

Assessment of liver fibrosis in chronic hepatitis: comparison of shear wave elastography and transient elastography

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Abstract

Purpose: To evaluate the diagnostic accuracy of shear wave elastography (SWE) and transient elastography (TE) in the evaluation of liver fibrosis in chronic hepatitis B (CHB) and C (CHC) patients taking liver biopsy as gold standard.

Methods: Ethics committee approved this prospective cross-sectional study. Between October 2012 and December 2014, consecutive CHB/CHC patients fulfilling the inclusion criteria were included—age more than 18 years, informed written consent, willing and suitable for liver biopsy. SWE, TE, and biopsy were performed the same day. Liver stiffness measurement (LSM) cut-offs for various stages of fibrosis were generated for SWE and TE. AUC, sensitivity, specificity, and positive/negative predictive values were estimated individually or in combination.

Results: CH patients ($n = 240$, CHB 172, CHC 68), 176 males, 64 females, mean age 32.6 ± 11.6 years were enrolled. Mean LSM of patients with no histological fibrosis (F0) was 5.0 ± 0.7 and 5.1 ± 1.4 kPa on SWE and TE, respectively. For differentiating F2 and F3–4 fibrosis on SWE, at 7.0 kPa cut-off, the sensitivity was 81.3% and specificity 77.6%. For TE, at 8.3 kPa cut-off, sensitivity was 81.8% and specificity 83.1%. For F3 vs. F4, SWE sensitivity was 83.3% and specificity 90.7%. At 14.8 kPa cut-off, TE showed similar sensitivity (83.3%)

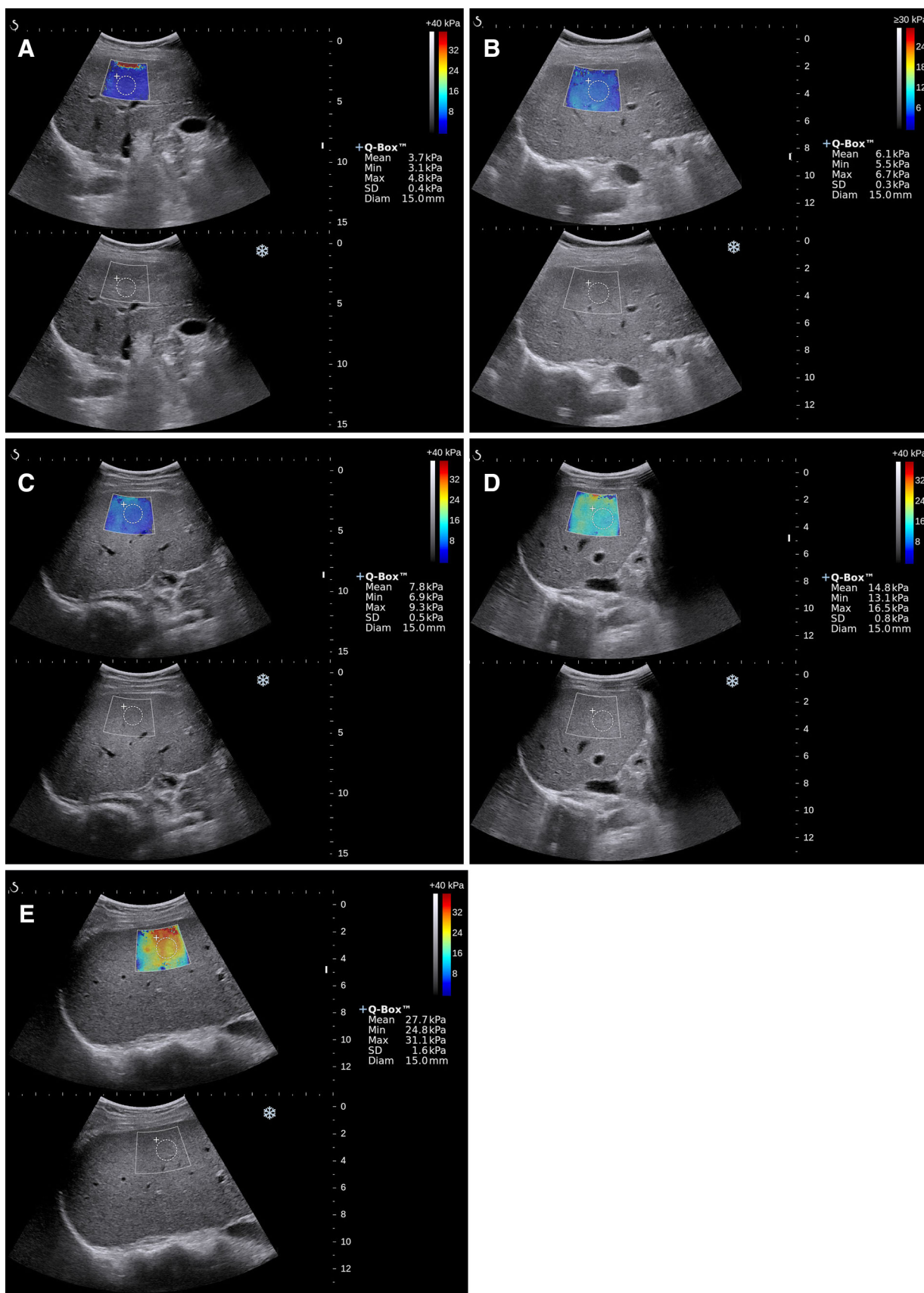
but specificity increased to 96.5%. Significant correlation between SWE and TE was observed ($r = 0.33$, $p < 0.001$). On combining SWE and TE, a drop in sensitivity with increased specificity for all stages of liver fibrosis occurred.

Conclusion: SWE is an accurate technique for evaluating liver fibrosis. SWE compares favorably with TE especially for predicting advanced fibrosis/cirrhosis. Combining SWE and TE further improves specificity.

Key words: Shear wave elastography—Transient elastography—Liver fibrosis—Chronic hepatitis—Diagnostic accuracy

Liver fibrosis is the outcome of untreated chronic liver injury occurring due to numerable causes and leads to serious long-term morbidity and mortality. Among the various causes, the important ones include hepatitis B, C infections, alcohol, non-alcoholic fatty liver disease, drugs, and autoimmune liver disease. With the emerging evidence that early fibrosis is reversible with effective treatment, many clinicians believe that patients with at least significant fibrosis should be subjected to therapy [1–4]. Precise estimation of the degree of liver fibrosis for accurate prognostication, surveillance, and treatment decisions in chronic hepatitis (CH) is thus crucial [5, 6].

Liver biopsy is the “gold standard” for grading liver fibrosis. However, it is an invasive procedure having small but significant risk of morbidity and mortality and



◀**Fig. 1. A–E** Shear wave elastography (SWE) showing different stages of fibrosis based on the metavir stage: **A** Metavir F0 fibrosis: SWE image showing a *rectangular box* depicting *deep blue* homogenous map (qualitative SWE) representing normal soft elasticity of liver. Color code interpretation (displayed on the *top right* corner of the screen) showing increasing tissue elasticity from *deep blue color* (soft) to *red color* (hard). For quantitative SWE, a circular region of interest of 15 mm diameter is marked within the *rectangular box* and the software displays the measured liver stiffness (LSM) on the screen—mean 3.7 kPa, min (minimum) 3.1 kPa, max (maximum) 4.8 kPa, SD (standard deviation) 0.4 kPa. **B** Metavir F1 fibrosis: SWE image showing color map of shades of *blue* with a mean LSM of 6.1 kPa. **C** Metavir F2 fibrosis: SWE color display of shades of *blue*, with mean LSM of 7.8 kPa. **D** Metavir F3 fibrosis: SWE image showing a *light blue color* map and a mean LSM of 14.8 kPa. **E** Metavir F4 fibrosis: SWE color map of *yellow to orange*, mean LSM 27.7 kPa and biopsy confirming metavir F4 stage fibrosis.

results in high patient refusal rate [4, 7, 8]. Additionally, many patients are unsuitable for the procedure due to associated coagulopathy. Liver biopsy has a moderate sensitivity and specificity due to sampling errors and small tissue sample retrieval [9, 10]. Repeating an invasive procedure for monitoring treatment response is also not advisable. Hence, there was a need for a technique which could estimate hepatic fibrosis by non-invasive methods.

Elastography is a technique which has the ability to estimate hepatic fibrosis based on the assessment of tissue stiffness. Among the available armamentarium, transient elastography (TE), was the earliest and most extensively used [11]. TE is difficult to perform in patients with obesity, ascites, shrunken liver, or those with narrow intercostal spaces [12]. Further technological advances led to the emergence of a novel technique of Shear wave elastography (SWE). This uses information of acoustically generated shear wave propagation speed through the liver to provide qualitative (stiffness-based color-coded maps) and quantitative assessment (average value in the region of interest in terms of the Young modulus, kilopascals) of liver fibrosis [13–16].

How do these techniques of SWE and TE perform with regard to the evaluation of different stages of fibrosis in patients of chronic viral hepatitis, needs comparison. Available literature on elastography has originated from the developed world and largely focused on chronic hepatitis C (CHC) patients. In India, about 50% of patients with chronic liver diseases occur due to hepatitis B and 20% due to hepatitis C [17]. HBV is the most common cause of chronic hepatitis, cirrhosis, and primary liver cell cancer [18].

This study was designed to evaluate chronic hepatitis B (CHB) and CHC patients for the presence of different grades of hepatic fibrosis using SWE and TE taking liver biopsy as the reference method.

Methods

This cross-sectional study was approved by our Institute's Ethics committee. A written informed consent was obtained. Between October 2012 and December 2014, consecutive patients of CH (CHB and CHC) reporting to our hospital were studied.

Patient work up

A detailed history pertaining to the source of infection, alcohol consumption, and co-morbidities like diabetes, hypertension, and any past history of decompensation was obtained. Liver function tests including serum bilirubin, aspartate transaminase (AST), alanine transaminase (ALT), serum protein, serum albumin, prothrombin time, complete hemogram, renal function tests, blood sugar, ultrasonography, and alpha-fetoprotein levels were done in all patients. Serologies for HBsAg, hepatitis B e antigen (HBeAg), antibodies to HBeAg (anti-HBe), hepatitis C virus (anti-HCV), and human immunodeficiency virus (HIV) were done using standard commercially available enzyme immunoassays (Biorad, Marnes-la-Coquette, France). CHB or CHC was diagnosed based on the positive serology of HBsAg or anti-HCV, respectively. In patients who were HBsAg positive, HBV DNA level was measured using a fluorescent probe-based detection kit (PG Biotech, Life River, Shanghai, China) on real-time polymerase chain reaction system (Mx 3000 5T) with a range of detection from 100 to 10⁹ copies/mL. In patients who were anti-HCV positive, HCV RNA was detected by reverse transcription-nested polymerase chain reaction.

The inclusion criteria were diagnosed patients of chronic hepatitis B or C of 18 years of age or more, willing to undergo liver biopsy, providing informed written consent, and having normal coagulation profile. Pregnant females, known case of cirrhosis, those with co-morbid illnesses like coronary artery disease, congestive cardiac failure, or coexistent chronic ailments, any contraindication for liver biopsy (coagulopathy, thrombocytopenia, history of bleeding diathesis) were excluded. Enrolled patients were subjected to SWE, TE, and liver biopsy on the same day by different investigators located in different departments who were blinded to the other two investigations of the same patient.

Shear wave elastography: technique

SWE was performed on the ultrasound machine (Aixplorer, Supersonic Imagine). Patients reported after 5 h of fasting, were made to lie supine with right arm in maximum abduction. Breath holding for few seconds was rehearsed (avoiding deep inspiration and expiration) for obtaining liver stiffness measurement.

Placing a convex broadband probe in the right intercostal space, a B-Mode ultrasound (US) image of the right lobe of the liver was obtained. SWE mode that had a simultaneous display of B-mode US and SWE, was put on. SWE box was placed onto a vessel-free hepatic parenchyma at a depth of 3–5 cm below the liver capsule. Ensuring image stabilization, while the patient held breath, a color image depicting different grades of stiffness was obtained. Quantitative SWE was performed by choosing a region of interest (ROI) of 10–15 mm diameter in the center of the SWE box displaying a homogeneous color map and the mean, minimum, maximum liver stiffness measurements (LSM) were displayed on the monitor (Fig. 1A–E). Six such LSMs were obtained at different sites in the right lobe of liver. Subsequently, the mean and standard deviation (SD) of six means with SD were derived depicting the final LSM, which was correlated with the histological grading (metavir score) on biopsy.

Transient elastography (TE)

TE was performed on the machine (Echosens, Paris, France) using either M or XL probe. Patients reported after fasting for 5–6 h, were made to lie supine with right arm in full abduction. The probe was placed perpendicular to the skin in the midaxillary line and in the ninth to eleventh intercostal space and on pressing the probe button, ten successful measurements per patient were obtained. TE measures liver stiffness in a volume (1 cm wide, 4 cm long) at 2.5–6.5 cm below the skin surface. If the success rate was <60% or inter-quartile range >30% of the final median liver stiffness, the study was considered unsuccessful.

Liver biopsy: technique

After obtaining informed written consent, the procedure was performed under ultrasound guidance using local anesthesia. Two intercostal spaces above the costal margin, in midaxillary line, the biopsy was done under aseptic precautions using 16 gauge Menghini needle. About 1.5–2.0 cm core of liver tissue was obtained and the punctured site was sealed. The sample was immersed in the neutral buffered formalin vial and sent to the pathology department. The patient was observed for 3 hours for any untoward complication and discharged when stable.

Histological grading of liver biopsy

Biopsies were reviewed by the investigators who were blinded to the SWE and TE findings and the report was conveyed by consensus. Biopsies without adequate number of portal tracts (<10, except in patients with cirrhosis) and/or insufficient length (10 mm) were ex-

cluded from the study. In all biopsies hematoxylin-eosin stain was performed, along with reticulin silver stain, Masson's trichrome stain, and Sirius red stain for the assessment of liver fibrosis. Metavir staging for liver fibrosis was done based on the METAVIR Cooperative Study Group [19]. Five stages ranging from F0 to F4 were assigned—F0, no fibrosis; F1, minimal fibrosis (portal fibrosis with no fibrous septa); F2, significant fibrosis (portal fibrosis with a few porto-portal fibrous septa); F3, advanced fibrosis (numerous porto-portal fibrous septa without cirrhosis); F4, cirrhosis with complete nodule formation.

Statistical analysis

Statistical analysis was performed on Stata, version 14.2. Continuous variables were expressed as mean with standard deviation (SD) or median with inter-quartile range (IQR). All statistical tests were two-sided and statistical significance was taken as $p < 0.05$. Liver stiffness values determined by the two tests were correlated with Metavir staging using Spearman's correlation coefficient. The diagnostic accuracy and cut-offs of liver stiffness determined by SWE and TE in detecting histological minimal, significant, and advanced fibrosis and cirrhosis were calculated using the receiver operating characteristics (ROC curves) and the best cut-off value of LSM, area under the curve (AUC), sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) were determined. Subsequently, the diagnostic accuracy was estimated by combining SWE and TE by either/or method.

Results

Baseline demographic and clinical characteristics

Two hundred and fifty-six consecutive patients of chronic viral hepatitis reported to our hospital during the study period (Fig. 2). Liver biopsy could not be done in 14 patients due to associated coagulopathy and in two patients the tissue biopsy sample was inadequate. Hence, 240 patients of CH (CHB-172 and CHC-68) were included who underwent SWE, TE, and liver biopsy.

These patients were 176 males and 64 females, of mean age 32.6 ± 11.6 years (range 15–75 years). Their clinical profile is illustrated in Table 1. All patients were subjected to three investigations of TE, SWE, and liver biopsy on the same day. Both SWE and TE could not be done in one patient, TE could not be done in four and SWE failed in two patients. Thus, the success rate of SWE was 98.7% (237/240) while that of TE was 97.9% (235/240) and there was no difference in the success rate between the two techniques ($p = 0.47$). Hence, a total of 237 patients underwent SWE while TE could be done in 235 patients.

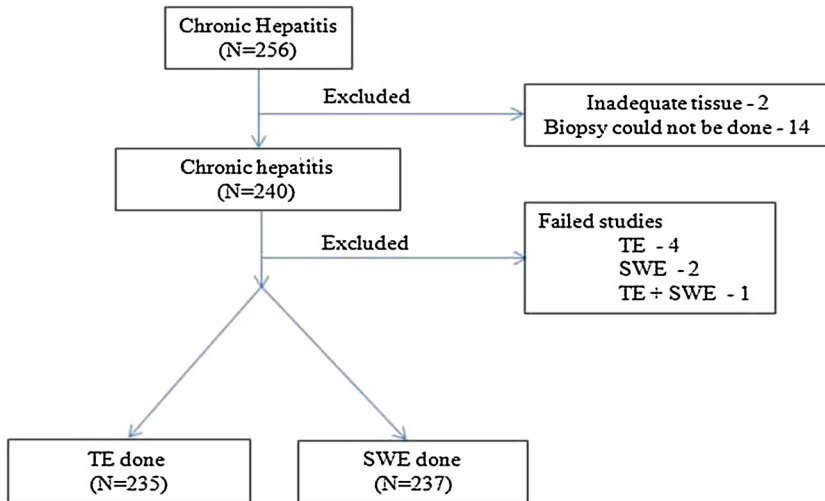


Fig. 2. Flow diagram of the study population.

Table 1. Profile of chronic hepatitis patients enrolled in the study (n = 240)

Parameter	Values
Age (years)	
Mean ± SD	32.6 ± 11.6
Range	15–75
Sex	
Males	176 (73.3%)
Females	64 (26.7%)
Etiology	
CHB	172 (72%)
CHC	68 (28%)
Diabetes (n = 238)	16 (6.7%)
BMI (kg/m ²)	22.3 ± 4.1
ALT (IU/L)	71.7 ± 89.0
AST (IU/L)	54.3 ± 59.0
SAP (IU/L)	243.2 ± 108.6
Serum bilirubin (mg/dL)	0.8 ± 0.9
Serum protein (gm/dL)	7.5 ± 0.6
Serum albumin (gm/dL)	4.7 ± 0.7
Platelet count (mm ³)	190.8 ± 74.9

All continuous data are presented as mean ± SD
 CHB, chronic hepatitis B; CHC, chronic hepatitis C; BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SAP, serum alkaline phosphatase

Liver stiffness measurements according to the fibrosis stage

There was moderately significant correlation between liver biopsy and both SWE (0.533, $p < 0.001$) as well as TE (0.614, $p < 0.001$) (Fig. 3). Mean LSM of patients with ‘no fibrosis’ (F0) was 5.0 ± 0.7 and 5.1 ± 1.4 kPa on SWE and TE, respectively. The mean LSM assessed by both SWE and TE increased progressively with the increase in histological fibrosis from F0 to F4 (Table 2).

Cut-offs values of liver stiffness for detecting various stages of fibrosis

For the diagnostic accuracy of SWE and TE with respect to histological fibrosis, the AUC and the best cut-offs were

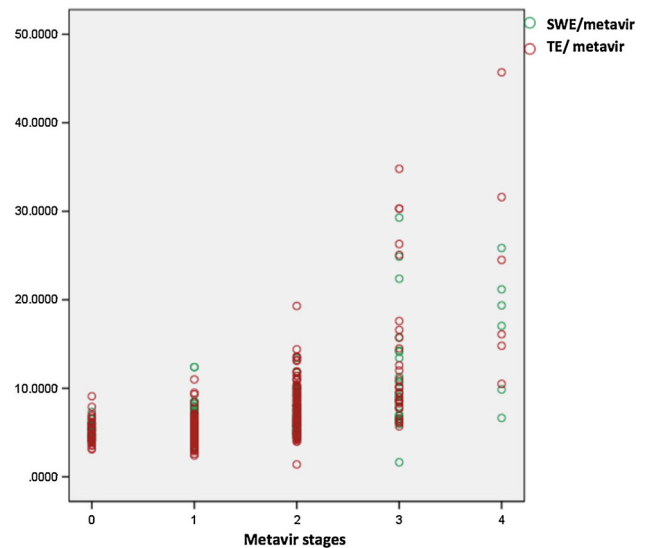


Fig. 3. Scatter plot depicting correlation between metavir stage and TE and shear wave elastography.

obtained on the ROC curve. The SWE and TE correlated significantly with each other ($r = 0.52$, $p < 0.001$).

For SWE

AUC of SWE for the presence of minimal fibrosis (F0 vs. F1–4), significant fibrosis (F0–1 vs. F2–4), advanced fibrosis (F0–2 vs. F3–4), and cirrhosis (F0–3 vs. F4) was 0.81 (95% CI 0.74–0.88), 0.76 (95% CI 0.70–0.82), 0.90 (95% CI 0.85–0.94), and 0.93 (95% CI 0.84–1.00), respectively. The cut-off of 7.0 and 9.7 kPa had a sensitivity and specificity of 81.3% and 77.6%, and 83.3% and 90.7% in discriminating F3–4 from F0 to F2 fibrosis and F4 from F0 to F3 fibrosis, respectively (Table 3).

For TE

AUC of TE for minimal fibrosis (F0 vs. F1–4), significant fibrosis (F0–1 vs. F2–4), advanced fibrosis (F0–2 vs.

Table 2. Liver stiffness values of different stages of fibrosis on shear wave elastography and transient elastography as per Metavir staging

Metavir stage	LSM in kPa on SWE			LSM in kPa on TE		
	<i>N</i> (237)	Mean \pm SD	Median (IQR)	<i>N</i> (235)	Mean \pm SD	Median (IQR)
0	31	5.0 \pm 0.8	5.0 (3.7–6.9)	31	5.1 \pm 1.4	4.8 (3.1–9.1)
1	89	5.9 \pm 1.5	5.7 (3.6–13.2)	88	5.3 \pm 1.5	5.3 (2.4–11.0)
2	83	6.9 \pm 2.0	6.4 (4.6–13.1)	83	7.8 \pm 2.9	7.4 (4.0–19.3)
3	28	11.8 \pm 6.2	9.4 (6.0–29.3)	27	13.7 \pm 8.3	10.1 (5.7–34.8)
4	6	17.0 \pm 7.8	18.2 (7.0–28.5)	6	23.9 \pm 13.1	20.3 (10.5–45.7)

LSM, liver stiffness measurement; *TE*, transient elastography; *IQR*, inter-quartile range; *kPa*, kilopascals; *SD*, standard deviation

Table 3. Diagnostic accuracy of shear wave elastography ($n = 237$) and transient elastography ($n = 235$) for different stages of liver fibrosis in chronic hepatitis patients

Metavir staging (numbers)	AUC	Cut-off (kPa)	Se (%)	Sp (%)	PPV (%)	NPV (%)
Shear wave elastography						
F0 vs. F1234 (31 vs. 206)	0.81 (0.74–0.88)	5.5	71.3	74.2	94.7	28.4
F01 vs. F234 (120 vs. 117)	0.76 (0.70–0.82)	6.0	66.7	69.7	67.9	68.6
F012 vs. F34 (203 vs. 34)	0.90 (0.85–0.94)	7.0	81.3	77.6	36.6	96.3
F0123 vs. F4 (231 vs. 6)	0.93 (0.84–1.0)	9.7	83.3	90.7	19.2	99.5
Transient elastography						
F0 vs. F1234 (31 vs. 304)	0.72 (0.64–0.80)	5.6	64.9	67.7	92.9	22.8
F01 vs. F234 (119 vs. 116)	0.84 (0.79–0.89)	6.2	75.4	78.2	76.8	76.9
F012 vs. F34 (202 vs. 33)	0.90 (0.85–0.95)	8.3	81.8	83.1	43.3	96.5
F0123 vs. F4 (229 vs. 6)	0.97 (0.93–1.0)	14.8	83.3	96.5	38.5	99.5

AUC, area under the curve; *kPa*, kilopascals; *Se*, sensitivity; *Sp*, specificity; *PPV*, positive predictive value; *NPV*, negative predictive value

Table 4. Diagnostic accuracy of shear wave elastography and transient elastography by combining or using either technique

Metavir staging	Se	Sp	PPV	NPV
F0 vs. F1–F4				
SWE \geq 5.5 kPa and TE \geq 5.6 kPa	53.5	87.1	96.4	22.3
SWE \geq 5.5 kPa or TE \geq 5.6 kPa	82.7	54.8	92.3	32.7
F1 vs. F2–F4				
SWE \geq 6.0 kPa and TE \geq 6.2 kPa	55.3	87.4	80.8	67.1
SWE \geq 6.0 kPa or TE \geq 6.2 kPa	86.8	60.5	67.8	82.8
F2 vs. F3–F4				
SWE \geq 7.0 kPa and TE \geq 8.3 kPa	71.9	91.0	56.1	95.3
SWE \geq 7.0 kPa or TE \geq 8.3 kPa	90.6	69.7	32.2	97.9
F3 vs. F4				
SWE \geq 9.7 kPa and TE \geq 14.8 kPa	83.3	97.4	45.5	99.5
SWE \geq 9.7 kPa or TE \geq 14.8 kPa	83.3	89.9	17.9	99.5

Se, sensitivity; *Sp*, specificity; *PPV*, positive predictive value; *NPV*, negative predictive value; *SWE*, shear wave elastography; *TE*, transient elastography

F3–4), and cirrhosis (F0–3 vs. F4) was 0.72 (95% CI 0.64–0.80), 0.84 (95% CI 0.79–0.89), 0.90 (95% CI 0.85–0.95), and 0.97 (95% CI 0.93–1.00), respectively. The cut-off of 8.3 and 14.8 kPa had a sensitivity and specificity of 81.8% and 83.1%, and 83.3% and 96.5% in discriminating F3–4 from F0 to F2 fibrosis and F4 from F0 to F3 fibrosis, respectively (Table 3).

For both SWE and/or TE

On using the combination of SWE and TE for all stages of liver fibrosis, there was a drop in the sensitivity whereas the specificity increased markedly in all stages of liver fibrosis (Table 4). The PPV showed improvement

for diagnosing F2 and F3 fibrosis. When the elastography techniques were used in either/or method, the reverse was true, that is, increase in sensitivity with drop in specificity (Tables 3 and 4).

Comparison of diagnostic accuracies of SWE and TE (Fig. 4)

The accuracies of SWE and TE were comparable for differentiating F0–2 fibrosis from F3 to F4 [SWE 0.90 (0.85–0.94) vs. TE 0.89 (0.85–0.95), $p = 0.87$] and for F0–3 from F4 fibrosis [SWE 0.93 (0.84–1.0) vs. TE 0.97 (0.93–1.0), $p = 0.23$]. However, TE had a better accuracy for differentiating between F0 and F1 from F2 to F4

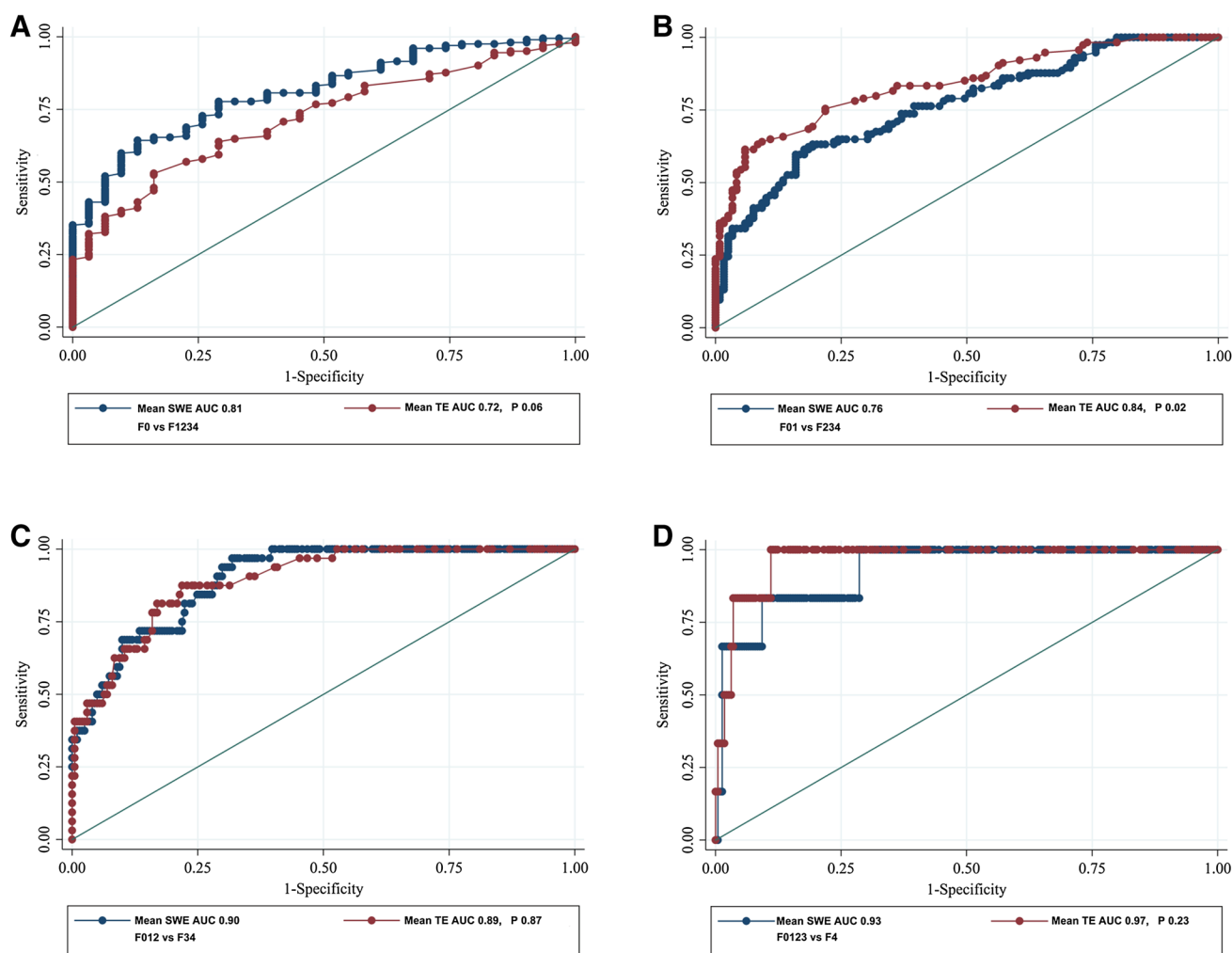


Fig. 4. Comparison of area under the curve (AUC) of SWE and TE at different stages of fibrosis.

fibrosis [SWE AUC 0.76 (0.70–0.82) vs. TE AUC 0.84 (0.79–0.89), $p = 0.02$].

Factors affecting liver stiffness measured by SWE and TE

A univariate analysis of the association of individual factors affecting LSM was undertaken. Factors like age, BMI, ALT, platelet levels, serum albumin, viral marker positivity for HBeAg, HBVDNA, and HCVRNA, duration of disease at the time of evaluation, and presence of steatosis did not show significant association with the mean LSM of individual stages of fibrosis (results not shown).

Discussion

Published literature for estimating liver fibrosis has mainly originated from the developed world [20–22] with majority of the studies focused on CHC [23, 24], and scanty literature on CHB patients [25, 26]. Further,

limited work comparing SWE with other techniques or serum markers is available [20, 23, 25, 27]. To the best of our knowledge, this is the first study of its kind from South Asia for estimating liver fibrosis in patients with chronic viral hepatitis (CHB and CHC), using SWE and TE on the same cohort with liver biopsy as the reference method.

In our study on 240 patients, SWE could be performed in 237/240 patients (success rate 98.7%) while TE in 235/240 (success rate 97.9%), and there was no difference in the success rate between the two techniques ($p = 0.47$). These patients in whom elastography failed were either very obese, had BMI $> 30.5 \text{ kg/m}^2$, or had narrow intercostal spaces. For both techniques, obesity posed a significant hurdle (a known limitation), which was faced more with TE than SWE.

Different cut-offs and AUC values for discriminating between different stages of fibrosis by elastography are published. These studies are from different geographical locations and on patients of varied etiologies. Additionally, factors like age, sex, ethnicity, medication, and

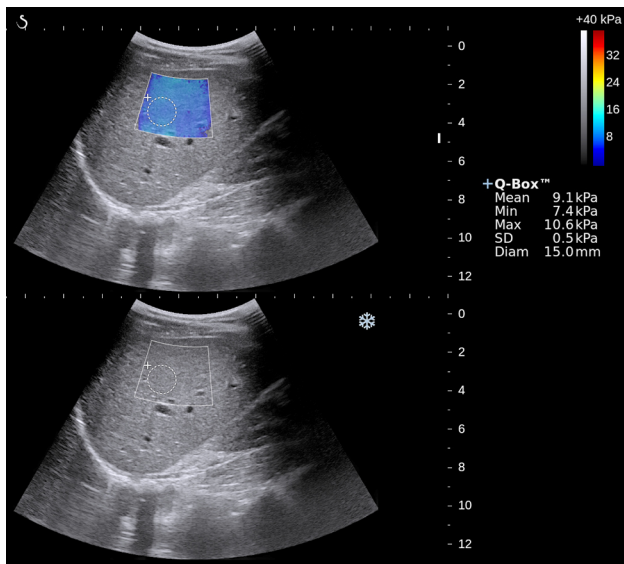


Fig. 5. Discordance of metavir stage of fibrosis on SWE and TE: SWE image of a 25-year-old CHB patient showing a light blue color map with mean stiffness of 9.1 kPa and the stiffness measured on TE was also high, 11.0 kPa, suggestive of F3 fibrosis on both SWE and TE. However, the biopsy revealed metavir F1 fibrosis.

post prandial status, etc., which are known to cause variability in liver stiffness, are also not known [28]. Hence, the available liver stiffness cut-offs cannot be generalized and data based on our own population are much needed. Further, even the European Federation of Societies for Ultrasound in Medicine and Biology [29] and World Federation for Ultrasound in Medicine and Biology [11] have only specified the guidelines for the use of elastographic techniques but not laid any specific thresholds for diagnosing different stages of fibrosis.

The technique of TE was available at our center earlier than SWE and a significant co-relation between LSM and histological fibrosis ($r = 0.58$, $p < 0.01$) was depicted [30]. In this study, we performed SWE and TE in the same cohort and the cut-off values for different stages of fibrosis on SWE were generated for the first time. The mean LSM on SWE in our patients with no histological fibrosis was 5.0 ± 0.7 kPa (range 3.6–6.9 kPa). This value is in good agreement with a retrospective study by Suh et al. (4.4 kPa) who collected LSM data of those patients who underwent SWE and liver biopsy for various other clinical indications and had normal hepatic histology [31]. Additionally, the mean LSM of 4.6 and 4.9 kPa respectively have also been shown in two studies on healthy volunteers without histopathological confirmation [32, 33].

It is difficult to accurately differentiate between adjacent stages of fibrosis due to a substantial overlap in median liver stiffness values. Same was true in our study for both SWE and TE, particularly, for early fibrosis (F1

and F2, Table 2) where we found a modest performance of the two techniques and TE showed an edge over SWE in discriminating between F1 and F2 fibrosis (TE, AUC 0.84 (0.79–0.89) vs. SWE AUC 0.76 (0.70–0.82), $p = 0.02$) (Table 4).

The degree of liver fibrosis has a positive correlation with the complications of cirrhosis including variceal bleed, ascites and risk of hepatocellular carcinoma, and has been correlated with prognosis [34]. Hence, the differentiation with high precision is clinically important particularly for patients with significant fibrosis and beyond who would require therapy and regular follow-up for the assessment of complications. With increasing fibrosis, a parallel increase in the LSM values as well as in the diagnostic performance of both techniques of SWE and TE was seen (Table 3). SWE and TE had cut-offs of 7.0 kPa (AUC: 0.90) and 9.7 kPa (AUC: 0.93), and 8.3 (AUC: 0.89) and 14.8 kPa (AUC: 0.97) for detecting advanced fibrosis (>F2) and cirrhosis (>F3), respectively. The diagnostic accuracy of TE to detect advanced fibrosis and cirrhosis was almost similar to a study published from our center on CHB patients [30]. However, the accuracy for significant fibrosis in the present study was slightly lower than the previous study which could be because of the difference in the overall number and proportion of patients with different stages of fibrosis. The cut-offs exhibited in the other published studies from different centers were higher than ours for all stages of fibrosis. This difference could be attributed to the heterogeneity in the patients studied and geographic regional variations.

SWE and TE came across as useful non-invasive elastography techniques particularly for evaluation of advanced fibrosis (F3) and cirrhosis (F4). A recent meta-analysis of twelve studies of SWE performed on patients of different etiologies of CH has also illustrated similar sensitivities (89% and 88%) and specificities (84% and 86%) for advanced fibrosis and cirrhosis [35]. Similarly, a meta-analysis of 40 studies on TE for estimating liver fibrosis, concluded that TE had a high sensitivity and specificity for cirrhosis and less for lesser degrees of fibrosis. No optimal stiffness cut-offs for individual fibrosis stages were validated and the wide range of cut-offs with overlap between stages was encountered, the results being quite similar to the observations in the present study. [36]

LSM evaluated by SWE or TE did not have any association with age, BMI, ALT, platelet count, serum albumin, hepatitis B/C viral marker positivity, duration of disease at time of evaluation, and steatosis. However, in the previous study from our center, ALT was shown to be an independent predictor of LSM. This discrepancy could be explained by the difference in the proportion of patients with ALT $\times 5$ times normal in the present and previous study, as in the previous study, it was ALT $\times 5$ times that correlated with LSM rather than all values of ALT. In the previous study 7% (25/352) patients had

ALT \times 5 times as compared to present study where only 2.5% (6/240) patients had ALT \times 5 times normal. Similarly, no factor had any association with LSM in the study by Ferraioli et al. [23] and Samir et al. [14]. However, Poynard et al. [37] on assessing the impact of steatosis and necro-inflammation have shown a less impact of both (steatosis and necro-inflammation) on SWE in comparison to TE in non-advanced fibrosis patients.

We found a modest correlation between SWE and TE ($r = 0.52, p < 0.001$). Diagnostic accuracy of SWE and TE in discriminating advanced fibrosis and cirrhosis was high. Comparison studies on SWE and TE have documented variable results, some showing superiority of SWE over TE while others depicting comparable outcomes. However, all these studies have been performed on CH patients with different etiologies. Kim et al [38], in a retrospective study showed significant conformity of SWE and TE ($p < 0.05$) with higher precision of SWE (higher kappa index) in patients of CHB. Leung et al [25] showed that SWE was superior to TE especially for evaluating F2 fibrosis (SWE AUC 0.82 (0.74–0.89), specificity 84.8% and TE AUC was 0.78 (0.69–0.86), specificity 80.9% in chronic B carriers). In our study, for $>$ F2 fibrosis, the AUC of SWE and TE was comparable with similar sensitivities (0.90 (0.85–0.94 vs. 0.89 (0.85–0.95), $p = 0.87$) but TE depicted a higher specificity of 83.1% compared to that of SWE (77.6%). In contrast, a cohort of 226 CH patients, showed that the performance of SWE and TE was similar for diagnosing fibrosis; however, the SWE applicability was greater than that of TE in patients with ascites [39]. Comparable results of SWE with TE and ARFI (acoustic radiation force impulse) have also been elicited [27].

We also explored the predictive value of fibrosis by combining SWE and TE. Combination resulted in drop in sensitivity with increase in specificity for discriminating between all stages of fibrosis. Hence, SWE and TE combination would be highly specific for predicting fibrosis. Similar findings have been reported by the use of a combination of TE with ARFI. However, the feasibility of using two techniques is rather difficult and would not be cost-effective. This approach may be reserved for cases having high index of suspicion or contraindications for biopsy.

Our study had few limitations. We evaluated patients of chronic hepatitis B and C only, thus, these cut-offs may not be applicable to CH patients of other etiologies in our population. Patients who had definite diagnosis of cirrhosis (clinically or by ultrasound/ CT abdomen or endoscopy) were not included as the identification of these patients can be made on conventional ultrasound. Due to this, we had few patients in the F4 stage on histology and better numbers could have provided us with a more robust data. SWE, by virtue of being a real-time ultrasound technique has the ability to depict the color-coded maps of stiffness (qualitative) and quantitative

information of tissue stiffness of the entire liver. We encountered some cases in which both SWE and TE depicted high stiffness values, but their metavir stage was low (Fig. 5). Since fibrosis affects the liver in a heterogenous manner, the liver biopsy is prone to sampling errors. In such cases, liver biopsy performed under SWE guidance (from depicted harder areas) could have helped in obtaining a better represented tissue sample. We could not undertake this due to the logistics and feasibility issues and this perhaps has led to an underestimation of the diagnostic potential of SWE.

To conclude, SWE is an accurate non-invasive technique for evaluating liver fibrosis especially for predicting advanced fibrosis and cirrhosis and the results compare favorably with TE. Combination of the two techniques results in increased specificity for detecting liver fibrosis. Future studies comparing SWE with liver biopsy performed under SWE guidance may help in clarifying the role of SWE further.

Acknowledgments Authors want to acknowledge Mr. Sanjeev Negi and Mr. Dilshad Ali, the research staff, for handling the data.

Compliance with ethical standards

Funding No funding was received for this study.

Conflict of interest The authors have no conflict of interest.

Ethical approval The study was performed after approval from the Ethics committee of our institute and all procedures performed on human participants were in accordance with the ethical standards.

Informed consent A written informed consent was obtained from all individual participants included in the study.

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