Use of shear wave elastography in the evaluation of liver fibrosis

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ABSTRACT

Background and objective: Chronic liver disease promotes hepatic inflammation and fibrosis. When diagnosing and treating hepatic diseases such as chronic hepatitis C, it is important to evaluate the degree of liver fibrosis. We aimed to determine the diagnostic capabilities of shear wave elastography (SWE) in patients with liver disease. Materials and methods: Hepatic stiffness, size of liver and spleen, portal vein flow velocity, portal vein diameter and flow pattern of hepatic veins were evaluated in 24 patients with diagnosed liver disease and 15 healthy subjects. All measurements were performed using the Philips ElastPQ SWE. The hepatic stiffness was expressed in kilopascals (kPa). Results: The mean liver stiffness value was 4.18±1.15 kPa in the control group and 16.19±12.31 kPa inpatient group ($p<0.001$). An optimal SWE cut-off value of 5.51 kPa had predicted 88% sensitivity and 93% specificity for detecting liver fibrosis. The liver stiffness was positively correlated with the portal vein diameter and the flow pattern of hepatic veins ($r=0.4$, $P<0.008$), no significant correlation between liver stiffness and the size of the liver, spleen and portal vein flow velocity was found. **Conclusions:** The liver is stiffer in subjects with diagnosed liver disease than in those who are healthy. The sensitivity of the SWE is 88%, specificity 93% with a cut-off value of 5.51 kPa. Greater hepatic stiffness is associated with increased portal vein diameter, monophasic and biphasic flow patterns of hepatic veins.

Keywords: ultrasound; shear wave elastography; liver stiffness; liver fibrosis; cirrhosis

INTRODUCTION

Based on the latest scientific research, shear wave elastography (SWE) is a sensitive and specific diagnostic tool [1] that may become a standard method in evaluating patients with chronic liver disease. Currently, liver biopsy is the most commonly used method in clinical practice to determine the degree of liver fibrosis. However, it is a painful and risky intervention. A first non-invasive method used for liver stiffness evaluation was transient elastography (TE), implemented in a FibroScan device. It is a painless and safe method, but has several technical limitations: the scan is "blind," it is not accurate on patients with ascites and on individuals who are morbidly obese or have a thick subcutaneous fat in the abdomen [2].

Newer techniques such as ultrasound-based SWE show results that correlate with the histological fibrosis scores [3], so using such non-invasive methods may reduce the number of patients undergoing potentially dangerous liver biopsy [4] and therefore reduce the risk of complications and medical costs. Measuring liver and spleen shear wave velocity may help to predict prognosis in patients with liver cirrhosis and portal hypertension [5]. SWE may be used to evaluate liver stiffness in patients with chronic hepatitis C virus infection who received antiviral therapy and may help to avoid repeating biopsy and add valuable information about disease progression [6]. The recent imaging phantom experiment showed that observers' experience levels had little impact upon the accuracy of SWE results [7]. Little impact of observers' experience suggests that specific training is not needed prior to performing SWE making this method easily implemented into the clinical practice.

This study proves SWE being useful, valuable and accurate method in measuring liver stiffness which may help to avoid the liver biopsy and threatening complications associated with it.

MATERIALS AND METHODS

The study protocol was approved by the local institutional ethics committee. Before the start of the study, written informed consent was obtained from all participants. Between March and December of 2016, we examined 39 subjects. The patient group consisted of subjects with diagnosed cirrhosis and another liver disease (cholecystitis, steatohepatitis, etc.). The control group consisted of apparently healthy volunteers.

All measurements were performed using ElastPQ SWE on Philips EPIQ 7 ultrasound system. Scans were conducted by one observer with 30 years of abdominal US experience. The ultrasonographer was blinded to the subject's clinical data.

Participants were in the supine position. First, the size of the liver and spleen, portal vein flow velocity, portal vein diameter and flow pattern of hepatic veins were evaluated. Next, the liver stiffness of the right hepatic lobe was measured. The detection site was fixed at least 1.5 cm beneath the liver capsule, away from the intrahepatic vessels and gallbladder (Figure 1). When the elasticity imaging mode was selected, subjects were asked to hold the breath at mid-respiration for 3–5 s. When the region of interest (ROI) was located, the ultrasonographic initiated the SWE measurement (the median elastic modulus in kilopascals (kPa) was calculated automatically). The mean value of 10 consecutive measurements was used for statistical analysis.

We used the following values proposed by Phillips for staging liver fibrosis: no fibrosis (F0) – 2.0-4.5 kPa, normal or mild fibrosis (F0-F1) – 4.5-5.7 kPa, mild-moderate fibrosis (F2-F3) – 5.7-12.0 kPa and moderate-severe fibrosis (F3-F4) – 12.0-21.0+ [8].

To determine the diagnostic accuracy of SWE for the prediction of liver stiffness development in patients with liver disease, receiver operating characteristic (ROC) curve analysis was performed. Statistical analysis was performed using IBM SPSS statistics 24.0 software. Statistical significance was defined as $p<0.05$.

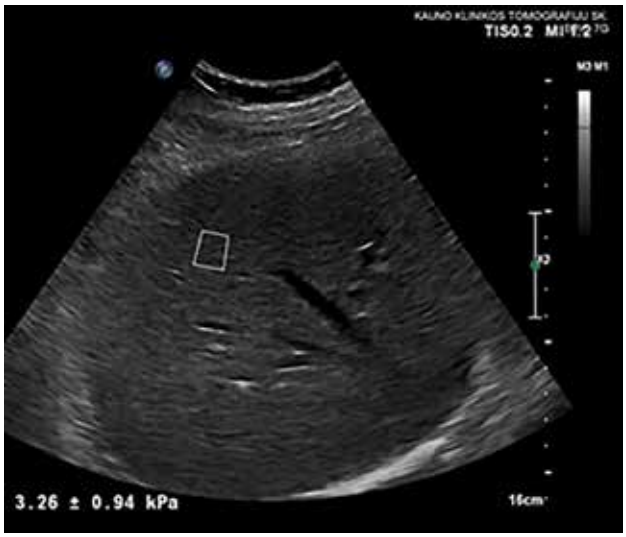


Figure 1. The image shows how measurements were obtained. The quadrangular white box is ROI. The median stiffness, in this case, is 3.26 kPa.

RESULTS

Ultrasound examination of the abdomen was used to evaluate liver stiffness, size of the liver and spleen, portal vein flow velocity, portal vein diameter and flow pattern of hepatic veins in 39 participants. The baseline characteristics of all participants are listed in Table 1.

The mean liver stiffness value was 4.18±1.15 kPa and 16.19±12.31 kPa in control and patient group, respectively ($p<0.001$). In this study, the mean liver stiffness values were found to be increased inpatient group compared with the control group ($p<0.001$). ROC curve analysis showed that, with an optimal SWE cut-off value of 5.51 kPa, the predicted sensitivity and specificity for detecting liver fibrosis is 88% and 93%, respectively (Figure 2).

Table 1. The main participants' characteristics and SWE results.

Characteristic	Control group (n=15)	Patient group (n=24)	P Value
Sex (n)[1]			0.542
Female	6 (40.0)	12 (50.0)	
Male	9 (60.0)	12 (50.0)	
Age (y)[2]	52.73 ± 11.73	57.21 ± 14.42	0.338

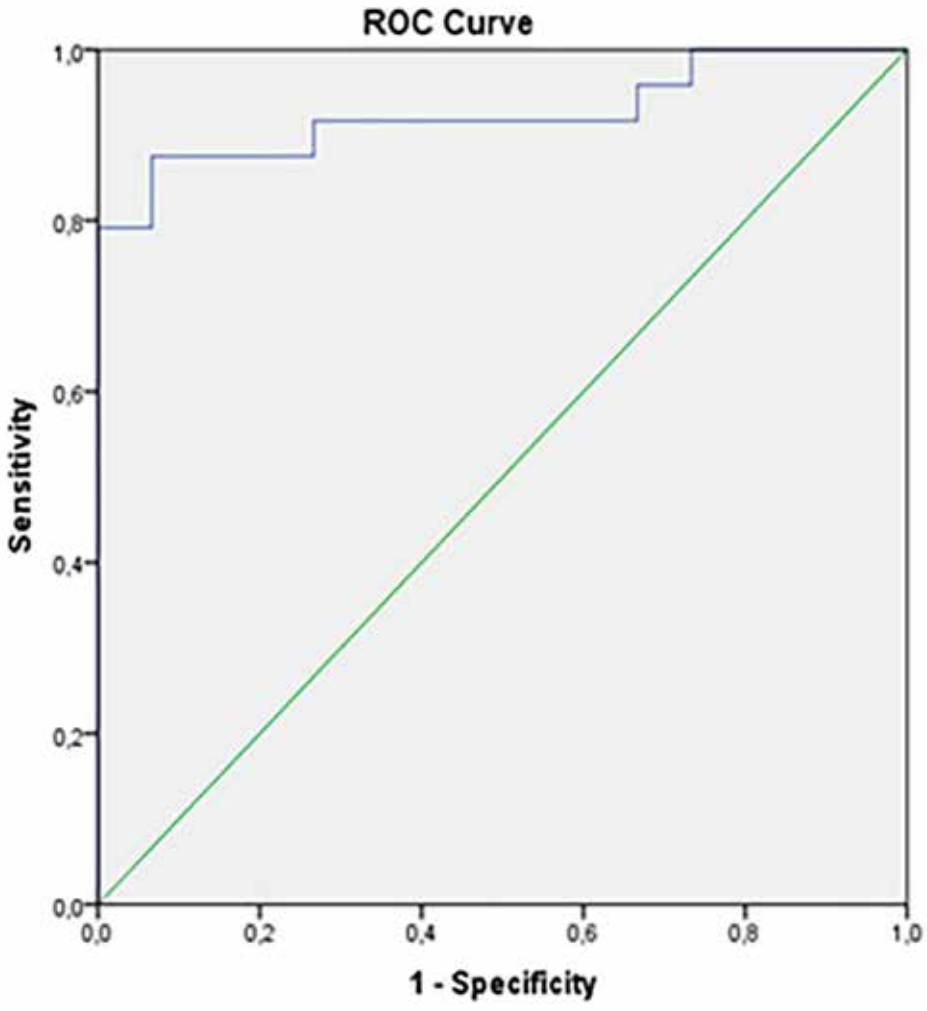
[1] *Data are numbers of patients or volunteers with percentages.*

[2] *Data are means ± standard deviations.*

Fibroscan was performed on 3 (12.5 %) participants in the patient group. Comparing the diagnostic performance of Fibroscan and SWE, the same stage of hepatic fibrosis was found in 2 out of 3 participants, in one patient SWE showed a lower degree of fibrosis (F2-F3) than Fibroscan (F4).

Liver stiffness was found to be positively correlated with the portal vein diameter and the flow pattern of hepatic veins (r=0.4, P<0.008). The analysis showed that SWE is 9.87 kPa higher than the average value when hepatic vein flow pattern is biphasic and 12.28 kPa higher when monophasic. No significant correlation between liver stiffness and the size of the liver and spleen or portal vein flow velocity was found.

Figure 2. The performance of ElastPQ for predicting liver fibrosis.



DISCUSSION

To our knowledge, we were first to use SWE in the evaluation of liver fibrosis in Lithuania. When we started our study, we had to obtain ten measurements to evaluate the stiffness of the liver. At mid-respiration participants were asked to hold breaths, the measurements were obtained by placing a small white box (ROI) in the right lobe of the liver. The method is simplified now because it's enough to put an ROI box on site once and obtain all ten measurements within. This makes the scan much faster and easier to perform.

One of the limitations of our study was that only a few patients that we examined underwent Fibroscan testing before. There is no database where the results of TE are registered in our clinic so we couldn't confidently compare TE and SWE results. However, TE demonstrated more severe liver fibrosis than SWE in 1 patient. Based on a single case, we cannot make any conclusions, but it may be explained by studies performed on elasticity phantoms that found TE to be better at soft and hard tissues comparing with SWE, both were found equally good at intermediate levels of elasticity [9]. Another study that compared ElastPQ (the same SWE method that we used) and TE results found similar accuracy for staging liver fibrosis [10].

Comparing SWE and TE, an observer who uses SWE has more influence on final results as he or she can exclude several measurements. In contrast, the exclusion is not available in Fibroscan [11]. That may be one of the reasons why the mean stiffness values in control groups vary in different studies. The mean liver stiffness value in our control group was 4.18±1.15 kPa. However, research with a larger sample found it to be higher (5.49 ± 1.59 kPa). They have also found it to be higher in men than in women [12]. However, several studies found it to be less than four kPa in the control group [13, 14].

The fact that liver stiffness was found to be positively correlated with the flow pattern of hepatic veins and the portal vein diameter is not surprising as liver fibrosis is associated with increased portal vein diameter and changing of the flow pattern of hepatic veins into the biphasic and monophasic as fibrosis progresses. In contrast, typical hepatic venous waveform shows a triphasic pattern. No association with liver and splenic size may be explained due to the small sample and the fact that more than half of the subjects inpatient group (58.3%) had mild-moderate fibrosis or no fibrosis (<12 kPa).

CONCLUSIONS

SWE is a promising method to diagnose liver fibrosis that has the potential to replace liver biopsy, although more extensive prospective studies are needed to define the role of SWE in liver fibrosis staging.

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Conflicts of Interest: The authors declare no conflict of interest.

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