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Comparative Utility of Transient and 2D Shear Wave Elastography for the Assessment of Liver Fibrosis in Clinical Practice

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Abstract

The aim of the study was to investigate the feasibility and correlation of liver stiffness measurements (LSM) between 2D-shear wave elastography (2D-SWE) and transient elastography (TE) in patients with chronic liver disease. Over 4 months, 421 patients with chronic liver disease of any cause underwent LSM by 2D-SWE and TE (M and/or XL probe) and controlled attenuation parameter at the same visit. LSM was not feasible by TE in 16 (3.8%) and by 2D-SWE in 17 (4.0%) patients. Median LSM were 8.9 and 8.7 kPa with TE and 2D-SWE, respectively, having a strong correlation ($r=0.774$, $p<0.001$) in the total cohort and in any cause of liver disease ($r=0.747$–0.806, $p<0.001$). There was a strong agreement on diagnosis of severe fibrosis (k-statistic: 0.841, $p<0.001$) or cirrhosis (*k*-statistic: 0.823, $p<0.001$). Both methods had increased failure rates in patients with obesity and/or increased waist circumference. Among 104 obese patients, TE was more feasible than 2D-SWE (92.3% vs 85.6%, $p<0.001$]. LSM by 2D-SWE are strongly correlated to LSM by TE independently of the etiology of chronic liver disease, stage of fibrosis, degree of liver steatosis, and patients' characteristics. TE with the XL probe may be superior in a minority of obese patients.

Keywords Transient elastography · Liver stiffness · 2D-shear wave elastography · Liver fibrosis

Abbreviations

TE	Transient elastography
2D-SWE	2D-shear wave elastography
LSM	Liver stiffness measurements
CAP	Controlled attenuation parameter
ALD	Alcoholic liver disease
NAFLD	Non-alcoholic fatty liver disease
HCC	Hepatocellular carcinoma
BMI	Body mass index
ROI	Region of interest
IQR	Interquartile range
SD	Standard deviation
AUROC	Area under the receiving operating characteristic

Introduction

The assessment of liver fibrosis is of great value in patients with chronic liver disease of any etiology, as the presence of severe fibrosis and particularly cirrhosis is associated with increased risk of clinical events and liver-related morbidity and mortality [1]. Liver biopsy has been considered as the "gold standard" for the estimation of liver fibrosis severity, but as any invasive procedure, it has some limitations including potential risks of complications [2]. Furthermore, there may be intra-observer and inter-observer variability and even sampling errors especially in small length liver specimens [3]. Considering these drawbacks, there has been a lot of research for the non-invasive assessment of liver fibrosis severity mainly focusing on the development of laboratory tests, combined markers and liver elastography [4]. Currently, such methods have almost completely replaced liver biopsy in the diagnosis of severe fibrosis and cirrhosis, particularly in patients with chronic viral hepatitis [4]. Thus, non-invasive methods have become irreplaceable tools for the optimal management of patients with chronic liver diseases.

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The first elastographic technique was transient elastography (TE) (Fibroscan®, Echosens; France) [5]. A lot of studies and meta-analyses comparing TE to liver biopsy confirmed the good accuracy of TE for the diagnosis of at least significant liver fibrosis and the excellent accuracy of TE for the diagnosis of cirrhosis [6–8]. However, TE is limited by a high rate of unreliable results (15–20%) [9], even though a new probe (XL) may be used to optimize the applicability of the method in obese patients [10]. Two-dimensional shear wave elastography (2D-SWE) (Aixplorer®, SuperSonic Imagine; France) is a newer elastographic technique, which can be performed by an ultrasound imaging machine with conventional ultrasound probes without the need of any extra equipment. 2D-SWE requires some expertise on ultrasonography by the operator, but it has some advantages compared to TE including the ability to examine larger size of liver tissue, to identify the most appropriate region for liver stiffness measurements (LSM) and to be performed without extra probes even in difficult for elastographic measurements patients such as those with ascites or obesity [11]. Till now, there have been several studies showing non-inferiority of 2D-SWE compared to TE for the assessment of liver fibrosis severity in patients with liver biopsy [12–14]. Nevertheless, there are some issues that have not been thoroughly investigated, such as the comparability of the feasibility rates of the two methods and the potential effects of the individual patients' characteristics on each method, as well as the extent of correlation in their assessments of stage of liver fibrosis.

Therefore, the primary aim of our study was to assess the feasibility and correlations of LSM by 2D-SWE and TE using standard (M) or (XL) probe in patients with any cause of chronic liver disease, as well as in relation to the etiology of liver disease. In addition, we tried to determine factors that influence the feasibility and comparability of the two methods.

Material and Methods

Patient Population

In total, 443 consecutive adult patients (≥ 16 years old) with chronic liver disease referred to our liver clinic during a 4-month period underwent LSM by both TE and 2D-SWE at the same visit. Controlled attenuation parameter (CAP) by TE was also measured. Patients with chronic viral hepatitis, alcoholic liver disease (ALD), non-alcoholic fatty liver disease (NAFLD), autoimmune hepatitis, and cholestatic liver diseases were included. In contrast, patients with hepatocellular carcinoma (HCC), Budd-Chiari syndrome, thrombosis of portal vein, liver congestion due to heart disease, ALT levels > 150 IU/L, alcoholic hepatitis, or patients with bile duct dilatation documented by abdominal ultrasound were excluded.

For all patients, main epidemiological characteristics were recorded and clinical examination was performed. Measurements of body weight and height, as well as of waist circumference, were also performed, and body mass index (BMI) was calculated. Obese patients were defined those with BMI > 30 kg/m^2, while the waist circumference was considered as increased when it was > 88 cm in women and > 102 cm in men [15]. The study was approved by the local Ethics Committee and was conducted in accordance with the Helsinki Declaration of 1975 as revised in 1983. All subjects provided written informed consent.

Transient Elastography

TE was performed by a FibroScan® 530 compact device equipped with both M and XL probes and CAP™ (Echo-Sens, Paris, France) [5]. In each patient, 10 valid LSM were carried out under fasting conditions in supine position by inter-costal approach, with the right arm in maximum abduction, using M-probe or XL probe at a measurement depth of 25–65 mm or 35–75 mm, respectively. The XL probe was used in patients with BMI > 30 kg/m^2 or patients with increased subcutaneous soft tissue in whom LSM was not feasible by using the M-mode. Results were expressed in kPa. We used only successful LSM defined by interquartile range (IQR)/median ratio < 0.3 [4, 16, 17]. The examinations were performed by an experienced user (DK or TV) who had previously completed more than 500 LSM by TE.

In order to diagnose more accurately the presence of severe fibrosis (≥ F3) or cirrhosis (F4) by TE, we used different LSM cut-offs according to the etiology of chronic liver disease. In particular, the diagnosis of fibrosis ≥ F3 or cirrhosis was based on LSM cut-off of 8.2 kPa and 11.3 kPa in chronic hepatitis B [18], 9.5 kPa and 13 kPa in chronic hepatitis C [19], 9.7 kPa and 13.6 kPa in NAFLD [20], and 9.5 kPa and 12 kPa in chronic liver disease of any other etiology [21]. Based on the recent Baveno VI criteria, which have been validated for ruling out patients at high risk for variceal bleeding, we evaluated our patients after dividing them into those with liver stiffness above or below the threshold of 20 kPa [22].

2D-Shear Wave Elastography

2D-SWE was performed by an Aixplorer® ultrasound system (Super Sonic Imagine S.A., Aix-en-Provence, France) with a SC6-1 convex probe [11]. The examinations were conducted in accordance with the manufacturer's instructions on the right lobe of the liver, through inter-costal spaces, under fasting conditions with the patient lying in dorsal decubitus position and the right arm in maximal

abduction. A liver portion of at least 6 cm thick and free of large vascular structures and 15-mm depth below the liver capsule was targeted using real-time B-mode ultrasonography. Only successful LSM were considered; they were defined by a region of interest (ROI) of 15-mm diameter with a complete and homogeneous fulfilling, while the patient was in a complete apnea state for 3 s [16, 17]. Though the manufacturer of the system recommends three measurements for each examination, we decided to undertake 10 valid LSM in order to further increase the reliability of the examinations [23]. The median value and standard deviation (SD) of 10 valid measurements were selected and expressed in kPa. We used only those results reported with an SD/median ratio < 0.3 [16, 17]. The examinations were performed by an experienced user (DK or TV) who had previously completed more than 500 LSM by 2D-SWE.

Again, different LSM cut-offs in relation to the etiology of chronic liver disease were used in order to diagnose more accurately the presence of fibrosis ≥ F3 or cirrhosis (F4). In particular, LSM cut-off of 8.1 kPa and 11.5 kPa was used for the diagnosis of fibrosis ≥ F3 or cirrhosis in chronic hepatitis B and 9.2 kPa and 13 kPa, respectively, in all other etiologies of chronic liver disease [13].

Statistical Analysis

Statistical analysis was done by SPSS software (SPSS Inc, Chicago, IL, USA). Data were expressed as frequencies, mean ± SD, or median (interquartile range [IQR]), as appropriate. Quantitative variables were compared between groups by Student's *t* test or Mann–Whitney test for normally distributed and non-normally distributed variables, respectively. Qualitative variables were compared by corrected chi-squared test or two-sided Fisher's exact test, as appropriate. The relationship between quantitative variables was assessed by the Spearman's correlation coefficient (*r*). The agreement between qualitative variables was determined by *k*-statistics. Multivariate linear regression analysis was used to identify independent factors associated with the presence of at least severe fibrosis. The area under the receiving operating characteristic (AUROC) curves for 2D-SWE predictability of severe fibrosis, as well as sensitivity and specificity, was calculated. The c-statistics of AUROC curves were provided with their 95% confidence intervals. Diagnostic accuracy was considered to be poor in case of a c-statistic < 0.65, moderate in case of a *c*-statistic 0.65–0.75, good in case of a *c*-statistic 0.76–0.85, and excellent in case of a c-statistic > 0.85. The optimal cutoff was selected from the AUROC curves as the point which provided the maximum sum of sensitivity and specificity. *P* values of < 0.05 were considered to be statistically significant.

Results

Of the 443 patients, 421 were finally included in this study, while 22 cases were excluded (bile duct dilatation: 10, HCC: 5, portal vein thrombosis: 3, Budd-Chiari syndrome: 2, refusal to sign informed consent: 2). Of the 421 patients, 207 (49.2%) were males and 214 (50.8%) females, whereas their mean age was 53 ± 14 years and their mean BMI was 27 ± 5 kg/m^2. Patients' main characteristics including the etiology of chronic liver disease are presented in Table 1.

Feasibility

LSM by TE with either M or XL probe was not technically feasible in 16 (3.8%) patients, while LSM by 2D-SWE was not feasible in 17 (4.0%) patients. XL probe for TE was used in 35 (8.3%) patients. TE provided successful LSM in 15 (88.2%) of 17 patients in whom 2D-SWE was not technically feasible, while 2D-SWE provided successful LSM in 14 (87.5%) of 16 patients in whom TE was not feasible. There were only 2 (0.5%) patients in whom LSM by both TE and 2D-SWE was not feasible, while LSM was determined by both methods in 386 (91.6%) patients.

CAP measurements were successful in 408 of 421 patients (feasibility rate of 96.9%), and the mean CAP value was 262 ± 62 dB/m.

TE feasibility was associated with lower BMI ($p < 0.001$), lower waist circumference ($p = 0.001$), and lower CAP value ($p = 0.030$), but not with age, sex or the etiology of liver disease. 2D-SWE feasibility was also found to be associated with lower BMI ($p < 0.001$), lower

Table 1 Main characteristics of 421 patients who underwent liver stiffness measurements

Sex (males)	207 (49.2%)
Age (years)	53 ± 14
Waist circumference (cm)	99 ± 15
Body mass index (kg/m^2)	27 ± 5
Liver stiffness measurements by TE (kPa)	8.88 (2.5–75)
Liver stiffness measurements by 2D-SW (kPa)	8.72 (3.72–46.2)
Controlled attenuation parameter (db/m)	262 ± 62
Etiology of liver disease	
Chronic hepatitis B	106 (25.2%)
Chronic hepatitis C	45 (10.7%)
Non-alcoholic fatty liver disease	181 (43%)
Alcoholic liver disease	26 (6.2%)
Cholestatic liver disease	28 (6.7%)
Other	35 (8.3%)

Quantitative variables are expressed as mean ± SD or median (min–max) values

TE transient elastography, *2D-SWE two-dimensional* shear wave elastography

waist circumference ($p < 0.001$), and lower CAP value ($p = 0.001$), but not with age, sex, or the etiology of liver disease. Finally, the feasibility of CAP was not associated with any of patients' characteristics.

Liver Stiffness Measurements and Their Correlations

The median LSM by TE was 8.9 (2.5–75.0) kPa with IQR: 0.8 (0–16.1) kPa. Severe fibrosis ≥ F3 by the predefined cut-offs for TE was observed in 78 (19.3%) patients. Multivariate linear regression analysis showed that LSM by TE was independently correlated with patients' age ($p = 0.002$) and waist circumference ($p = 0.034$), but not with sex, BMI, CAP value, or the etiology of liver disease.

The median LSM by 2D-SWE was 8.7 (3.7–46.2) kPa with SD: 0.8 (0.2–6.4) kPa. Severe fibrosis ≥ F3 by the predefined cut-offs for 2D-SWE was observed in 88 (18.5%) patients. LSM by 2D-SWE was independently associated with patients' age ($p < 0.001$), marginally not to BMI ($p = 0.052$) and not with sex, waist circumference, CAP value, or the etiology of liver disease.

In the total cohort, there was a strong correlation between LSM by TE and 2D-SWE ($r = 0.774$, $p < 0.001$). In addition, TE and 2D-SWE showed a strong agreement on classifying patients with or without severe fibrosis (≥ F3) (k-statistic: 0.841, $p < 0.001$), as well as on differentiating patients with or without cirrhosis (F4) (k-statistic: 0.823, $p < 0.001$) (Table 2).

Compared to the total cohort, the correlation of LSM between TE and SWE was numerically stronger in patients with ≥ F3 fibrosis by both methods ($r = 0.862$, $p < 0.001$), as well as in patients with cirrhosis ($r = 0.876$, $p < 0.001$), while it was still significant but numerically lower in patients with < F3 fibrosis by both methods ($r = 0.606$, $p < 0.001$).

LSM ≥ 20 kPa was detected in 33 (7.8%) patients by TE and 34 (8.1%) patients by 2D-SWE (k-statistic: 0.868, $p < 0.001$). Only 4 out of 421 (0.95%) patients had LSM ≥ 20 kPa only by TE or 2D-SWE. In patients with LSM ≥ 20 kPa, the correlation of LSM by the two methods was strong ($r = 0.729$, $p < 0.001$).

Liver Stiffness Measurements in Patients with Obesity and/or Increased Waist Circumference

There were 104 obese patients having a mean BMI of 34.2 ± 3.8 kg/m^2. Of them, 29 (27.9%) had BMI > 35 kg/m^2 and 9 (8.7%) had BMI > 40 kg/m^2. Increased waist circumference was found in 51 (49%) of the 104 obese patients. LSM by TE was not feasible in 8 (7.7%) obese patients regardless of the probe used (M or XL). Of the 96 remaining patients, LSM by TE was feasible by the M probe in 69 (71.9%) and by the XL probe in 27 (28.1%) cases. Regardless of the probe, LSM by TE was most likely to be unsuccessful in obese compared to non-obese patients (8/104 (7.7%) vs 8/317 (2.5%), $p < 0.001$).

Among the total cohort of 421 patients, 193 (45.8%) had increased waist circumference (51 of the 104 obese patients and 142 of the 317 non-obese patients). LSM by TE was not feasible in 14 (7.3%) cases with increased waist circumference irrespective of the probe (M or XL). Of the 179 remaining patients, LSM by TE was feasible by the M probe in 150 (83.8%) and the XL probe in 29 (16.2%) cases. Regardless of the probe, LSM by TE was most likely to be unsuccessful in patients with increased compared to normal waist circumference (14/193 (7.3%) vs 2/228 (0.9%), $p = 0.001$).

LSM by 2D-SWE was not feasible in 15 (14.4%) of the 104 obese patients. Again, LSM by 2D-SWE was more frequently not feasible in obese than non-obese patients (15/104 (14.4%) vs 2/317 (0.6%), $p < 0.001$). LSM by 2D-SWE was also not feasible in 16 (8.3%) of 193 patients with increased waist circumference. The failure rates by 2D-SWE were higher in patients with increased compared to those with normal waist circumference (16/193 (8.3%) vs 0/228 (0%), $p < 0.001$).

LSM was successfully performed by TE in 13 (86.7%) of the 15 obese patients without feasible LSM by 2D-SWE. Among the 104 obese patients, LSM was significantly more frequently feasible by TE using M or XL probe compared to 2D-SWE (96 (92.3%) vs 89 (85.6%), $p < 0.001$). In the obese patients evaluated by both TE and 2D-SWE, there was a strong correlation of the LSM by these two methods ($r = 0.860$, $p < 0.001$).

In contrast, the failure rate of LSM in patients with increased waist circumference did not differ between TE

Table 2 Classification of patients in advanced stages of fibrosis (≥ F3 fibrosis) or cirrhosis according to liver stiffness measurements by using transient elastography (TE) and *two-dimensional* shear wave elastography (2D-SWE)

	By TE only	By 2D-SWE only	By both methods	k statistic	p value
< F3 fibrosis	0	0	272 (64.6%)	0.841	< 0.001
≥ F3 fibrosis	3 (0.7%)	17 (4%)	69 (16.4%)		
No cirrhosis	0	0	341 (81%)	0.823	< 0.001
Cirrhosis	5 (1.2%)	11 (2.6%)	44 (10.4%)		

and 2D-SWE (14 (7.3%) vs 16 (8.3%), $p=0.326$); once more, there was a strong correlation between LSM by the two methods ($r=0.802$, $p<0.001$).

Liver Stiffness Measurements in Relation to the Etiology of Chronic Liver Disease

There was strong correlation of LSM by TE and 2D-SWE in patients with chronic hepatitis B ($r=0.758$, $p<0.001$), chronic hepatitis C ($r=0.756$, $p<0.001$), NAFLD ($r=0.747$, $p<0.001$), cholestatic liver disease ($r=0.806$, $p<0.001$), or ALD ($r=0.774$, $p<0.001$).

Of the 106 patients with chronic hepatitis B, 100 were successfully evaluated by both TE and 2D-SWE. Seventeen (17%) of them were found to have ≥ F3 fibrosis and 73 (73%) to have < F3 fibrosis by both methods, while 3 patients were found to have ≥ F3 fibrosis only by TE and 7 to have ≥ F3 fibrosis only by 2D-SWE respectively (k-statistic: 0.709, $p<0.001$). The correlation of LSM by the two methods remained strong in chronic hepatitis B patients with ≥ F3 fibrosis ($r=0.866$, $p<0.001$) and significant but numerically lower in those with < F3 fibrosis ($r=0.592$, $p<0.001$).

LSM by both TE and 2D-SWE was feasible in 42 of the 45 patients with chronic hepatitis C. Among them, 8 (19%) were found to have ≥ F3 fibrosis and 33 (78.6%) to have < F3 fibrosis by both methods (k-statistic: 0.926, $p<0.001$). Only 1 (2.4%) patient was classified to have ≥ F3 fibrosis by 2D-SWE and none by TE alone. The correlation of LSM between the two methods was strong in patients with ≥ F3 fibrosis ($r=0.922$, $p=0.001$) and significant but numerically lower in patients with < F3 fibrosis ($r=0.541$, $p=0.001$).

Of the 181 patients with NAFLD, 163 were successfully examined by both TE and 2D-SWE. Twenty-seven (16.6%) of the 163 patients were found to have ≥ F3 fibrosis and 130 (79.7%) to have < F3 fibrosis by both methods (k-statistic: 0.878, $p<0.001$). No patient was found to have ≥ F3 fibrosis by TE alone, while 6 (3.7%) patients were found to have ≥ F3 fibrosis only by 2D-SWE. Again, in patients with NAFLD, the correlation of LSM by the two methods was stronger in patients with ≥ F3 fibrosis ($r=0.902$, $p<0.001$) and remained significant but became numerically lower in patients with lower fibrosis stages ($r=0.576$, $p<0.001$).

TE as a Reference Method

Considering TE as the reference method and using its proposed cut-offs for diagnosis of severe fibrosis or cirrhosis, we evaluated the discriminatory ability of LSM by 2D-SWE and tried to identify the optimal respective LSM cut-off values of 2D-SWE in relation to the most common causes of chronic liver disease. In patients with chronic hepatitis B, LSM by 2D-SWE had an AUROC of 0.960 ($p<0.001$) for detecting patients with at least severe fibrosis and 0.964 ($p<0.001$) for detecting cirrhosis. In patients with chronic hepatitis C, the AUROC of LSM by 2D-SWE was 1.000 for both detection of severe fibrosis or cirrhosis ($p<0.001$). Finally, in patients with NAFLD, the AUROC of LSM by 2D-SWE for discriminating at least severe fibrosis or cirrhosis was 0.992 or 0.999, respectively ($p<0.001$). The optimal LSM cut-off values for detecting severe fibrosis and cirrhosis in relation to the etiology of liver disease are shown in Table 3.

Discussion

Nowadays, liver elastography has almost substituted liver biopsy in the assessment of liver fibrosis, as it is based on non-invasive, cheap, and easily performed techniques [24]. TE is the most validated method, as lot of studies and meta-analyses have shown its ability in diagnosing or ruling out different stages of fibrosis, especially cirrhosis, regardless of the etiology of liver disease [25–27]. 2D-SWE is a newer elastographic method that has been increasingly used worldwide. Though many studies have shown its excellent accuracy for predicting various stages of liver fibrosis, TE still remains the reference method in the international guidelines [4, 17, 18]. In our study, we tried to compare these two methods and to assess whether there are any differences in LSM between them in relation to patients' characteristics, etiology of liver disease, and stage of fibrosis.

According to our findings, there was no significant difference in the feasibility rates of TE by M or XL probe and 2D-SWE. The failure rate by each method was approximately 4% in all patients, reaching 8% and 15% in obese patients evaluated by TE and 2D-SWE, respectively. Our

Table 3 Accuracy of 2D-SWE to diagnose severe fibrosis (≥ F3) and cirrhosis according to the etiology of liver disease, when TE has been used as a reference method

	Severe fibrosis (≥ F3) by TE			Cirrhosis by TE		
	2D-SWE cut-off (kPa)	Sensitivity	Specificity	2D-SWE cut-off (kPa)	Sensitivity	Specificity
Chronic hepatitis B	8	95%	92%	11.5	87.6%	97.6%
Chronic hepatitis C	10	100%	100%	11.9	100%	100%
NAFLD	9.4	100%	96.3%	12.35	100%	98.6%

NAFLD non-alcoholic fatty liver disease

feasibility rates by TE are better than those of previous studies which reported failure rates ranging between 15 and 20% [9]. However, only the M probe was used in the previous studies, while we used either the M or the XL probe. Nevertheless, our technical failure rates by TE in the difficult for LSM obese patients were lower (8%) even compared to a recent study using TE with XL probe in obese patients and reporting failure rates of 20–40% [28]. The increasing experience in the use of this method and differences in the patients' characteristics (such as number of patients with BMI > 35 or > 40 kg/m^2) that affect the feasibility rates could be responsible for such discrepant results.

In the difficult to assess obese patients, both methods were less feasible in comparison to non-obese patients. However, TE with the use of XL probe seemed to be superior than 2D-SWE. In particular, TE using the XL probe was successful significantly more frequently compared to 2D-SWE and managed to give valid LSM in the majority of cases with 2D-SWE failures. This is in agreement with the results of the retrospective study by Staugaard et al. which reviewed 1975 patients and concluded that TE with the XL probe outweighs 2D-SWE in difficult patients [29]. It seems that 2D-SWE probably needs some extra equipment or programming in order to overcome difficulties in that small, but not negligible proportion of patients.

Based on the studies published so far, the LSM cut-offs for the diagnosis of fibrosis stages in patients with the same etiology of chronic liver disease differ slightly between TE and 2D-SWE [21, 25–27]. In our study, using the LSM cut-offs proposed for each method by the latest EASL guidelines and the most recent meta-analyses [13, 18, 19], there were no significant differences in the proportions of patients diagnosed with or without severe fibrosis or cirrhosis by each method. Moreover, there was a strong correlation of LSM by the two methods, which was even stronger in patients with at least severe fibrosis.

The good correlation of LSM by TE and 2D-SWE was also verified when patients with different causes of liver disease were examined separately. In patients with chronic hepatitis B, chronic hepatitis C, NAFLD, or cholestatic liver diseases, the correlation of LSM by the two methods remained strong and was even stronger in patients with at least severe fibrosis, similar to that observed in the total study population. Even when the widely proposed LSM cut-off values of TE for the diagnosis of at least severe fibrosis or cirrhosis were used as reference, 2D-SWE showed excellent diagnostic accuracy regardless of the etiology of liver disease. Such a finding questions whether different LSM cut-off values for TE and 2D-SWE are required, or the same values could be safely used without increased risk of misdiagnosis.

Another interesting finding was the agreement between the two methods for the diagnosis of LSM values < 20 kPa, which has been suggested by the Baveno VI recommendations to be used in combination with platelets > 150,000/mm^3 for selection of patients who can safely avoid screening gastroscopy [22]. Since these criteria have been validated only for LSM by TE, it was reassuring that the above criteria may be safely applied for LSM by 2D-SWE as well.

Another observation of our study was that LSM by both TE and 2D-SWE was not associated with liver steatosis as determined by CAP in the total cohort of patients. These findings are in agreement with previous reports suggesting that liver steatosis does not affect LSM by elastography [22, 30], but different findings have been also reported [31–34]. Thus, more data seem to be required to further clarify this issue.

In conclusion, this prospective study showed that LSM by 2D-SWE are strongly correlated to LSM by TE using the M or XL probe independently of the etiology of chronic liver disease, stage of fibrosis, degree of liver steatosis, and patients' main characteristics. These findings suggest that 2D-SWE can be safely used as an equal alternative to TE for the assessment of liver fibrosis in most patients with chronic liver disease. However, TE with the XL probe may be superior in a minority of obese patients.

Author Contribution All authors have significantly contributed and are in agreement with the content of the manuscript. Specifically, D. Karagiannakis was involved in the design of the trial, performed liver elastographies, and wrote the initial draft. T. Voulgaris performed elastographies as well. T. Aggelopoulos and P. Ioannidou contributed to the collection of the clinical and biochemical data. E. Cholongitas contributed to the collection of clinical data and performed the statistical analysis. J. Vlachogiannakos helped to the designation of the study and reviewed the manuscript. G.V. Papatheodoridis performed the statistical analysis, and was involved in the interpretation of the data, the improvement of the protocol, and in the finalization of the manuscript.

Availability of Data and Material Any data and material are available.

Declarations

Ethics Approval The study was approved by the local Ethics Committee.

Research Involving Human Participants and/or Animals The study was conducted in accordance with the Helsinki declaration of 1975 as revised in 1983.

Consent to Participate All subjects provided written informed consent.

Consent for Publication This manuscript has been approved by all authors, has not been previously published, and is not under consideration (in whole or in part) for publication elsewhere. In case of acceptance of the manuscript, the copyright is transferred to the Journal of Digital Imaging.

Conflict of Interest The authors declare no competing interests.

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