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ORIGINAL ARTICLE

Clinical relevance of shear wave elastography compared with transient elastography and other markers of liver fibrosis

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Key words
liver fibrosis, chronic liver disease, elastography, ultrasound, endoscopy, portal hypertension.

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Abstract

Background: Early and accurate non-invasive diagnosis of liver fibrosis is important for reducing the burden of cirrhosis and related complications.
Aim: This cross-sectional study compares shear wave elastography (SWE), transient elastography (TE) and clinical markers of chronic liver disease in patients with various liver disorders.
Methods: Liver ultrasound with SWE was performed on 421 adult patients, 227 of whom also had TE. Patient age, gender, body mass index (BMI), liver disease aetiology and laboratory results were recorded. Associations between SWE, TE and other tests for liver fibrosis and chronic liver disease severity were sought. Advanced liver fibrosis was defined as liver stiffness measurement (LSM) equivalent to ≥F3 using Metavir staging.
Results: Patients were predominantly male (68%), with mean (standard deviation) age 54 (13) years, BMI 28 (6) kg/m^2 and serum alanine aminotransferase (ALT) 39 (27) U/L. Liver disorders were predominantly non-alcoholic fatty liver disease (NAFLD), chronic hepatitis B (CHB), chronic hepatitis C (CHC) and alcohol-related liver disease. The median (interquartile range) LSM was 10 (6–20) kPa with SWE and 9.2 (6–21) kPa with TE. Advanced liver fibrosis was associated with older age, higher BMI, model for end-stage liver disease score, aspartate aminotransferase (AST), AST/ALT ratio, AST to platelet ratio index, fibrosis-4 index and Hepascore. SWE and TE LSM were positively correlated, particularly for NAFLD and CHC. SWE LSM predicted ultrasound and endoscopy-diagnosed portal hypertension and oesophageal varices.
Conclusions: Across various liver diseases, SWE is at least comparable with TE and other non-invasive tests of liver fibrosis. SWE is accurate for predicting liver-related portal hypertension.

Introduction

The global burden of chronic liver disease is substantial, with geographical disparities in the aetiologies.[1] The dominant aetiologies of chronic liver disease in 'Western' and Latin American countries are alcohol-related chronic liver disease, non-alcoholic fatty liver disease (NAFLD) and to a lesser degree viral hepatitis.[2,3] In contrast, chronic viral hepatitis and alcohol-related chronic liver disease are more prevalent in African and Asian countries, although rising rates of NAFLD have been observed.[4,5]

Liver fibrosis

Liver fibrosis is the harbinger of many chronic liver disease complications, as it reflects increased risk for progression to cirrhosis and its complications, including hepatocellular cancer and portal hypertension.[6] Since different stages of liver fibrosis in various liver disorders can sometimes be reversed,[7] early and accurate diagnosis of liver fibrosis identifies individuals who would potentially benefit from targeted lifestyle recommendations, disease-specific or antifibrotic pharmacotherapy.

Abbreviations: CI, confidence intervals; OR, odds ratio

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Liver biopsy

Liver biopsy has had a historical and ongoing role in assessment of liver disease aetiology and severity.[8] However, liver biopsy risks include pain, bleeding and rarely death.[9] A single-site liver biopsy is not always representative of overall liver fibrosis burden, since liver fibrosis is not necessarily uniformly distributed.[10] Therefore, there is a need for accurate, non-invasive tests for liver fibrosis.

Non-invasive liver fibrosis assessment

There is no approved propriety liver fibrosis test funded in the Medicare Benefits Schedule in Australia. Liver imaging using B-mode ultrasound or computed tomography are not sensitive for diagnosing liver fibrosis in the absence of cirrhosis or features of portal hypertension.[7,11] Non-invasive liver fibrosis tests are now an integral part of routine hepatology clinical practice and for assessing results of interventions in clinical trials for chronic liver disorders. These incorporate blood-based biomarker algorithms and imaging techniques.[12,13] An elastography-based test or liver biopsy is sometimes used as a confirmatory test if blood-based tests produce an indeterminate or high result suggestive of liver fibrosis or cirrhosis.[14] The pioneer ultrasound-based elastography technique, transient elastography (TE) using liver Fibroscan® is best known and has been validated against liver histology.[15] Shear wave elastography (SWE) is an emerging ultrasound (US)-based alternative for assessment of liver fibrosis.[16,17] Several studies have shown good correlation between TE and SWE-measured liver stiffness measurements (LSM).[18,19]

In Australia, there is limited understanding of the utility of SWE for assessment of liver fibrosis and clinically relevant chronic liver disease outcomes, such as cirrhosis and portal hypertension. Therefore, we aimed to compare the associations between SWE, TE and other markers of liver fibrosis in a group of patients with varied liver diseases against clinically relevant liver endpoints of liver fibrosis, sonographic and endoscopic portal hypertension. We hypothesised that: (i) liver elastography determined using SWE and TE are correlated; (ii) SWE may have diagnostic utility for staging of liver fibrosis in various liver diseases; and (iii) SWE is accurate for predicting the presence of liver-related portal hypertension.

Methods

This is a cross-sectional study relying on pre-existent data from liver ultrasound, SWE, TE, clinical and laboratory assessment, and endoscopic findings.

Study population

The study population comprised of serial adult patients attending liver ultrasound assessment at a tertiary/quaternary hospital Medical Imaging service between April 2015 and June 2019 (50 months). Liver ultrasound and SWE data were prospectively recorded. SWE assessment was performed concurrently with liver ultrasound examination on 421 patients with known or suspected liver disease. Inclusion criteria included age over 18 years and absence of a known acute hepatitis. Among these patients, 227 had also attended the Hepatology outpatient clinic and had liver TE examination. For comparison purposes, SWE and TE had to have been performed within 6 months of each other. To avoid the potential confounding of acute hepatitis we excluded data on 26 patients with serum ALT >150 U/L from statistical analyses, leaving 395 patients. Institutional approval to conduct this study was obtained from the South Metropolitan Health Service Governance, Evidence, Knowledge, Outcomes Committee that did not require written/informed consent because of the low-risk retrospective, non-interventional design of this study.

Patient clinical information

Patient age (years), gender, bodyweight (kg), height (cm) and derived body mass index (BMI; kg/m^2), alcohol history (per 10 g standard drink), liver disease aetiology and laboratory results were obtained from the clinical records. Laboratory results of relevance included serum liver biochemistry (alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin), alpha fetoprotein, blood platelet count, fasting serum glucose, glycosylated haemoglobin (HbA1c) and the liver fibrosis test Hepascore®.[20] Liver fibrosis risk scores were calculated, including AST/ALT ratio, AST to platelet ratio index (APRI)[21] and fibrosis-4 index (FIB-4).[22] The model for end-stage liver disease (MELD) score,[23] which is an accurate predictor of survival among different populations of patients with advanced liver disease, was calculated. Baveno VI criteria for exclusion of high-risk oesophageal varices (liver stiffness <20 kPa and a platelet count $>150 \times 10^9$ cells/L)[24] were adapted to SWE.

Liver ultrasound and SWE methodology

Liver ultrasound and SWE were performed by accredited liver sonographers. The sonographer relied on the information provided in the referral form and did not have access to additional clinical or laboratory results at the time of the ultrasound. 2D liver ultrasound was

performed with the patient having completed a minimum 4 h fast. The ultrasound examination was conducted using a Focussed Chronic Liver Disease ultrasound protocol. This requires assessment of hepatic size and echogenicity, presence or absence of hepatic vein wall and liver surface irregularity, exclusion of hepatic masses, splenic size, assessment for the presence of ascites and Doppler examination of the portal and splanchnic circulation for assessment of portal hypertension. This examination typically took 30 min scanning time and around 40 images were archived. 2D-SWE examination was performed using a Toshiba Aplio 500 or Canon Aplio i800 machine, concurrently with liver ultrasound examination. SWE was conducted in line with the World Federation for Ultrasound in Medicine and Biology guidelines,[16] that is, with the patient in a supine position, with the transducer positioned to visualise hepatic segments 5 or 8, with the capsule parallel to the transducer. The patient suspends respiration gently and an elastogram region of interest (ROI) is placed within homogenous hepatic tissue free of vessels and artefacts, at a distance ≥10 mm beneath the liver capsule. A 10-mm circular analysis ROI was placed within the elastogram at 4–5 cm depth from the skin, and a minimum of 3–5 successful measurements were recorded (Supporting Information Fig. S1). In line with manufacturer guidelines, a SWE propagation map was utilised as a quality indicator for the elastogram and analysis ROI placement. Examinations with a standard deviation (SD) of >20% were excluded from the SWE data, resulting in a liver stiffness to median interquartile range of ≤30%. The combined liver ultrasound and SWE took approximately 40 min. The skin-to-liver-capsule distance was measured in millimetres.

TE methodology

TE was performed on 227 patients by accredited hepatology registered nurses certified to perform TE, using Fibroscan® 502 Touch and either the M- or XL-probe, according to the manufacturer recommendations. Each hepatology nurse had experience with at least 500 TE assessments and had access to the patient anthropometry but not the results of the SWE. TE was performed with the patient in the supine position, preferably fasting for at least 2 h, and in mid-expiration. TE results were included in the final analysis if at least 10 valid measurements were obtained, with an interquartile range to LSM ratio ≤30%. Suspected advanced liver fibrosis was defined by an LSM interpreted as ≥F3 equivalent for different liver disorders using manufacturer cut-offs for Metavir staging. Liver fat quantification using the controlled attenuation parameter was measured.

Endoscopy

Upper gastrointestinal endoscopy was performed on 250 patients at the discretion of the managing hepatologist for screening or surveillance for varices as part of routine care. The presence or absence of portal hypertensive gastropathy and oesophageal varices noted during endoscopy was recorded. High-risk oesophageal varices were defined as those needing treatment due to size or high-risk stigmata (i.e. Grade II/III or Grade I with high-risk stigmata). Overall, 151 (38%) patients had a complete dataset of ultrasound, SWE, TE and endoscopy.

Statistical analysis

Associations between SWE, TE and patient factors were sought. Continuous descriptive data are summarised as means (SD) or median (interquartile range). The main outcome variables are advanced liver fibrosis (≥F3) based on TE as reference and the presence of portal hypertension determined by ultrasound or endoscopy. Differences in anthropometric, laboratory and calculated blood-based liver fibrosis test scores between those with and those without advanced liver fibrosis were computed with the independent *t*-test for parametric variables and the Mann–Whitney *U*-test for non-parametric variables. Correlations were examined between the various liver fibrosis measures, using Spearman's correlation coefficient. Multivariable logistic regression analysis was used to calculate the odds of advanced liver fibrosis, portal hypertension or varices. The area under the receiver operating characteristics curve (AUROC) was used to predict the probability of a patient having significant, advanced fibrosis or cirrhosis or portal hypertension based on different non-invasive fibrosis tests. The DeLong test was used to compare differences in the AUROC. All *P*-values were two-sided and were interpreted at the 5% level of significance. Data were analysed using IBM SPSS statistics for Windows (version 25.0; IBM Corp., Armonk, NY, USA) and MedCalc (version 19.8; MedCalc Software Ltd, Ostend, Belgium).

Results

Patient characteristics

Three hundred and ninety-five patients (68% male) had SWE performed concurrently with liver

Table 1 Comparison of patient characteristics between patients with or without significant liver fibrosis diagnoses with shear wave elastography (SWE)

Characteristic	SWE subgroup					Transient elastography (TE) subgroup				
	n	SWE subgroup ($n = 395$)	SWE fibrosis F0–F2 ($n = 189$)	SWE fibrosis ≥F3 ($n = 206$)	*P*-value	*n*	TE subgroup ($n = 218$)	TE fibrosis F0–F2 ($n = 114$)	TE fibrosis ≥F3 ($n = 104$)	*P*-value
Age (years)	395	53.7 (13.0)	48.7 (13.6)	58.0 (11.6)	<0.001	218	54.5 (11.3)	51.8 (12.4)	57.5 (9.2)	<0.001
BMI	302	27.9 (6.2)	26.2 (5.5)	29.3 (5.9)	<0.001	210	28.0 (5.4)	26.6 (4.9)	29.5 (5.6)	<0.001
SWE (kPa)	395	9.9 (6.4–20.0)	6.2 (5.0–7.6)	19.4 (13.4–31.5)	<0.001	218	9.7 (6.6–16.8)	6.8 (4.9–8.7)	16.1 (11.8–25.7)	<0.001
TE (kPa)	218	9.2 (5.7–21.2)	6.2 (4.6–8.6)	19.7 (11.8–34.6)	<0.001	218	9.2 (5.8–20.9)	6.0 (4.5–7.3)	21.4 (14.2–35.3)	<0.001
CAP (dB/m)	193	254 (212–301)	235 (198–273)	267 (230–321)	<0.001	196	245 (207–303)	237 (199–276)	269 (228–324)	0.001
Skin to capsule (mm)	376	20.3 (7.2)	17.7 (5.1)	22.0 (8.0)	<0.001	218	19.8 (6.2)	18.4 (4.8)	21.4 (7.2)	<0.001
ALT (U/L)	378	39.6 (26.1)	38.6 (24.4)	39.5 (28.6)	0.75	218	39.1 (26.6)	36.2 (18.5)	43.5 (28.5)	0.03
AST (U/L)	219	47.6 (30.9)	38.5 (19.3)	53.8 (36.4)	0.001	147	48.1 (31.9)	32.0 (10.2)	49.5 (27.4)	<0.001
Albumin (g/L)	378	39.1 (7.2)	41.4 (4.4)	37.6 (6.0)	<0.001	214	39.4 (5.7)	42.0 (3.8)	39.9 (4.9)	0.001
Platelet count ($\times 10^9$/L)	377	202 (90)	226 (92)	167 (83)	<0.001	214	197 (87)	223 (63)	166 (69)	<0.001
AST/ALT	219	1.1 (0.8–1.6)	0.9 (0.8–1.2)	1.3 (1.0–1.8)	<0.001	147	1.1 (0.8–1.6)	0.9 (0.7–1.2)	1.2 (0.9–1.6)	<0.001
APRI	219	0.6 (0.3–1.1)	0.4 (0–3–0.6)	0.8 (0.4–1.3)	<0.001	147	0.6 (0.3–1.1)	0.4 (0.3–0.4)	0.7 (0.4–1.2)	<0.001
FIB-4	219	2.2 (1.4–4.0)	1.3 (1.0–1.8)	3.0 (1.9–4.5)	<0.001	147	2.2(1.4–3.8)	1.3 (1.0–1.6)	2.5 (1.8–4.6)	<0.001
Hepascore	173	0.9 (0.3–1.0)	0.5 (0.2–0.9)	1.0 (0.9–1.0)	<0.001	144	0.9 (0.4–1.0)	0.4 (0.2–0.9)	1.0 (0.9–1.0)	<0.001
AFP (kU/L)	274	3.0 (2.0–4.0)	2.0 (2.0–3.0)	3.0 (2.0–5.0)	0.001	190	3.0 (2.0–4.0)	2.0 (2.0–3.0)	3.0 (2.0–5.0)	<0.001
MELD score	273	7.0 (6.0–10.0)	7.0 (6.0–7.0)	7.0 (6.0–12.0)	<0.001	86	7.0 (6.0–7.0)	6.0 (6.0–6.7)	7.0 (6.0–7.0)	0.12

Data are presented as numbers, mean (standard deviation) or median (interquartile range). *P*-values <0.05 are considered statistically significant. ALT, alanine aminotransferase; APRI, AST to platelet ratio index; AST, aspartate aminotransferase; BMI, body mass index; CAP, controlled attenuation parameter; FIB-4, fibrosis-4 index; SWE, shear wave elastography; TE, transient elastography.

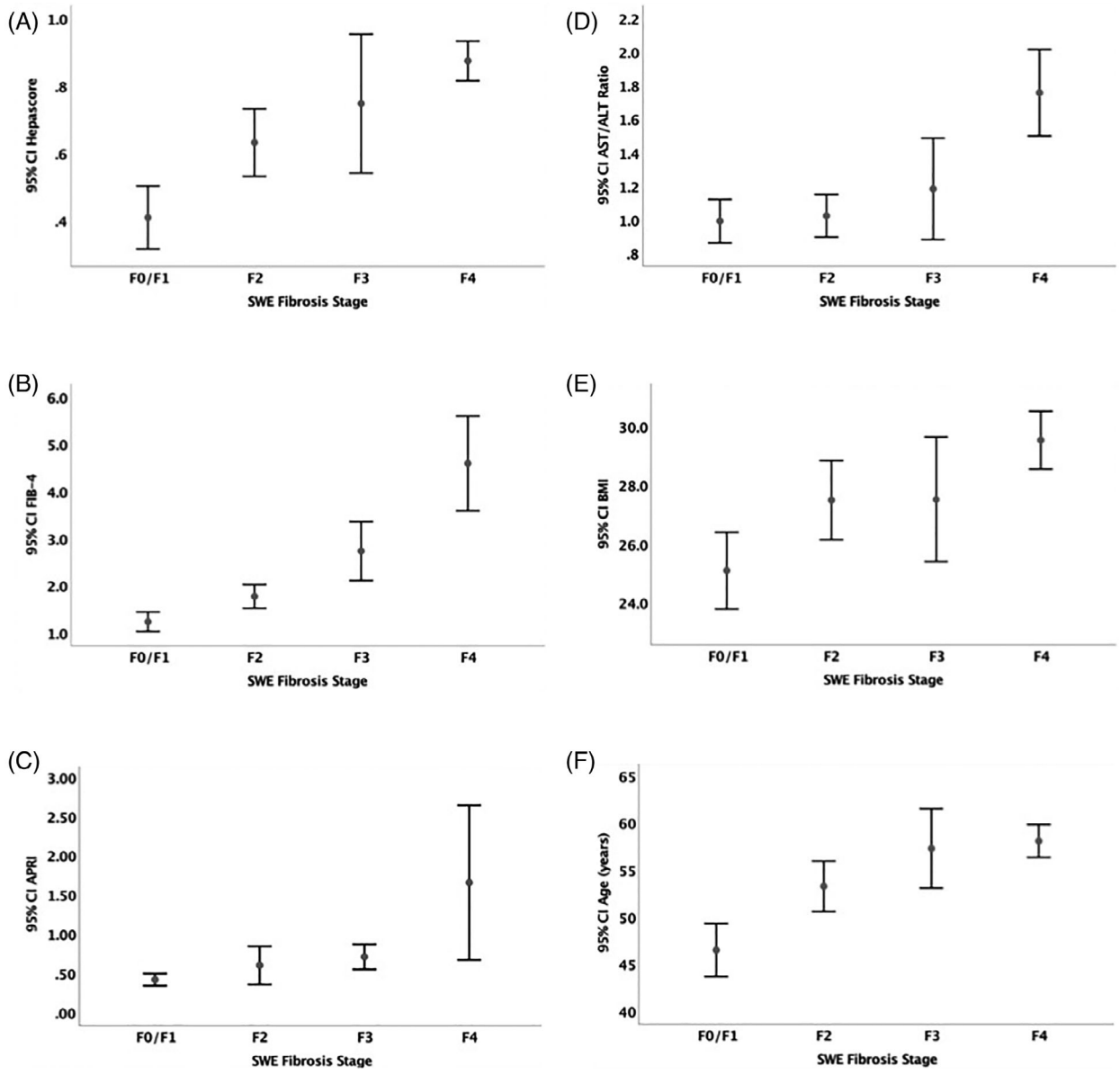


Figure 1 Relationship between shear wave elastography (SWE) liver stiffness measurement and age, body mass index (BMI) and other risk factors for liver fibrosis. Error bars represent the means and standard deviations. ALT, alanine aminotransferase; APRI, AST to platelet ratio index; AST, aspartate aminotransferase; CI, confidence interval; FIB-4, fibrosis-4 index.

ultrasound. Males and females had similar mean age and BMI. Indications for the assessments included NAFLD (10%), chronic hepatitis B (24%), chronic hepatitis C virus infection (37%), alcohol-related liver disease (18%) and others (11%). The mean (SD) age was 54 (13) years, BMI 28 (6) kg/m^2, ultrasound-measured skin to liver capsule distance 20 (7) mm, serum ALT 40 (26) U/L and AST 48 (32) U/L (Table 1). Characteristics of patients in the SWE and TE subgroups are summarised in Table 1.

Liver stiffness measurement

Reliable TE measurements were obtained in 218 of 227 (96%). The median (interquartile range) LSM using SWE was 9.9 (6.4–20.0) kPa and with TE was 9.2 (5.8–20.9) kPa. Using TE, one-quarter of patients were diagnosed with F2/F3 liver fibrosis (Fig. S2). There was a strong positive correlation between SWE and TE LSM (Table S1). Increasing age, liver fibrosis severity determined by FIB-4, Hepascore, APRI and AST/ALT ratio were all associated with increasing SWE severity of

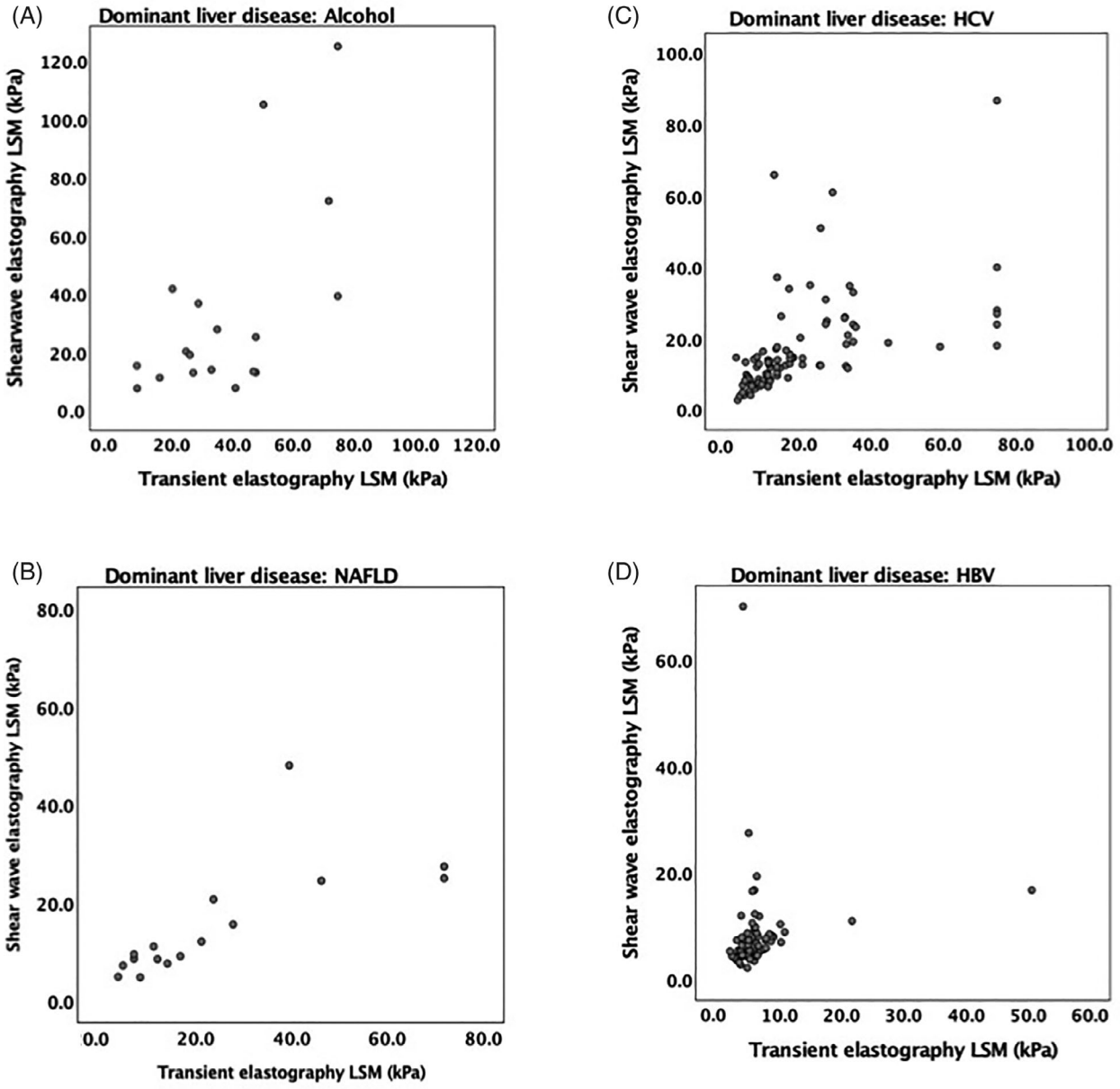
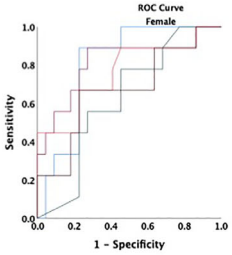


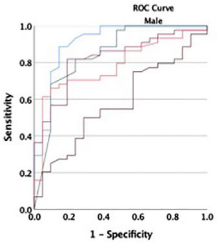
Figure 2 Correlations between shear wave elastography and transient elastography liver stiffness measurement (LSM) in different liver disorders: alcohol ($r = 0.53$, $P = 0.03$); non-alcoholic fatty liver disease (NAFLD) ($r = 0.87$, $P < 0.001$); hepatitis C virus (HCV) ($r = 0.76$, $P < 0.001$); hepatitis B virus (HBV) ($r = 0.50$, $P < 0.001$).

liver fibrosis (Fig. 1). Both SWE and TE-LSM were positively correlated with skin to liver capsule distance, BMI, amount of alcohol consumed, AST, AFP, AST/ALT ratio, APRI and FIB-4, and negatively correlated with platelet count and albumin. The strength of correlation between SWE and TE varied by aetiology of liver disease: alcohol ($r = 0.53$, $P = 0.03$); hepatitis B virus ($r = 0.50$, $P < 0.001$); hepatitis C virus (HCV) ($r = 0.76$, $P < 0.001$); NAFLD ($r = 0.87$, $P < 0.001$) (Fig. 2).

Using SWE, patients with advanced liver fibrosis were older, had more general adiposity (BMI), subcutaneous adiposity (skin to liver capsule distance), liver fat and higher serum AST, but lower serum albumin and blood platelet count compared with those without advanced liver fibrosis ($P < 0.005$ for all). The levels of all blood-based

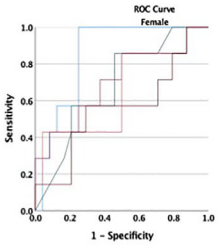
(A)

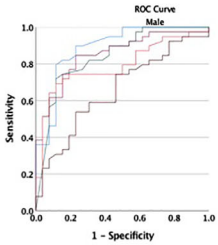




	Female			Male		
Test	**AUROC**	**95% CI**	***P* value**	**AUROC**	**95% CI**	***P* value**
SWE	0.80	0.62–0.92		0.91	0.81–0.97	
Hepascore	0.62	0.43–0.79	0.12	0.85	0.74–0.93	0.31
FIB-4	0.81	0.63–0.93	0.93	0.82	0.71–0.91	0.17
APRI	0.77	0.58–0.90	0.80	0.78	0.66–0.87	0.04
AST/ALT	0.67	0.48–0.83	0.34	0.58	0.45–0.70	0.0003

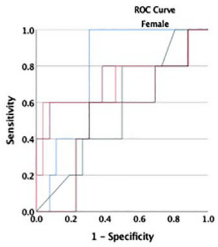
(B)

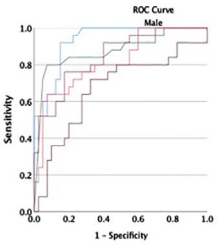




	Female			Male		
Test	**AUROC**	**95% CI**	***P* value**	**AUROC**	**95% CI**	***P* value**
SWE	0.85	0.69–0.95		0.89	0.79–0.95	
Hepascore	0.68	0.49–0.84	0.13	0.84	0.73–0.92	0.42
FIB-4	0.71	0.52–0.86	0.26	0.85	0.74–0.93	0.54
APRI	0.65	0.45–0.81	0.16	0.79	0.67–0.88	0.12
AST/ALT	0.55	0.36–0.73	0.02	0.66	0.53–0.77	0.008

(C)





	Female			Male		
Test	**AUROC**	**95% CI**	***P* value**	**AUROC**	**95% CI**	***P* value**
SWE	0.78	0.59–0.91		0.93	0.84–0.98	
Hepascore	0.57	0.38–0.75	0.08	0.88	0.77–0.94	0.22
FIB-4	0.73	0.54–0.87	0.77	0.85	0.74–0.94	0.13
APRI	0.73	0.54–0.87	0.76	0.81	0.70–0.90	0.06
AST/ALT	0.53	0.34–0.71	0.07	0.67	0.54–0.78	0.002

Figure 3 Diagnostic ability of various tests for (A) transient elastography (TE) significant fibrosis (≥F2); (B) TE advanced liver fibrosis (≥F3); (C) TE-diagnosed cirrhosis (F4). Tables display area under the receiver operating characteristics curve (AUROC) and 95% confidence intervals (CI). *P*-values compare shear wave elastography (SWE) AUROC with AUROC for Hepascore, fibrosis-4 index (FIB-4), AST to platelet ratio index (APRI) and aspartate aminotransferase/alanine aminotransferase (AST/ALT) ratio.

liver fibrosis tests (Hepascore, APRI, FIB-4) were higher in patients with liver fibrosis compared with those without liver fibrosis ($P < 0.001$). There was no difference in serum ALT between patients with or without advanced liver fibrosis (Table 1) and no significant correlation between SWE LSM and serum ALT (Table S1).

Prediction of liver fibrosis/cirrhosis

Using multiple logistic regression analysis, independent predictors of TE-diagnosed advanced liver fibrosis were SWE-LSM ≥F3 (odds ratio (OR) 10.02; 95% confidence interval (CI) 3.75–26.76), FIB-4 (OR 3.35; 95% CI 1.70–6.62) and male gender (OR 2.85; 95% CI 1.03–7.95) (after adjusting for other covariates that were statistically significant in univariate analysis). SWE-LSM (OR 1.07; 95% CI 1.02–1.12) and FIB-4 (OR 3.67; 95% CI 2.09–6.44) were also associated with cirrhosis, after adjusting for age, Hepascore, APRI, AST/ALT ratio and serum AFP. Within each gender the AUROC for diagnosing advanced liver fibrosis or cirrhosis was not significantly different, comparing SWE, Hepascore, FIB-4 and APRI. In contrast, AST/ALT ratio provided weaker discrimination for all stages of liver fibrosis, particularly in males (Fig. 3).

There was 87.9% agreement regarding a cirrhosis diagnosis, comparing SWE and TE. There was no significant difference in ability of TE and SWE to predict varices. TE-AUROC 0.80 (95% CI 0.72–0.86) versus SWE-AUROC 0.84 (95% CI 0.77–0.90), *P*-value for difference in AUROC = 0.21.

Portal hypertension

We found a strong association between SWE-LSM and the presence or absence of portal hypertension. In particular, increasing SWE-LSM predicted the presence of portal hypertension and high-risk oesophageal varices diagnosed with ultrasound and endoscopy respectively (Table 2). SWE-LSM had an AUROC of 0.82 (95% CI 0.76–0.92) for any varices and 0.68 (95% CI 0.49–0.87) for high-risk oesophageal varices.

Baveno VI criteria

The Baveno VI criteria, adapted to SWE, were fulfilled by 74.2% of patients and associated with a low likelihood of detecting high-risk oesophageal varices during endoscopy (odds ratio 0.18; 95% confidence interval 0.05–0.61), sensitivity 78.6%, specificity 66.1%%, negative predictive value (NPV) 96.1% and positive predictive value (PPV) 22.4%. This equates to Baveno VI criteria missing approximately 4% of high-risk varices.

Discussion

In this population of adults with various liver disorders, we found SWE and TE results to be highly correlated, confirming existent literature.[18,19] The strength of the association varied by chronic liver disease aetiology, being highest for NAFLD and chronic HCV infection, as previously observed.[25] The applicability and diagnostic accuracy of 2D SWE has previously been shown to closely resemble that of TE (AUROC 0.80–0.92 for oesophageal varices),[26] which is confirmed in the present study. SWE has been shown to have high diagnostic accuracy for staging liver fibrosis in adults with NAFLD.[27] SWE is comparable with MRE for diagnosing advanced liver fibrosis but has lower accuracy for significant fibrosis.[28] MRE is limited by availability and cost, while SWE is limited by heterogeneity in interpretation of results. Different estimates of shear wave speed (SWS) are obtained with different ultrasound manufacturer systems and at different depths for each system, reducing comparability of results. TE-measured LSM is positively correlated with the hepatic venous pressure gradient, with LSM values >20–25 kPa being highly specific for clinically significant portal hypertension.[29] There has been a paucity of data regarding associations between SWE-measured LSM and portal hypertension, with studies finding variable applicability for reducing rates of endoscopic variceal screening.[30–32] The gender difference in associations of SWE-LSM with liver fibrosis may impact the interpretation of SWE results in everyday use and warrants further examination.

Reduced SWE availability, standardisation, reproducibility and understanding of results has limited its utility. However, SWE has been demonstrated to have better diagnostic performance than serum fibrosis indices (APRI, FIB-4, Forns score, King's score, FibroIndex, red cell distribution width-to-platelet ratio, Hepascore, type IV collagen and hyaluronic acid).[33,34] SWE prediction of significant fibrosis, advanced fibrosis and cirrhosis was similar to that of Hepascore, FIB-4 and APRI. Age and

Table 2 Association between SWE LSM and portal hypertension

SWE LSM (kPa)	Clinical characteristic	Unadjusted odds ratio	95% confidence interval
≥22.0	Ultrasound portal hypertension	9.49	5.08–17.71
≥25.0	Endoscopic portal hypertensive gastropathy	8.41	4.41–16.07
≥27.2	High-risk oesophageal varices	7.62	2.30–25.20

Data are presented as odds ratios and 95% confidence intervals for associations between SWE LSM and features of portal hypertension. LSM, liver stiffness measurement; SWE, shear wave elastography.

BMI were associated with increasing SWE liver fibrosis Metavir stages. SWE-LSM was also associated with risk measures for chronic liver disease severity, including portal hypertension, platelet count, serum albumin and the MELD score, making SWE-LSM a clinically useful tool for establishing chronic liver disease severity. While serum AST and blood-based liver fibrosis tests that utilised AST were positively associated with elastography-diagnosed liver fibrosis, liver biochemistry incorporating serum ALT without AST was not significantly associated with liver fibrosis.

Concordant with the literature,[31,35] SWE-LSM noninvasively predicted the likelihood of portal hypertension determined by ultrasound and endoscopy. SWE-LSM was useful for diagnosing the likelihood of CSPH with oesophageal varices. Other studies have shown that favourable Baveno VI status using TE is unlikely to be associated with oesophageal varices in patients with advanced chronic liver disease.[24,35] Our findings are consistent with those observations but extend the relevance to include different severities of liver fibrosis and also portal hypertension determined by ultrasound and endoscopy. We have shown that SWE-LSM used alone when the platelet count is unavailable, as well as when utilised as a part of the Baveno VI criteria, has predictive value for portal hypertension and varices. We did not find either TE or SWE to be superior for determining the study outcomes. However, SWE performed as well or better than blood-based assessments.

Strengths of the present study include the large study population size and patient characterisation using liver ultrasound, SWE, TE, anthropometry, endoscopy, and blood test results, including blood-based liver fibrosis tests. These have allowed comparisons for clinically relevant outcomes in a population with various liver disorders, abnormalities in liver biochemistry and liver fibrosis severities. Limitations of the present study include ascertainment bias of the TE + 2D-SWE subset. Since TE was performed in a random selection of patients having SWE, there is a risk of spectrum bias. TE and SWE measurements were sometimes performed under different conditions up to 6 months apart. Although all patients were fasting for at least 4 h for SWE, fasting was not universally fulfilled for TE. There could also have been interventions such as alcohol cessation, weight changes or antiviral treatment between one assessment and the other. We also did not have liver histology. However, liver biopsy is invasive and was not deemed necessary for clinical management in the majority of patients, given the detailed biochemical and imaging characterisation of the patients. It is plausible that adiposity from abdominal subcutaneous fat thickness, hence the skin to liver capsule distance or hepatic steatosis may have contributed to the combined association between SWE and TE-determined significant fibrosis.[16] However, this is less relevant to our study, because although the mean SCD was 21.5 mm, we excluded unreliable measurements with SD >20%. Similarly, we excluded patients with liver biochemistry evidence of acute hepatitis. Therefore, an impact of these on LSM in our study would not be expected to result in clinically relevant diagnostic uncertainty. Further, the ultrasound descriptions of portal hypertension and the endoscopic descriptions of portal hypertensive gastropathy and varices were based on the proceduralist report, hence potentially subjective and creating some bias. Despite these limitations, SWE and TE results were significantly correlated. Overall, SWE results have a potential diagnostic and therapeutic consequence for management of patients with chronic liver disease.

Conclusion

In conclusion, SWE is a useful addition to the physician's armamentarium for assessing the severity of suspected liver fibrosis in various liver disorders. SWE-LSM results were found to correlate with TE-LSM plus relevant clinical and laboratory measures of chronic liver disease. SWE-LSM performs equivalently or better than blood-based tests of liver fibrosis, with possible gender differences. SWE LSM >22 kPa was associated with a high likelihood of cirrhosis-related portal hypertension in our study. Further studies examining gender differences in SWE are required.

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Supporting Information

Additional supporting information may be found in the online version of this article at the publisher's web-site:

Figure S1. B mode liver ultrasound with SWE elastogram and propagation map. A 10-mm analysis ROI is utilised.
Figure S2. Distribution of liver fibrosis stages based on transient elastography.
Table S1. Correlations between SWE LSM and other patient variables. There were significant associations between SWE LSM and patient age, adiposity and measures of liver fibrosis or chronic liver disease, but not serum ALT.