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Shear wave elastography: An accurate technique to stage liver fibrosis in chronic liver diseases

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Abstract
Objectives: The goals of this study were to assess the diagnostic accuracy of shear wave elastography (SWE) using the results of histopathological analysis as a standard of reference and compare the results of SWE and those of transient elastography (TE) to the degree of fibrosis as evaluated by histomorphometry.
Patients and methods: Adult patients who were scheduled to undergo liver biopsy were prospectively enrolled in the study. The diagnostic performances of SWE were assessed using AUROC curve analysis according to fibrosis thresholds defined by $\geq$ F2 (significant fibrosis), $\geq$ F3 (advanced fibrosis) and F4 (cirrhosis). Additional analyses using the Obuchowski measures for pairwise comparisons of fibrosis stages were performed. In a subgroup of 55 patients, the relationships between stiffness as measured using SWE and TE and the percentage of fibrosis were compared using Spearman's rank coefficient.

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Results: Among the initially enrolled 170 patients, 148/170 (87%) had successful SWE acquisition and formed the study population. SWE sensitivity and specificity were respectively 85.1% and 82.7% ($\geq$ F2), 88.9% and 90.3% ($\geq$ F3), 93.3% and 98.3% (F4). The AUROC curves of SWE along with their 95% confidence intervals (CI) were respectively 0.904 (95%CI: 0.845—0.946) for fibrosis $\geq$ F2; 0.958 (95%CI: 0.912—0.984) for fibrosis $\geq$ F3 and 0.988 (95%CI: 0.955—0.999) for fibrosis = F4. The global Obuchowski measure was 0.953 ± 0.007. In the subgroup study, a significant correlation was found between the percentage of fibrosis and stiffness as assessed by SWE ($r = 0.77$; 95%CI: 0.63—0.86; $P < 0.0001$) and by TE ($r = 0.65$; 95%CI: 0.47—0.78; $P < 0.01$). *Conclusion:* SWE is accurate to assess liver fibrosis in patients with chronic liver disease.

Chronic liver diseases are major public health concerns, with an estimated mortality of 1.5 million per year worldwide due to cirrhosis and its complications [1]. The assessment of liver fibrosis is a key element to determine prognosis, to manage treatment, to monitor disease progression and assess response to therapy in patients with chronic liver disease. Histopathological assessment using liver biopsy remains the standard of reference to evaluate liver fibrosis. However, this procedure is painful and may lead to hemorrhage (0.3%) or death (0.01%). In addition, the biopsy analysis depends on the experience of the pathologist, the size of the biopsy sample (usually about 1/50,000 of the total liver mass) and the site of sampling [2]. The heterogeneous distribution of liver fibrosis as well as intra- and inter-observer variability explain why the diagnosis of cirrhosis can be missed in up to 30% [3].

To address these limitations, non-invasive methods have been investigated for estimating liver fibrosis in patients with chronic liver diseases. Among the available non-invasive approaches shear wave-based techniques such as FibroScan®, also named transient elastography (TE), or acoustic radiation force impulse (ARFI) have been developed [4]. With TE, liver stiffness is assessed by estimating the speed of shear waves mechanically generated at the surface of the skin. Several studies have reported good performances of TE in patients with specific causes of liver fibrosis (hepatitis C virus [HCV] or hepatitis B virus [HBV] infections, alcoholic liver disease [5], non-alcoholic steatohepatitis, non-alcoholic fatty liver disease [6], primary biliary cirrhosis or primary sclerosing cholangitis) [7]. However, TE does not allow measuring stiffness in patients with ascites and fails in up to 20%, particularly when body mass index (BMI) is high [8]. ARFI has the advantage to provide a steerable point estimate of liver tissue stiffness, which can be guided by ultrasound. When compared to the results of histopathological analysis, both techniques have shown similar diagnostic performances [6,9,10].

Shear wave elastography (SWE), also named supersonic shear imaging or two-dimensional (2D) SWE, implemented on the Aixplorer® unit (SuperSonic Imagine, Aix-en-Provence, France) provides in real-time, a 2D quantitative map of tissue stiffness, that can be used in several organs [11,12]. This image enables adjustment of the region of interest (ROI) to assess a region of tissue (up to 4 cm long, 4 cm wide), to perform the measurements while assessing artifacts from tissue movement pulsation around larger vessels and reverberation under the liver capsule [13]. In HCV- and HBV-infected patients, SWE allows assessment of severe fibrosis and cirrhosis as accurately as TE does with better diagnostic performances in livers with significant fibrosis [14,15].

The main objective of this study was to evaluate the diagnostic accuracy of SWE compared to the results of liver biopsy. We also assessed the relationships between stiffness and METAVIR fibrosis scores, METAVIR activity and steatosis as well as the inter-observer reproducibility of SWE. In a subgroup of patients, we compared the diagnostic accuracy of SWE and TE according to fibrosis thresholds and assessed the relationships between stiffness measured by SWE or TE and the percentage of fibrosis, evaluated by histomorphometry.

Materials and methods

Study population

All consecutive patients were eligible if they were at least 18 year old, if they were scheduled to undergo liver biopsy whatever its indication in the Department of Radiology at Lyon Hospitals (France) from September 2010 to May 2012. Exclusion criteria were a liver transplantation for less than 6 months or contra-indications for liver biopsy (marked coagulation abnormalities, anticoagulant therapy, cardiac insufficiency, ascites, acute liver disease). This study protocol conformed to the ethical guidelines of the 1975 declaration of Helsinki. Informed written consent was obtained from each patient.

Study procedures

After a 6-hour fasting period, venous blood samples were collected to assess liver function. A standard Doppler ultrasound examination was then performed to identify the site of biopsy and to perform SWE. An ultrasound machine Aixplorer® (SuperSonic Imagine, Aix-en-Provence, France) with the low frequency convex probe (SC6-1) suitable for liver imaging was used.

SWE was first performed in the segment 5 of the liver. The right arm was placed in maximum abduction to enlarge the space between the ribs. During SWE acquisition, the patient was asked to stop breathing during 5 seconds. The elastographic acquisition was repeated 5 times for each

patient. For each acquisition, real-time SWE 2D color map of the stiffness (in kPa) was frozen after a stabilization of at least 3 seconds. The placement of the SWE color map could be moved, enabling an extended visual evaluation of liver stiffness. The size of the SWE color box was 3×4 cm. The measurements were performed in a 1.6 to 3 cm-diameter region of interest (ROI), within the chosen liver biopsy area. The subcapsular region was avoided because reverberation artifacts are often found beneath the capsule of Glisson. Similarly, perivascular areas were avoided because they may alter liver stiffness estimate. The shear wave images were qualitatively evaluated off-line on a computer by two radiologists, with more than 2 years of experience in SWE imaging. The assessment was made with the operators blinded to the histological diagnosis. An acquisition was considered to be successful if 2 or 3 of these following criteria were fulfilled: the SWE color box filled of more than 2 thirds of the total SWE box surface, the elastographic signal within the vessels missed, the minimal stiffness was superior to 0.2 kPa in the ROI as previously recommended [16]. For each patient, stiffness was defined as the median of several SWE successful measurements. In a subgroup of randomly selected patients, 5 additional acquisitions were also performed by a third physician, blinded to the previous results in order to study the inter-observer reproducibility.

Liver biopsy was performed immediately after SWE, under ultrasound guidance, through the same intercostal space and in the same area of segment 5 as in SWE. A biopsy gun 16G Magnum® (Bard Ltd, UK) was used to collect histological samples. To be eligible for analysis, biopsy samples had to be at least 20 mm long and to contain at least 11 portal tracts as recommended by the American Association of Study of Liver Disease guidelines [17], except for obvious cirrhosis. In case of a small sample size, repeat liver biopsy was immediately performed. The tissue sample was then processed according to the standard techniques, fixed in formaldehyde and embedded in paraffin. Four μm-thick sections were cut. One section was stained with hematoxylin, eosin and saffron for complete histopathological examination and activity grading. Another section was stained with Picrosirius Red for fibrosis staging. Biopsies were scored according to the METAVIR system [18] by a single pathologist blinded to SWE results. Liver activity was graded as A0 (absence of inflammation), A1 (small), A2 (moderate), A3 (severe). Liver fibrosis was scored as: F0, absent; F1, enlarged fibrotic portal tract; F2, periportal or initial portal-portal septa with intact architecture; F3, architectural distortion but no obvious cirrhosis and F4, cirrhosis. Additionally, steatosis was assessed using the Kleiner scoring system: S0: < 5%, S1: 5—33%, S2: 33—66%, S3: > 66% [19].

Subgroup analysis

All patients who underwent one successful TE within one month prior to liver biopsy were included in a sub-study. TE was performed by trained and experienced technicians. The probe was applied perpendicularly on the skin, in the right intercostal space of the midaxillary line, in the area used for the biopsy. Ten acquisitions were recorded for each patient. A successful acquisition was defined as an interquartile range of less than 30% of the median elasticity and a success rate of more than 60% [20].

In patients who had successful SWE and TE acquisitions, the percentage of fibrosis was assessed by histomorphometry on the liver biopsy samples. The area of fibrosis was studied using one 4 μm-thick tissue section of formalin-fixed, paraffin-embedded liver tissue stained with Sirius red and lightly counterstained with hematoxylin. Image analysis was performed on an optical microscope (Eclipse E400, Nikon, Japan) supplied with a scanning device and with a dedicated software (Histolab, Microvision Instruments, Ivry, France) aimed to digitize images of the complete section. The percentage of fibrosis, corresponding to the collagen proportionate area, was determined, as previously described [21]:

- the area of fibrosis was determined by measuring the surface specifically stained with Sirius red;
- the total area of the tissue sample was determined after manual contouring of the whole biopsy sample;
- the percentage of fibrosis was the ratio between the surface of fibrosis and the surface of the whole tissue sample.

No distinction was made between portal and periportal fibrosis, perisinusoidal fibrosis and perivenular fibrosis. A quality control was performed by a single supervisor on all images used for analysis.

Statistical analysis

The diagnostic performances of SWE and their 95% confident interval (95% CI) were assessed using the areas under the receiver operating characteristic curves (AUROC) as variables for comparison. Several fibrosis thresholds were evaluated: F0—F1 versus F2 to F4 ($\geq$ F2) for significant fibrosis, F0 to F2 versus F3 to F4 ($\geq$ F3) for advanced fibrosis, F0 to F3 versus F4 (F4) for cirrhosis. For each threshold, the optimal stiffness cut-off was estimated in maximizing the Youden's index defined as sensitivity + specificity-1. Further analyses were performed using the Obuchowski measures [22]. This measure summarizes all pairwise comparisons of fibrosis stages defined by liver biopsy, with a weighting scheme and a penalty function. Comparison between the Obuchowski measures was made using DeLong et al. method [23].

The relationship between stiffness and METAVIR fibrosis was described according to the steatosis and METAVIR activity scores. The correlation between SWE and steatosis, SWE and METAVIR grade (inflammation), SWE and METAVIR stage (fibrosis) was evaluated using the Spearman's rank coefficient and multivariate regression analysis.

Inter-observer reproducibility was studied using an intraclass correlation coefficient (ICC).

In the sub-study, AUROC calculated from SWE and TE diagnostic performances were compared within the same thresholds as the whole study. Correlation between stiffness measured by SWE or TE and the total fibrosis area were assessed using the Spearman rank coefficient. Statistical calculations were performed using Stata statistical package (StataCorp LP, College Station, TX).

Results

One hundred and seventy consecutive patients were included in this study between September 2010 and May

2012. SWE failure was observed in 18 of the 170 patients (10.5%). The causes of failure were poor acoustic windows in 14 patients (78%) including 9 patients with a BMI above 30 kg/m^2 and excessive tissue movement in 4 patients (22%) due to breathing. Moreover, four patients were excluded due to poor liver biopsy sampling. Therefore, 148 patients were finally included in the analysis. They were 95 men and 53 women with a mean age of 54.3 years $\pm$ 13.2 (SD) (Table 1).

According to fibrosis thresholds, AUROCs ranged between 0.90 (95%CI: 0.85–0.95) and 0.99 (95%CI: 0.96–0.99) and were statistically significant (Fig. 1). The optimal stiffness cut-off to assess significant fibrosis, advanced fibrosis and cirrhosis were, respectively, 8.8 kPa, 11.5 kPa and 18.1 kPa. Whatever the fibrosis thresholds, sensitivity and specificity of SWE were above 80% and increased with the fibrosis threshold. Same trends were shown for positive and negative predictive values (Table 2).

Table 1   Baseline characteristics of 148 patients included in the main analysis and 55 patients included in the sub-study.

Characteristics	Total n = 148	Sub-study n = 55
Male gender	95 (64.2%)	34 (61.9%)
Age (years)	54.3 ($\pm$13.2)	49.6 ($\pm$14)
BMI (kg/m^2)	24.9 ($\pm$4.3)	24.7 ($\pm$3.8)
AST (IU/L)	41.9 ($\pm$24)	44.9 ($\pm$27.6)
ALT (IU/L)	48.7 ($\pm$29.8)	57.4 ($\pm$36.8)
Alkaline phosphatase (IU/L)	104.8 ($\pm$40.1)	103.2 ($\pm$46.3)
GGT (IU/L)	158.1 ($\pm$152)	152.7 ($\pm$148.9)
Total bilirubin (μM/L)	16.6 ($\pm$12)	11.7 ($\pm$6.2)
Serum albumin (g/L)	40.8 ($\pm$3.6)	41.6 ($\pm$4.1)
Platelets count (10^3/mm^3)	183 ($\pm$60.1)	195.2 ($\pm$60.9)
Prothrombin time (%)	90.1 ($\pm$13.5)	96.1 ($\pm$6.7)
Liver transplantation	57 ($\pm$38.5)	21 ($\pm$38.3)
Chronic liver condition in native liver		
Non-alcoholic steatohepatitis	30 (20.3%)	13 (23.6%)
Viral chronic hepatitis B or C	22 (14.8%)	9 (16.4%)
Alcoholic liver disease	17 (11.5%)	2 (3.6%)
Auto-immune hepatitis	4 (2.7%)	2 (3.6%)
Chronic biliary disease	4 (2.7%)	2 (3.6%)
Other	14 (9.5%)	6 (10.9%)
Fibrosis score (METAVIR)		
F0–F1	81 (54.7%)	34 (61.8%)
F2	22 (14.9%)	7 (12.7%)
F3	15 (10.1%)	8 (14.6%)
F4	30 (20.3%)	6 (10.9%)

Qualitative variables are expressed as raw numbers (%) and quantitative variable as mean value $\pm$ standard deviation. BMI: body mass index; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma glutamyltransferase.
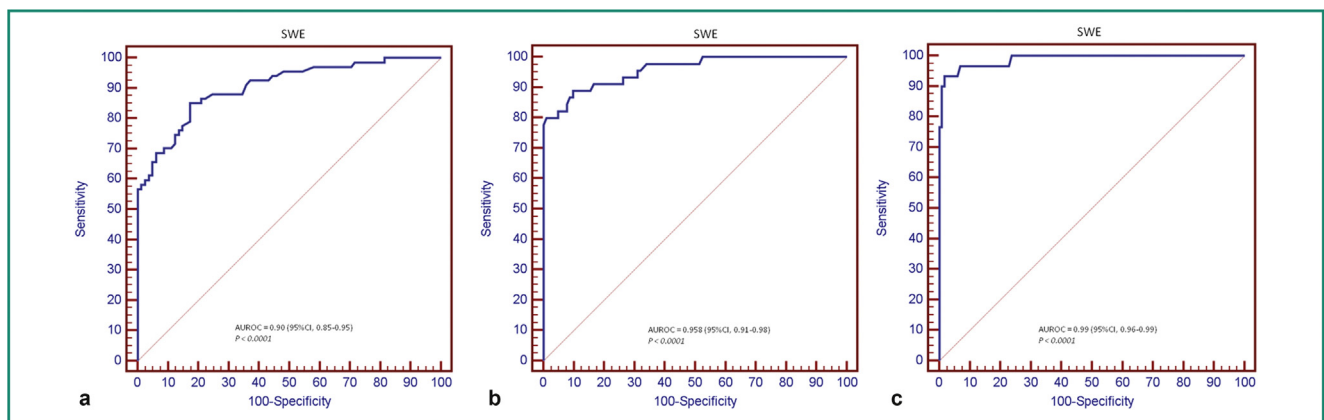

Figure 1.   Receiver Operating Characteristic curves for shear wave elastography for different fibrosis thresholds: (a) significant fibrosis (F0–F1 versus F2 to F4: $\geq$ F2), (b) advanced fibrosis (F0 to F2 versus F3 to F4: $\geq$ F3), (c) cirrhosis (F0 to F3 versus F4) (n = 148).

Table 2 Diagnosis accuracy of share wave elastography and optimal stiffness cut-off according level of fibrosis ($n = 148$).

	F $\geq$ 2	F $\geq$ 3	F = 4
Optimal stiffness cut-off (kPa)	8.8	11.5	18.1
Sensitivity	85.1 (74.3—92.6)	88.9 (75.9—96.3)	93.3 (77.9—99.2)
Specificity	82.7 (72.7—90.2)	90.3 (82.9—95.2)	98.3 (94.0—99.8)
Positive predictive value	80.3 (69.0—88.8)	80.0 (66.1—90.1)	93.3 (77.6—99.2)
Negative predictive value	87.0 (77.3—93.6)	94.9 (88.5—98.3)	98.3 (94.0—99.8)
Positive likelihood ratio	4.9 (4.3—5.7)	9.16 (8.1—10.3)	55.1 (49.9—60.8)
Negative likelihood ratio	0.18 (0.09—0.4)	0.12 (0.04—0.3)	0.07 (0.01—0.5)

Significant fibrosis: $\geq$ F2 (F0—F1 versus F2 to F4), advanced fibrosis: $\geq$ F3 (F0 to F2 versus F3 to F4), cirrhosis: F4 (F0 to F3 versus F4). Values of sensitivity, specificity, positive predictive value and negative predictive value are in percentage (95% confidence interval).

The median stiffness was 7.0 kPa (IQR: 6.0; 8.3) for F0—F1, 9.5 kPa (IQR: 7.8; 11.4) for F2, 13.0 kPa (IQR: 10.4; 16.7) for F3 and 25.8 kPa (IQR: 21.7; 34.5) for F4, and was significantly associated with METAVIR fibrosis whatever the fibrosis score (F0—F1 vs. F2, $P = 0.0001$; F2 vs. F3, $P = 0.04$; F3 vs. F4, $P = 0.0002$) (Fig. 2).

The global Obuchowski measure was significantly high (0.953 ± 0.007) (Table 3).

The relationships between the METAVIR fibrosis and stiffness did not significantly differ according to steatosis or METAVIR activity (Fig. 3). Nevertheless, at univariate analysis, median stiffness was significantly associated with METAVIR fibrosis ($r = 0.758$, $P < 0.0001$) or activity ($r = 0.252$, $P < 0.01$) but not with steatosis ($r = 0.103$, $P = 0.24$), but at multivariate analysis, METAVIR fibrosis remained the only independent variable associated with median stiffness ($r = 0.697$; $P < 0.001$).

Twenty-five patients were included in the inter-observer reproducibility study. The ICC was 0.92 (95% CI: 0.81—0.96).

Table 3 Diagnostic performances of SWE using the Obuchowski method in 148 patients.

	Estimate	Standard error
wAUC	0.953	0.007
Details between all pair		
F0 versus F1	0.593	0.065
F0 versus F2	0.807	0.061
F0 versus F3	0.943	0.030
F0 versus F4	0.996	0.004
F1 versus F2	0.742	0.064
F1 versus F3	0.899	0.046
F1 versus F4	0.996	0.004
F2 versus F3	0.765	0.086
F2 versus F4	0.989	0.011
F3 versus F4	0.947	0.032

wAUC indicates the Obuchowski measure of the AUC.

Sub-study

Among the 148 patients, 55 patients had additional histomorphometrical assessment of fibrosis percentage and a successful TE acquisition. Main characteristics of this sub-study population did not differ than those of the whole study population (Table 1).

No significant differences on AUROCs were found between TE and SWE, according to the fibrosis thresholds ($P = 0.75$, 0.62 and 0.21 respectively for $\geq$ F2, $\geq$ F3 and F4) (Fig. 4). Sensitivity, specificity, positive and negative predictive values did not differ regarding the confidence intervals, although fibrosis thresholds were not the same between the two techniques (Table 4). Liver stiffness was significantly associated with the percentage of fibrosis for SWE ($r = 0.77$; 95%CI: 0.63—0.86; $P < 0.0001$) and for TE ($r = 0.65$; 95%CI: 0.47—0.78; $P < 0.01$) (Fig. 5).

Discussion

Our results suggest that SWE is an accurate and reproducible non-invasive method to assess liver fibrosis, especially for the diagnosis of significant fibrosis in patients with various
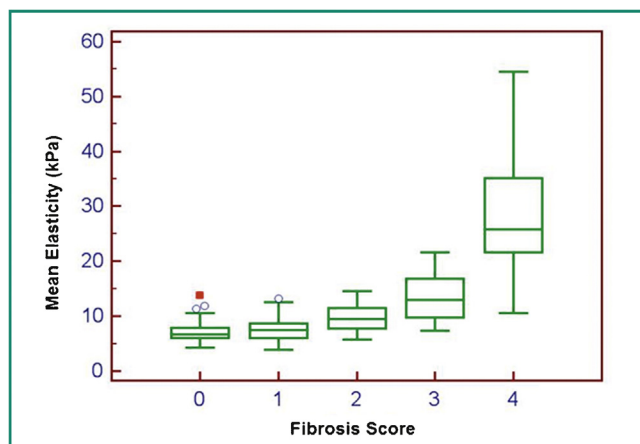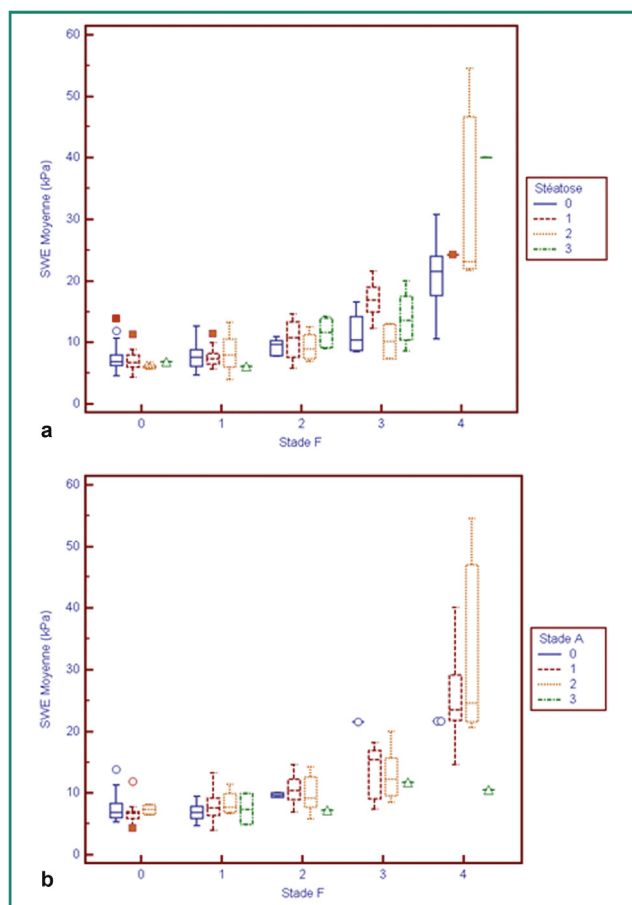

Figure 2. Box and whisker plots of values obtained with SWE measurements, according to each METAVIR fibrosis stage. Each box represents the interquartile range (from the 25th to the 75th percentile) within which 50% of the elasticity values are represented. The line crossing horizontally each box represents the median. The error bars show the minimum and maximum non-extremes values (median values). The median values (in kPa) were for F0—F1: 7.0 (IQR = 6.0—8.3), F2: 9.5 (IQR = 7.8—11.4), F3: 13.0 (IQR = 10.4—16.7) and F4: 25.8 (IQR = 21.7—34.5).

Figure 3. Box and whisker plots of SWE values for each METAVIR stage in relation to the degree of (a) steatosis and (b) necrotico-inflammatory activity (METAVIR grade) (*n* = 148). The central box represents values from the interquartile range. The line through the box represents median value. Bars represent minimum and maximum non-extreme values.

causes of liver fibrosis. Moreover, liver stiffness assessed by SWE is well correlated to liver biopsy using METAVIR score. This is the first study that compares the liver stiffness estimated by SWE and TE with fibrosis assessed both by the semi-quantitative METAVIR score and a quantitative histological score estimating percent fibrosis.

The AUROC is widely used to measure the diagnostic performance of non-invasive fibrosis techniques. Nevertheless, its use needs a binary gold standard whereas fibrosis staging is based on the five-stage METAVIR score. This difference implies that fibrosis stages have to be aggregated into 2 groups, a process that can lead to discordant conclusions, depending on how the groups are aggregated. Moreover, in case of spectrum bias [24] (i.e. when extreme stages of fibrosis (F0 and F4) are over-represented in the study population) the sensitivity and specificity of the test will be artificially increased as compared to the general population [20]. To overcome these issues in case of ordinal gold standards, the use of the Obuchowski multinomial measures was suggested [22]. In our study, the use of these measures strengthened the overall performance of SWE as assessed by AUROCs analysis, although they underlined a lower performance when discriminating between F0 and F1 [16]. Fortunately, the potential misclassification between F0 and F1 has little impact on the management of patients with liver fibrosis.

In our study, the SWE performances according to fibrosis thresholds using METAVIR score were similar to those of previous studies in patients with both various [25] or specific fibrosis etiologies such as HCV [14] or HBV [15] infections. However, our optimal stiffness cut-off values were slightly higher than those in these studies [14,15,25]. In this regard, we found 8.8 kPa in our study for significant fibrosis versus 7.1—8.0 kPa in other studies [14,15,25], 11.5 kPa in our study for severe fibrosis versus 7.9—8.9 kPa in other studies and 18.1 kPa for cirrhosis versus 10.1—10.7 kPa in other studies. Variability in METAVIR scoring might explain some of these differences, especially for significant and severe fibrosis [2]. We also believe that the METAVIR scale itself might contribute to explain a higher cirrhosis cut-off. Whereas each fibrosis stage matches with a well-defined level of fibrosis, the cirrhosis stage includes all levels of cirrhosis severity without upper limit. Thus, the optimal stiffness cut-off of cirrhosis would be highly related to the study population: higher, when mainly severe cirrhosis would be included in the study, lower, when ''overt cirrhosis'' would be excluded
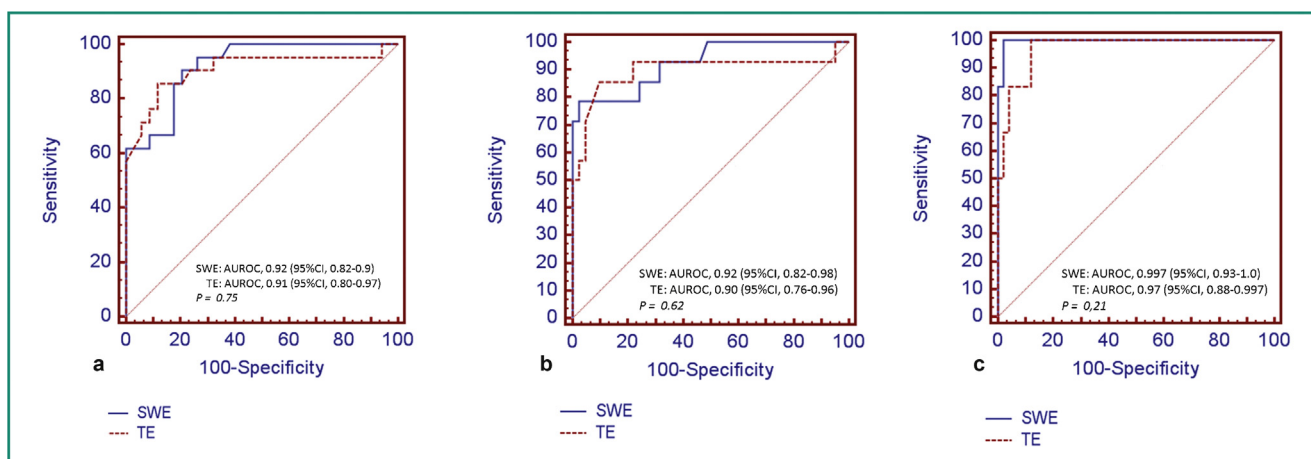

Figure 4. ROC curves for SWE and TE for different fibrosis thresholds: (a) significant fibrosis (F0—F1 versus F2 to F4: ≥ F2), (b) advanced fibrosis (F0 to F2 versus F3 to F4: ≥ F3), (c) cirrhosis (F0 to F3 versus F4) (*n* = 55).

Table 4 Optimal stiffness cut-off and diagnosis accuracy of share wave elastography (SWE) and transient elastography (TE), according to level of fibrosis (n = 55).

Procedure	F ≥ 2	F ≥ 3	F = 4
Optimal stiffness cut-off (kPa)			
SWE	8.5	11.5	15.8
TE	7.3	8.6	11.8
Sensitivity			
SWE	90.5 (69.6—98.8)	78.6 (49.2—95.3)	100 (54.1—100)
TE	85.7 (63.7—97.0)	85.7 (57.2—98.2)	100 (54.1—100)
Specificity			
SWE	79.4 (62.1—91.3)	97.6 (87.1—99.9)	98.0 (89.1—99.9)
TE	88.2 (72.5—96.7)	90.2 (76.9—97.3)	87.8 (75.2—95.4)
Positive predictive value			
SWE	73.1 (52.2—88.4)	91.7 (59.7—99.8)	85.7 (42.1—99.6)
TE	81.8 (59.7—94.8)	75.0 (46.6—93.1)	50.0 (21.1—78.9)
Negative predictive value			
SWE	93.1 (76.8—99.2)	93.0 (80.9—98.5)	100 (92.6—100)
TE	90.9 (75.3—98.1)	94.9 (82.7—99.4)	100 (91.6—100)
Positive likelihood ratio			
SWE	4.4 (2.2—8.6)	32.2 (4.6—227.6)	49.0 (7.0—340.9)
TE	7.3 (5.9—9.0)	8.8 (6.9—11.1)	8.17 (7.4—9.1)
Negative likelihood ratio			
SWE	0.12 (0.03—0.5)	0.22 (0.08—0.6)	0
TE	0.16 (0.04—0.7)	0.16 (0.03—0.8)	0

Values of sensitivity, specificity, positive predictive value and negative predictive value are in percentage (95% confidence interval).

as in the study by Ferraioli et al. [14], with a median stiffness for cirrhosis of 15.6 kPa (range: 8.0—22.5) in their study versus 25.8 kPa (range: 10.5—54.5) in our study. This also explains the differences of cut-off for cirrhosis between our main population and those of the sub-study.

Normal liver tissue contains 5.5 mg of collagen per gram of parenchyma, while a cirrhotic liver contains more than 30 mg/g [26]. Semi-quantitative histological scores like the METAVIR score are markers of fibrosis architecture without an absolute quantitative estimate of liver fibrosis. The addition of a quantitative assessment liver fibrosis from liver biopsy could reduce some of the reader variability and misclassification associated semi-quantitative histological scores.
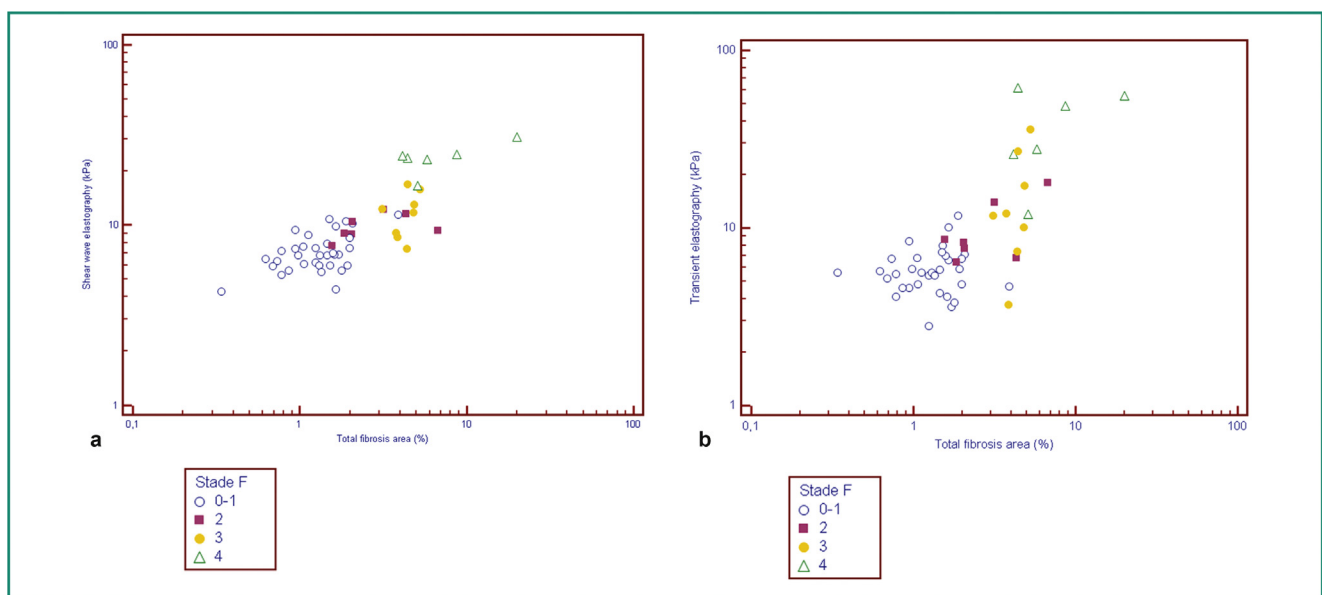

Figure 5. Correlation between total fibrosis area and liver stiffness measurements with details of the METAVIR stages obtained with (a) SWE and (b) TE (n = 55). Stiffness is significantly associated with the percentage of fibrosis for SWE and TE.

Consistent with the results of prior studies using TE [27], ARFI [28] or even SWE [14,29] our results support that steatosis has no major effect on stiffness measurements. Although the role of inflammation on stiffness measurements with TE [30], ARFI [31] or SWE [14] is debated, no correlation was shown in our study.

In our study, we observed a failure rate similar to those reported with SWE [14,16,25,32] or with TE [8,9,33]. Causes of failure of SWE were similar to those reported in other studies [14,16,25,32]. In case of high BMI, SWE does not seem to improve the success rate of a liver stiffness estimate over other share wave techniques.

Whereas SWE has an excellent inter-observer reproducibility as previously shown [15,32], the intra-observer reproducibility was not evaluated. SWE has shown improved reliability and repeatability [29,32] over TE.

Although our study has evaluated SWE in a relatively small population, we believe that it is representative of patients followed for different causes of liver fibrosis in clinical routine. As liver transplantation is known to influence stiffness during the early weeks [29], we excluded patients transplanted for less than 6 months.

Our study has some limitations. Of these, we did not study the influence of liver viscosity on the results of SWE. However, this was recently done by Deffieux et al. who reported a correlated between viscosity and the degree of liver fibrosis, but not with steatosis or disease activity [34].

In conclusion, SWE might be a useful tool to screen for liver fibrosis in the general population during a conventional ultrasound examination, especially when laboratory tests and ultrasound examination are negative despite the potential underlying fibrosis [35]. However, epidemiological studies are needed to fully investigate the performance and utility of SWE in this setting.

Acknowledgements

Disclosure of interest

The authors have not supplied their declaration of competing interest.

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