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Comparison of acoustic radiation force impulse imaging with the convex probe 6C1 and linear probe 9L4

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Abstract

Background: Acoustic radiation force impulse imaging (ARFI) is a noninvasive method to detect liver fibrosis. The aims of the study were to evaluate the difference between 2 different probes, 6 C1 and 9 L4, and to study inter- and intraobserver reproducibility for the probes.

Methods: We enrolled 100 patients in this cross-sectional comparative study. All patients underwent liver stiffness measurement with both probes. Intraobserver, interobserver, intralobe, and interlobe agreement was analyzed using the intraclass correlation coefficient.

Results: A significant difference in success rates was observed for both probes between the right and left liver lobes. A success rate of 91% was observed in the right liver lobe compared with 77% in the left liver for the convex probe ($P = .007$), and 91% vs 68% for the linear probe ($P < .001$). There was a significant correlation in ARFI-shear wave velocity (ARFI-SWV) between both probes in the right liver lobe ($P = .01$; r = .508) and in the left liver lobe ($P = .05$; r = .278); however, there was no significant correlation in ARFI-SWV between the liver lobes for both probes (convex probe r = .19 $P = .112$; linear probe r = .144 $P = .23$). Good or excellent inter- and intraobserver was detected for both probes. Poor agreement was found only for the interobserver agreement in the left lobe with the convex probe (ICC = .320).

Conclusion: ARFI can be performed successfully with both probes in both liver lobes. There was no significant correlation in ARFI between the liver lobes for both probes; however, the right liver lobe should be favored. Standardization of the procedure is needed for the comparability of different studies.

Abbreviations: ARFI = acoustic radiation force impulse imaging, ARFI-SWV = ARFI-shear wave velocity, BMI = body mass index, CI = convergence interval, F-test = Fisher exact test, ICC = intraclass correlation coefficient, m = meter, ROI = region of interest, s = second, SWV = shear wave velocity.

Keywords: acoustic radiation force impulse imaging, liver stiffness, probes, shear wave velocity

1. Introduction

Chronic liver diseases lead to liver fibrosis and cirrhosis. Liver cirrhosis is associated with complications, such as hepatocellular carcinoma, bleeding of esophageal varices, hepatorenal syndrome, hepatopulmonary syndrome, and hepatic encephalopathy. Liver biopsy has long been the gold standard for assessing hepatic fibrosis or cirrhosis.[1] However, it is an invasive procedure, with a risk of rare but potentially life-threatening complications. In addition, the accuracy of liver biopsy for assessment of fibrosis may suffer from sampling errors and interobserver variability.[2–6] Noninvasive methods for assessment of liver fibrosis have become the focus of interest. The first method to measure liver elasticity was transient elastography. Liver stiffness is measured at a fixed depth and without a visual control.[7]

Acoustic radiation force impulse (ARFI) imaging technology is also a noninvasive tool to detect liver fibrosis.[8–10] ARFI imaging has been incorporated into a conventional ultrasonographic device (Acuson S2000; Siemens Medical Solutions, Mountain View, CA). This technology involves mechanical excitation of tissue using short-duration acoustic pulses in a region of interest (ROI), producing shear waves that spread away from the ROI.[11–13] By recording the shear wave-front and correlating these measurements with the elapsed time, the shear wave velocity (SWV) can be measured and quantified in meter/second (m/s) (ARFI-SWV). The SWV increases with stiffness. Thus, the measured SWV is an intrinsic and reproducible property of tissues.[14,15] A few pilot studies reported that ARFI imaging and serum fibrosis marker test results are significantly correlated with histologic fibrosis stage Determination of liver stiffness is

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considered valid when a success rate of at least 60% is obtained and the interquartile range is less than 30%.[16–19]

Based on the fact that ARFI is incorporated into a conventional ultrasonographic device, measurement of ARFI-SWV can be performed with different transducers. ARFI-SWV is recommended to be performed in the right liver lobe through the intercostal space. In this study, we aimed to perform a comparison of ARFI-SWV with 2 probes in both liver lobes. ARFI-SWV was initially measured with the convex probe 6C1 and then with the linear probe 9L4. The differences between the probes were investigated in each liver lobe. Furthermore, we also aimed to analyze inter- and intraobserver reproducibility for the probes.

2. Materials and methods

2.1. Patients

A total of 100 patients who had consulted the Academic Teaching Hospital Bethesda Duisburg, Germany were included in this study. There were no exclusion criteria. Written informed consent was obtained from all participating subjects. The informed consent was obtained in accordance with the WORLD Medical Association Declaration of Helsinki. This study was approved by the ethics committee of Heinrich Heine University (Ref. No. 5009). Patient characteristics are shown in Table 1.

2.2. ARFI-SWV measurement

In all patients, ARFI imaging (Acuson S2000, Siemens AG, Erlangen, Germany; Virtual Touch Tissue Quantification mode) was performed with both transducers (convex probe 6C1 and linear probe 9L4) during the same session. The examination was performed in the right lobe of the liver through the intercostal space and in the left lobe of the liver. A measurement depth of 2 cm below the liver capsule was chosen to standardize the examination for ARFI-SWV. The mean value of ten measurements was taken as representative.

Determination of liver stiffness was considered valid when a success rate of at least 60% was obtained and the interquartile range was less than 30%.

2.3. Statistical analysis

Data were analyzed using SPSS (version 17.0; SPSS Inc., Chicago, IL, USA). A χ^2 or Fisher exact test (F-test) was used for the comparison of categorical variables, and Mann–Whitney test for the comparison of continuous variables. The significance level was set at 0.05, and all P values were two-tailed. Pearson test was performed to study the correlation of ARFI-SWV between the liver lobes and between the probes.

Intraobserver, interobserver, intralobe, and interlobe agreements were analyzed using the intraclass correlation coefficient (ICC) (18). ICC values ranged from +1 (100% agreement, all the variability being due to patient characteristics) to −1 (100% disagreement, all the variability being due to the raters performance). Interobserver agreement was calculated as the agreement between the first liver ARFI measurements of the 2 observers. Intraobserver agreement was calculated as the agreement between the first and second ARFI evaluation. Intralobe agreement was calculated as the agreement between the first and second ARFI in the same liver lobe with the same probe. Interlobe agreement was calculated as the agreement between the first ARFI in the right and left lobes with the same probe. Interprobe agreement was calculated as the agreement between the first ARFI in the same liver lobe with different probes. The agreement of liver stiffness between the right and left liver lobes was calculated using ICC. Agreement was classified as poor (ICC, .00–.40), fair (ICC, .40–.59), good (ICC, .60–.74), or excellent (ICC >.75).

Table 1

Characteristics of patients at the time of liver stiffness measurement (n = 100).

Patients, n	100
Male, n (%)	41 (41%)
Age (years)	41 ± 18
ALT (IU/L)	25 ± 9
AST (IU/L)	23 ± 13
GGT (IU/L)	41 ± 58
Total bilirubin (mg/dL)	0.1 ± 1.4
Weight (kg)	66 ± 14
Height (m)	1,68 ± 0.08
BMI (kg/m^2)	22.3 ± 3.9

ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, GGT = gamma-glutamyl transpeptidase.

3. Results

One hundred patients comprising 41 males and 59 females were included in the study. The mean age was 41 ± 18 years, the mean weight was 66 ± 14 kg, and the mean body mass index (BMI) was 22.3 ± 3.9 kg/m^2 (28 patients with BMI < 20, 52 patients with 20 ≤ BMI ≤ 25, 16 with 25 < BMI ≤ 30, and 4 patients with 30 < BMI < 35).

Six patients had chronic liver disease: 5 with steatosis hepatis and 1 with primary biliary cholangitis. Because only 6 patients had chronic liver disease, no subgroup was defined. There were no BMI subgroups, because only 4 patients had a BMI > 30. Patient characteristics are shown in Table 1.

3.1. Comparison of success rates

A valid liver stiffness determination (success rate of at least 60% and ICR less than 30%) was observed in 91/100 (91%) with both probes in the right liver lobe. A trend to a higher success rate was observed in the left liver lobe with the convex probe (77/100 (77%)) compared with the linear probe (68/100 (68%)) (P = .205). This difference may be due to the significantly larger distance between the skin surface and the left liver lobe capsule (right lobe 2.53 ± 0.72 cm; left lobe 3.32 + 0.99 cm; P < .001).

A significant difference in the success rates was observed for both probes between the right and left liver lobes. A success rate of 91% was observed in the right liver lobe compared with that of 77% in the left liver lobe for the convex probe (P = .007), and 91% vs. 68% for the linear probe (P < .001) (Table 2).

After excluding all patients with an invalid liver stiffness determination from one of the probes, 84 patients were analyzed for the right liver lobe and 55 for the left liver lobe. The difference between lobes was significant (P < .001).

3.2. Correlation of ARFI between both probes

Pearson test was performed to analyze the correlation between both probes and both lobes. A significant correlation of ARFI-

Table 2

Comparison of success rate, skin liver capsule distance, and ARFI-SWV between the right and liver lobes independence on the probes.

Characteristic	Right liver lobe	Left liver lobe	P
Success rate			
Convex probe	91%	77%	.007
Linear probe	91%	68%	<.001
Skin liver capsule distance (cm)	2.53 ± 0.72	3.32 ± 0.99	<.001
ARFI-SWV (m/s)			
Convex probe	1.19 ± 0.21	1.26 ± 0.26	.083
Linear probe	1.07 ± 0.17	1.23 ± 0.23	<.001

ARFI-SWV = Acoustic radiation force impulse imaging - shear wave velocity.

SWV was found between both probes in the right liver lobe ($P = .01$, r = .508; Fig. 1a) and in the left liver lobe ($P = .05$, r = .278; Fig. 1b).

Mean ARFI-SWV was significantly higher with the convex probe than that with the linear probe (1.19 ± 0.21 m/s vs 1.07 ± 0.17 m/s; $P < .001$) in the right liver lobe. The same observation was noted for ARFI-SWV in the left lobe (1.26 ± 0.26 m/s vs 1.23 ± 0.23 m/s; $P < .001$).

Next, ARFI-SWV was analyzed between the liver lobes for each probe. ARFI-SWV was not significantly different between the right and left liver lobes measured with the convex probe (1.19 ± 0.21 m/s vs. 1.26 ± 0.26 m/s; $P = .083$) but was significantly different with the linear probe (1.07 ± 0.17 m/m vs 1.23 ± 0.23 m/s; $P < .001$).

After correlation of both probes for each lobe, we investigated the ARFI-SWV for each probe in both lobes. ARFI-SWV was successfully performed in 71 patients in both liver lobes with the convex probe and in 71 patients with the linear probe. No significant correlation of ARFI-SWV was found between the liver lobes for both probes (convex probe r = .19, $P = .112$, Fig. 1c; linear probe r = .144, $P = .23$, Fig. 1d).

ICC was calculated to study the agreement between both probes in different liver lobes. A successful ARFI-SWV measurement was performed in 84 patients in the right lobe with both probes. A good agreement was observed in the right lobe (ICC, .612; 95% CI .402–.748). A fair agreement was detected in the left lobe for ARFI-SWV between both probes (n = 55; ICC, .429; 95% CI .020–.667).

3.3. Reproducibility of ARFI

3.3.1. Intra- and interobserver reproducibility in the right liver lobe

3.3.1.1. Convex probe. Twenty patients were examined repeatedly to evaluate the reproducibility of ARFI-SWV measurements. For the intraobserver reproducibility, 1 observer examined the patients twice directly in series. An excellent agreement between both measurements was found for observer 1 (ICC, .814; 95% CI .592–.930) and observer 2 (ICC, .900; 95% CI .778–.955). To study the interobserver agreement, 2 observers examined the patients consecutively. A good agreement was found for the interobserver agreement in the right lobe with the convex probe ((ICC, .679; 95% CI .296–.854) (Table 3).

3.3.1.2. Linear probe. An excellent agreement was found between both measurements for observer 1 (ICC = .961; 95% CI .921 to .981) and observer 2 (ICC = .771; 95% CI .526 to .889). An excellent agreement was also found for the interobserver agreement in the right lobe with the linear probe (ICC = .815; 95% CI .617 to .911) (Table 3).

3.4. Intra- and interobserver reproducibility in the left liver lobe

3.4.1. Convex probe. An excellent agreement was found between both measurements for observer 1 (ICC, .893; 95% CI .757–.953) and observer 2 (ICC, .824; 95% CI .514–.936). A poor agreement was found for the interobserver agreement in the left lobe with the convex probe (ICC, .320; 95% CI .819–.745) (Table 3).

3.4.2. Linear probe. An excellent agreement was found between both measurements for observer 1 (ICC, .932; 95% CI .845–.970) and observer 2 (ICC, .897; 95% CI .753–.957). A good agreement was also found for the interobserver agreement in the right lobe with the linear probe (ICC, .603; 95% CI .043–.835) (Table 3).

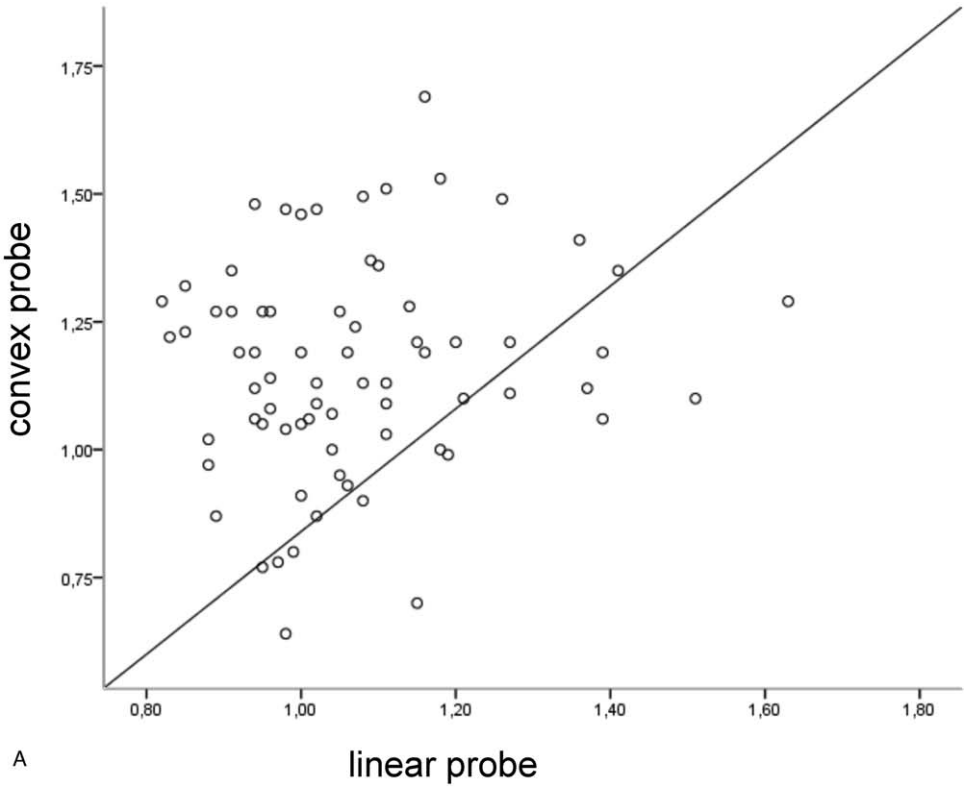
4. Discussion

Noninvasive measurement of liver fibrosis has attracted great interest. Various tools and noninvasive methods have been described and used clinically. ARFI is an ultrasound-based method with the advantage that the ROI can be selected under ultrasound control. A good correlation was observed between ARFI and the determined histological stage of fibrosis in several studies.

We compared ARFI-SWV between convex (6C1) and linear probes (9L4) in both liver lobes. ARFI is generally performed in the right lobe, but it can also be performed in the left lobe. Optimal conditions for share wave speed imaging have been published by the World Federation for Ultrasound in Medicine and Biology. These conditions include fasting, dorsal decubitus position, resting respiratory position, ROI placement beneath Glisson capsule by 1.5 to 2.0 cm, ROI placement to avoid large liver vessels, and the median of 5 to 10 measurements. However, no recommendation on which probe type and probe position to use has been made. In this study, we investigated these factors. The European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) guidelines recommend measurement of liver stiffness by SWV through the right intercostal space in supine position, with the right arm in extension. The guidelines also recommend patients to fast for a minimum of 2 hours, but they have no suggestions on which probe to use.

ARFI-SWV could be performed with the same success rate with both probes in the right liver lobe but was different in the left liver lobe. A significant difference in the success rates was observed when the success rates for each probe were compared in the right and left liver lobes. A reason for this trend may be due to the significantly larger distance between the skin surface and the left liver lobe capsule (right lobe 2.53 ± 0.72 cm; left lobe 3.32 ± 0.99 cm; $P < .001$). In view of the requirement of a success rate of at least 60% for valid liver stiffness detection, the right liver lobe should be preferred.

ARFI-SWV correlation between both probes was significant for both liver lobes, with a better correlation index in the right liver lobe (r = .508) compared with the left liver lobe (r = .278). However, there was poor correlation for both lobes. The agreement between both probes was different in the liver lobes. While a good agreement for both probes was observed in the right



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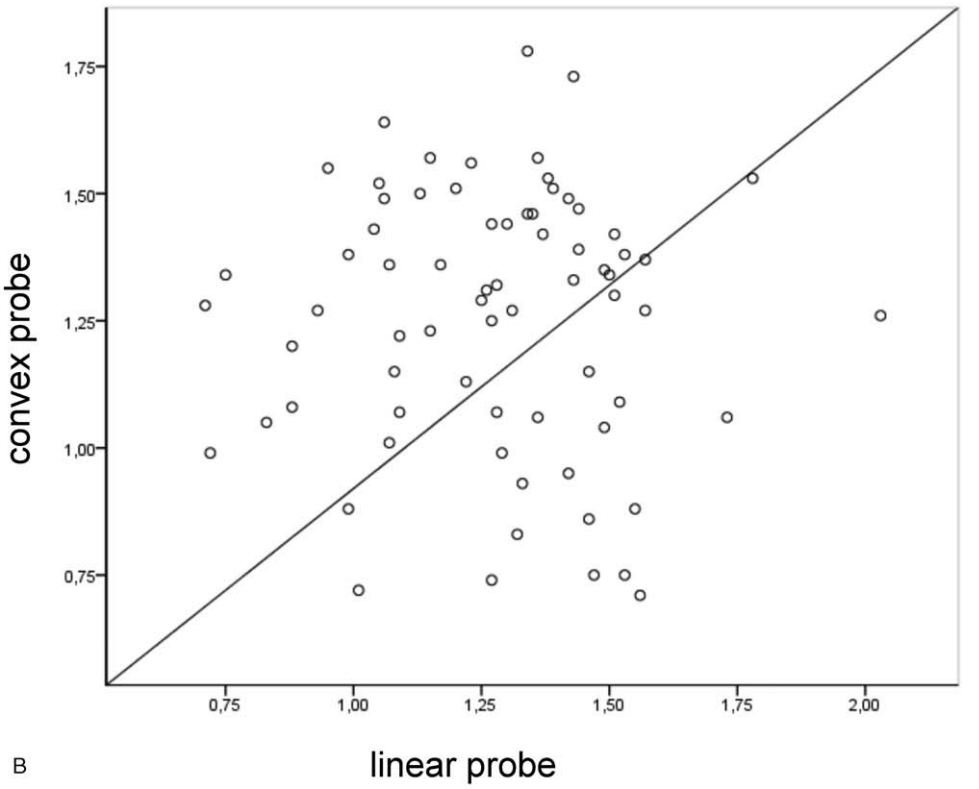

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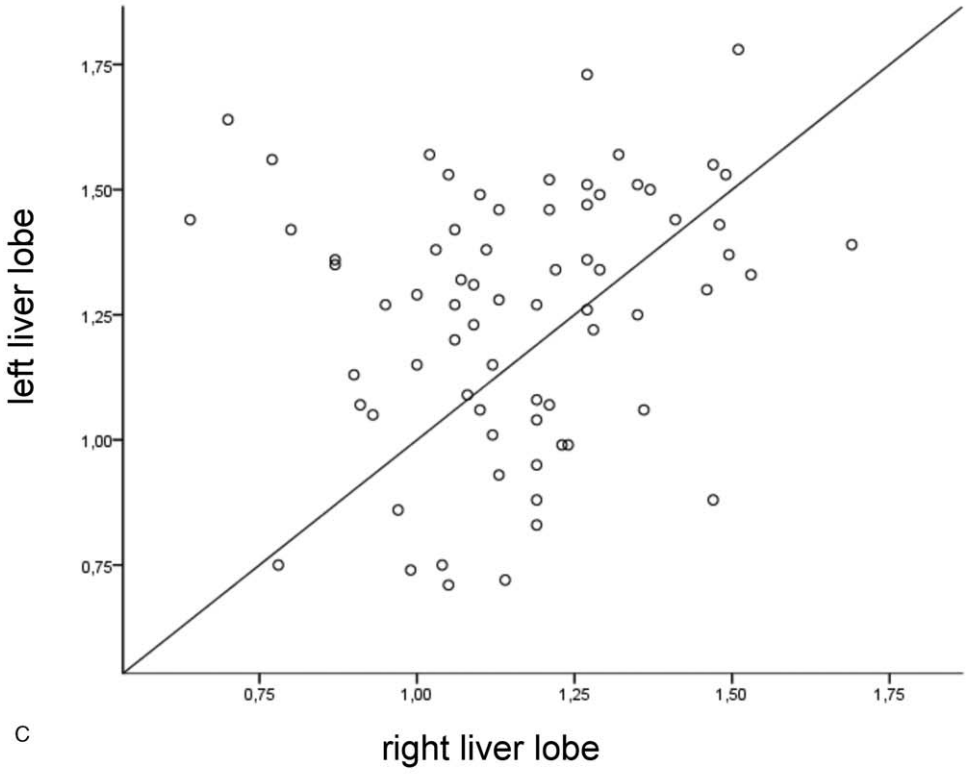
Figure 1. Correlation of liver stiffness measured by ARFI (a) in the right liver lobe with the convex and linear probes (n = 84; r = .508; *P* = .01), (b) in the left liver lobe with the convex and linear probes (n = 55; r = .278; *P* = .05), (c) with the convex probe in the right and left liver lobes (n = 71; r = .19; *P* = .112), and (d) with the linear probe in the right and left liver lobes (n = 71; r = .144; *P* = .23).



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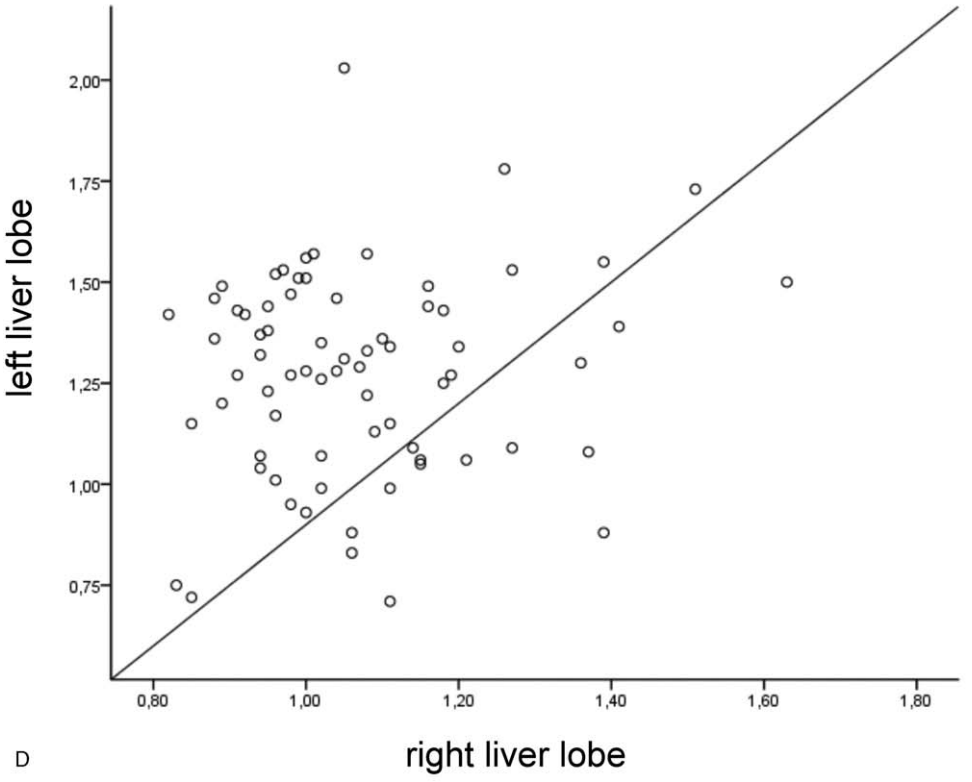

D

Figure 1. (Continued).

Table 3

Intraclass correlation coefficient (ICC) for inter- and intraobserver reproducibility for the different probes in the right and left liver lobes.

	ICC
Interobserver reproducibility	
Right liver lobe	
Convex probe	.679
Linear probe	.815
Left liver lobe	
Convex probe	.320
Linear probe	.603
Intraobserver reproducibility	
Convex probe	
Right liver lobe (observer I)	.814
Right liver lobe (observer II)	.900
Left liver lobe (observer I)	.893
Left liver lobe (observer II)	.824
Linear probe	
Right liver lobe (observer I)	.961
Right liver lobe (observer II)	.771
Left liver lobe (observer I)	.932
Left liver lobe (observer II)	.887

liver lobe, only a fair agreement was detected in the left liver lobe. Nonetheless, a good agreement was observed for both in the right liver lobe; a significant trend to higher ARFI-SWV was found for the convex probe. These results suggest that the right liver lobe seemed less susceptible to the used probe. This was indicated by the following results. When we investigated ARFI-SWV for both probes in both liver lobes, no significant correlation was observed for one of the probes (the probe when we measured liver stiffness in the right and left liver lobes with the same probe). These results imply a standard position for performance and for comparability among different studies.

Pfeifer et al investigated 2 convex probes (6C1HD and 4C1) and found slightly higher ARFI-SWV with the 6C1HD probe in an ARFI phantom and patients with liver cirrhosis.[20] Because the difference was small, they suggested that current cut-off values should maintain their usefulness; nevertheless, their results should be interpreted with caution when measurements are close to the cut-off. Potthof et al investigated the correlation of C4–1 and L9–4 convex probes.[21] They found a significant correlation between the probes, with significantly higher mean values in patients with significant fibrosis or with cirrhosis for the linear probe than for the convex probe.[21] This is in contrast to our findings; however, they used other probes in their study. The difference between their results and our findings indicates that ARFI-SWV depends on the probe used.

When we compared ARFI-SWV in both lobes that were dependent on the probe, a significant difference was detected for the linear probe, with lower ARFI values in the right hepatic lobe. This result is comparable with the observation reported by Fontanilla et al.[22] They showed that the site of measurement had a significant effect, with lower ARFI values in the right hepatic lobe. Eiler et al investigated the interlobar difference in children and adolescents and found lower values in the right liver lobe than in the left liver lobe.[23] These results support the EFSUMB recommendations that liver stiffness measurement should be performed in the right liver lobe.

Reproducibility is important for observer-independence method. In this study, we investigated the intra- and interobserver reproducibility for both probes in both liver lobes. The intraobserver reproducibility was excellent for both probes in the right liver lobe. While an excellent interobserver agreement was detected for the linear probe in the right liver lobe, a good interobserver agreement was demonstrated for the convex probe only. These results are comparable in the left liver lobe, with a trend to poorer interobserver agreement for both probes. Other studies also found excellent inter- and intra-observer agreement for ARFI-SWV. Fang et al found an excellent inter- and intraobserver reproducibility in healthy volunteers.[24] Balakrishnan et al measured liver and spleen stiffness by ARFI-SWV.[25] They found an excellent intra- and interobserver reproducibility for the liver but not for the spleen. These results are consistent with our results. ARFI seems not to depend on the observer, but our results indicated that ARFI-SWV should be performed in the right liver lobe for a better reproducibility.

There were several limitations in this study. First, we had a sample size of only 100 subjects; therefore, we could not study the influence of BMI or chronic liver disease. Second, the study was conducted at 1 site by 2 experienced operators. If the study had been performed at more sites, differences among sites may have been identified.

In conclusion, ARFI-SWV could be performed with both probes in both liver lobes. Higher success rates and a better correlation could be detected in the right liver lobe. Intraobserver agreement was excellent for both probes in both liver lobes, but interobserver agreement was better in the right liver lobe. Therefore, we suggest that the convex probe be used in the right liver lobe to standardize the examination.

Author contributions

Mirja Wegner: conception and design of the study, acquisition of data, drafting of the manuscript/critical revision, approval of final version of the manuscript.

Erol Iskender: conception and design of the study, acquisition of data, drafting of the manuscript/critical revision, approval of final version of the manuscript.

Ahmed Azzarok: conception and design of the study, data analysis/interpretation, drafting of the manuscript/critical revision, approval of final version of the manuscript.

Abdurrahman Sagir: Conception and design of the study, data analysis/interpretation, drafting of the manuscript/critical revision, approval of final version of the manuscript.

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