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Feasibility and reliability of the FibroScan S2 (pediatric) probe compared with the M probe for liver stiffness measurement in small adults with chronic liver disease

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ABSTRACT

Background. The success of liver stiffness measurement (LSM) by transient elastography (TE, FibroScan) is influenced by anthropometric factors. In smaller adults, the M probe may fail due to narrow intercostal spaces and rib interference. We aimed to compare LSM using the FibroScan S2 (pediatric) probe with the M probe in small adults with chronic liver disease. **Material and methods.** In this prospective study, 41 liver disease patients and 18 controls with a thoracic perimeter ≤ 75 cm underwent LSM using the FibroScan M and S2 probes. TE failure was defined as no valid LSMs and unreliable examinations as < 10 valid LSMs, an interquartile range (IQR)/LSM > 30%, or success rate < 60%. **Results.** TE failure was not observed and reliability did not differ between the M and S2 probes (86% *vs.* 95%; P = 0.20). Liver stiffness measured using the M and S2 probes was highly correlated (ρ = 0.81; P < 0.0005) and median liver stiffness did not differ between probes (4.5 *vs.* 4.4 kPa; P = 0.10). However, in participants with a skin-capsular distance ≥ 15 mm, median liver stiffness was higher using the S2 probe (5.5 *vs.* 4.9 kPa; P = 0.008). When compared with validated liver stiffness cut-offs, the S2 probe would have overestimated the stage of fibrosis compared with the M probe in 10% of patients. **Conclusions.** The FibroScan S2 probe does not improve the feasibility of LSM in adults of smaller stature and may overestimate liver stiffness compared with the M probe. The FibroScan M probe should remain the preferred tool for LSM in small adults with chronic liver disease.

Key words. Biopsy. Diagnosis. Fibrosis. Hepatitis. Noninvasive.

INTRODUCTION

In patients with chronic liver disease, accurate staging of fibrosis is critical for estimating prognosis and management decisions. Transient elastography (TE) using the FibroScan (Echosens; Paris, France) is an accurate, noninvasive method for evaluating liver stiffness as a surrogate of liver fibrosis.[1,2] TE was first studied in patients with chronic hepatitis C,[3,4] but has now been validated in adult and pediatric populations with various liver disorders.[5-8] The diagnostic performance of TE is excellent for cirrhosis and moderate for significant fibrosis.[5,9,10] In light of its accuracy, simplicity, rapid results, patient acceptance, and ease of incorporation into an outpatient clinical setting, TE has gained widespread use in many countries.[5,6]

While TE represents an attractive alternative to liver biopsy, the feasibility and accuracy of liver stiffness measurement (LSM) using the FibroScan are heavily influenced by anthropometric factors. Numerous studies have shown that obesity and other correlated factors (e.g. thoracic fold thickness, waist circumference, and the distance between the skin and liver capsule) are important determinants of FibroScan failure and unreliable results, which occur in approximately 5% and 15% of patients, respectively.[6,11-19] Moreover, subcutaneous adipose tissue may lead to overestimation of liver stiffness. As a result, a novel FibroScan probe (the 'XL' probe) that has a greater vibration amplitude and measurement depth compared with the standard M probe has been designed specifically for use in obese patients.[14,15] The XL probe facilitates LSM in a significantly greater

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number of obese patients than the M probe, while maintaining comparable accuracy.[17]

Thus far, minimal attention has been paid to patients at the opposite end of the size spectrum; namely adults of smaller stature. Although the prevalence of obesity is rising, smaller adults represent an important reservoir of liver disease in many regions (e.g. those with chronic viral hepatitis in Southeast Asia). In these patients, the standard FibroScan M probe (with a 9 mm tip diameter) may inaccurately assess liver stiffness because the narrow intercostal spaces in these patients may make it difficult to obtain an unobstructed window for LSM. This interference may cause TE failure, an unreliable result, or overestimation of liver stiffness. Therefore, it may be more appropriate to use the FibroScan S2 probe, which was designed for use in pediatric patients due to the smaller diameter of its probe (7 mm). Although a reasonable approach, the more superficial measurement depth of the S2 probe compared with the M probe (20 to 50 mm *vs.* 25 to 65 mm from the skin) could lead to liver stiffness overestimation due to interference from subcutaneous adipose tissue within the region of measurement.

In light of these uncertainties, the objective of this prospective study was to compare the feasibility and reliability of LSM using the FibroScan M and S2 probes, and to compare the correlation between these measures, in adults of small stature and chronic liver disease.

MATERIAL AND METHODS

Patients and recruitment

In this prospective study, adults (≥ 18 years) with chronic liver disease of any etiology and a thoracic perimeter measured at the xiphoid process ≤ 75 cm were recruited from the University of Calgary Liver Unit between March and April 2012. A cohort of healthy controls with no history of liver disease and a thoracic perimeter ≤ 75 cm were also recruited. Individuals with a thoracic perimeter > 75 cm or contraindications to LSM (e.g. pregnancy, ascites, implantable cardiac devices, etc.) were ineligible. The Conjoint Health Research Ethics Board at the University of Calgary approved the study protocol.

Clinical data

Before TE examination, demographic information (age, gender, race/ethnicity), etiology of liver disease, and anthropometric measurements (weight, height, BMI, and thoracic perimeter) were obtained. In addition, biochemical data including liver biochemistry, platelets, albumin, and bilirubin were recorded.

Liver stiffness measurement

All study participants underwent LSM using the FibroScan M and S2 probes by a single experienced operator with > 3,000 prior examinations.[6] Previous studies have shown that intraobserver agreement by experienced operators is nearly perfect (intraclass coefficient, 0.99).[20] Briefly, with the patient lying in the dorsal decubitus position, the tip of the transducer probe was placed on the skin between the ribs over the right lobe of the liver. Assisted by a sonographic image, a portion of the liver at least 6 cm thick and free of large vascular structures was identified using a portable 10 MHz ultrasound transducer (Mindray DP-6600; Mindray, Shenzhen, China). At this site, the distance between the skin and liver capsule (skin-capsular distance) was measured and at least 10 valid measurements were collected with each probe. Specific differences between the M and S2 probes include their central ultrasound frequency (3.5 *vs.* 5 MHz), vibration amplitude (2 *vs.* 1 mm), tip diameter (9 *vs.* 7 mm), and measurement depth from the skin surface (25-65 *vs.* 20-50 mm). The manufacturer recommends that the S2 probe be used in patients with a thoracic perimeter ≤ 75 cm (Appendix). Examinations with no successful measurements after at least 10 attempts were deemed failures. The median liver stiffness value (in kPa) was considered representative of the elastic modulus of the liver. As an indicator of variability, the ratio of the interquartile range (IQR) of liver stiffness to the median value (IQR/M) was calculated. Examinations with fewer than 10 valid measurements or an IQR/M > 30% or a success rate < 60% were considered potentially unreliable.

Statistical analyses

Patient characteristics and clinical data were descriptively summarized and are reported as medians (IQR) and proportions. Between groups comparisons were made using Fisher's exact for categorical variables, and Mann-Whitney and Wilcoxon matched pairs sign-rank tests for continuous variables, as appropriate. Spearman correlation coefficients (ρ) between liver stiffness measured using the M and S2 probes were determined. Further analyses of the agreement between probes were performed using Bland-Altman plots of the intra-individual differences

in LSMs with each probe versus the mean measurement.[21] In a post hoc fashion, the same analysis was repeated using FibroScan data that was reprocessed by Echosens to measure liver stiffness in the same region of interest (25-50 mm from the skin). To determine the extent to which any differences in liver stiffness measured using the two probes may influence clinical decision-making, patients were categorized into four fibrosis categories with each probe using universal liver stiffness cut-offs identified as optimal in the systematic review by Tsochatzis, *et al*. These thresholds were derived for use with the M probe (no or minimal fibrosis [F0-F1], < 7.2 kPa; moderate fibrosis [F2], 7.2-9.5 kPa; severe fibrosis [F3], 9.6-14.4 kPa; and cirrhosis [F4], > 14.4 kPa).[22] The proportion of patients with a discrepancy in fibrosis classification between the two probes was determined. Finally, subgroup analyses were conducted according to median BMI (< 21 *vs.* ≥ 21 kg/m^2) and skin-capsular distance (< 15 *vs.* ≥ 15 mm). We hypothesized that any differences in liver stiffness measured using the M and S2 probes would be greatest in patients with higher BMI and/or skin-capsular distance due to the influence of subcutaneous adipose tissue in larger patients (i.e. overestimation of liver stiffness).[17]

All statistical analyses were performed using Stata v11 software (StataCorp; College Station, TX). Two-sided P-values < 0.05 were considered statistically significant.

RESULTS

Patient characteristics

Between 1 March 2012 and 2 April 2012, 43 patients and 19 controls were screened for the study. Three subjects were excluded (2 patients and 1 control) due to a thoracic perimeter > 75 cm. Characteristics of the remaining 59 participants (41 patients and 18 controls) are outlined in Table 1. Eighty-eight percent (n = 52) were female and the median age was 38 (IQR 30-50) years. The majority was of Asian (46%) or Caucasian (32%) race/ethnicity. The median thoracic perimeter, body weight, and BMI were 71 cm (IQR 69-73; range 57-75 cm), 51 kg (IQR 48-55; range 40-64 kg), and 20.6 kg/m^2 (IQR 18.5-21.9; range 15.6-25.1 kg/m^2), respectively. The median skin-capsular distance was 14.8 mm (IQR 12.2-16.2; range 10.0-19.7 mm); no participant had a skin-capsular distance exceeding 20 mm (the measurement depth of the S2 probe). The majority of patients (66%) had chronic hepatitis B or C; 10% had primary biliary cirrhosis; 7% had autoimmune hepatitis; and 5% had alcoholic liver disease. Compared with liver disease patients, control subjects were younger (median age, 45 *vs.* 28 years; P = 0.0001) and had a shorter median skin-capsular distance (15.3 *vs.* 13.1 mm; P = 0.007), but the median BMI (20.8 *vs.* 20.3 kg/m^2; P = 0.66) and thoracic perimeter (72 *vs.* 70 cm; P = 0.09) did not differ between groups (Table 1).

Feasibility and reliability of LSM with the FibroScan M and S2 probes

Table 2 compares the feasibility and reliability of LSM using the S2 and M probes. Both probes achieved at least 10 valid measurements in every participant (i.e. no failures were observed). Variability between LSMs, as assessed by the ratio of IQR/M, was not significantly different between probes (P = 0.24). Similarly, reliable LSM (defined as ≥ 10 valid measurements, an IQR/M ≤ 30%, and a success rate ≥ 60%) did not differ between the S2 and M probes (95% *vs.* 86%; P = 0.20). Subgroup analyses according to BMI (< *vs.* ≥ 21 kg/m^2) and skin-capsular distance (< vs. ≥ 15 mm) revealed no differences in reliability between probes (data not shown).

Correlation between liver stiffness measured using the M and S2 probes

Liver stiffness measured using the M and S2 probes was highly correlated (ρ = 0.81; P < 0.0005) (Figure 1). The correlation between measurements was higher among patients with liver disease (ρ = 0.90; P < 0.0005) than controls (ρ = 0.53; P = 0.02) and at lower liver stiffness values. The latter relationship was confirmed in a Bland-Altman plot (Figure 2) which demonstrated a greater difference in LSMs between probes at higher mean values (Pitman's test of difference in variance: r = 0.89; P < 0.0005). Overall, median liver stiffness did not differ significantly between the M and S2 probes (4.5 kPa [IQR 3.7-6.1] *vs.* 4.4 kPa [IQR 3.6-6.5]; P = 0.10). The mean and median differences between measurements were 0.8 kPa (95% CI -0.2 to 1.7) (Figure 2) and 0.1 kPa (IQR -0.4 to 1.2), respectively (with positive values indicating higher liver stiffness with the S2 probe). When expressed as a percentage of liver stiffness measured using the M probe, the median difference was 2.5% (IQR -11% to 24%; range -54% to 53%).

When the liver stiffness data was reprocessed to measure the same region of interest using both probes (25 to 50 mm from the skin), the mean and

Table 1. Characteristics of the study cohort.

Characteristics	Patients (n=41)	Controls (n=18)	P-value
• Demographics			
Female	90% (37)	83% (15)	0.66
Age, years	45 (33-53)	28 (26-36)	0.0001
Race			
Asian	61% (25)	11% (2)	0.001
Caucasian	27% (11)	44% (8)	-
South Asian	7% (3)	39% (7)	-
Black	5% (2)	6% (1)	-
• Anthropometrics			
Weight, kg	52 (48-60; range 40-64)	50 (48-52; range 42-59)	0.22
BMI, kg/m^2	20.8 (19-22; range 17-25)	20.3 (19-21; range 16-24)	0.66
Thoracic perimeter, cm	72.0 (70.0-73.0)	70.0 (69.0-71.5)	0.09
Skin-capsular distance, mm	15.3 (13-17; range 10-19.7)	13.1 (12-15; range 11-16)	0.007
• Liver disease etiology			
Viral (HBV, HCV)	66% (27)	-	-
Primary biliary cirrhosis	10% (4)	-	-
Autoimmune hepatitis	7% (3)	-	-
Alcohol	5% (2)	-	-
Other	12% (5)	-	-
• Biochemistry*			
ALT, IU/L (n = 38)	30 (18-60)	-	-
AST, IU/L (n = 25)	32 (24-50)	-	-
GGT, IU/L (n = 34)	29 (16-98)	-	-
Alkaline phosphatase, IU/L (n = 36)	72 (60-103)	-	-
Platelets, x 10^9/L (n = 36)	203 (170-248)	-	-
INR (n = 28)	1.0 (1.0-1.0)	-	-
Bilirubin, umol/L (n = 30)	8 (5-15)	-	-
Albumin, g/L (n = 33)	38 (36-40)	-	-

All data are median (IQR) or % (n), unless otherwise indicated. *Numbers in parenthesis indicate the number of patients with complete laboratory data.

Table 2. Feasibility and Performance of the FibroScan M and S2 Probes (n = 59).

Characteristic	M Probe	S2 Probe	P-value
Failure (no valid measurements)	0% (59)	0% (59)	-
≥ 10 valid measurements	100% (59)	100% (59)	-
Median success rate	100% (100-100%)	100% (100-100%)	0.85
Median IQR/M	17% (12-25%)	17% (13-23%)	0.24
IQR/M ≤ 30%	86% (51)	95% (56)	0.20
Reliable LSM (≥ 10 valid measurements, IQR/M ≤ 30%, and success rate ≥ 60%).	86% (51)	95% (56)	0.20
Median liver stiffness, kPa			
Overall	4.5 (3.7-6.1)	4.4 (3.6-6.5)	0.10
BMI < 21 kg/m^2 (n=33)	4.9 (4.0-6.0)	4.6 (3.6-6.5)	0.44
BMI ≥ 21 kg/m^2 (n = 26)	4.2 (3.7-6.6)	4.4 (3.9-6.1)	0.11
SCD < 15 mm (n = 33)	4.5 (3.7-5.7)	4.1 (3.4-5.7)	0.73
SCD ≥ 15 mm (n = 26)	4.9 (3.8-6.1)	5.5 (4.2-7.1)	0.008

All data are percentage (n) or median (IQR). BMI: body mass index. LSM: liver stiffness measurement. SCD: skin-capsular distance.

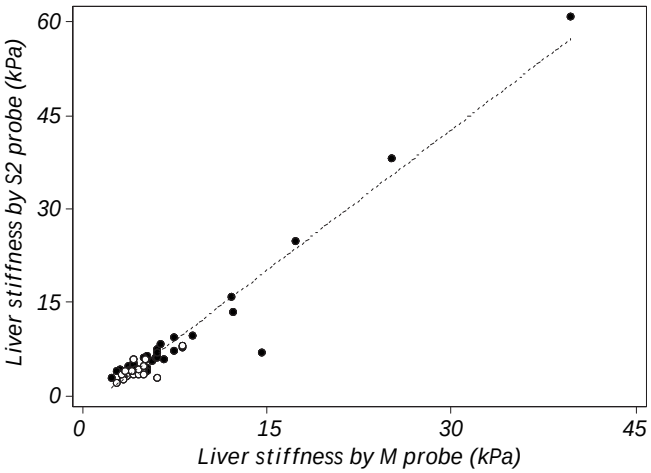

Figure 1. *Correlation between liver stiffness values measured using the M and S2 probes in patients with chronic liver disease (black circles) and controls (white circles) (ρ = 0.81; P < 0.0005).*

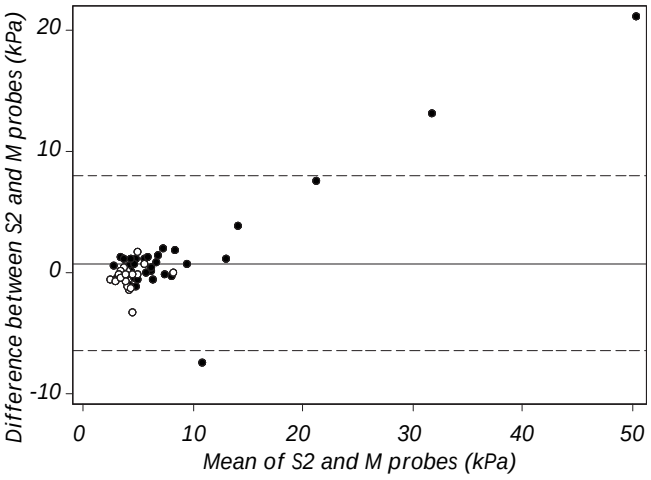

Figure 2. *Bland-Altman plot of the difference between liver stiffness measured using the S2 and M probes vs. the mean measurement in patients with chronic liver disease (black circles) and controls (white circles). A greater difference in liver stiffness between probes was observed at higher mean liver stiffness values (P < 0.0005). The solid horizontal line represents the mean difference between probes (0.8 kPa higher with the S2 probe; 95% CI -0.2 to 1.7) and the dashed lines the 95% limits of agreement (-6.5 to 8.0 kPa).*

median differences between measurements were -0.15 kPa (95% CI -0.6 to 0.3) and -0.10 kPa (IQR -0.5 to 0.4), respectively (Figure 3). The absolute difference between measurements within individual patients did not differ significantly between the analysis of raw and reprocessed data (P = 0.15). However, among cases with a skin-capsular distance

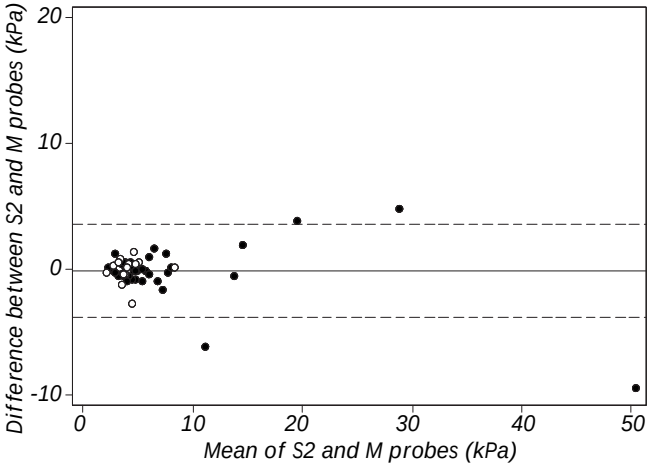

Figure 3. *Bland-Altman plot of the difference between liver stiffness measured using the S2 and M probes versus the mean measurement using FibroScan data reprocessed to measure the same region of interest (25 to 50 mm below the skin) for both probes. Patients with chronic liver disease are denoted with black circles and controls with white circles. The solid horizontal line represents the mean difference between probes (-0.15 kPa; 95% CI -0.6 to 0.3) and the dashed lines the 95% limits of agreement (-3.9 to 3.6 kPa).*

Table 3. Distribution of fibrosis stages as estimated by the S2 and M probes.

Fibrosis according to S2 probe	Fibrosis according to M probe F01 (n = 48)	F2 (n = 5)	F3 (n = 2)	F4 (n = 4)
F01 (n = 47)	46	0	0	1
F2 (n = 6)	2	4	0	0
F3 (n = 2)	0	1	1	0
F4 (n = 4)	0	0	1	3

Discordance ≥ 1 stage between LSM using the S2 and M probes indicated by grey squares. Universal liver stiffness cut-offs derived by Tsochatzis, *et al.* for use with the M probe: F0-F1, < 7.2 kPa; F2, 7.2-9.5 kPa; F3, 9.6-14.4 kPa; and F4, > 14.4 kPa.[22]

≥ 15 mm, the difference between the S2 and M probe measurements was reduced with the reprocessed data compared with the raw data (P = 0.02).

In 54% of subjects (n = 32), liver stiffness was greater using the S2 probe; in 41% (n = 24) it was greater using the M probe; and in 5% (n = 3), there was no difference. Subgroup analyses comparing liver stiffness results measured using the M and S2 probes among participants with a BMI < 21 kg/m^2 (4.9 *vs.* 4.6 kPa; P = 0.44) and ≥ 21 kg/m^2 (4.2 *vs.* 4.4 kPa; P = 0.11), and skin-capsular distance < 15 mm (4.5 *vs.* 4.1 kPa; P = 0.73) revealed no significant differences. However, among those with a skin-capsular distance exceeding 15 mm,

median liver stiffness was higher when measured using the S2 probe (5.5 kPa *vs.* 4.9 kPa using the M probe; P = 0.008).

The clinical relevance of differences in liver stiffness values measured using the M and S2 probes are illustrated in Table 3. In 5 participants (8.5%) – all with chronic liver disease– a clinically relevant difference in fibrosis classification would have been observed had the S2 probe been used instead of the M probe. Excluding controls, the discordance rate was 12% (5/41). In all but one patient with discordance, the predicted fibrosis stage would have been overestimated by one stage by the S2 probe. The discordance rate did not differ between patients with a skin-capsular distance < 15 mm (6% [2/33]) *vs.* ≥ 15 mm (12% [3/26]; P = 0.65).

DISCUSSION

This is the first study to prospectively compare the feasibility and reliability of LSM using the FibroScan M and S2 probe in adults of smaller stature. We hypothesized that the S2 probe may facilitate LSM in this patient population due to the smaller diameter of the tip of its probe compared with the M probe, yet may overestimate liver stiffness due to its more superficial region of measurement. Our findings demonstrate that the S2 and M probes are comparable with respect to feasibility and reliability. However, the S2 probe may overestimate liver stiffness in some patients, particularly those with a larger distance between the skin and liver capsule.

In our assessment of TE feasibility, the M and S2 probes had similar performance. Although most series report a TE failure rate of 3% to 5% in unselected cohorts,[6,11-19] no failures were observed in our study. This likely relates to our exclusion of patients with a thoracic perimeter > 75 cm, in whom the skin-capsular distance may exceed the measurement depth of the probes. Indeed, no study participant had a skin-capsular distance greater than 20 mm – the measurement depth of the S2 probe. As the larger diameter of the M probe is not associated with an increased risk of TE failure in smaller adults, interference with the propagation of TE impulses by the ribs in these patients (who often have narrow intercostal spaces) is a not of significant clinical concern. We also failed to detect a significant difference between probes in the ability to obtain a reliable LSM, defined as ≥ 10 valid measurements, an IQR/M ≤ 30%, and a success rate ≥ 60%. Overall, a reliable result was obtained in 86% of participants using the M probe and 95% with the S2 probe (P = 0.20). The individual criteria composing this definition of reliability were also similar between probes (Table 2). Based on these findings, our data suggest that LSM using the S2 probe does not improve measurement success compared with the M probe in smaller adults. Therefore, our findings do not justify the additional cost of acquiring and maintaining an S2 probe for clinicians who evaluate only adult patients with liver disease.

In addition to comparing the feasibility of the M and S2 probes, we confirmed the strong correlation between liver stiffness measured using these devices ($\rho = 0.81$; $P < 0.0005$). In a large multi-center study of obese adults, Myers et al. observed similar findings when comparing LSMs obtained using the M and XL probes.[17] Unlike that study, however, we did not observe a statistically significant difference between liver stiffness values obtained using the S2 and M probes (Figure 2). Indeed, the mean and median differences between measurements were only 0.8 kPa (95% CI -0.2 to 1.7) and 0.1 kPa (IQR -0.4 to 1.2), respectively (not significantly different from zero). However, in the report of Myers and colleagues, liver stiffness was approximately 1 to 2 kPa higher when measured using the M probe compared with the XL probe. Elimination of this bias in analyses in which the probes were recalibrated to measure the same region of interest (both 35-65 mm and 35-75 mm from the skin) suggests that these findings reflect the influence of adipose tissue in the region of interest explored by the M probe in obese patients, causing overestimation of liver stiffness.[17] In addition, heterogeneity in hepatic fibrosis (e.g. greater fibrous tissue deposition in the subcapsular region) and the differences in measurement depth between probes were postulated to play a role. In the current study, the only difference in LSMs between the S2 and M probes was identified in subjects with a skin-capsular distance exceeding 15 mm. In these individuals, median liver stiffness was approximately 0.6 kPa higher when measured using the S2 probe (Table 2). As recalibration of our data to the same region of interest (25 to 50 mm from the skin) reduced the bias between probes in these patients, we hypothesize that the more superficial measurement region of the S2 probe at least partly explains this discrepancy due to overestimation of liver stiffness. Moreover, when tested on phantoms with homogeneous stiffness distribution, the M and S2 probes give nearly identical results (V. Miette, Echosens; unpublished data).

In general, the interpretation of TE results is based on comparisons with liver stiffness thresholds validated for the diagnosis of specific fibrosis categories (e.g. F0-F1 *vs*. F2-F4).[2] As such, we evaluated the clinical relevance of differences in liver stiffness measured using the M and S2 probes using universal cut-offs validated for the M probe versus liver histology.[22] As shown in Table 3, a discordance in fibrosis stage estimated by the M and S2 probes was observed in 8.5% (5 of 59) of cases. In all but one of these patients, the stage of fibrosis would have been overestimated had the S2 probe been used instead of the M probe. Although all discordant cases involved overestimation by one stage only, these findings could have important implications for individual patients. For example, in patients with chronic hepatitis B –many of whom would qualify for our study due to their smaller stature (e.g. Asians)– antiviral treatment is often targeted to patients with at least stage 2 fibrosis. In our study, two of 48 patients with no to mild fibrosis (F0-F1) using the M probe would have been classified as having F2 fibrosis using the S2 probe and potentially subjected to unnecessary antiviral treatment. Likewise, one of two patients with bridging fibrosis according to the M probe would have been considered cirrhotic using the S2 probe and enrolled in surveillance programs for hepatocellular carcinoma and esophageal varices. Although our study lacks histological data to confirm the true fibrosis stage in these patients, these data lead one to further question the merits of adopting the S2 probe for LSM in smaller adults.

Our study has several limitations. First, the small sample size may have limited our ability to detect significant differences between probes for various outcomes. We included healthy controls to augment our power, a reasonable strategy considering the fact that TE has been proposed as a screening tool for liver disease at the population level.[23,24] As discrepancies in liver stiffness between probes were greatest at higher values of liver stiffness (Figure 2), the inclusion of healthy controls and a preponderance of patients with mild disease may have inadvertently reduced our power to detect significant differences in liver stiffness between probes. In addition, in our analysis of discordances in expected fibrosis staging between probes, we used liver stiffness cut-offs that were derived in predominantly normal and overweight populations. Since our cohort included 20% underweight individuals (BMI < 18.5 kg/m^2), the applicability of these cut-offs to this population requires validation. Finally, and as previously mentioned, our study lacked histological data to confirm the true fibrosis stage of our patients. Nevertheless, since TE using the FibroScan M probe has been validated extensively as a noninvasive method for fibrosis assessment in adult populations, we felt it unnecessary to obtain liver biopsies in our study.

In summary, the FibroScan S2 probe, which was designed for use in pediatric populations, does not improve the feasibility or reliability of LSM in adults of smaller stature. Moreover, the S2 probe may overestimate liver stiffness in some patients, particularly those with a larger distance (≥ 15 mm) between the skin and liver capsule. In light of these findings, the FibroScan M probe should remain the preferred tool for LSM in small adults with chronic liver disease.

ABBREVIATIONS

- **CI:** confidence interval.
- **IQR:** interquartile range.
- **IQR/M:** IQR over the median.
- **INR:** International normalized ratio.
- **LSM:** liver stiffness measurement.
- **NAFLD:** nonalcoholic fatty liver disease.
- **NAS:** NAFLD activity score.

COMPETING INTERESTS

Dr. Myers has received speaking fees from KNS Canada (distributors of the FibroScan in Canada) and research support from Echosens.

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Appendix. *Manufacturer recommendations regarding FibroScan probe selection based on patient specifications.*

Probe	*Diameter of probe tip*	*Depth of measurement (from skin)*	*Recommended thoracic perimeter (TP) and body mass index (BMI)*
S2 (pediatric)	*7 mm*	*20-50 mm*	*TP > 45 cm and ≤ 75 cm*
M (adult)	*9 mm*	*25-65 mm*	*TP > 75 cm, BMI ≤ 30 kg/m²*
XL (adult)	*12 mm*	*35-75 mm*	*TP > 75 cm, BMI > 30 kg/m²*