Radiology

Quantitative Elastography of Liver Fibrosis and Spleen Stiffness in Chronic Hepatitis B Carriers: Comparison of Shear-Wave Elastography and Transient Elastography with Liver Biopsy Correlation[1]

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Purpose: To document utility of shear-wave (SW) elastography for assessing liver fibrosis in chronic hepatitis B and to compare its performance with that of transient elastography.

Materials and Methods: Ethics committee approved the study, and informed consent was obtained. Patients with liver biopsy correlation (n = 226) and healthy patients (n = 171) were analyzed. Results of SW elastography of liver, SW elastography of spleen, and transient elastography of liver were compared and correlated according to METAVIR scores. Areas under the receiver operating characteristic curve (AUCs), binary logistic regression, and Delong test were used.

Results: AUC for SW elastography of liver, transient elastography of liver, and SW elastography of spleen was, respectively, 0.86, 0.80, and 0.81 for fibrosis (≥F1 stage); 0.88, 0.78, and 0.82 for moderate fibrosis (≥F2 stage); 0.93, 0.83, and 0.83 for severe fibrosis (≥F3 stage); and 0.98, 0.92, and 0.84 for cirrhosis (F4 stage). SW elastography of liver showed significantly higher accuracy than transient elastography of liver and SW elastography of spleen in all fibrosis stages (P = .01–.04). SW elastography of spleen showed similar accuracy with transient elastography of liver (P = .21–.99). Combination SW elastography of liver and SW elastography of spleen to predict fibrosis staging showed diagnostic accuracy not further improved compared with SW elastography of liver alone (similar AUC; ≥F1, P = .87; ≥F2, P = .81; ≥F3, P = .84; ≥F4, P = .88). SW elastography of liver had higher successful rate than transient elastography of liver (98.9% vs 89.6%). Prevalence of discordance in at least two stages with liver histologic staging was 10.2% (23 of 226) for SW elastography of liver and 28.2% (58 of 206) for SW elastography of spleen.

Conclusion: SW elastography provides more accurate correlation of liver elasticity with liver fibrosis stage compared with transient elastography, especially in identification of stage F2 or greater.

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Patients with chronic hepatitis B are at increased risk of cirrhosis. Assessment of fibrosis has important prognostic implications that guide clinical therapy (1,2). Though liver biopsy is still the reference standard for diagnosis and grading of fibrosis, it is invasive and carries risk of complications.

Ultrasonography (US) provides ideal noninvasive assessment for diffuse liver disease because of its low cost and wide availability. Conventional B-mode US is good for diagnosis of advanced cirrhosis, but is insensitive for fibrosis (3). Elastography can act as a surrogate diagnostic marker of fibrosis. Currently, transient elastography (FibroScan; Echosens, Paris, France), shear-wave (SW) elastography, and acoustic radiation force impulse imaging are the three main techniques that allow direct and indirect quantification of liver stiffness (1–6). Among these technologies, transient elastography is the most widely used but shows unreliable results in 15.8% of cases (7).

Magnetic resonance (MR) elastography is based on the use of SW elastography induced in tissues by external surface vibrators. MR elastography also showed promising results for quantification of liver fibrosis with high accuracy (8–10). However, MR elastography has limitations. It is imprecise for detection of early levels of fibrosis and for quantitation of intermediate levels of fibrosis. There is overlap between adjacent stages of fibrosis, especially in the precirrhotic stage of liver disease. The difference is small in grade F0–F2 fibrosis, but it is larger in grades F3 and F4 (10,11). The acquisition time for MR elastography is long (10–15 minutes), and therefore it is limited to static organs and precludes freehand applicability (12). Technically, the delivery of SW elastography by MR elastography into the abdomen may be imperfect, and it may lead to error in interpretation and calculation (11).

SW elastography permits absolute quantification of tissue stiffness in terms of pressure unit of kilopascals versus a semiquantitative estimate that corresponds to relative tissue strain (6).

The purpose of this study was to document the utility of SW elastography for assessment of liver fibrosis in chronic hepatitis B and to compare its performance with that of transient elastography.

Advances in Knowledge

- Shear-wave (SW) elastography shows better correlation with histologic staging in assessment of liver fibrosis when compared with transient elastography and has more accurate detection and classification of early fibrosis (P = .001–.04).
- SW elastography of the spleen shows change in stiffness in accordance with severity of liver fibrosis (r = 0.67; $P < .001$).
- SW elastography is a sensitive tool for screening, with sensitivity that ranged from 83.5% to 97.4% at various fibrosis stages.

Materials and Methods

Patients

Ethics committee approved the study and informed consent was obtained from all patients. Between April 2011 and March 2012, 454 consecutive patients with chronic viral hepatitis B, verified with serologic testing, were prospectively recruited. All patients were aged 18 years or older and did not receive any antiviral or antifibrotic therapy. Patients with liver tumor, clinically overt liver failure, or gross ascites were excluded. Patients who could not get satisfactory SW elastography of the liver or transient elastography liver readings (n = 52) were excluded from the analysis. The reasons for failure in both techniques were recorded. Of the remaining 402 patients, 226 underwent liver biopsy within 12 months of elastographic imaging and formed the final cohort (Table 1). A previous study (4) showed that an interval between biopsy and study inclusion of up to 15 months was acceptable,and the expected changes were minimal. In our study, 176 did not undergo biopsy either because of patient refusal or lack of clinical indications.

In addition, 171 healthy control patients were recruited. These were hospital staff or their relatives older than 18 years. They were all volunteers who had no substantial past medical history, including diabetes or hypertension. They had no substantial alcohol intake (defined as <30 g alcohol daily for men, <20 g for women), negative hepatitis B and hepatitis C serology, and no biochemical or US features of liver or splenic disease. They had no history of chronic drug use or substance abuse.

For all patients and healthy control patients, anthropometric tests were measured that included body weight and height, body mass index, waist and hip circumference, and systolic and diastolic blood pressure. Venous blood samples were obtained after fasting for 12 hours. Blood profile tests that were performed included alanine aminotransferase, aspartate aminotransferase, γ-glutamyltransferase, alkaline

Implications for Patient Care

- SW elastography is an accurate noninvasive method for assessing liver fibrosis.
- Screening for fibrosis can be performed by SW elastography, thus reducing the risk from biopsy.

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Abbreviations:
AUC = area under receiver operating characteristic curve
ICC = intraclass correlation coefficient
SW = shear wave

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Conflicts of interest are listed at the end of this article.

Table 1

Summary of Demographic Data, Blood Test, and Histologic Results in Patients with Chronic Hepatitis B (Index Patients) and Healthy Volunteers (Control Patients)

Parameter	Healthy Control Patients (*n* = 171)	Index Group Patients (n = 226)	*P* Value
No. of men*	68 (40)	146 (65)	.001
No. of women*	103 (60)	80 (35)	.001
Mean age (y)†	40.6 ± 10.8	48.8 ± 12.3	.31
Median no. of men‡	40.4 (16.2–61.3)	48.6 (22.7–78.3)	.02
Median no. of women‡	41.6 (19.2–67.2)	48.9 (25.1–87.2)	.52
Mean body weight (kg)†	65.8 ± 12.5	69.5 ± 18.6	.58
Median body mass index (kg/m^2)‡	22.9 (20.8–24.3)	24.2 (21.6–27.3)	.18
Mean waist circumference (cm)†	78 ± 8	85.9 ± 12.6	.05
Median hip circumference (cm)‡	88 (85–93)	94 (90.2–101.5)	.06
No. of patients with hypertension*	0 (0)	78 (33)	…
Median fast blood sugar (mmol/L)‡	4.8 (4–6)	5.2 (4.8–6)	.22
Median HbA1c (%)‡	5.3 (4.9–6)	6.0 (5.7–6.6)	.42
Mean total cholesterol (mmol/L)†	5 ± 0.8	5.0 ± 1.0	.72
Median alanine aminotransferase (IU/L)‡	36 (26.3–70.2)	69.0 (37.5–105)	.004
Median triglyceride (mmol/L)‡	1.2 (0.8–1.5)	1.2 (0.9–1.6)	.91
Mean hemoglobin (g/dL) †	12.6 ± 0.9	14.4 ± 1.4	.51
Median total bilirubin (μmol/L)‡	5 (4–8)	12 (9–16)	.22
Median aspartate aminotransferase (IU/L) ‡	24 (15–52)	48.6 (20–108)	.003
Median γ-glutamyltransferase (U/L) ‡	13.6 (6.8–30.3)	7.34 (14.2–125.4)	.004
Mean alkaline phosphatase (IU/L)†	58 ± 21.7	119 ± 52.3	.04
Mean platelet count (× 10^9/L)†	174.2 ± 60.9	194.2 ± 54.5	.58
HBe antigen: positive (%)	0	100	…
Mean HBV-DNA (log IU/mL)†	…	5.6 ± 3.1	…
Histologic fibrosis stage (no. of patients)*			
F0	…	38 (17)	…
F1	…	52 (23)	…
F2	…	56 (25)	…
F3	…	45 (20)	…
F4	…	35 (15)	…

* Data in parentheses are percentages.

† Data are ± standard deviation.

‡ Data in parentheses are interquartile range.

phosphatase, platelet count, glucose, total cholesterol, HbA1c and triglycerides, total bilirubin, and hemoglobin (Table 1). SW elastography of the liver and spleen and transient elastographic imaging of the liver were performed on the same day. All operators were blinded to the clinical data and one another's findings.

SW Elastographic Imaging

All patients underwent SW elastography examination by using a curvilinear transducer (bandwidth, 6–1 MHz) (Aixplorer; SuperSonic Imagine, Aix-en-Provence, France). Patients were instructed to relax and hold their breath in the natural breathing cycle (neither full inspiration nor expiration) while measurements were taken. Breathing rehearsals were allowed before the actual scanning to avoid variation between patients. For the liver, all patients were studied in right decubitus position with right arm extended above head. For the spleen, they were studied either supine or by lying in the left decubitus position with left arm extended above the head. Different positioning for the spleen was to obtain the maximum scanning area and avoid gas shadowing from the lung.

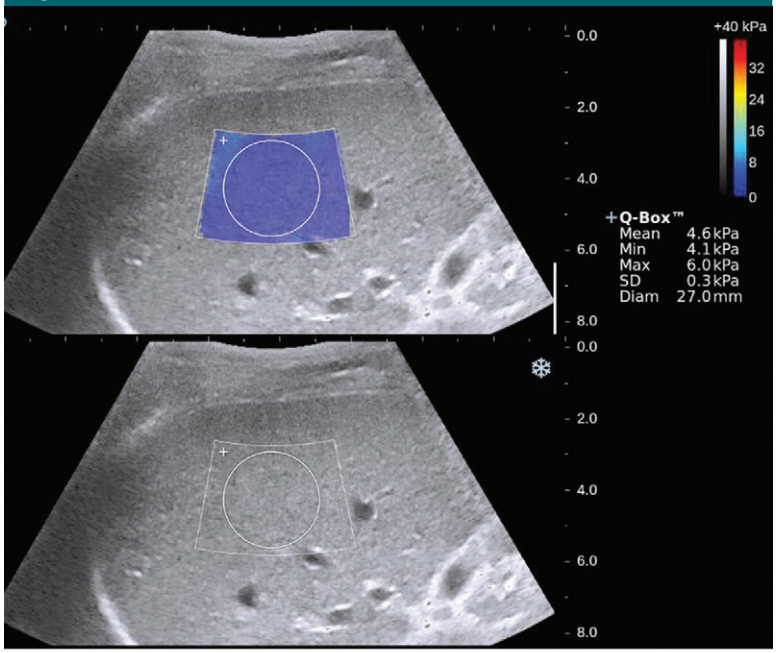
All SW elastographic examinations were performed by a single sonographer (V.Y.L., >20 years of experience). SW elastography of the liver was performed on segment VIII of the liver over three consecutive intercostal spaces (ranged from either sixth to eighth or seventh to ninth intercostal spaces, depending on the habitus of the patients). They were assigned as anterior, mid, and posterior sections. SW elastography of the spleen was measured at a single intercostal space with the best visualization of spleen.

SW elastography was performed in dual mode (ie, elastograms displayed alongside gray-scale sonograms in real time). The operator chose the best static SW elastographic display images onto which a rectangular electronic region of interest (3 × 4 cm for SW elastography of the liver and 2 × 3 cm for SW elastography of the spleen, which could be adjusted to a smaller size to fit patients with narrow intercostal spaces) and a circular region of interest (placed within the center of the rectangular region of interest) for analysis were positioned within 1–3 cm and 0.5–2 cm, respectively, from the capsular surface of the liver and spleen (Fig 1). Once the optimal sizes of the regions of interest were chosen, they were fixed for subsequent measurement in each subject. Special attention was paid to avoid any focal lesion, vessels, biliary tracts, or artifacts from nearby lung gas or cardiac movement. From the circular region of interest, the mean, standard deviation, and minimum and maximum kilopascal values were recorded. The average values from the three readings in each organ were used for subsequent statistical analysis.

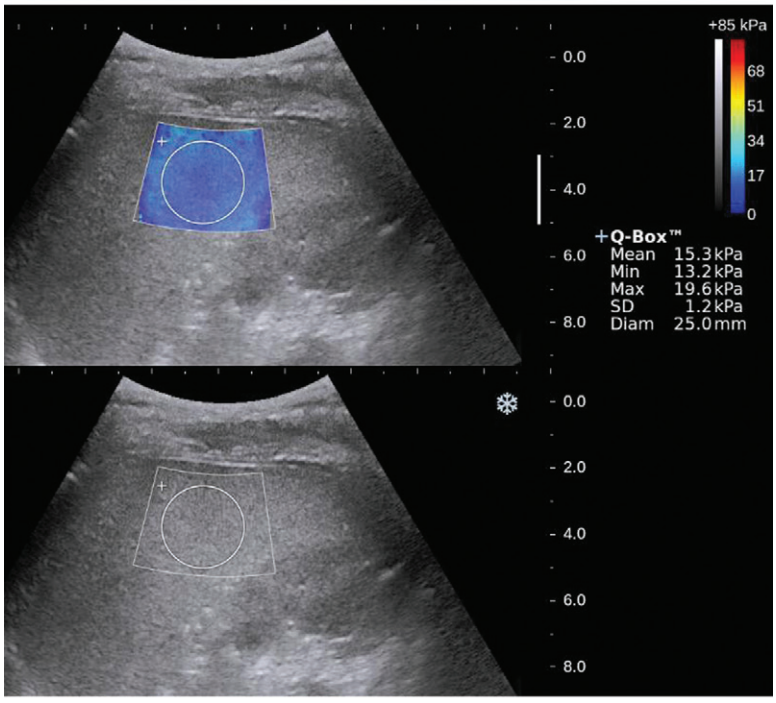
Tests of Reproducibility and Observer Variability

The reproducibility and degree of agreement of measurements for SW elastography of the liver were compared among three operators (V.Y.L., W.C.C. [radiologist with >20 years of experience] and J.A. [radiologist with >15 years of experience]) in 21

Figure 1



a.



b.

Figure 1: Real-time SW elastographic images of **(a)** liver and **(b)** spleen overlaid on gray-scale images in a healthy 40-year-old man. Rectangular and circular regions of interest are positioned. The color scale shows the distribution of the measured elasticity within the rectangular region of interest. Since liver and spleen are mostly soft (low kPa value), the majority of the color is blue. *Min* = minimum, *Max* = maximum, *SD* = standard deviation, and *Diam* = diameter.

randomly selected patients (10 healthy patients and 11 patients who had hepatitis B). To determine the intraobserver error, three measurements were obtained for one intercostal space by each operator. Three intercostal spaces per subject were assessed, giving a total of nine measurements for analysis. To determine interobserver error, the mean values from all intercostal measurements were compared between operators.

Transient Elastography

Following SW elastography, patients underwent transient elastographic imaging of the liver (FibroScan; Echosens). Transient elastography was performed by a single operator (S.H.C., research nurse with >5 years of experience). Transient elastography liver measurement was taken at either the seventh or eighth intercostal space of each subject over the right lobe of the liver. The measuring depth ranged from 2.5 to 6.5 cm below the skin surface. Only transient elastography results obtained with 10 valid measurements, with a success rate of at least 60% and an interquartile range of 30% or lower, were considered reliable (13,14).

Liver Histology

Liver biopsy (length, >15 mm) was performed in the right lobe of the liver by using a 16-gauge needle (Temno; CareFusion, San Diego, Calif) (13). All histologic slides were read by single pathologist (A.W.C., >10 years of experience).

Histologic staging of fibrosis was based on the METAVIR scoring system and divided into the following five stages: F0, no fibrosis; F1, early fibrosis (ie, portal fibrosis without septa); F2, moderate fibrosis (ie, portal fibrosis with rare septa); F3, severe fibrosis (ie, numerous septa without cirrhosis); and F4, cirrhosis (15). We considered grades of F2 or higher to indicate substantial fibrosis.

Statistical Analysis

Statistical tests were performed by using statistical software (Predictive Analytics Software version 18.0; SPSS,

Chicago, Il). Data were first tested for normality by using a one-sample Kolmogorov-Smirnov test. Data were expressed as mean ± standard deviation or median (interquartile range) as appropriate. Spearman correlation coefficients were used to analyze the correlation between SW elastographic imaging of the liver, transient elastographic imaging of the liver, and SW elastographic imaging of the spleen with histologic fibrosis stage. One-way analysis of variance with post hoc test (multiple range tests) was used to evaluate the level of significance of the difference in SW elastography among fibrosis stages. Receiver operating characteristic curves were constructed to assess which liver section (anterior, mid, or posterior) showed the best accuracy for prediction of fibrosis, and for the overall accuracy of SW elastography and transient elastography. Areas under the receiver operating characteristic curve (AUCs) were used to estimate the probability of correctly predicting the degree of fibrosis. Differences between various AUCs were compared by using a Delong test. The optimal cutoff points for prediction of the different fibrosis stages were identified from the highest Youden index. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated. Binary logistic regression was used for analysis of improvement in diagnostic accuracy by combining SW elastography of the liver and SW elastography of the spleen in various fibrosis stages. *P* values less than .05 indicated statistical significance.

By using cutoff values for the different fibrosis stages, substantial discordance between SW elastography of the liver and spleen and histologic staging was defined as a difference in fibrosis stage by at least two points. In the assessment of discordance, categorical variables between groups were compared by using χ^2-test or Fisher exact test as appropriate. Continuous variables were compared by using independent samples *t* test or Mann-Whitney *U* test.

For observer variability testing, repeated measures of analysis of variance were used to compare the difference in mean SW elastographic values between the three liver sections in the same patient. If the difference was statistically significant, a post hoc test (with multiple range tests) was used to compare the variables in pairs. To assess intraobserver and interobserver error, intraclass correlation coefficients (ICCs) were used. ICCs and 95% confidence intervals were calculated. ICC greater than 0.75 indicated excellent reliability.

Table 2

Intraobserver Error of SW Elastographic Liver Measurement at Three Sections

Operator	Anterior ICC	Mid ICC	Posterior ICC
1	0.86 (0.71, 0.94)	0.91 (0.80, 0.96)	0.97 (0.94, 0.99)
2	0.91 (0.82, 0.96)	0.95 (0.90, 0.98)	0.94 (0.88, 0.98)
3	0.98 (0.95, 0.99)	0.97 (0.93, 0.99)	0.95 (0.90, 0.98)

Note.—Numbers in parentheses are 95% confidence intervals.

Results

SW elastography of the liver had a significantly higher success rate (98.9%; 449 of 454 patients) compared with transient elastography of the liver (89.6%; 407 of 454 patients) (*P* = .001). In a total of 52 patients, either SW elastography or transient elastographic examinations had failed. The main reasons for failure in either technique were similar and included obesity (10 of 52 patients), inability of optimal breath-holding (29 of 52 patients), or narrow intercostal space of the patients that leads to an inadequate scanning window (13 of 52 patients). A total of 226 patients with valid liver SW elastography, transient elastography, and satisfactory liver biopsy specimens (median biopsy length, 18 mm [interquartile range, 15–23]; 15 portal tracts [interquartile range, 9–20]) were included in the final analysis and formed the index group, which consisted of 146 men and 80 women. The control group consisted of 68 men and 103 women (Table 1).

Liver and Spleen Elasticity in Normal Patients by Using SW Elastography

In normal control subjects, the mean SW elastography of the liver was 5.5 kPa ± 0.7 (standard deviation), with a range of 3.7–6.7 kPa. Men had significantly higher SW elastography of the liver than did women (5.7 kPa ± 0.5 vs 5.4 kPa ± 0.7, respectively; *P* = .02). The mean SW elastography of the spleen was 17.3 kPa ± 2.6 (range, 8.05–24.9 kPa). There was no statistically significant difference between sexes (*P* = .66).

Reproducibility of SW Elastography

There was excellent correlation in repeated measurements made by the operators. The ICC for the three operators in three different sections of the liver ranged from 0.86 to 0.98, and the 95% confidence interval ranged from 0.71 to 0.99 (Table 2). Additionally, there was very good reproducibility between the three operators (ICC, 0.85; 95% confidence interval: 0.70, 0.94).

In the control group, there was no significant difference in mean SW elastography of the liver taken at the anterior (5.5 kPa ± 0.7, *P* = .65), mid (5.5 kPa ± 0.7, *P* = .82), and posterior (5.5 kPa ± 0.8, *P* = .54) sections of the liver. In the index group, SW elastographic values in the three sections showed similar accuracy for prediction of various stages of fibrosis (AUC, 0.86–0.98; *P* = .11–.87).

Liver Elasticity in Chronic Hepatitis with SW and Transient Elastography

In the index group, values for SW elastography of the liver ranged from 4.3 to 40.5 kPa (Fig 2a). SW elastography of the liver had a very strong positive correlation with fibrosis stage (*r* = 0.81; *P* < .001). SW elastography of the liver overlapped between F0 (*P* = .59), F1 (*P* = .31), and the healthy control group (*P* = .63), but SW elastography

Figure 2

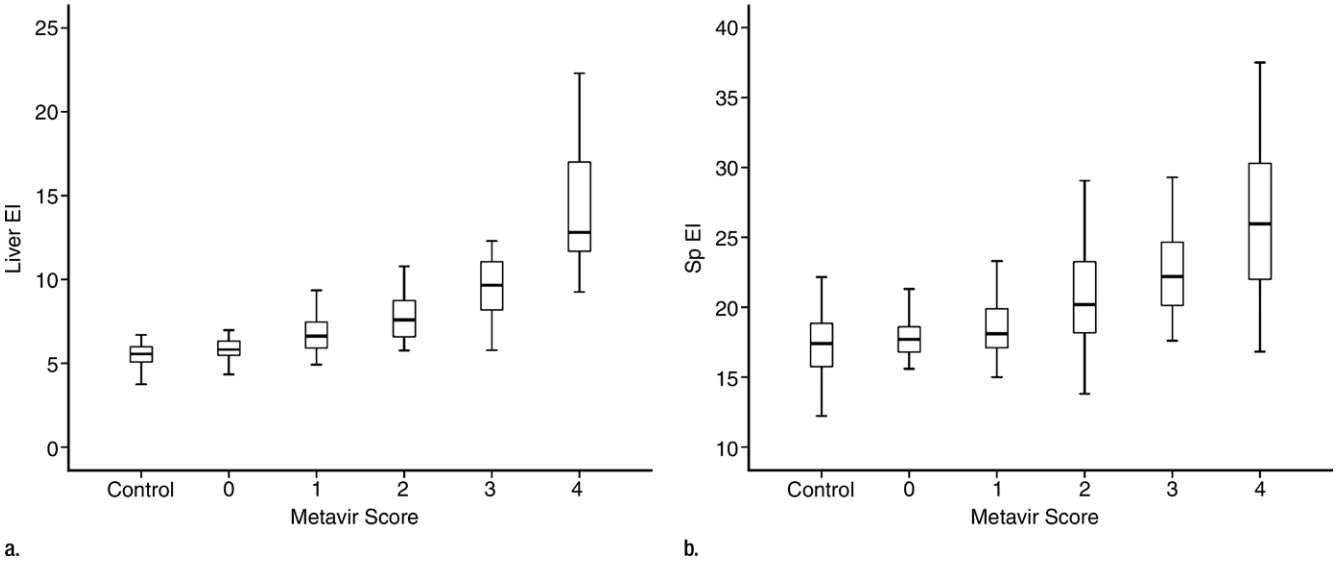


Figure 2: Box and whisker plots of **(a)** SW elastography of the liver and **(b)** SW elastography of the spleen at each fibrosis stage.

of the liver could distinguish among F2 (P = .002), F3 (P = .001), and F4 (P = .001) stages. Transient elastographic liver values ranged from 3.2 to 36.6 kPa and showed strong positive correlation with fibrosis stage (r = 0.58; $P < .001$). The optimal cutoff values in kilopascals of SW and transient elastography liver for the identification of fibrosis stage are listed in Table 3, in which SW elastography of the liver achieved an overall accuracy of 86%–98% and specificity of 90%–93%.

The difference in AUC between SW elastography of the liver and transient elastography of the liver at various fibrosis stages was significant (Table 4). The accuracy of SW elastography of the liver was significantly higher (P = .001) than that of transient elastography liver in all fibrosis stages.

Discordance between SW Elastography of the Liver and Histologic Staging

There were 10.2% (23 of 226) of patients who had discordance of at least two stages between SW elastography of the liver and histologic staging. Eleven patients were upstaged (ie, SW elastography predicted a higher fibrosis stage than biopsy stage) and 12 were downstaged (ie, SW elastography predicted a lower fibrosis stage than the biopsy stage). There was no significant difference in demographic and serologic profile between patients with and without discordance (P = .99).

Spleen Elasticity in Chronic Hepatitis by Using SW Elastography

In the index group, the values for SW elastography of the spleen ranged from 13.3 to 45.3 kPa, which showed strong positive correlation with fibrosis stage (r = 0.67; $P < .001$) (Fig 2b). There was overlap in SW elastography of the spleen between F0 (P = .53), F1 (P = .68), F2 (P = .33), and healthy control subjects (P = .85), but SW elastography of the spleen could distinguish among F3 and F4 stage (P = .01). AUCs and the optimal cutoffs for the identification of fibrosis stage are listed in Table 3, which achieved an overall accuracy of 81%–84% and specificity of 81%–86%.

The accuracy of SW elastography of the spleen was comparable to that of transient elastography of the liver in all fibrosis stages without any significant differences (Table 4). Accuracies for SW elastography of the liver and SW elastography of the spleen were comparable for stage F1 or greater, but for higher grades of fibrosis, SW elastography of the liver was significantly more accurate than SW elastography of the spleen. When combining SW elastography of the liver and spleen to predict fibrosis staging, the diagnostic accuracy was not improved compared with SW elastography of the liver alone (similar AUC generated by binary logistic regression; ≥F1, P = .87; ≥F2, P = .81; ≥F3, P = .84; and ≥F4, P = .88) (Tables 3, 4).

Prevalence of Discordance for SW Elastography of the Spleen

We found that 28.2% (58 of 206) of patients had discordance in at least two stages between SW elastography of the spleen and liver histologic staging. Of the patients, 30 were upstaged and 28 were downstaged. Patients with discordance had higher body mass index (33.0 vs 25.1 kg/m^2; P = .003), while other anthropometric and laboratory parameters were similar between patients with and without discordance (P = .94).

Discussion

To the best of our knowledge, this study included a cohort of patients who had

Table 3

Accuracy of SW Elastography of Liver, SW Elastography of Spleen, Transient Elastography of Liver, and Combination of SW Elastography of Liver and Spleen

Stage of Fibrosis	AUC	Cutoff Point (kPa)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
SW elastography of liver						
≥F1	0.86 (0.79, 0.93)	6.5	83.5	91.2	90.8	85.3
≥F2	0.88 (0.82, 0.94)	7.1	84.7	92.1	85.3	91.7
≥F3	0.93 (0.88, 0.97)	7.9	89.8	90.3	71.8	97.0
F4	0.98 (0.95, 0.99)	10.1	97.4	93.0	60.1	99.6
SW elastography of spleen						
≥F1	0.81 (0.73, 0.88)	19.4	66.3	85.9	86.3	65.5
≥F2	0.82 (0.74, 0.89)	19.8	75.8	84.8	78.1	83.0
≥F3	0.83 (0.76, 0.90)	20.6	79.8	82.8	62.6	91.9
F4	0.84 (0.74, 0.94)	22.0	82.4	80.9	38.5	96.9
Transient elastography of liver						
≥F1	0.80 (0.71, 0.89)	6.7	82.6	83.2	76.1	88.5
≥F2	0.78 (0.69, 0.86)	6.9	78.3	80.9	70.5	84.0
≥F3	0.83 (0.76, 0.91)	8.2	81.1	91.6	65.4	90.5
F4	0.92 (0.86, 0.97)	11.4	92.0	91.7	72.4	93.2
Combined SW elastography of liver and spleen						
≥F1	0.86 (0.79, 0.93)	…	…	…	…	…
≥F2	0.88 (0.82, 0.94)	…	…	…	…	…
≥F3	0.93 (0.88, 0.97)	…	…	…	…	…
F4	0.98 (0.95, 0.99)	…	…	…	…	…

Note.—Numbers in parentheses are 95% confidence interval range. For the combined SW elastography of liver and spleen, the cutoff point (represent by the combined probability) was generated by logistic regression. It was very complicated, and was neither easy nor useful for clinical use. More importantly, the combined SW elastography of the liver and spleen did not show better accuracy than SW elastography of the liver alone. This made the combined probability less important and less clinically useful; therefore, we did not put these values for the combined SW elastography of the liver and spleen in the Table. NPV = negative predictive value, PPV = positive predictive value.

Table 4

Comparison of AUC for Transient Elastography of Liver, SW Elastography of Liver, and SW Elastography of Spleen at Different Stages of Liver Fibrosis

Stage of Fibrosis	SW Elastography of Liver versus Transient Elastography Liver	SW Elastography of Spleen versus Transient Elastography of Liver	SW Elastography of Liver versus SW Elastography of Spleen
≥F1	.04*	.87	.11
≥F2	.01*	.38	.03*
≥F3	.01*	.99	.01*
F4	.04*	.21	.01*

Note.—Data are *P* values

* Delong test indicated statistical significance of difference of two AUC curves.

chronic hepatitis B for comparison of the test performances of SW elastography of the liver and spleen and transient elastography together with liver biopsy correlation. Recently, there was a study (16) that used SW elastography to assess liver fibrosis in 121 patients with hepatitis C. Our study showed similar mean and cutoff values in various fibrosis stages.

While US elastographic imaging is now widely recognized as a reliable method to assess liver fibrosis, various techniques that use transient elastography and acoustic radiation force impulse imaging are imprecise for detection of early and intermediate levels of fibrosis (2,15,17–19). Previous studies reported high accuracy with transient elastography only for detection of the more advanced fibrosis stages F3 and F4 (13). In our study, we found that SW elastography enabled identification of the earlier fibrosis stage F2 by using a cutoff of 7.1 kPa, with 92.1% specificity for diagnosis of fibrosis stage F2 or greater. Because stage F2 or greater marks the beginning of progressive liver disease, and therefore alludes to a stronger indication to initiate treatment, our findings suggested that SW elastography may serve as a better screening tool to differentiate patients with substantial fibrosis (≥F2) from those without substantial fibrosis (F0–F1). Furthermore, the high negative predictive value of SW elastography of the liver enhances the clinical utility of SW elastography for screening liver fibrosis. The same observation has been made by Bavu et al (20), but the main weakness of his study was that the fibrosis level was not exclusively derived from the liver biopsy.

Our results for SW elastography of the liver yielded higher AUCs compared with previous reports with transient elastography, but slightly lower AUCs compared with prototype SW elastography studies and other SW elastography studies for fibrosis stages F0–F2 (6,17,20). This variation could be operator and patient related.

Interestingly, lower AUCs in Asian countries have been noted in a meta-analysis (17) that involved 50 transient elastography studies. This geographic regional variation in AUCs was ascribed to different ethnic groups in different studies. We only recruited Chinese patients for this study. The values for SW elastography of the liver in healthy patients in this study (mean, 5.5 kPa) were comparable to those in a Western

study (mean, 6.6 kPa in 15 healthy volunteers, Muller et al [6]). This suggested that elasticity in a normal liver was not influenced by ethnicity. In our study, a high AUC of 0.93–0.98 was achieved for diagnosis of severe fibrosis (F3 and F4) by using cutoff values for SW elastography of the liver of 7.9 kPa and 10.1 kPa, respectively, which were similar to transient elastography cutoff values reported by a previous study (13) conducted in our institution. These values could therefore be regarded as a reference standard for US elastographic liver studies in Chinese populations with hepatitis B.

SW elastography of the liver correlated with SW elastography of the spleen, which was in accordance with previous studies that used transient elastography (14). Hemodynamic alterations related to the presence and progression of liver fibrosis may lead to architectural changes in the spleen. It was found that the effect of spleen stiffness (reflected by the SW elastography values of the spleen) was small during stages F1–F3 of liver involvement, but became more apparent at stage F4. The diagnostic accuracy of SW elastography of the spleen for hepatic fibrosis staging was poorer than SW elastography of the liver, but it was similar to that of transient elastographic imaging of the liver. Previous studies that used transient elastography advocated the combination of transient elastography liver and transient elastography spleen measurement, which increased the accuracy for prediction of the presence of esophageal varices in patients with liver cirrhosis (17). In our study, however, the combination of SW elastography of the spleen with SW elastography of the liver did not enhance the diagnostic accuracy. This may be explained by the intrinsic high specificity of SW elastography of the liver for prediction of all stages of liver fibrosis. SW elastography of the spleen can be used as an ancillary parameter to support the diagnosis of patients suspected of having fibrosis.

Transient elastography has been used in our institution as a quantitative measure of elasticity in kilopascals for the last 5 years. Both SW elastography and transient elastography were found to have good reproducibility in the current study and in previous studies (13). However, transient elastography was reported to have unreliable results in 15.8% of cases in clinical practice (7). This is in agreement with our study. SW elastography had higher successful rate (98.9% vs 89.6%) and higher accuracy (ie, AUC) in all fibrosis stages than did transient elastography of the liver. Transient elastography had limited clinical acceptance in other centers because of bulky external vibrators, while SW elastography had its own built-in transducer that generated acoustic radiation force impulses. Furthermore, transient elastography cannot be used in patients with obesity (body mass index, >28 kg/m^2) and ascites because of poor penetration; however, obesity only accounted for a small proportion of unsuccessful cases (2.2% [10 of 454]) of SW elastography in our study. This was also supported by the finding in our study that the discordance of at least two stages of histologic staging of the liver was rather low (10.2% in liver and 28.2% in spleen). We found that for the spleen, higher body mass index was an important factor that caused discordance for SW elastography, but not in liver.

This study had limitations. We used a Chinese study population, which made it possible that results would not be similar in other ethnic populations. Similarly, we have only assessed patients with hepatitis B, and only those patients with liver biopsy, and the time lag between biopsy and elastography could be up to 12 months. We excluded patients with clinically overt liver failure and gross ascites at the initial recruitment because of potential technical difficulty in SW elastography and transient elastography. We need to expand the current study to include more patients with other types of liver disease. In addition, healthy control subjects were not matched well according to sex or body habits. Other limitations include potential selection bias in the patients, and long interval between biopsy and elastography for some patients.

SW elastography enables a better biopsy-correlated assessment of liver fibrosis compared with transient elastography, especially for early fibrosis, and SW elastography also gives objective assessment of splenic elasticity, correlated with liver fibrosis staging in patients with chronic hepatitis B.

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