

The Value of Shear-wave Ultrasonography in Calculating Elastographic Values in Liver Pathologies

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Abstract

Objective: Liver pathologies consist of multiple benign and malignant diseases; shear-wave elastography values vary according to the lesions. In our study, we tried to figure out how to measure the mean shear-wave elastography values in different liver lesions.

Methods: Seventeen focal nodular hyperplasia (FNH), 41 hemangiomas, 25 cysts, and 45 malignant lesions were evaluated in 112 patients who had liver pathology. Twenty patients had hepatosteatois, and fibrosis was present in 26 patients. B-mode and shear wave ultrasonography examinations were performed on defined pathologies. Malignant lesions were histopathologically diagnosed and benign lesions were evaluated according to cross-sectional examination (computerized tomography and magnetic resonance imaging) methods.

Results: In our study, the average elastography values were determined as 50.38 kilopascals (kPa) and 3.69 meters per second (m/s) in FNH; 12.54 kPa and 1.97 m/s in hemangiomas; 116.47 kPa and 6.34 m/s in malignant lesions; 8.97 kPa and 1.57 m/s in cysts; 16.54 kPa and 2.30 m/s in cases with hepatosteatois; and 90.98 kPa and 5.44 m/s in cases with liver fibrosis. Mean values in cysts, hepatosteatois, and hemangiomas were close to normal; in liver fibrosis, malignant lesions, and FNH, they were higher than normal.

Conclusion: We think that shear wave elastography is a promising method for distinguishing benign from malign liver lesions by calculating quantitative values where a biopsy-free diagnosis is preferred in the present day.

Keywords: Diffuse liver diseases, FNH, hemangioma, shear wave ultrasound

INTRODUCTION

Every year, many patients are referred to radiology clinics with the diagnosis of a liver mass. The majority of malignant masses are metastases. But benign lesions of the liver are also frequently observed. Using radiological diagnostic methods correctly is crucial for detecting carcinoma early, determining the most effective treatment, and reducing disease-related fatalities.

Elastography is a new technique that contributes to ultrasonography in the characterization of liver lesions (1,2). This technique gives information about the stiffness of the lesion, as in clinical palpation. There are two methods, strain elastography and shear-wave elastography, in clinical use (1-4).

Shear-wave elastography provides quantitative measurement of lesion stiffness (in kPa).

Liver pathologies consist of many benign and malignant diseases; shear-wave elastography values vary according to lesions. In our study, we determined the mean shear-wave elastography values in different liver lesions. In clinical use, we believe that these values may be helpful in the diagnosis of lesions that are unidentified with imaging modalities without a biopsy.

METHODS

The study received the approval of the Human Subjects Ethics Committee, and informed written consent was obtained from



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all subjects. We evaluated 17 focal nodular hyperplasias (FNH), 41 hemangiomas, 25 cysts, and 45 malignant lesions in 112 patients aged between 22 and 76 years who had liver pathology and were referred to our clinic for an abdominal examination, and mean kilopascals (kPa) and meter per second (m/s) values were calculated. Hepatosteatosi was present in 20 patients and fibrosis was present in 26 patients.

The Toshiba Aplio 500 Premium (Tokyo, Japan) device was subjected to a B-mode and shear wave ultrasonography examination for defined pathologies. All individuals were lying in a supine position. Pathologies were evaluated using a 10-megahertz linear probe while patients were holding their breath with shear wave elastography. The region of interest (ROI) was at its minimum size in our study. After elastographic mapping, at least 4-5 measurements were taken from the hardest sections of each pathology, and average values were obtained. Malignant lesions were histopathologically diagnosed, and benign lesions were evaluated according to cross-sectional examination (computerized tomography and magnetic resonance imaging) methods. Patients with indeterminate lesions were not included in the study.

Statistical Analysis

The IBM Statistical Package for the Social Sciences (SPSS) Statistics 20 program was used for statistical analysis. The Independent Samples t-test and F-test (ANOVA) were used, as well as descriptive statistical methods (mean, standard deviation, median, frequency, minimum, and maximum), to determine whether the difference between two groups of variables with normal distribution compared to quantitative data is coincidental or statistically significant. Significance was evaluated at $p < 0.05$. Matrix Laboratory R2007b program was used to plot the data. A column graph was drawn using the IBM SPSS Statistics 20 program.

RESULTS

The average elastography values in FNH lesions were 50.38 kPa and 3.69 m/s; 12.54 kPa and 1.97 m/s in hemangiomas (Figure 1); 116.47 kPa and 6.34 m/s in malignant lesions (Figure 2); 8.97 kPa and 1.57 m/s in cysts; 16.54 kPa and 2.30 m/s in cases of hepatosteatosi; and 90.98 kPa and 5.44 m/s in liver fibrosis (Tables 1 and 2).

In our clinic, we found a mean elastography value of 10.49 in the shear wave elastography measurements in healthy subjects with normal laboratory and liver USG findings (Table 3).

In our study, we found that the elastography values were low in lesions with lower stiffness. The mean values in cysts, hepatosteatosi, and hemangiomas were close to those in normal liver parenchyma (slightly lower in cysts, slightly higher in hemangiomas, and hepatosteatosi) (Figure 3). The values were higher in liver fibrosis and FNH lesions and were significantly higher in malignant lesions than in normal lesions (Figure 4).

DISCUSSION

Liver diseases are an important global health problem. Diseases like fatty liver disease, autoimmune and chronic viral hepatitis, and primary biliary cirrhosis cause fibrosis that leads to portal hypertension, liver failure, and hepatocellular carcinoma development.

Correct classification of the degree of fibrosis is critical for treatment planning and for predicting response to treatment and the likelihood of malignancy. Liver biopsy is an invasive

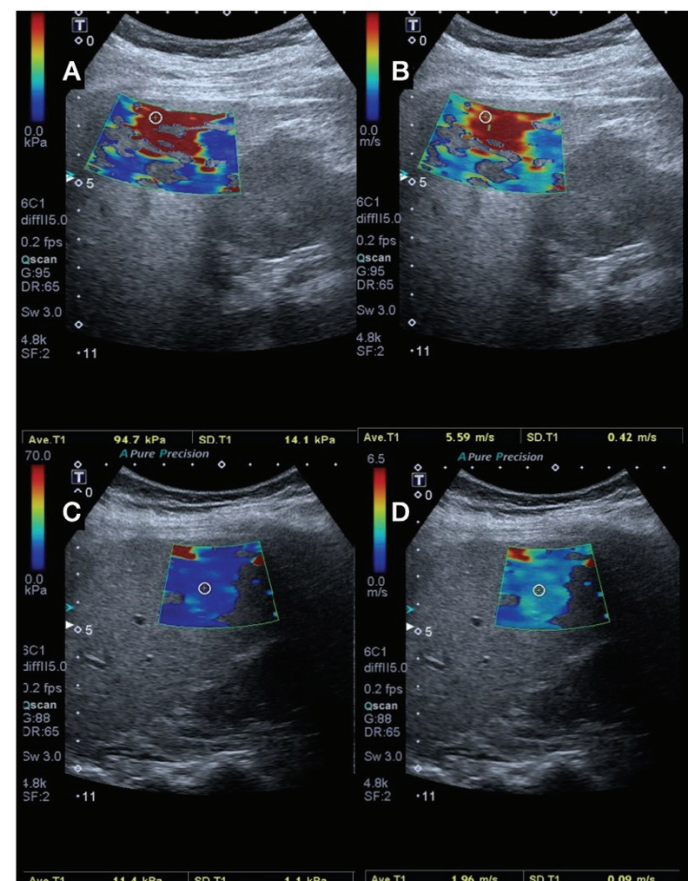


Figure 1. A 48-year-old female patient with focal nodular hyperplasia. Shear wave images are noticeable in kPa (a) and in m/s (b). Another example is a 44-year-old female patient with hemangioma. We can see hyperechoic solid lesion and elastography values in kPa (c) and in m/s (d). Circles depict the area of interest where the measurement is calculated

procedure that includes complications like severe pain and bleeding, despite having been the gold standard method for diagnosis (5,6). However, because of the small sample size from a heterogeneous organ, sampling error is an inherent problem (7), and diagnostic consistency can be affected by interobserver variability (8-10). Therefore, non-invasive techniques to evaluate liver fibrosis have attracted great attention. There are many studies in the literature on the use of serum markers such as the transaminase/platelet ratio index, hyaluronic acid, platelets, and collagen type IV (11). However, they may also be affected by non-hepatic causes.

Elastography can be used to noninvasively assess liver stiffness. Magnetic resonance imaging or ultrasound that applies mechanical stress evaluates tissue response. The optimal conditions in the examination include the patient being

hungry, the decubitus position where the right hand is above the head to provide an optimum intercostal approach, resting breathing, placing ROI approximately 1.5-2.0 cm underneath the Glisson capsule to prevent increased subcapsular stiffness and reverberation artifacts, and taking at least 4 measurements.

Point shear wave velocity measurement and slip wave velocity (SWSI) are the two major shear wave methods. The two basic methods used in the PSWSM method are the Virtual Touch Tissue Quantification (VTTQ) method, which shows the results in m/s, and the ElastPQ technique, which shows the results in m/s or kPa. There are countless studies using the VTTQ technique available, but there are very few studies using ElastPQ. The repeatability of the VTTQ method is high, with correlation coefficients ranging from 0.84 to 0.87 (12-15). Training the operator is not required (13). Similarly, the interobserver values

	kPa	m/s
FNH	50.3765	3.6947
Hemangioma	12.5439	1.9685
Hepatosteatois	16.545	2.306
Liver fibrosis	90.9808	5.4431
Cyst	8.9708	1.5744
Malignant lesions	116.4756	6.3398

Liver right lobe					
ave t1(m/s)	31	2.20	1.75	1.36	11.48
SD t1(m/s)	31	0.27	0.51	0.08	3.00
kPa	34	10.49	3.30	5.40	17.70
SD t1 kPa	34	2.01	1.05	0.50	5.00

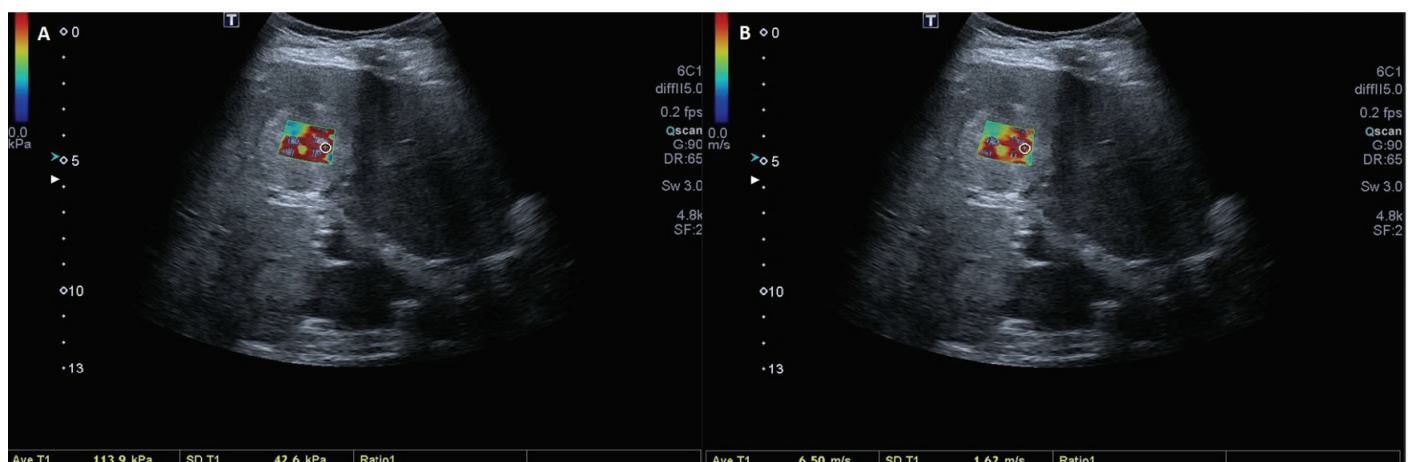
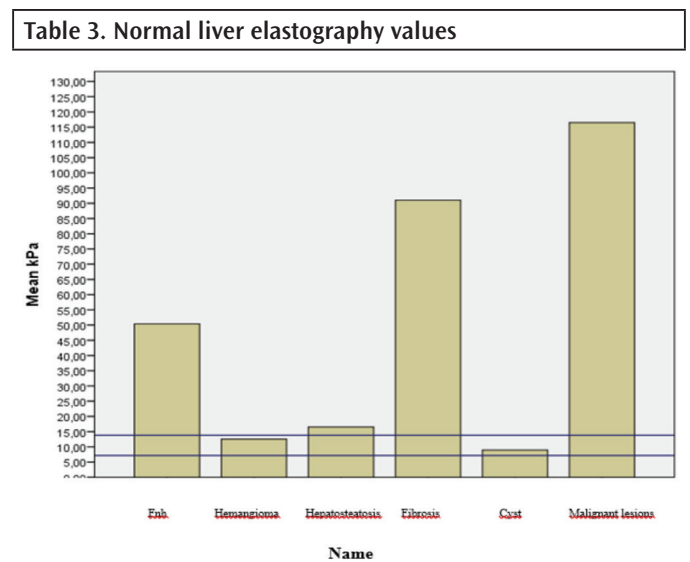


Figure 2. A 62-year-old male patient with hepatocellular carcinoma. Heterogeneous hyperechoic solid lesion and elastography values can be seen in kPa (a) and in m/s (b). The area of interest where the measurement is calculated is represented by circles

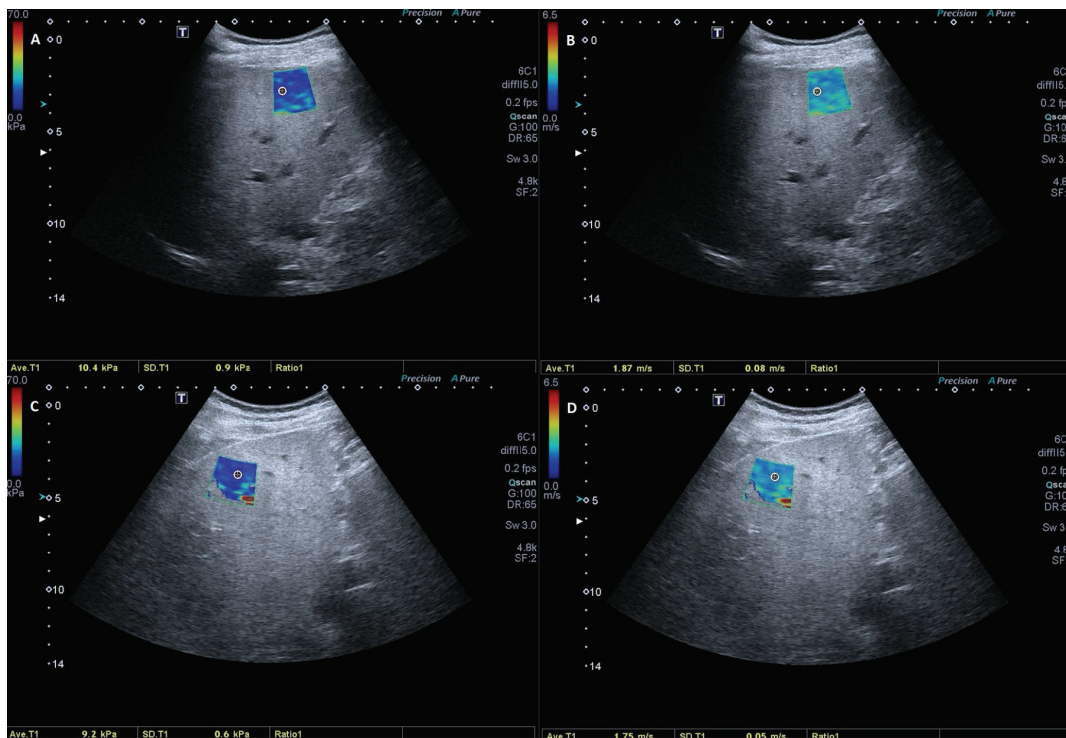


Figure 3. A pure cyst in a 52-year-old male patient; shear wave images are shown in kPa (a) and m/s (b). 36-year-old female patient with hepatosteotosis. Shear wave images are displayed in kPa (c) and m/s (d). Circles depict the area of interest where the measurement is calculated

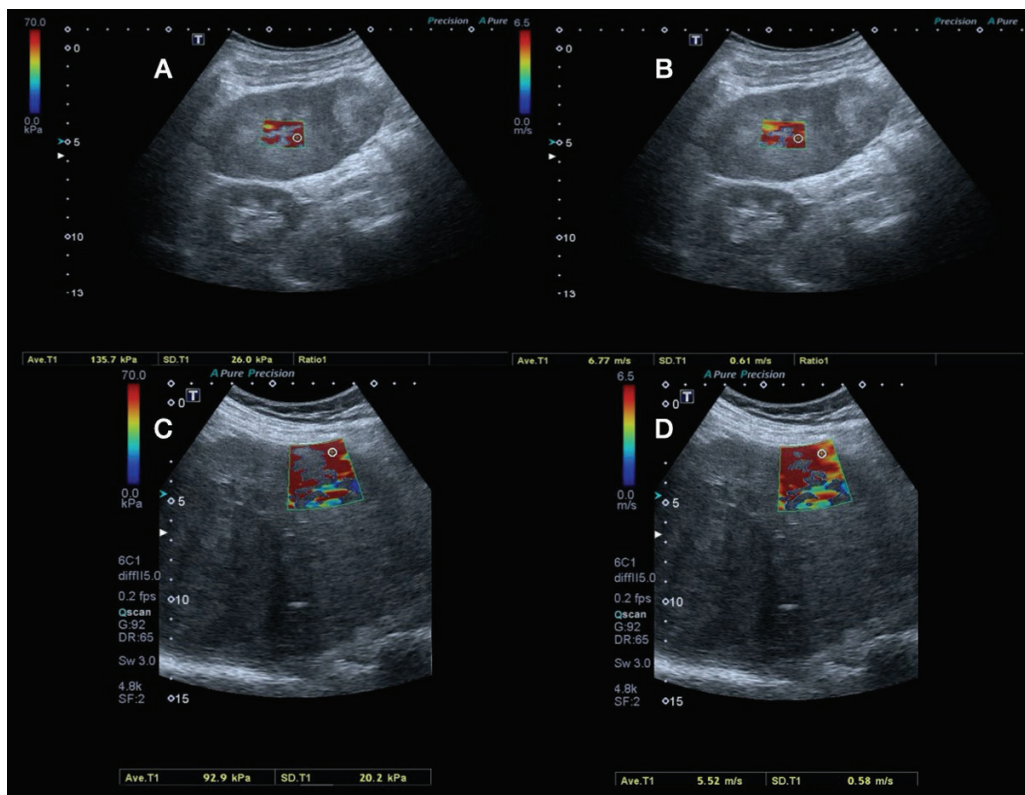


Figure 4. Multiple liver metastases in a 72-year-old male patient; shear wave images can be seen in kPa (a) and m/s (b). 62-year-old male patient with liver fibrosis. Shear wave images are shown in kPa (c) and m/s (d). The area of interest where the measurement is calculated is represented by circles

for the ElastPQ technique range from 0.83 to 0.93 (16), which shows that it is easy to repeat.

In healthy volunteers, PSWSM values with VTTQ can be found in various publications (17-19). In all of these studies, the values were lower than those of chronic hepatitis patients (<1.2 m/s). Liver stiffness increases significantly with food intake (20). The average PSWSM value obtained with ElastPQ is 3.5 kPa in healthy volunteers (21).

The cutoff range for each fibrosis stage is quite wide. The values of early-stage fibrosis ranged from 1.13 to 1.55 m/s, whereas they were 1.36-2.13 at the advanced stage (21). The largest series included more than 600 patients with chronic liver disease of various etiologies; the cut-off values for fibrosis, severe fibrosis, and cirrhosis in patients with chronic liver disease due to different causes were 1.34, 1.55, and 1.80 m/s, respectively. According to the PSWSM method, TE showed higher diagnostic accuracy for fibrosis and liver cirrhosis, whereas PSWSM and TE sensitivity were similar for the diagnosis of severe fibrosis (22).

In a meta-analysis (12), Bota et al. (12) showed that the PSWSM method had a similar predictive value for liver fibrosis and cirrhosis. In our study, the mean elastography values were found to be 90.98 kPa and 5.44 m/s in patients with liver fibrosis. In an international multicenter study with 181 patients with chronic hepatitis B and 914 patients with chronic hepatitis C, the correlation of PSWSM with histological fibrosis was found to be significantly higher in patients with chronic hepatitis C than in patients with chronic hepatitis B ($r=0.653$ vs. $r=0.511$, $p=0.007$). Similar PSWSM values were determined for each fibrosis stage in both groups (23).

Rizzo et al. (24) showed that PSWSM cut-off values were 1.3 m/s for fibrosis, 1.7 m/s for severe fibrosis, and 2.0 m/s for cirrhosis. In patients with severe hepatic inflammation, TE may exaggerate fibrosis (25). The same limitations were observed in several studies using PSWSM. It was observed that the degree of hepatosteatosis did not affect PSWSM values (24). Likewise, we found similar values for hepatosteatosis in normal liver parenchyma in our study. SWSI shows results in m/s and kPa. Ferraioli et al. (26) determined that the correlation between the expert and novice operators was to be 0.95 and 0.93 on the same day and 0.84 and 0.65 on different days by comparing the measurements. These results were confirmed by Hudson et al. (27) in the study they published.

Poynard et al. (28) found that the feasibility of SWSI was lower than that of TE in a cohort study of 442 patients in whom liver fibrosis was evaluated, in which no gold standard method

was used, although the performance of the two methods is similar. Stiffness values were reported not to be associated with hepatosteatosis or necroinflammation (29). In our study, we evaluated the mean elastography values in patients with hepatosteatosis as 16.54 kPa and 2.30 m/s

PSWSM and SWSI can be used to evaluate the severity of liver fibrosis in patients with chronic viral hepatitis, best demonstrated in patients with hepatitis C. However, the available studies are limited to SWSI. In PSWSM and SWSI as TE, the results are accurate when figuring out if someone has mild fibrosis or cirrhosis.

The mean shear wave values were evaluated as 57.91 kPa for malignant tumors and 23.87 kPa for hemangiomas, and the cut-off value was 23.62 kPa in a study on the stiffness of malignant masses and hemangiomas in 20 patients (30). Similarly, in our study, we found that the elastography values of malignant tumors were significantly higher than those of hemangiomas.

Average values were found to be 1.80 ± 0.57 m/s for hemangiomas, 2.66 ± 0.94 m/s for hepatocellular carcinomas, 3.27 ± 0.64 m/s for cholangiocarcinomas, 3.70 ± 0.61 m/s for colon cancer metastases, and 2.82 ± 0.96 m/s for other metastases with the analysis using the ARFI method in the study on 74 patients with 101 benign and malignant tumors (31). According to these results, the mean SW values were significantly higher in hepatic tumor groups than in the hemangiomas.

Brunel et al. (32) determined the mean elastography values as 46.99 ± 31.15 kPa for FNH and 12.08 ± 10.68 kPa for adenomas in a study of 76 liver lesions of FNH and adenomas, which were confirmed by MRI imaging, contrast-enhanced USG, or histologically in 56 patients. In this study, a cut-off value of 18.8 kPa was determined for the differentiation of FNH and adenoma.

Benign liver tumors that develop in healthy livers continue to be important problems in diagnosis and treatment. Conservative treatment is performed most often in patients with FNH. In contrast, treatment of hepatic adenomas is more invasive because of the risk of bleeding and malignant transformation.

There are studies using the ARFI or SWE method in a variety of malignant and benign multiple liver lesions, and some have reported differences between the degrees of hardness of FNH and hepatic adenomas.

Gallotti et al. (33) did not find a significant difference between the elasticity values measured in the adenoma and surrounding healthy liver tissue using the ARFI method. They also reported that FNH was the second most severe lesion after metastases, irrespective of the presence or extent of the central scar. Frulio et al. (34) found that FNHs were the stiffest lesions in benign liver

lesions. In their study with SWE on FNH and adenomas, Guibal et al. (35) found similar results. In our study, we determined that the elastography values in FNH were higher than those in other benign lesions.

Using point shear-wave elastography, Qiu et al. (36) compared the focal fatty change group with the liver mass group. They evaluated the lesion stiffness value, absolute stiffness difference, and stiffness ratio of lesions and found that the liver mass groups' shear wave values were significantly higher than those of the focal fatty change group. They concluded that this technique could reduce the need for additional contrast-enhanced imaging or biopsies when diagnosing mass-like focal fatty changes (36). Wang et al. (37) compared the diagnostic accuracy of SWE and shear wave dispersion (SWD) in the evaluation of hepatic parenchyma in patients with liver malignancies. They found that the optimal SWE cut-off values for $S \geq 1$, $S \geq 2$, $S \geq 3$, and $S = 4$ were 6.9, 7.9, 8.7, and 10.6 kPa, respectively, and determined that SWE was a more accurate predictor of severe fibrosis ($S \geq 3$) and cirrhosis ($S = 4$) than SWD (37).

Although the SWE and ARFI methods are based on the principle of measuring local shear wave velocities from the liver, the former has the advantage of providing real-time imaging and adding mapping of lesion stiffness to B-mode images. This mapping method can help you see the differences in elasticity between the lesion and the surrounding tissue and determine how different the tumoral parenchyma is.

To our knowledge, there is no study that evaluated liver masses with kPa and m/s at the same time. There are some limitations in studies, as in ours. SWSI accuracy was evaluated only on the right lobe at the intercostal space. Interlobar variations were reported with PSWSM at liver stiffness levels. Body structures such as obesity and a narrow intercostal space may hinder the results from being obtained. Because the elastic properties of the tissue show frequency dependence techniques should be used with care and caution when comparing the quantitative results obtained from these techniques. The results determined in kPa are not comparable between TE, PSWSM, and SWSI. Since most studies were conducted in patients with chronic hepatitis C, cut-off values may not apply to non-alcoholic fatty liver disease and other viral etiologies. Non-alcoholic fatty liver diseases were examined in only a small series of patients, and the cut-off values in these patients require further studies. Values may be higher in patients whose hepatic enzyme levels are 5 times the upper limit. Therefore, the influence of inflammation should be considered, and results should always be assessed in the presence of clinical information. Similar to

TE, congestive heart failure is probably associated with more severe liver tissue.

Error rates have increased in the elastographic evaluation, especially in the left lobe lesions, depending on the localization and depth of the tumor, the patient's breathlessness, and the heart rate. These conditions make elastography examinations difficult for patients. Although we did not have and could not include enough patients with hepatic adenomas diagnosed histopathologically, the average elastography values we found for FNH were high, and compared with the studies in the literature about hepatic adenomas with relatively low stiffness, this suggests that shear wave elastography may be helpful in differentiating these 2 benign liver lesions (38).

CONCLUSION

We found that shear wave elastography could be helpful in the differential diagnosis of liver lesions by calculating quantitative values in accordance with previous studies. We observed that it could be useful in the differentiation of malignant hepatic tumors from hemangiomas because of their high elastography values. In patients with liver fibrosis, we found that the elastography values increased in parallel with the increased stiffness of the tissue secondary to fibrosis. We calculated lower shear wave values in the cystic lesions of the liver because of the liquid content. In conclusion, shear wave elastography is a promising method for the differentiation of benign and malignant lesions in our study as well as in the literature, where a biopsy-free diagnosis is preferred.

Ethics

Ethics Committee Approval: The study received the approval of the Human Subjects Ethics Committee.

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

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: M.O.N., E.İ., Design: M.O.N., E.İ., Data Collection or Processing: M.O.N., E.İ., Analysis or Interpretation: M.O.N., E.İ., Literature Search: M.O.N., E.İ., Writing: M.O.N., E.İ.

Conflict of Interest: No conflict of interest was declared by the authors.

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