The Role of Liver Elastography Point Quantification in the Assessment of Fibrosis in Non-Alcoholic Fatty Liver Disease and Comparison with Other Non-Invasive Methods

Non-Alkolik Yağlı Karaciğer Hastalığında Fibrozisin Değerlendirilmesinde Karaciğer Elastografi Point Quantification Ölçümünün Rolü ve Diğer Non-İnvazif Yöntemlerle Karşılaştırılması

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ABSTRACT

Objective: The aim of this study was to determine the availability of a new liver stiffness (LS) measurement, the elastography point quantification (ElastPQ) method, in non-alcoholic fatty liver disease (NAFLD) and to compare it with other noninvasive Liver fibrosis (LF) investigations.

Material and Methods: A total of 108 patients with or without NAFLD were included in this study. LS measurement was done by the ElastPQ method. Noninvasive LF investigations; the AST/Platelet-ratio-index (APRI), Fibrosis-4 (FIB-4) index, NAFLD fibrosis score, AST/ALT ratio and BARD score were evaluated.

Results: Liver size, LS, APRI, FIB-4 index, NAFLD fibrosis score, AST/ALT ratio and BARD score were all significantly higher in NAFLD patients. It was determined that only LS among these parameters independently determined the NAFLD status. It was found that each 0.5-kPa increase in LS increased the risk of having NAFLD 2.12 fold. When the ROC analysis was performed for the NAFLD determination of the LS value, it was determined that the area under the ROC curve was 0.967, and when the limit value for LS was taken as 5-kPa, the risk of having NAFLD was determined with 88.9% sensitivity and 94.4% specificity.

Conclusion: The LS value obtained by ElastPQ has high diagnostic accuracy for NAFLD and performs better than other noninvasive laboratory methods in the assessment of NAFLD. At the same time, the LS value is closely related to the FIB-4 index, NAFLD fibrosis score and BARD score.

Key Words: Non-alcoholic fatty liver disease, Liver stiffness, Elastography, Non-invasive liver fibrosis investigations

ÖZ

Amaç: Bu çalışmanın amacı; yeni bir karaciğer sertlik (LS) ölçümü incelemesi olan elastografi point quantification (ElastPQ) yönteminin non-alkolik yağlı karaciğer hastalığında (NAFLD) kullanılabilirliğinin tespiti ve bu incelemenin diğer non-invaziv karaciğer fibrozis (LF) incelemeleri ile karşılaştırılmasıdır.

Gereç ve Yöntemler: Çalışmaya NAFLD olan ve olmayan 108 hasta alındı. LS ölçümü ElastPQ yöntemi ile yapıldı. Hastalara noninvaziv LF incelemelerinden; AST/Platelet oranı indeksi (APRI), Fibrosis-4 (FIB-4) indeksi, NAFLD fibrozis skoru, AST/ALT oranı ve BARD skoru değerlendirildi.

Bulgular: Karaciğer boyutu, LS, APRI, FIB-4 indeksi, NAFLD fibrozis skoru, AST/ALT oranı ve BARD skoru değerlerinin hepsi NAFLD olan hastalarda olmayanlara göre belirgin olarak yüksekti. Bu parametrelerden sadece LS' nin NAFLD olma durumunu bağımsız olarak belirlediği saptandı. LS' da her 0.5 kPa artış NAFLD olma durumunu 2.12 kat artırdığı tespit edildi. LS' nin NAFLD belirlemesi için ROC analizi yapıldığında, ROC eğri altında kalan alanın 0.967 olduğu ve LS için sınır değer 5 kPa olarak alındığında NAFLD olma riskini %88.9 duyarlılık ve %94.4 özgüllük ile belirlediği saptandı. Ayrıca HbA1c, LDL kolesterol, FIB-4 indeksi, NAFLD fibrosis skoru ve BARD skorunun, LS ile yakın ve bağımsız ilişkili olduğu bulundu.

Sonuç: ElastoPQ yöntemi ile ölçülen LS değeri NAFLD varlığını diğer non-invasiv LF incelmelerinden daha iyi ve bağımsız olarak belirler. Aynı zamanda, LS değeri non-invasiv LF belirleyicilerinden FIB-4 indeks, NAFLD fibrozis skoru ve BARD skoru ile yakın olarak ilişkilidir.

Anahtar Sözcükler: Non-alkolik yağlı karaciğer hastalığı, Karaciğer sertliği, Karaciğer elastografi, Non-invaziv karaciğer fibrozis incelemeleri

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the most common cause of liver disease worldwide and NAFLD is present in 1 out of every 4 patients (1). NAFLD can progress from simple liver fat deposition to non-alcoholic steato-hepatitis (NASH), cirrhosis and hepatocellular carcinoma (1). The most important parameter in the progression of the disease is the presence and degree of liver fibrosis (LF). To assess liver steatosis and fibrosis occurring in NAFLD, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels from biochemical tests or liver ultrasound (US) can be used but liver biopsy is still the gold standard (2). If only 10% of patients with NAFLD are biopsied, this invasive procedure should be done to more than 100 million people. Therefore, noninvasive imaging and laboratory methods developed for LF evaluation have been taking the place of liver biopsy in recent years. Liver US is a non-invasive, inexpensive and easily accessible investigation that can be used in detecting fatty liver.

Elastography is a newly developed US technique that can measure tissue stiffness and fibrosis development noninvasively and quantitatively. For the last 10 years, LF evaluation with the liver elastography (LE) method has been critical and gives clearer and more objective information. This investigation technique has been started with transient elastography (TE) (3-5), and continued with acoustic radiation force impulse (ARFI) technique (6), two dimensional shear wave elastography (SWE) (7) and point SWE (pSWE) (8). All of these studies gave good results in LF detection. It was shown that liver stiffness (LS) measurement detected in LE studies and the LF detected by biopsy were closely related (3,5,9,10). In 2016, 9 noninvasive fibrosis tests including LS obtained with TE were compared in NAFLD patients (BARD, NAFLD fibrosis score, Fibrometer^{NAFLD}, AST/platelet ratio index (APRI), Fibrosis-4 (FIB-4), FibroTest, Hepascore, FibroMeter^{V2G} and LS) (11). LS was reported to be the most accurate noninvasive fibrosis assessment to detect LF (11). However, there is a measurement problem for TE examination in patients with obesity, metabolic syndrome, acid and narrow intercostal space (12,13). Point SWE studies can be done on new model US devices. The most important features of these new tests when compared to TE are their ease of use, the ability to take measurements at high rates and the high power to predict liver pathology (8,14). In the literature, the use of this new ElastPQ study in patients with NAFLD and the comparison of other noninvasive LF parameters with those of the LS value determined by the ElastPQ study in patients with NAFLD have not been studied.

Therefore, the purpose of this study was to compare the use of the ElastPQ method, a new and objective LS study, in patients with NAFLD and to compare this investigation with other noninvasive LF scans.

MATERIALS and METHODS

A total of 108 patients (mean age; 54.9 + 7.7 years, male / female; 46/62) who underwent liver US to evaluate NAFLD and who were or were not diagnosed with NAFLD were included in this study at our Radiology Clinic. NAFLD was identified according to NAFLD diagnosis and treatment guidelines using the clinical history, biochemical data and radiology findings (15). Those with chronic liver diseases mentioned in the guidelines were not included in the study (15). Patients with previously known acute or chronic liver disease history, presence of Hepatitis B and C, NASH, regular alcohol intake (> 20gr/day), serious valvular heart disease, right or left heart failure, pulmonary or portal hypertension (HT), inflammatory diseases, hematological diseases, active thyroid disease, cancer and suspected pregnancy were excluded from the study. Ethics committee approval was received for this study from the ethics committee of Cukurova University (date: 01.06.2018; approval number: 2018– 78-40). All forms of voluntary consent for all patients were explained in detail and patients were included in the study after receiving written approval.

After all the patients were included in the study, a detailed anamnesis was obtained and a physical examination were performed. Subsequently, the baseline demographic characteristics of all groups were examined for age, gender, presence of HT, diabetes mellitus (DM), impaired fasting glucose (IFG), smoking, hyperlipidemia, and obesity. In determining these risk factors, the latest guidelines were taken into account. Systolic and diastolic blood pressures were recorded. The waist circumference was measured from the umbilicus level with subjects standing. Body mass index (BMI) was calculated by measuring weight and height. Baseline total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglyceride (TG), HbA1c, blood glucose, AST, ALT,

albumin, blood urea nitrogen (BUN), creatinine and high sensitivity C reactive protein (hs-CRP) levels of the patients were measured.

Liver Ultrasonography

All patients had undergone liver US screening using a high resolution US device (Philips EPIQ 7) 5-1 MHz high resolution convex probe (Philips Health Care, Bothell, WA, USA). Liver US examinations were performed after at least 6 hours of fasting, and B-mode US evaluation was first performed on the gray scale. Liver length and parenchyma echogenicity were assessed on gray scale. While the patient was in the supine position, the liver length was determined by the widest craniocaudal measurement in the mid-clavicular area. Normally the liver parenchyma has a homogenous echo which is equal to or slightly more echogenic than the normal renal cortex or spleen (grade 0). The presence of increased echogenicity in the liver parenchyma indicates mild fattiness (or grade 1) when the hepatic and portal venous walls are clearly visible. The parenchyma being more echogenic compared with the kidney or spleen shows moderate fattiness (or grade 2) when the hepatic and portal venous walls are undetectable and severe fattiness (or grade 3) when posterior attenuation, which means that the posterior segments of the liver cannot be assessed due to sonographically intense shadowing, and failure to detect the diaphragm are also present. Grade 1-3 was considered NAFLD. LS was performed in the left lateral decubitus position using the pSWE investigation and ElastPQ technique (Figure 1A-D). During liver ultrasound, the probe was compressed as lightly as possible and was placed in a stable position while the patient was asked not to breathe for a few seconds to minimize the movement of the liver

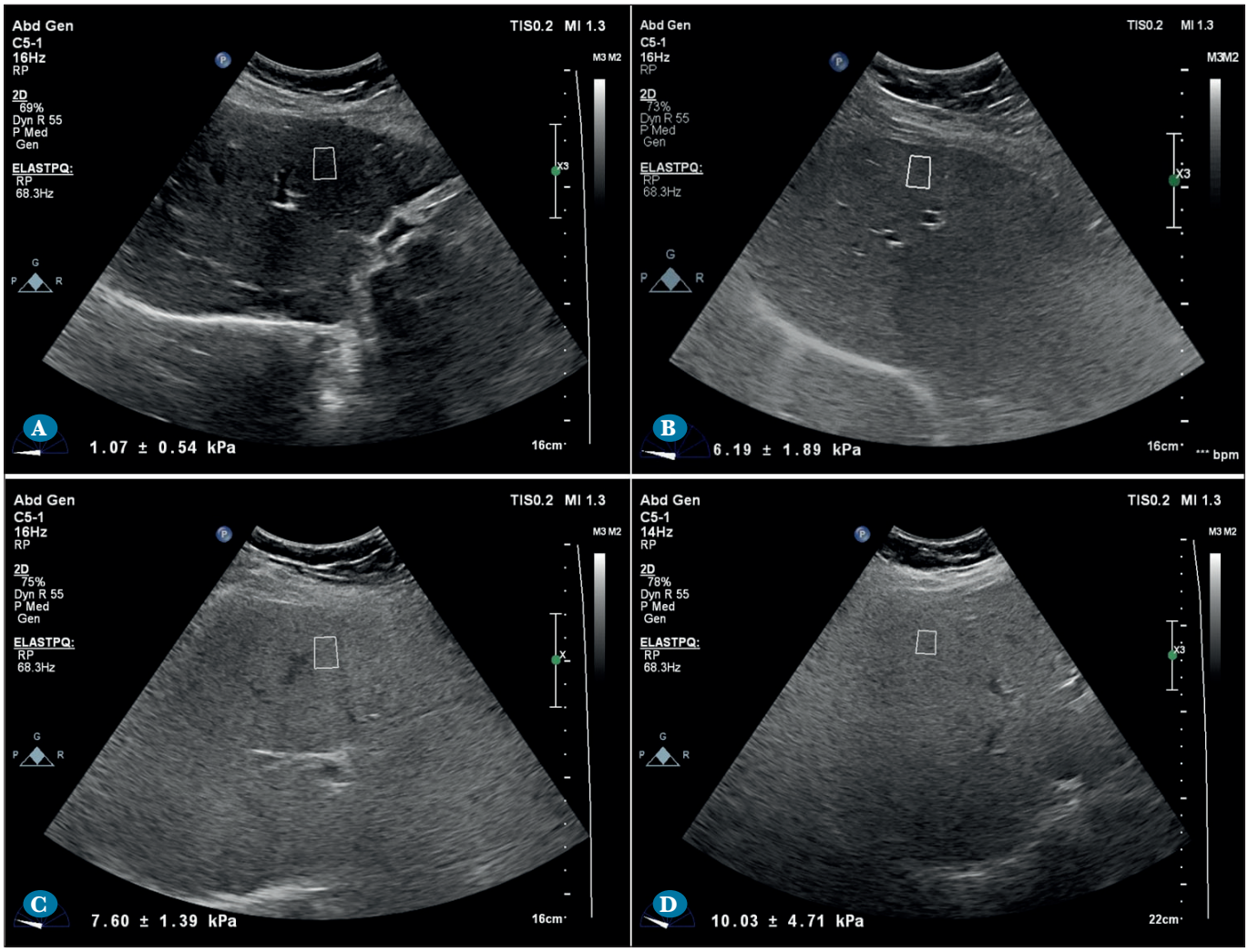

Figure 1: Liver stiffness measurement by liver elastography in patients with and without NAFLD **(A)** grade 0 parenchyma (no liver steatosis) and normal liver stiffness measurement in 1.07 ± 0.54 kPa is displayed in the lower left corner; **(B)** grade I parenchyma (mild liver steatosis) and increased liver stiffness measurement in 6.19 ± 1.89 kPa is displayed in the lower left corner; **(C)** grade II parenchyma (moderate liver steatosis) and increased liver stiffness measurement in 7.60 ± 1.39 kPa is displayed in the lower left corner; **(D)** grade III parenchyma (severe liver steatosis) and severely increased liver stiffness measurement in 10.03± 4.71 kPa is displayed in the lower left corner.

with respiration. The measurement was calculated by placing the region of interest (ROI) on the target on the conventional US image of the liver, after the target region was determined. The ROI was placed perpendicularly to a vessel-free or space occupying lesion-free zone. In our study, the ROI target distance was maximum 8cm and the ROI fixed box size was 1cm – 0.5cm. In each case, 10 valid measurements were obtained from the varying segments of the liver parenchyma and the mean value was calculated. If the measurement reliability is low, a result of 0.00 kPa was displayed. The result was expressed in kPa. All subjects were evaluated by a single experienced radiologist for conventional and SWE evaluations. The investigator had more than 5 years of experience in SWE studies and performed at least 500 SWE procedures a year.

Determination of non-invasive liver fibrosis scores

The 5 scoring systems previously identified for LF were calculated using appropriate formulas using clinical, demographic and laboratory results of the patients. APRI was calculated by the ratio of AST to platelet count (16). FIB-4 index (17) was calculated using the formula: [age (years) x AST (u/L)] / [(platelets ($x10^9$/l) x $ALT^{1/2}$ (u/L)]. NAFLD fibrosis score (18) was calculated using the formula: "–1.675 + [0.037 x age (years)] + [0.094 x BMI (kg/m^2) + [1.13 x IFG/DM (yes = 1, no = 0)] + [0.99 x AST/ALT ratio] – [0.013 x platelet count ($x10^9$/l)] – [0.66 x albumin (g/dl)]". AST/ALT ratio was calculated by the ratio of AST to ALT (19). There were 3 variables for BARD score; 2 points for AST/ALT ratio ≥ 0.8, 1 point for BMI ≥ 28 and

Table I: Clinical, demographic and laboratory findings presence or absence NAFLD.

Variable	NAFLD (-) *n*=54	NAFLD (+) *n*=54	*p*
Age (year)	54.3 ± 6.8	55.6 ± 8.5	0.376
Sex (male/female)	19/35	27/27	0.173
Hypertension, n (%)	12 (22%)	14 (26%)	0.822
Diabetes mellitus, n (%)	9 (17%)	34 (63%)	**<0.001**
Impaired fasting glucose status, n (%)	6 (11%)	8 (15%)	0.649
Current smoker, n (%)	11 (20%)	7 (13%)	0.439
Hyperlipidemia, n (%)	10 (19%)	19 (35%)	0.081
Obesity, n (%)	10 (19%)	12 (22%)	0.406
Systolic blood pressure (mmHg)	127 ± 10	128 ± 11	0.487
Diastolic blood pressure (mmHg)	83 ± 8	86 ± 8	0.059
Waist circumference (mm)	94.2 ± 7.9	98.1 ± 7.9	**0.015**
Body mass index (kg/m^2)	27.6 ± 2.4	28.0 ± 2.2	0.395
White blood cell (uL)	7.2 ± 2.6	8.7 ± 2.3	**0.002**
Hematocrit (%)	38.4 ± 4.2	39.9 ± 4.5	0.096
Platelet cell (10^3 mmc)	289 ± 62	265 ± 65	0.061
Fasting plasma glucose (mg/dL)	112 ± 48	190 ± 97	**<0.001**
HbA1c (%)	6.2 ± 1.7	8.5 ± 2.3	**<0.001**
LDL cholesterol (mg/dL)	115 ± 30	130 ± 38	**0.036**
HDL cholesterol (mg/dL)	55 ± 11	46 ± 16	**0.001**
Triglycerides (mg/dL)	125 ± 93	237 ± 188	**<0.001**
Aspartate aminotransferase (u/L)	20.2 ± 4.9	24.0 ± 8.7	**0.006**
Alanine aminotransferase (u/L)	25.9 ± 6.7	23.2 ± 8.3	0.055
Serum albumin (gr/dL)	4.19 ± 0.25	4.08 ± 0.49	0.176
Blood urea nitrogen (mg/dL)	25.9 ± 4.6	33.4 ± 16.8	**0.003**
Creatinine (mg/dL)	0.59 ± 0.13	0.73 ± 0.19	**<0.001**
hs-CRP (mg/dL)	0.49 ± 0.64	0.93 ± 0.64	**0.012**

The values were shown as mean ± standard deviation or (%).
HDL: high density lipoprotein, **hs-CRP:** high sensitive C reactive protein, **LDL:** low density lipoprotein, **NAFLD:** non-alcoholic fatty liver disease.

1 point for DM presence or IFG, and scores between 0 and 4 points were obtained (20).

Statistical Analysis

All analyses were performed with the SPSS 20.0 (Chicago, IL, USA) statistical software package. The variables were divided into two groups as categorical and continuous variables. The continuous variables in the group were expressed as mean ± standard deviation. Categorical variables are given in numbers and percentages. Continuous variables that showed a normal distribution were compared using Student's t test and ANOVA (only steatosis grade), whereas the Mann-Whitney U test were used for non-normally distributed samples. Chi-square ($\chi 2$) test was used to compare categorical variables. In univariate analyses, logistic regression analysis was performed to identify independent indices among different results in NAFLD patients. Determination of the parameters associated with LS was performed using Pearson's and Spearman's correlation method of univariate correlation analysis. Statistically significant parameters were included in the linear regression analysis and the parameters most closely related to LS were determined. The statistical significance level was accepted as $p < 0.05$.

RESULTS

The study data was divided into two groups as NAFLD patients and non-NAFLD subjects and compared between them. LS measurements were made with the ElastPQ technique in all the patients studied.

Except for waist circumference and DM frequency, other clinical and demographic findings were similar (Table I). DM frequency and waist circumference values were found to be higher in patients with NAFLD (Table I). White Blood Cell Count, HbA1c, LDL cholesterol, TG, AST, BUN, creatinine and hs-CRP levels were higher in patients with NAFLD while HDL cholesterol levels were lower (Table I). Liver size and LS values were significantly higher in NAFLD patients (Table II). Non-invasive fibrosis scores; APRI, FIB-4 index, NAFLD fibrosis score, AST/ALT ratio, and BARD score were all higher in patients with NAFLD than non-NAFLD individuals (Table II).

In the univariate analysis, all parameters associated with NAFLD were evaluated by logistic regression analysis. LS and creatinine levels were independently determined with NAFLD. According to this analysis, an increase of 0.5 kPa in LS and an increase of 0.1 mg/dL in creatinine levels were found to increase NAFLD risk by 2.12 fold and 1.85 fold, respectively (Table III). In liver echogenicity evaluation of NAFLD patients; 20 patients had grade I (mild), 24 patients had grade II (moderate), and 10 patients had grade III (severe) liver steatosis. LS value increased in accordance with liver steatosis grade (grade I, grade II and grade III 6.6±2.1, 7.9±3.2, 9.8±3.3 respectively and $p=0.016$) and the most significant difference was found between grade I and grade III ($p=0.017$).

When the receiving operating characteristics (ROC) analysis was made for determining the importance of LS, BARD, NAFLD fibrosis score, FIB-4, AST/ALT ratio and APRI

Table II: Liver ultrasound and non-invasive fibrosis scores findings presence or absence NAFLD.

Variable	NAFLD (-) *n*=54	NAFLD (+) *n*=54	*p*
Caudal to cranial liver size (cm)	13.4 ± 1.9	15.7 ± 2.5	<0.001
Liver stiffness (kPa)	3.2 ± 1.2	7.8 ± 3.1	<0.001
APRI	0.073 ± 0.024	0.095 ± 0.038	<0.001
FIB-4 index	0.76 ± 0.25	1.21 ± 0.47	<0.001
NAFLD fibrosis score	– 2.58 ± 0.88	– 1.23 ± 1.33	<0.001
AST/ALT ratio	0.81 ± 0.31	1.10 ± 0.37	<0.001
BARD score	0.96 ± 0.95	2.50 ± 1.31	<0.001

The values were shown as mean ± standard deviation.
ALT: alanine aminotransferase, **APRI:** AST/Platelet ratio index, **AST:** aspartate aminotransferase, **NAFLD:** non-alcoholic fatty liver disease.

Table III: According to multivariate regression analysis, independent risk factors for presence of NAFLD.

	Odds Ratio	95% Confidence Interval	*p*
Liver stiffness (each 0.5 kPa)	2.119	1.538 - 2.920	<0.001
Creatinine (each 0.1 mg/dL)	1.854	1.085 - 3.167	0.024

NAFLD: non-alcoholic fatty liver disease.

values for identifying NAFLD, the area under the ROC curves was found to be 0.967, 0.809, 0.785, 0.782, 0.755 and 0.682 for LS, BARD, NAFLD fibrosis score, FIB-4, AST/ALT ratio and APRI, respectively (Table IV). In the same analysis, when the limit value for LS was taken as 5 kPa, the risk of NAFLD was determined with 87.8% sensitivity and 94.1% specificity (Table IV and Figure 2).

The demographic, clinical, laboratory, liver US and non-invasive LF parameters associated with LS in the univariate analysis are summarized in Table V. Linear regression analysis was performed with these LS-related parameters (Table V). HbA1c, LDL, FIB-4 index, NAFLD fibrosis score, and BARD score were found to be independently associated with LS (Table V). The relationship between liver stiffness measurement and HbA1c, FB-4, NAFLD fibrosis score, and BARD score was shown in Figure 3.

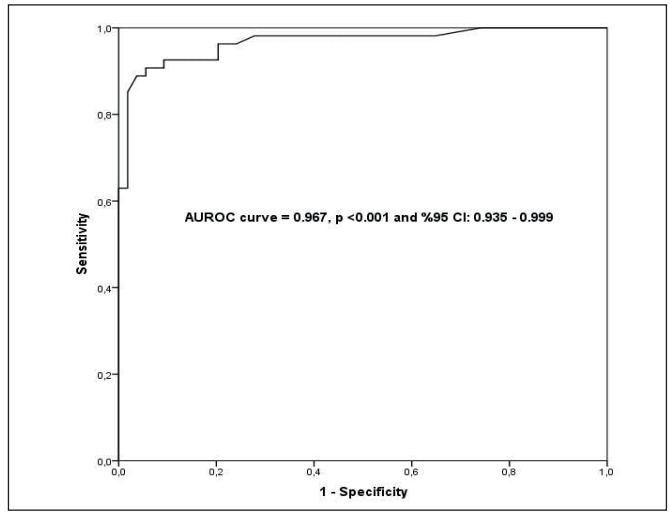

Figure 2: Receiver operating characteristic curves for LS for the diagnosis of NAFLD.

Table IV: Receiving operating characteristics curve analysis for presence of NAFLD.

Variable	AUROC Curve	*p*	Cut-off	Sensitivity	Specificity
Liver stiffness (kPa)	0.963 (0.927–0.998)	<0.001	5	87.8%	94.1%
APRI	0.682 (0.577–0.788)	0.002	0.08	61.2%	66.7%
FIB-4 index	0.782 (0.687–0.877)	<0.001	0.90	71.4%	70.6%
NAFLD fibrosis score	0.785 (0.687–0.882)	<0.001	– 2.0	75.5%	74.5%
AST/ALT ratio	0.755 (0.655–0.856)	<0.001	0.80	69.4%	76.5%
BARD score	0.809 (0.722–0.896)	<0.001	2	75.5%	78.4%

APRI: AST/Platelet ratio index, **ALT:** alanine aminotransferase, **AST:** aspartate aminotransferase, **NAFLD:** non-alcoholic fatty liver disease.

Table V: The parameters associated with liver stiffness and linear regression analysis for parameters significantly correlated with liver stiffness.

	Univariate analyze		Multivariate analyze	
	p	r	*p*	β
Waist circumference (mm)	0.018	0.227	0.126	0.145
Fasting plasma glucose (mg/dL)	<0.001	0.462	0.082	0.011
HbA1c (%)	<0.001	0.580	<0.001	0.520
LDL cholesterol (mg/dL)	<0.001	0.353	0.034	0.166
HDL cholesterol (mg/dL)	0.004	– 0.233	0.180	– 0.110
Triglycerides (mg/dL)	<0.001	0.396	0.095	0.165
Aspartate aminotransferase (u/L)	<0.001	0.462	0.149	0.097
Blood urea nitrogen (mg/dL)	0.009	0.250	0.022	0.244
Creatinine (mg/dL)	0.007	0.257	0.949	0.064
Caudal to cranial liver size (cm)	<0.001	0.446	0.813	0.022
APRI (AST/Platelet ratio index)	<0.001	0.450	0.179	0.229
FIB-4 index	<0.001	0.631	<0.001	0.616
NAFLD fibrosis score	<0.001	0.506	0.016	0.506
AST/ALT ratio	<0.001	0.546	0.728	0.038
BARD score	<0.001	0.601	0.015	0.298

$R^2_{Adjusted} = 0.668$ in multivariate analyses; **ALT:** alanine aminotransferase, **APRI:** AST/Platelet ratio index, **AST:** aspartate aminotransferase, **HDL:** high density lipoprotein; **hs-CRP:** high sensitive C reactive protein, **LDL:** low density lipoprotein, **NAFLD:** non-alcoholic fatty liver disease.

DISCUSSION

The main finding of this study is that the LS value obtained with the ElastPQ technique was found to be significantly higher in patients with NAFLD. In our study, similar to the previous literature, LS was found to have a better diagnostic value in determining the presence of NAFLD than other noninvasive laboratory methods. Considering this similarity, the most important difference in our study from previous studies is that the ElastPQ technique was used for the first time in the NAFLD patient group. According to our study, an LS limit value or 5 kPa was discovered to have very good sensitivity and specificity in detecting NAFLD and each 0.5 kPa increase in LS also increased the risk of NAFLD by 2.12 fold.

In all liver diseases including advanced NAFLD, the presence of LF is the most important determinant in terms of prognosis. Liver biopsy is a procedure that has been around for many years to show the presence of LF and is considered a reference in staging. However, liver biopsy evaluation is invasive, painful, and may have serious complications, including mortality, and is a study with inter- and intraobserver variability (1). Due to these limitations of liver biopsy, noninvasive laboratory and imaging methods have been developed and the need for liver biopsy is reduced. This is a very important development, especially for a disease seen in 1 out of every 4 people. These noninvasive evaluations can be evaluated in 2 groups; i) Laboratory methods in which biological serum biomarkers and demographic parameters are used, and ii) MRI and US elastography

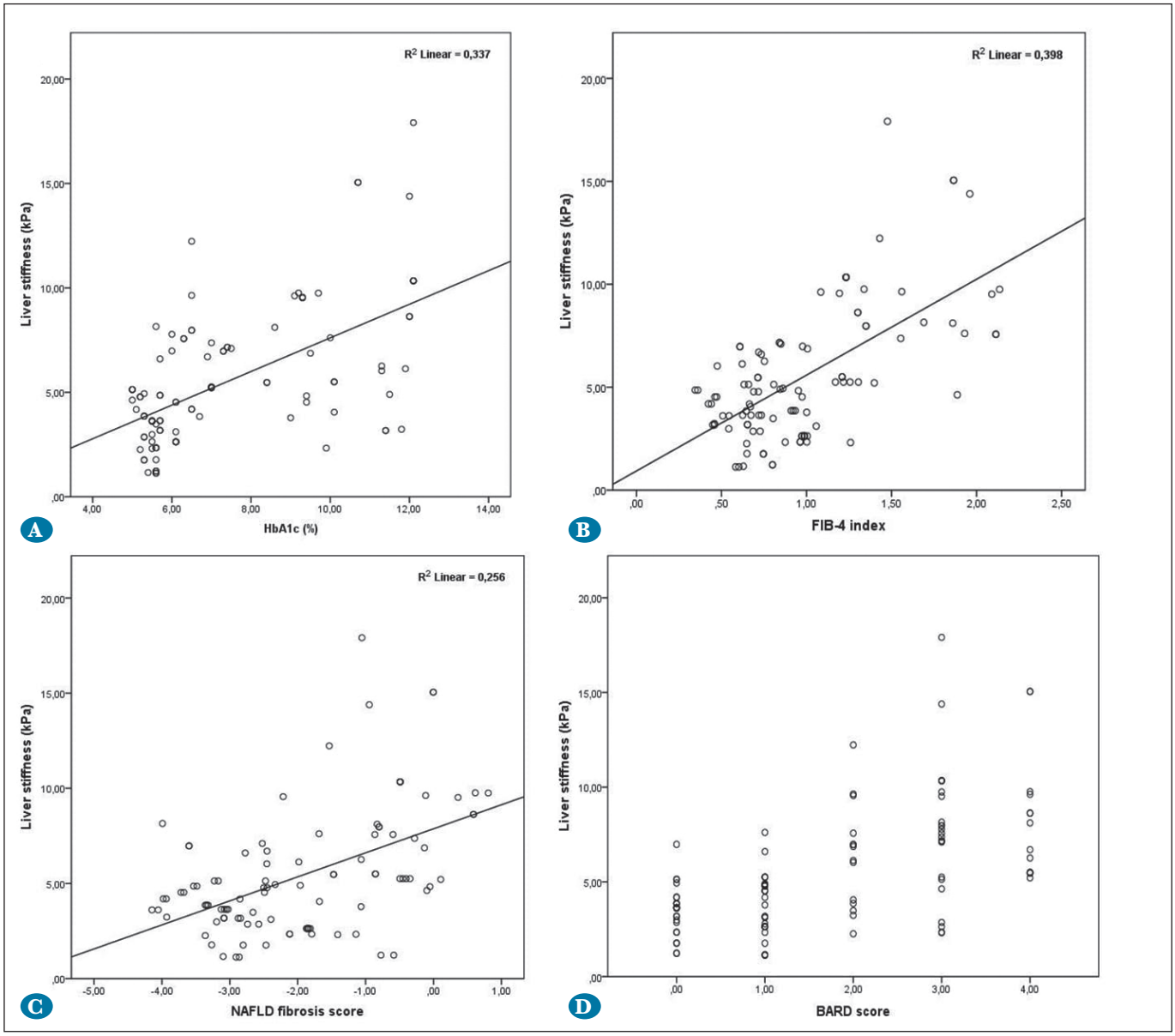

Figure 3: There is significant correlation between liver stiffness and **A)** HbA1c levels **B)** FIB-4 index **C)** NAFLD fibrosis score **D)** BARD score.

that measures tissue stiffness with physical US and MRI examinations (TE, ARFI technique, ElastPQ, and MRI elastography) The greatest advantages of noninvasive tests are being easy to use, cost effective and repeatable. Noninvasive laboratory methods are APRI [16], FIB-4 index (17), NAFLD fibrosis score (18), AST/ALT ratio (19), BARD score (20), Fibrometer^{NAFLD} (21) and FibroTest (21). Among these laboratory tests that determine NAFLD, FIB-4 has the highest sensitivity (85%) and NAFLD fibrosis score has the highest specificity (98%) (22). In our study, 5 different noninvasive laboratory examinations (BARD, NAFLD fibrosis score, FIB-4, AST/ALT ratio, and APRI) were evaluated as well as LS. When LS was not evaluated, ROC analysis revealed that NAFLD presence is determined by BARD, NAFLD fibrosis score, FIB-4, AST/ALT ratio, and APRI scores, respectively. FibroTest and FibroMeter assessments obtained in previous studies could not be evaluated in our study due to the fact that alpha2-macroalbumin and ferritin levels could not be obtained from all patients.

Apart from noninvasive laboratory studies, the most commonly used examination is TE. In 2016, 9 noninvasive fibrosis tests including LS obtained with TE were compared in NAFLD patients and LS was reported to be the most accurate noninvasive fibrosis assessment to detect LF (11). A recent meta-analysis of 13.046 patients with NAFLD reported that the diagnostic value of TE, FIB-4 and NAFLD fibrosis score was 0.88, 0.84, and 0.84, respectively, in diagnosing severe LF in patients with NAFLD (23). In another study, it was reported that the TE examination was better in detecting cirrhosis than FIB-4 and NAFLD fibrosis score in patients with NAFLD (11). Recent studies have also shown that NAFLD fibrosis score, TE and FIB-4 assessments in NAFLD patients can determine the cirrhosis, death, and transplantation need (11,24). It may be better to perform a screening test primarily because NAFLD is so common in the general population. Most of these screening studies have used TE and found that a value of > 8.0 kPa determines the state of Metavir F ≥ 2 (25,26). For this reason, these noninvasive evaluation methods are widely used in everyday practice and are also recommended in the guidelines (10,27). Although it is used in the first place to assess LF and assessed in many studies and is the US study recommended by the guidelines, TE has been shown to produce inadequate results in clinical practice (28,29). The most important reason is that the TE investigation may result in failure or inaccurate measurement in patients with obesity, DM, metabolic syndrome, and narrow intercostal space, which are the most important risk factors for NAFLD (12,13).

The pSWE examination in the new Philips US system features ElastPQ technology. This study began in 2012 and has been assessed for its utility with studies mostly conducted on chronic hepatitis (8,30-35). First among these studies are limit value studies in healthy controls in 2013 (30), followed by chronic viral hepatitis studies (8,31-35). The most recent retrospective study of 2018 evaluated the outcome of biopsy in different chronic liver disease patients and only 4 NAFLD patients were included in the study (35). In this last study, it has been reported that the ElastPQ technique predicts very well the presence and degree of LF, such as TE (35). In the same study, it was determined that the LS value obtained by ElastPQ was better than noninvasive laboratory methods to show LF presence (35). In the literature, it was not possible to obtain information on the evaluation of LF in the NAFLD patient group in the limited number of ElastPQ trials conducted. In addition, current guidelines point out that the effectiveness of the ElastPQ method in determining the presence and degree of LF is limited (10,27). In our study, the LS value obtained with ElastPQ technique was found to be significantly higher in patients with NAFLD and, similar to previous literature data, LS obtained by elastography examination had better diagnostic value in NAFLD detection compared to other noninvasive laboratory methods (APRI, BARD, FIB-4, AST/ALT, and NAFLD fibrosis score). In addition, our study showed that the most relevant noninvasive laboratory method for the LS value is the FIB-4 index. Apart from this high diagnostic value of ElastPQ, a significant advantage is that it can be measured with less effort and there is no need for unnecessary laboratory investigations of the patient for the repetition.

The previous study showed that LF was determined with good diagnostic value when the cut-off value was taken as 6.2 kPa in chronic liver disease (35). In our study, it was determined that the LF value of 5.0 kPa had high sensitivity and specificity in detecting NAFLD patients. In the literature, a comparative evaluation could not be done because of the lack of similar groups of patients and similar techniques that would be compared with this limit value obtained in our study in NAFLD patients. In clinical practice, the screening indications for NAFLD presence are not suggested due to the fact that the tests performed are not cost-effective and the diagnostic utility of these tests is unclear (10,15,27).

The incidence and prevalence of NAFLD is increasing with the increase in co-morbid diseases. Therefore, the identification of these patients and determining the progression of the disease and the prognosis are very important. People who are elderly or suffer from DM, obesity and metabolic syndrome are at high risk for NAFLD. The results of our study and previous studies suggest that the LS value obtained with ElastPQ is a simple, reproducible and powerful criterion that can be used in the diagnosis and follow-up of NAFLD patients.

An important limitation of our study is that our study data are not confirmed with liver biopsy. Liver biopsy and MRI were not performed in our study because they were invasive and expensive, respectively. If these studies were done, more objective results could be obtained. However, performing a liver biopsy in NAFLD patients would not be ethical. If the relationship between liver fibrosis grade and LS was objectively examined, the study could provide more clear findings. However, we saw in our study that the increase in steatosis resulted in increased LS values when patients were classified as grade I, grade II and grade III steatosis according to the liver US findings.

CONCLUSION

LS detected by the liver ElastPQ technique can be used as a powerful, reliable, objective, noninvasive, reproducible, and inexpensive US test in diagnosing NAFLD in clinical practice. This study is more effective in NAFLD diagnosis than other noninvasive laboratory methods. In addition, LS should be planned in situations with a high risk of NAFLD development such as patients with DM, metabolic syndrome and obesity. Patients with LS ≥ 5kPa in the Liver ElastPQ examination should be closely monitored and treated. However, we conclude that the results obtained in our study should be strengthened by new studies on different and larger numbers of NAFLD patients.

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