine Aixplorer US system (Aix-en-Provence, France) that was equipped with an SC6-1 convex array probe with a frequency of 1-6 MHz. In this study, it was reported that the mean value of the SWE measurements in 502 individuals was 5.10±1.02 kPa. It was also reported that BMI had no effect on the results, and gender were also important factor affecting SWE (26). However, in our study, although liver elasticity was higher in males than in females, this difference was not statistically significant (p=0.879-0.991). Additionally, there was no statistically significant difference between the liver elasticity values of BMI (p=0.118-0.267).

In a large study by Fang et al. (27) comparing the interobserver reproducibility of four operators the ICC was found to be 0.88-0.93 for two series of measurements, in which 880 2D-SWE and pSWE velocities were recorded, respectively. Hudson et al. (28) determined that the intra-observer reliability was better for same-day evaluations (ICC=0.91) than the inter-observer reliability (ICC=0.78), they also determined that intra-observer agreement decreased when scans were repeated on a different day. Our pSWE results for two observers are correlated with conventional US grading. High ICC values were found for patients without steatosis and patients with mild steatosis

Table 4. ICC values according to liver steatosis grades

	Researcher 1 vs. researcher 2	
Liver steatosis	P (r)#	ICC (95% CI)*
Grade 0	<0.001 (0.733)	0.853 (0.500-0.944)
Grade 1	<0.001 (0.914)	0.917 (0.847-0.956)
Grade 2	<0.001 (0.847)	0.976 (0.958-0.986)
Grade 3	<0.001 (0.370)	0.518 (0.057-0.799)

#Spearman correlation analysis, *Two-way random-absolute agreement, CI: Confidence interval, ICC: Intraclass Correlation Coefficient

Table 5. The cut-off pSWE values of grade 1-2 and 3 liver steatosis of both researchers

Grade	Researcher	Threshold	Sensitivity	Specificity
1	1	<101.05	0.969	0.954
	2	<89	0.969	0.907
2	1	<18.2	0.929	0.971
	2	<22.2	0.943	0.986
3	1	<5.85	0.944	0.938
	2	<6.55	0.919	1.000

pSWE: Point shearwave elastography

and moderate steatosis. Medium ICC values were found for patients with severe steatosis. Medium ICC values in severe steatosis, may be due to the two investigators' placement of the sample box at different locations due to increased echogenicity of the liver parenchyma or the variability of the pressure applied to the probe to clearly assess the parenchyma. In relation to that the other limitation of our study was that the investigators' intraobserver agreement was not evaluated.

CONCLUSION

Although there are many elastography studies in the literature for grading fibrosis, which is an important prognostic factor in NAFLD however there is no study published investigating pSWE values in liver steatosis grading. This prospective study determines the threshold values for pSWE method considering the steatosis grades and non-steatosis in the liver steatosis using the Esaote MyLab9 US machine and pSWE technique. Our study showed that the pSWE is a reproducible, noninvasive, and easily accessible method for evaluating fatty liver disease. But, more studies are needed, including histopathological verifications.

ETHICS

Ethics Committee Approval: This prospective study was conducted in accordance with the ethical standards of the local ethics committee on human experimentation and with the Helsinki Declaration of 1075, as revised in 2000 after getting approval from the University of Health Sciences Turkey, Haseki Training and Research Ethics Committee (decision no: 2019-54, date: 26.02.2020).

Informed Consent: Informed written consent was obtained from all volunteers.

Authorship Contributions

Surgical and Medical Practices: S.Ö., T.S.C., B.K.Y., R.T., Concept: S.Ö., Design: S.Ö., B.K.Y., Data Collection or Processing: S.Ö., T.S.C., B.K.Y., Analysis or Interpretation: S.Ö., R.T., Literature Search: S.Ö., B.K.Y., R.T., Writing: S.Ö., R.T.

Conflict of Interest: The authors declare that they have no conflict of interest.

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REFERENCES

1. da Silva LCM, de Oliveira JT, Tochetto S, de Oliveira CPMS, Sigrist R, Chammas MC. Ultrasound elastography in patients with fatty liver disease. Radiol Bras 2020;53:47-55.
2. Lindenmeyer CC, McCullough AJ. The Natural History of Nonalcoholic Fatty Liver Disease-An Evolving View. Clin Liver Dis 2018;22:11-21.
3. Kaya E, Yılmaz Y. Non-alcoholic fatty liver disease: A growing public health problem in Turkey. Turk J Gastroenterol 2019;30:865-71.
4. Baranova A, Lal P, Birerdinc A, Younossi ZM. Non-invasive markers for hepatic fibrosis. BMC Gastroenterol 2011;11:91.
5. Realdi G, Fattovich G, Hadziyannis S, Schalm SW, Almasio P, Sanchez-Tapias J, et al. Survival and prognostic factors in 366 patients with compensated cirrhosis type B: a multicenter study. The Investigators of the European Concerted Action on Viral Hepatitis (EUROHEP). J Hepatol 1994;21:656-66.
6. Schalm SW. The diagnosis of cirrhosis: clinical relevance and methodology. J Hepatol 1997;27:1118-9.
7. Fowell AJ, Iredale JP. Emerging therapies for liver fibrosis. Dig Dis 2006;24:174-83.
8. Friedman SL, Bansal MB. Reversal of hepatic fibrosis -- fact or fantasy? Hepatology 2006;43(2 Suppl 1):S82-8.
9. AlShaalan R, Aljiffry M, Al-Busafi S, Metrakos P, Hassanain M. Nonalcoholic fatty liver disease: Noninvasive methods of diagnosing hepatic steatosis. Saudi J Gastroenterol 2015;21:64-70.
10. Gharibvand MM, Asare M, Motamedfar A, Alavinejad P, Momeni M. Ultrasound shear wave elastography and liver biopsy to determine liver fibrosis in adult patients. J Family Med Prim Care 2020;9:943-9.
11. Ferraioli G, Soares Monteiro LB. Ultrasound-based techniques for the diagnosis of liver steatosis. World J Gastroenterol 2019;25:6053-62.
12. Kang BK, Kim M, Shin SJ, Kim YJ. Correlation of Clinical and Histopathologic Parameters with Ultrasonographic Grades in Pediatric Non-Alcoholic Fatty Liver Disease. J Korean Med Sci 2019;34:e298.
13. Suh CH, Kim SY, Kim KW, Lim YS, Lee SJ, Lee MG, et al. Determination of normal hepatic elasticity by using real-time shear-wave elastography. Radiology 2014;271:895-900.
14. Loomba R, Sanyal AJ. The global NAFLD epidemic. Nat Rev Gastroenterol Hepatol 2013;10:686-90.
15. Nassir F, Rector RS, Hammoud GM, Ibdah JA. Pathogenesis and Prevention of Hepatic Steatosis. Gastroenterol Hepatol (N Y) 2015;11:167-75.
16. Paschos P, Paletas K. Non alcoholic fatty liver disease and metabolic syndrome. Hippokratia 2009;13:9-19.
17. Leoni S, Tovoli F, Napoli L, Serio I, Ferri S, Bolondi L. Current guidelines for the management of non-alcoholic fatty liver disease: A systematic review with comparative analysis. World J Gastroenterol 2018;24:3361-73.
18. Arulanandan A, Ang B, Bettencourt R, Hooker J, Behling C, Lin GY, et al. Association Between Quantity of Liver Fat and Cardiovascular Risk in Patients With Nonalcoholic Fatty Liver Disease Independent of Nonalcoholic Steatohepatitis. Clin Gastroenterol Hepatol 2015;13:1513-20.e1.
19. Castera L, Friedrich-Rust M, Loomba R. Noninvasive Assessment of Liver Disease in Patients With Nonalcoholic Fatty Liver Disease. Gastroenterology 2019;156:1264-81.e4.
20. Lee SS, Park SH. Radiologic evaluation of nonalcoholic fatty liver disease. World J Gastroenterol 2014;20:7392-402.
21. Hernaez R, Lazo M, Bonekamp S, Kamel I, Brancati FL, Guallar E, et al. Diagnostic accuracy and reliability of ultrasonography for the detection of fatty liver: a meta-analysis. Hepatology 2011;54:1082-90.
22. Özkan MB, Bilgici MC, Eren E, Caltepe G, Yilmaz G, Kara C, et al.

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23. Harris N, Nadebaum D, Christie M, Gorelik A, Nicoll A, Sood S, et al. Acoustic radiation force impulse accuracy and thei mpact of hepatic steatosis on livervfibrosis staging. J Med Imaging Radiat Oncol 2016; 60:587-92.
24. Barr RG, Wilson SR, Rubens D, Garcia-Tsao G, Ferraioli G. Update to the Society of Radiologists in Ultrasound Liver Elastography Consensus Statement. Radiology 2020;296:263-74.
25. Sharma VK, Malhotra A, Chauhan TK. Evaluation of Liver Stiffness in Healthy Individuals by Sonoelastography. Journal of Clinical and Diagnostic Research 2017;11:13-6.
26. Huang Z, Zheng J, Zeng J, Wang X, Wu T, Zheng R. Normal liver stiffness in healthy adults assessed by real-time shear wave elastography and factors that influence this method. Ultrasound Med Biol 2014;40:2549-55.
27. Fang C, Konstantatou E, Romanos O, Yusuf GT, Quinlan DJ, Sidhu PS. Reproducibility of 2-Dimensional Shear Wave Elastography Assessment of the Liver: A Direct Comparison With Point Shear Wave Elastography in Healthy Volunteers. J Ultrasound Med 2017;36:1563-9.
28. Hudson JM, Milot L, Parry C, Williams R, Burns PN. Inter- and intra-operator reliability and repeatability of shear wave elastography in the liver: a study in healthy volunteers. Ultrasound Med Biol 2013;39:950-5.