Radiology

REVIEWS AND COMMENTARY • STATEMENTS AND GUIDELINES

Update to the Society of Radiologists in Ultrasound Liver Elastography Consensus Statement

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

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This multidisciplinary update of the Society of Radiologists in Ultrasound consensus statement on liver elastography incorporates the large volume of new information available in the literature since the initial publication. The recommended procedure for acquiring stiffness measurements is reviewed. There has been substantial improvement in the acoustic radiation force impulse (ARFI) technology—most notably the addition of a quality assessment of the shear wave propagation. Due to the efforts of the Quantitative Imaging Biomarkers Alliance, or QIBA, the variability of liver stiffness measurements between systems had decreased. There are now effective treatments for hepatitis B and hepatitis C, and follow-up after effective treatment should be based on the use of the delta change of the value obtained at viral eradication or suppression. Because the detection of compensated advanced chronic liver disease (cACLD) is very important, the new guidelines are made based on the probability of cACLD for given stiffness values. The panel recommends a vendor-neutral rule of four for interpretation for ARFI techniques. This new method simplifies interpretation of liver stiffness results and is more clinically relevant.

This statement is an update produced by the Society of Radiologists in Ultrasound (SRU). Authors include the clinical members of the original statement and comprise society representatives and hepatologists with expertise in liver elastography in the United States and the European Union. The revision process involved identifying a panel leader (R.G.B.), who then selected relevant previous panelists to participate in the update. The panel chair and cochair (G.F.) created a preliminary draft with recommended updates, which were reviewed by the panel. Consensus was obtained iteratively after successive reviews and revisions and finalized after review by the SRU Executive Board.

The use of shear-wave elastography (SWE) for the noninvasive assessment of liver fibrosis has grown rapidly, and substantial new information regarding disease-specific liver stiffness is available since the publication of the consensus statement of the SRU in September 2015 (1,2). Vibration-controlled transient elastography has been available for almost 20 years and has a large body of literature (3–5). Acoustic radiation force impulse (ARFI) techniques, both point SWE (pSWE) and two-dimensional (2D) SWE have been available for almost 10 years. Currently, several vendors implement ARFI technology (both pSWE and 2D SWE, which are described in detail elsewhere [2,6]) in their US equipment and provide suggestions for optimal technique and assessment of data quality. Since publication of the previous guidelines, several additional vendors have introduced ARFI techniques, and the development of quality or confidence maps have led to the ability to assess the quality of the results. With excellent, less-expensive treatments for both hepatitis C and hepatitis B, these patients are being treated regardless of the liver stiffness value. This led to a need to update the SRU recommendations on the use of ARFI SWE for the assessment of fibrosis in patients with diffuse liver disease, as a guide for performing and interpreting the examination, taking into account the interim technology advances and published studies.

Chronic liver disease is a world-wide problem. It can be due to a wide range of inciting factors. Its major consequence is increasing deposition of fibrous tissue within the liver leading to the development of cirrhosis, which in turn may give rise to portal hypertension, hepatic insufficiency, and hepatocellular carcinoma. The stage of liver fibrosis is important to determine the prognosis, for surveillance, for prioritization for treatment, and even to determine the potential for reversibility (1,2,7–9). The spectrum of fibrosis is a continuum, and patients with a higher stage of liver fibrosis (stage F3–F4) are at risk for clinical complications (eg, ascites, variceal hemorrhage, hepatic encephalopathy). For patients with severe fibrosis or liver cirrhosis who are asymptomatic, the term "compensated advanced chronic liver disease" (cACLD) has been proposed (10,11). In patients with cACLD, the degree of portal hypertension is predictive of decompensation and/or death (10,11). A portal pressure (as assessed by means of the hepatic venous pressure gradient) of 10 mm Hg or higher (normal, 3–5 mm Hg)—a threshold that is designated "clinically significant portal hypertension" (CSPH)—has been associated with an almost four-fold higher risk of decompensation compared with lower pressures (12).

Many clinical guidelines recommend the use of noninvasive tests for the detection and staging of liver fibrosis (3,5,13,14). Although biopsy is historically the reference standard for staging fibrosis, it is imperfect, with

Abbreviations

ARFI = acoustic radiation force impulse, cACLD = compensated advanced chronic liver disease, CSPH = clinically significant portal hypertension, IQR = interquartile range, NAFLD = non-alcoholic fatty liver disease, pSWE = point SWE, SRU = Society of Radiologists in Ultrasound, SWE = shear wave elastography, 2D = two-dimensional

Summary

To follow-up patients, the consensus suggests using the delta changes of liver stiffness over time instead of the absolute values, using as a baseline value in case of viral hepatitis that obtained after viral eradication or suppression.

Key Results

- The variability between consecutive liver stiffness acquisitions, assessed by means of the interquartile range–to-median ratio, is the most important quality criterion; when this ratio is higher than 30% for measurements given in kilopascals or higher than 15% for measurements given in meters per second, the accuracy of the technique is reduced.
- Given the large overlap of stiffness values for mild-to-moderate fibrosis, the Society of Radiologists in Ultrasound continues to recommend a low cutoff value below which there is a high probability of no or mild fibrosis and recommends a high cut-off value above which there is a high probability of compensated advanced chronic liver disease (cACLD).
- Because the overlap of liver stiffness values between METAVIR scores is as large if not larger than the difference between vendors, separate cut-off values for each vendor are not required.
- The panel recommends a vendor-neutral "rule of four" for the acoustic radiation force impulse techniques in the viral causes and non-alcoholic fatty liver disease (NAFLD): Liver stiffness less than or equal to 5 kPa (1.3 m/sec) has high probability of being normal, liver stiffness less than 9 kPa (1.7 m/sec), in the absence of other known clinical signs, rules out cACLD, and values greater than 13 kPa (2.1 m/sec) are highly suggestive of cACLD; in some patients with NAFLD, the cut-off values for cACLD may be lower and follow-up or additional testing in those with values between 7 and 9 kPa is recommended.
- For pediatric patients with liver disease or congenital heart disease with Fontan surgery, it is expert opinion that each patient becomes his or her own control, and the stiffness delta changes over time should be used to evaluate the efficacy of the treatment or the progression of disease.

considerable interobserver variability and κ values varying from 0.5 to 0.9 in the literature (15,16). It should be emphasized, however, that histologic examination of liver specimens does provide information on inflammation that is not yet possible to evaluate with US. Despite this benefit, the use of noninvasive tests is favored due to the need for longitudinal monitoring and to safely extend screening to larger populations.

There are many different causes of chronic liver disease worldwide. Chronic viral hepatitis (hepatitis C in the West, hepatitis B in the East) remains a major risk factor. Although the incidence of cACLD may be lower because of the advent of highly effective interferon-free antiviral therapies, staging of liver fibrosis is still necessary before treatment because patients with cACLD require continued surveillance for hepatocellular carcinoma and/or varices even after the clearance of the virus (17,18).

A rising cause of chronic liver disease worldwide is nonalcoholic fatty liver disease (NAFLD). NAFLD is currently the most common liver disease in the United States, with a worldwide prevalence of 25% with imaging estimation (19). NAFLD ranges from simple steatosis to nonalcoholic steatohepatitis, which may progress to liver fibrosis and cirrhosis with its complications. Although there is no specific therapy for nonalcoholic steatohepatitis, lifestyle modifications have been associated with a decrease in fibrosis and portal hypertension (20,21), and identification of cACLD allows for screening and surveillance of varices and hepatocellular carcinoma. Therefore, the availability of noninvasive tools to exclude or diagnose cACLD in these patients is of the utmost importance.

Protocol for ARFI SWE Acquisition

The patient preparation, imaging technique, and measurement recommendations for ARFI SWE (both pSWE and 2D SWE) are the same, and the recommended protocol in the original SRU consensus is unchanged and similar to the European Federation of Societies for Ultrasound in Medicine and Biology and World Federation for Ultrasound in Medicine and Biology guidelines (3,5). The protocol includes obtaining measurements between the ribs in the right upper quadrant, instructing the patient to fast for at least 4 hours, imaging the patient in a supine or slight left lateral decubitus position (not more than 30°) with their right hand above their head, obtaining measurements in a neutral breath hold, placing the transducer perpendicular to the liver capsule and the measurement box parallel to the liver capsule, and taking measurements 1.5–2.0 cm from the liver capsule to avoid reverberation artifact. A brief outline of how to perform the examination is included in Table 1.

Because B-mode is used to track the shear waves, high-quality B-mode imaging is required. Images should be free of artifacts. Several studies have shown that operators require only a short period of training to perform reliable liver stiffness measurements; however, the reproducibility of liver stiffness measurements over time is higher for expert operators than for novice operators (22–24).

Quality Criteria

The recommended quality criteria include the number of required acquisitions and the interquartile range (IQR)–to-median ratio (subsequently referred to as IQR/M). Furthermore, some vendors provide a quality or confidence factor for measurements obtained with 2D SWE. Some vendors also provide an assessment of the quality of each measurement for pSWE. Each vendor has recommendations for use of their quality criteria.

Obtaining Measurements

Measurements should be obtained in areas of high quality, which is determined by a high amplitude of the shear waves, a normal shear-wave propagation, and a linear slope of the time of the peak and distance from ARFI pulse of the displacement curves. Each vendor provides a confidence or quality number or map that combines these factors into one number for clinical use. Figure 1 demonstrates various methods used to assess the quality of an image. If the quality is poor in most of the image, a measurement should not be obtained from that image.

Table 1: Recommendations for Performing Liver Stiffness Measurements with the ARFI Technique

Recommendations
1. Patients should fast at least 4 hours before the examination
2. Measurement should be taken at an intercostal space with the patient in the supine or slight lateral decubitus (30°) position with right arm in extension
3. Measurements should be taken at neutral breathing during a breath hold
4. Measurement should be taken at least 15–20 mm below liver capsule in pSWE
5. The 2D SWE region of interest can be positioned closer to the liver capsule, if reverberation artifacts are avoided; however, the measurement box should be positioned at least 15–20 mm below the liver capsule
6. Results can be reported in meters per second or in kilopascals
7. In most systems, the maximum ARFI push pulse is at 4–4.5 cm from the transducer, which is the optimal location for obtaining measurements. In most systems, the ARFI push pulse is attenuated by 6–7 cm, limiting adequate shear wave generation
8. Major potential confounding factors include liver severe inflammation indicated by AST and/or ALT elevation greater than five times upper normal limits, obstructive cholestasis, liver congestion, acute hepatitis, and infiltrative liver disease (these all lead to overestimation of the stage of fibrosis)
9. Ten measurements should be obtained with pSWE, and the final result should be expressed as the median together with the IQR/M
10. Fewer than 10 measurements with pSWE can be obtained (at least five); however, the IQR/M should be within the recommended range
11. For 2D SWE, five measurements should be obtained when the manufacturer's quality criteria are available, and the final result should be expressed as the median together with the IQR/M
12. The most important reliability criterion is an IQR/M of ≤30% of the 10 measurements (pSWE) or five measurements (2D SWE) for kilopascals and ≤15% for measurements in velocity (in meters per second)
13. Adequate B-mode liver imaging is a prerequisite for point and 2D SWE as shear waves are tracked with B-mode

Note.—ALT = alanine aminotransferase, ARFI = acoustic radiation force impulse, AST = aspartate aminotransaminase, IQR/M = interquartile range–to-median ratio, pSWE = point SWE, SWE = shear-wave elastography, 2D = two-dimensional.

Number of Measurements

pSWE.—Ten measurements are still recommended; however, studies have shown that there is no loss in accuracy with five measurements when the quality criterion of IQR/M is fulfilled (25–28). In the study by Fang et al (25), six measurements were recommended; however, when only the values obtained with a high reliability (IQR/M, ≤30%) were considered, there was no difference between five and six measurements.

Two-dimensional SWE.—The measurement area is larger than that with pSWE, and thus each value is an average of several measurements. Hence, five measurements are adequate if a quality assessment is provided by the manufacturer. If a quality assessment is not available, 10 measurements are recommended.

IQR/M Values

Studies have shown that the level of variability between consecutive acquisitions, assessed by means of the IQR/M, is the most important quality criterion. When this ratio is higher than 30% (for measurements given in kilopascals), the accuracy of the technique is reduced (3,25,27). It is important to note that the IQR/M for measurements reported in kilopascals should be 30% or less, whereas that for measurements reported in meters per second (shear wave speed) should be 15% or less as the conversion of meters per second to kilopascals is nonlinear. If the IQR/M values are greater than 30% in kilopascals or 15% in meters per second, the measurement of liver stiffness should be judged as unreliable.

Cut-off Values

Cut-off values for fibrosis staging vary across US systems from different vendors; however, the variance has decreased due to the efforts of the Quantitative Image Biomarker Alliance, or QIBA (29,30). QIBA (an RSNA organization with vendors, scientists, members of the U.S. Food and Drug Administration, and clinicians) developed standardized phantoms that the vendors have used to standardize their measurements. The difference between various system measurements increases as liver stiffness increases. The difference in cut-off values is greatest as patients exceed the threshold of cACLD (31).

Given the large overlap of stiffness values for mild-to-moderate fibrosis, the SRU continues to recommend a low cut-off value below which there is a high probability of no or mild fibrosis and recommends a high cut-off value above which there is a high probability of cACLD. In this update, a new cut-off value to rule out CSPH has been added on the basis of some recent studies (32–35). The consensus panel also divides the liver stiffness values between no or minimal disease and cACLD into two categories. For these middle liver stiffness values, confirmation with an additional test may be needed to rule in or rule out cACLD. From a clinical perspective, it is more important to rule in or rule out significant disease than it is to provide an exact stage by using the METAVIR scoring system. Because of the large liver stiffness value overlap of METAVIR scores (1), which is greater than the measurement variability between vendors (31), separate cut-off values for each vendor are not required. Based on some published studies and mirroring the Baveno VI consensus conference (10,11), that is, the so-called "rule of five" (5, 10, 15, 20 kPa)

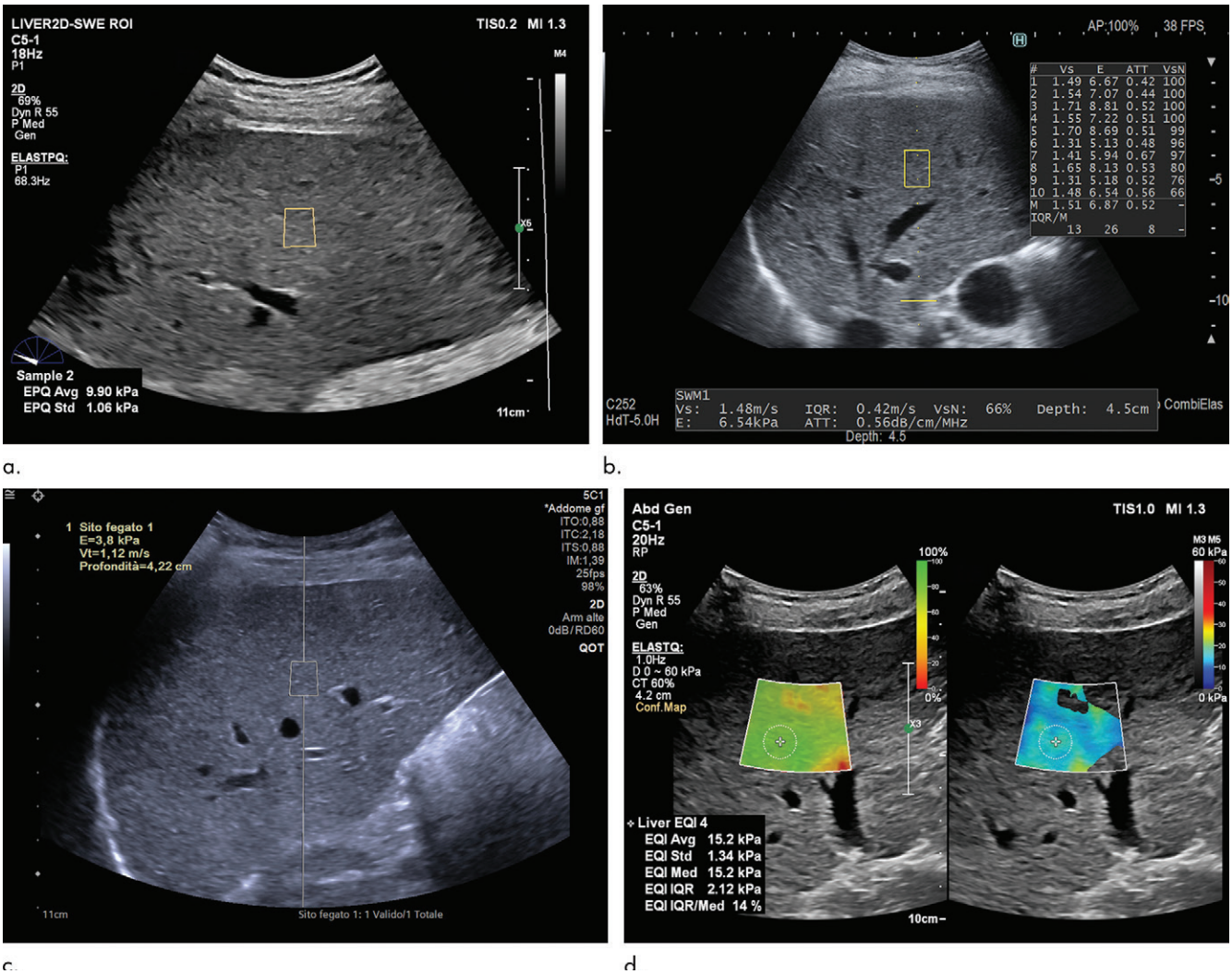


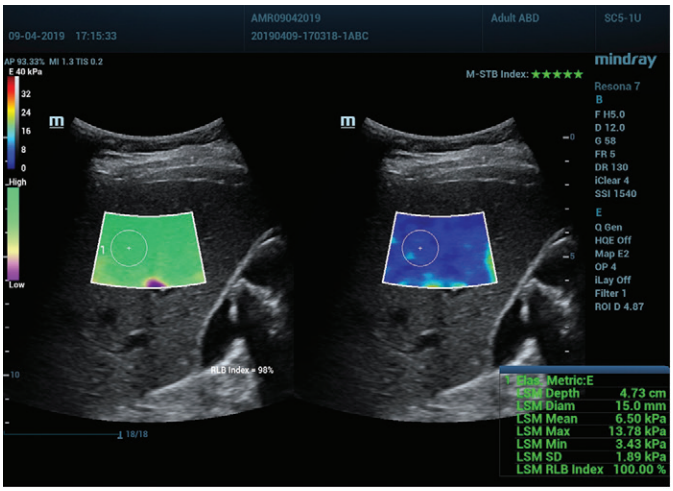
Figure 1: **(a)** Image obtained with point shear-wave elastography (pSWE) system (ElastPQ; Philips, Bothell, Wash). A standard deviation (Std) of 30% or less of the mean value is indicative of an acquisition of good quality. In this case, the standard deviation is 1.06/9.90 or 10.7%. When the signal-to-noise ratio of an acquisition is very low, the mean value is not shown. **(b)** Image obtained with pSWE (SWM; Hitachi, Tokyo, Japan). "VsN" is a reliability index that indicates the percentage of effective push-track sequences. When the signal-to-noise ratio of an acquisition is very low, the mean value is not shown. A good acquisition has a VsN of at least 50%. In this case, the VsN measurements are all above 66%. **(c)** Image obtained with pSWE (VTQ; Siemens, Mountain View, Calif). The system automatically filters out the measurements that are not good. In these cases, the numeric value of shear-wave speed is replaced by an "XXX" sequence. **(d)** Images obtained with two-dimensional (2D) shear-wave elastography (SWE) (EQI, Philips). The color-coded confidence map (left) is an evaluation of the quality of the acquired signals. The confidence threshold (CT) is set at 60%: Areas of low quality (red) are filtered out and left blank on the color-coded image of liver stiffness assessment (right); the yellow color on the confidence map is a warning, that is, it indicates that the acquisition in that area is not the highest quality (*Fig 1 continues*).

for the staging of liver fibrosis with vibration-controlled transient elastography, the consensus panel proposes a vendor-neutral "rule of four" (5, 9, 13, 17 kPa) for the ARFI techniques for viral etiologies and NAFLD: Liver stiffness of 5 kPa (1.3 m/sec) or less has high probability of being normal; liver stiffness less than 9 kPa (1.7 m/sec), in the absence of other known clinical signs, rules out cACLD; values between 9 kPa (1.7 m/sec) and 13 kPa (2.1 m/sec) are suggestive of cACLD but may need further test for confirmation; and values greater than 13 kPa (2.1 m/sec) are highly suggestive of cACLD. There is a probability of CSPH with liver stiffness values greater than 17 kPa (2.4 m/sec), but additional patient testing may be required. In some patients with NAFLD, the cut-off values for cACLD may be lower and follow-up or additional testing in those with values between 7 and 9 kPa is recommended.

For other causes such as alcoholic hepatitis, primary biliary cirrhosis, Wilson disease, autoimmune hepatitis, sclerosing cholangitis, and drug-induced liver disease, there is insufficient data to make a conclusion.

Table 2 summarizes these cut-off value recommendations and provides them in both kilopascals and meters per second. For those who would like a value to rule out significant fibrosis, most studies that used ARFI (pSWE and 2D SWE) suggest that a liver stiffness value of less than 7 kPa (1.5 m/sec) can help rule out significant fibrosis.

With vibration-controlled transient elastography, the alanine aminotransferase–adapted cut-off values of liver stiffness reportedly improved the staging of liver fibrosis in patients with chronic hepatitis B in a single study (36). The consensus



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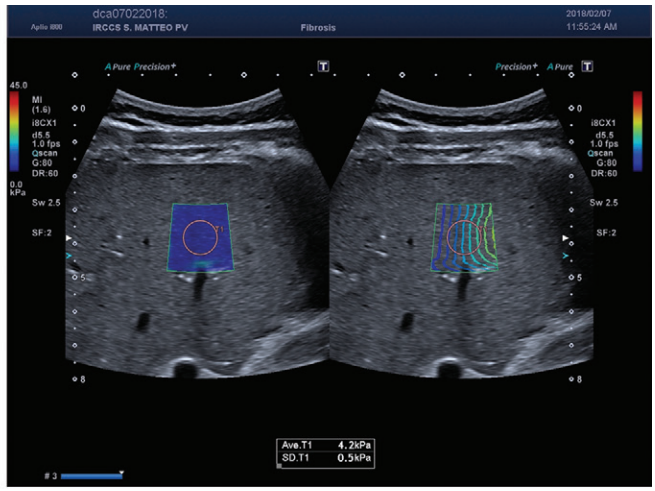

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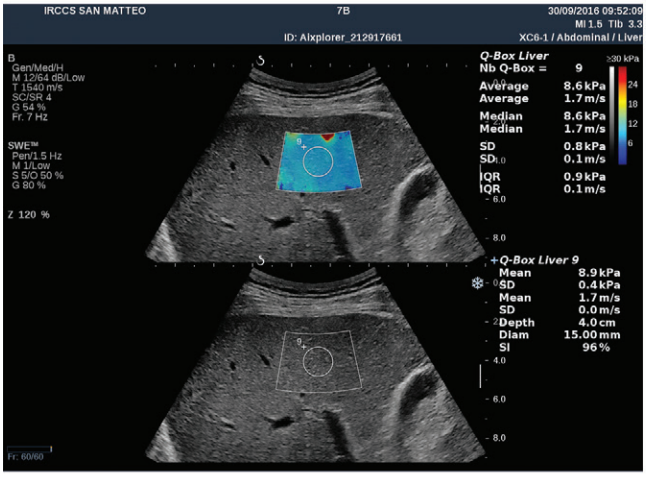


g.

Figure 1 (*continued*)**: (e)** Images obtained with 2D SWE (STE; Mindray, Shenzhen, China). Two quality criteria are provided: the motion stability (M-STB) index, which is indicated by stars (with the highest stability shown with five green stars), and the reliability (RLB) map, which goes from purple to green—with the latter indicating the highest reliability. The stars are an indicator of motion during the acquisition. When there are fewer than four stars, there is significant motion during the acquisition and that frame should not be used for liver stiffness measurement. **(f)** Images obtained with 2D SWE (Aplio; Canon, Tochigi, Japan). The system filters out values with a low signal-to-noise ratio, and these areas are left blank. The proprietary quality parameter is the propagation map (right). A proper propagation map is displayed with parallel lines, with the intervals between the lines constant. The propagation map is used to guide placement of the measurement box. Image on left is velocity map. **(g)** Images obtained with 2D SWE (SSI; SuperSonic, Aix-en-Provence, France). Values with a low signal-to-noise ratio are filtered out. The stability index (SI) is an indicator of temporal stability, and it is displayed while positioning the measurement box (Q-Box). An acquisition of good quality should have a stability index greater than 90%. Top image is velocity map, and bottom image is B-mode image.

Table 2: Recommendation for Interpretation of Liver Stiffness Values Obtained with ARFI Techniques in Patients with Viral Hepatitis and NAFLD

Liver Stiffness Value	Recommendation
≤5 kPa (1.3 m/sec)	High probability of being normal
<9 kPa (1.7 m/sec)	In the absence of other known clinical signs, rules out cACLD. If there are known clinical signs, may need further test for confirmation
9–13 kPa (1.7–2.1 m/sec)	Suggestive of cACLD but need further test for confirmation
>13 kPa (2.1 m/sec)	Rules in cACLD
>17 kPa (2.4 m/sec)	Suggestive of CSPH

Note.—ARFI = acoustic radiation force impulse, cACLD = compensated advanced chronic liver disease, CSPH = clinically significant portal hypertension, NAFLD = non-alcoholic fatty liver disease.

panel therefore does not recommend alanine aminotransferase–adapted cut-offs until additional publications confirm its usefulness. The updated World Federation of Ultrasound in Medicine and Biology guidelines provide a detailed review of the literature for several of the causes that progress to chronic liver disease and associated confounding factors (3).

Confounding Factors

There are several clinical conditions in which an increase of liver stiffness unrelated to liver fibrosis can be observed (1,3,5). These conditions include, but are not limited to, acute hepatitis, liver inflammation, transaminitis flares with alanine aminotransferase value more than five times the upper limit of normal, obstructive cholestasis, hepatic congestion, and infiltrative liver diseases such as amyloidosis, lymphoma, or extramedullary hematopoiesis. Other factors may also affect liver stiffness measurement, such as postprandial hyperemia or intense physical exercise. In all these conditions, however, stiffness values within the normal range exclude significant liver fibrosis.

Table 3: Recommendations for Performing Spleen Stiffness Measurements with the ARFI Technique

Recommendations
1. Patients should fast at least 4 hours before the examination (56)
2. Measurement should be taken at an intercostal space with the patient in supine position with left arm in extension
3. Measurements should be taken during breath hold at neutral breathing (57)
4. Measurement should be taken at least 15 mm below spleen capsule with pSWE and reverberation artifacts avoided with 2D SWE. The region of interest should be placed perpendicular to the splenic surface
5. Results can be reported in meters per second or kilopascals
6. In most systems, the maximum ARFI push pulse is at 4–4.5 cm from the transducer, which is the optimal location for obtaining measurements. In most systems, the ARFI push pulse is attenuated by 6–7 cm, limiting adequate shear wave generation
7. Ten measurements should be obtained with pSWE, and the final result should be expressed as the median together with the IQR/M
8. For 2D SWE, five measurements should be obtained, and the final result should be expressed as the median together with the IQR/M
9. The most important reliability criteria is a IQR/M of ≤30% of the recommended measurements for kilopascals and ≤15% for meters per second

Note.—ARFI = acoustic radiation force impulse, IQR/M = interquartile range–to-median ratio, pSWE = point SWE, SWE = shear-wave elastography, 2D = two-dimensional.

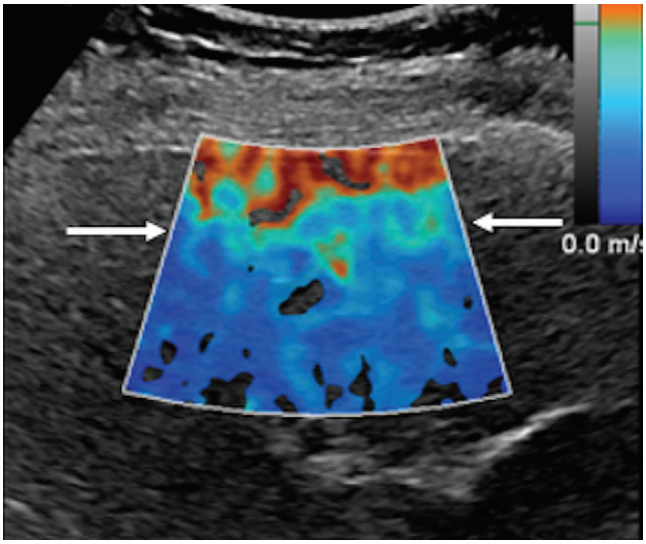


Figure 2: Image obtained with two-dimensional (2D) shear-wave elastography (SWE) demonstrates area of increased stiffness (red and teal, arrows) due to reverberation artifact. The reverberation artifact occurs below the liver capsule in both point SWE (pSWE) and 2D SWE. In pSWE, the artifact is not seen; therefore, it is important to obtain measurements at least 1.5 cm below the liver capsule to avoid the artifact. This area should be avoided when placing the measurement box for liver stiffness measurements.

Follow-up

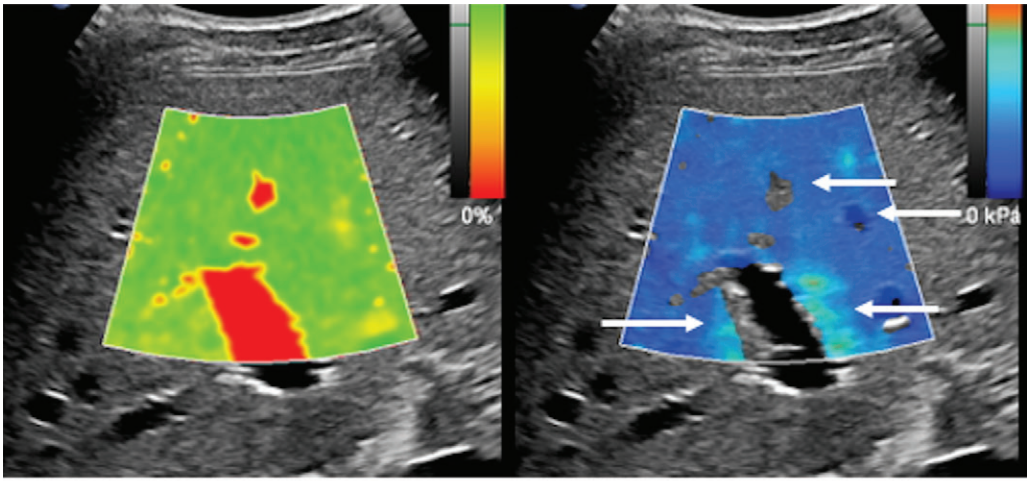
In patients with chronic hepatitis B virus or hepatitis C virus who have been successfully treated with antiviral drugs, the cut-offs obtained in viremic patients should not be used because a rapid decline of stiffness values has been observed in these patients, likely due to the decrease of liver inflammation (3,5). When liver cirrhosis is evident with B-mode findings, elastography should not be used to rule out the disease because a value in the low range of liver stiffness may only indicate a successful response to antiviral treatment.

On the basis of results of both prospective and retrospective studies with more than 1000 patients (37–41), the delta change of liver stiffness values over time should be used instead of the absolute values (37–40,42). Thus, every patient becomes his or her own control. Because there is an approximately 10% variability of the measurements within a vendor and between vendors (29,30), a clinically significant change should be considered when the delta change is greater than 10%. The panel recommends using the same equipment for follow-up studies. In patients with chronic viral hepatitis who are successfully treated, the baseline liver stiffness should be that obtained after viral eradication or suppression. Applying this rule, liver stiffness assessment can be suitable for evaluating all clinical conditions leading to an increase of liver stiffness, independent of the disease etiology including nonfibrotic causes of liver stiffness increase, such as congestive heart failure.

Spleen Stiffness

It has been reported that liver stiffness correlates with the severity of liver fibrosis up to the threshold of CSPH, defined as an increase in hepatic venous pressure gradient greater than 10 mm Hg (43). In patients with CSPH, the strength of the correlation between liver stiffness and fibrosis decreases, probably due to an increasing role played by extrahepatic factors, mainly the increase in portal venous inflow, as portal hypertension progresses (10,44). The acquisition technique is the same as that for liver, except the measurements are taken between the left ribs with the patient in a supine or slight right lateral position. It is the opinion of the expert panel that adequate studies have not been performed to provide cut-off values at this time. A review of the existing literature is provided below. In patients with chronic liver disease, splenic measurements should only be taken in patients with cACLD as significant portal pressures are not expected at lower levels of fibrosis.

CSPH is predictive of the development of complications of cirrhosis, including variceal rupture and death. However, it is also present in about 50%–60% of patients with compensated cirrhosis without gastroesophageal varices (12,45). It appears that spleen stiffness shows better correlation with portal pressure than does liver stiffness (46). Portal hypertension leads to splenic



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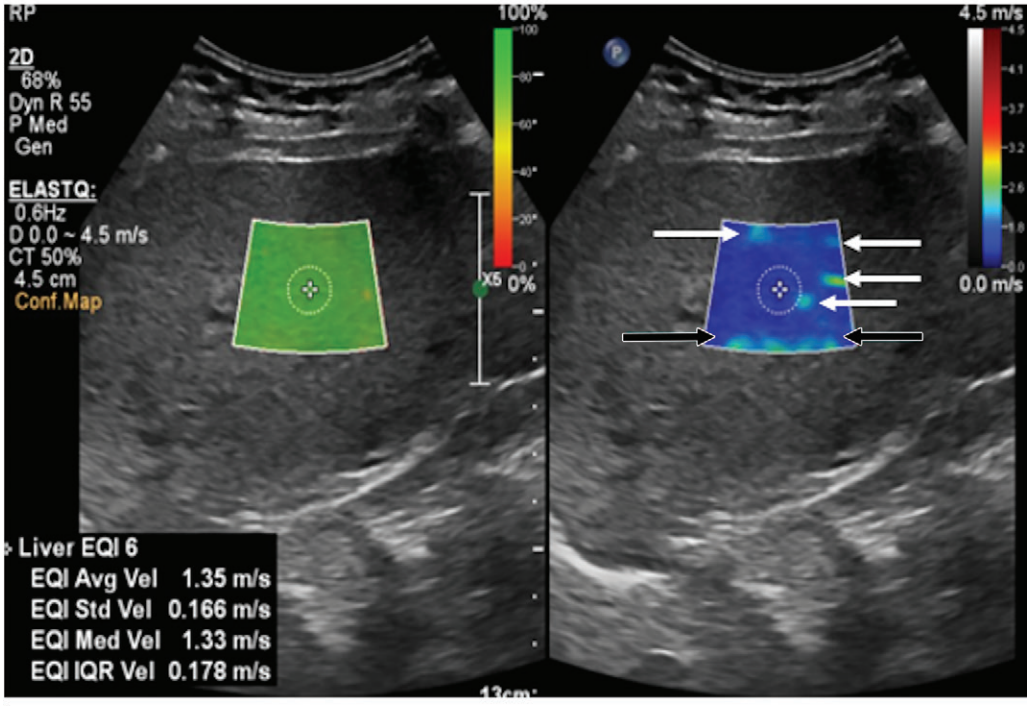

b.

Figure 3: **(a)** Artifacts occur around large blood vessels and bile ducts. These artifacts are not seen in point shear-wave elastography (SWE), and therefore measurements should be obtained at least 5 mm from these structures. In two-dimensional SWE, these artifacts can be identified and avoided. Image on right is velocity map, and image on left is quality map. Arrows indicate artifacts. Depending on the vendor, artifacts may not be color-coded or appear as areas of increased stiffness (teal). These areas should be avoided when placing the measurement box. **(b)** Shear-wave propagation occurs in all directions perpendicular to the acoustic radiation force impulse (ARFI) pulse. Therefore, artifacts from a blood vessel just out of the image plane can also produce artifacts. Velocity image (right) shows artifacts in teal (white arrows). These artifacts are most likely from vessels just out of the image plane. The measurement box should not include these areas. Black arrows point to teal areas at the deep part of the image. These are artifacts from the ARFI pulse strength decreased due to attenuation, leading to weak shear waves that make it difficult to obtain accurate estimates of shear-wave speed. Note that the quality map (left) in this case suggests high quality throughout the field of view. The quality map does not identify all artifacts, and both the quality map and velocity map should be evaluated for artifacts.

congestion, increasing splenic stiffness. In fact, portal hypertension may cause splenic fibrosis (47).

In healthy individuals, the spleen is stiffer than the liver. Several studies, most of which were performed with vibration-controlled transient elastography, have shown that, in patients with portal hypertension, spleen stiffness is more reliable than liver stiffness for assessing the risk of CSPH and esophageal varices (46,48–50). However, there are differences in cut-off values between studies, and the level of evidence is still too low to recommend spleen stiffness in the diagnostic work-up of patients with cirrhosis.

For ARFI-based techniques, limited studies suggest that abdominal wall thickness and splenic longitudinal diameter are independent predictors of successful spleen stiffness measurement (51,52). The feasibility of performing spleen

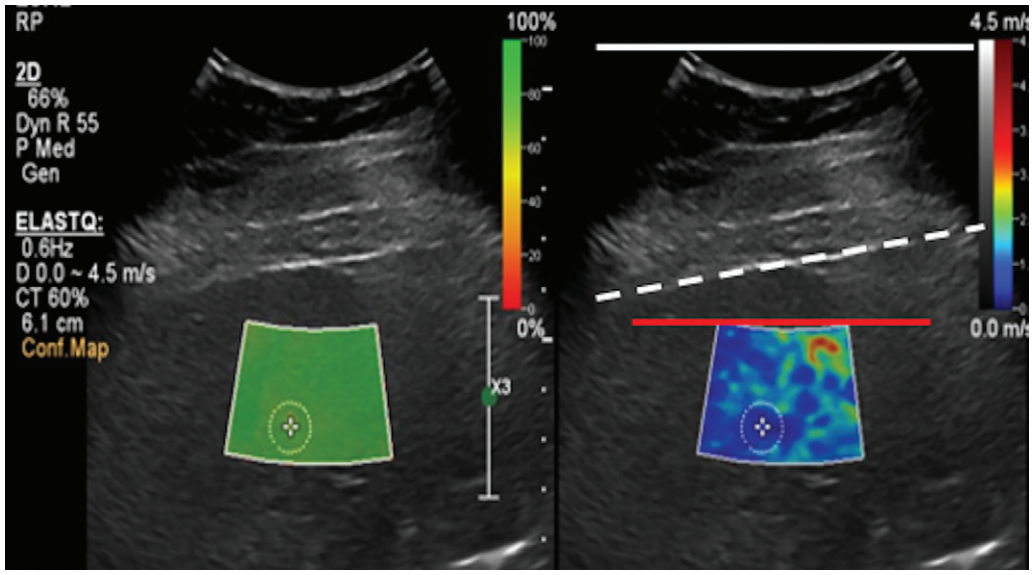

Figure 4: Images from two-dimensional shear-wave elastography. Image on left is confidence map, and image on right is velocity map. When the acoustic radiation force impulse pulse is not perpendicular to the liver capsule, artifacts occur. In this case, the liver capsule (dashed white line) is not parallel to the transducer (solid white line) or the field-of-view box (red line). The heterogeneous stiffness measurements in the field of view are due to artifacts occurring because the three lines are not parallel.

Suggested Reporting for Liver Stiffness Measurements

Liver stiffness measurements were obtained on a (list vendor and machine) using a (list probe) following the SRU guidelines. (# number of) valid measurements were obtained using a (point SWE or 2D SWE) method. The IQR-to-median ratio was (x), suggesting a (quality data set or poor-quality data set). The liver stiffness value was (X), suggesting **(rule of 4 recommended wording)**. Consider adding the following sentence(s) if appropriate: In the setting of (elevated liver function tests, nonfasting, vascular congestion, etc), the stage of liver fibrosis may be overestimated; In some patients with NAFLD, the cut-off values for cACLD may be lower (7–9 kPa); In causes other than viral hepatitis and NAFLD, the cut-off values are not well established.

Figure 5: Suggested reporting format for liver stiffness measurements. cACLD = compensated advanced chronic liver disease, IQR = interquartile range, NAFLD = non-alcoholic fatty liver disease, SWE = shear wave elastography, SRU = Society of Radiologists in Ultrasound, 2D = two-dimensional.

stiffness measurement was evaluated by Procopet et al (53) in 88 patients undergoing hepatic venous pressure gradient measurement for portal hypertension. The overall success rate of obtaining an accurate measurement, defined as the system being able to estimate a stiffness value, was 66%. In that series, the patients with failure of spleen stiffness had higher body mass index (mean, 28.3 kg/m^2 ± 5.0 vs 25.2 kg/m^2 ± 3.7; P = .002) and smaller spleen (mean bipolar diameter, 11.8 cm ± 2.7 vs 14.2 cm ± 4.0; $P < .0001$). In a series composed of 313 consecutive patients who underwent liver stiffness and spleen stiffness measurements on the same day (52), the success rate of spleen stiffness measurement was 80% in patients with splenomegaly. Technical success of spleen stiffness measurements was 78% in another small series (54), including 54 patients with cirrhosis who either had low-grade esophageal varices or were without esophageal varices at upper endoscopy.

Normal values of spleen stiffness with ARFI-based techniques in published studies range from 20.5 kPa (2.6 m/sec) to 24.4 kPa (2.85 m/sec) (52,53,55). The suggested procedure for performing spleen stiffness measurement is presented in Table 3.

With use of pSWE, investigators in one study reported a higher incidence of esophageal variceal bleeding in patients with a spleen stiffness value of at least 39 kPa (3.64 m/sec); no bleeding occurred in patients with spleen stiffness less than 36 kPa (3.48 m/sec) (58). With use of 2D SWE, other investigators showed that CPSH is unlikely in patients with spleen stiffness less than 26.6 kPa (3.0 m/sec) (35). Algorithms that combine liver stiffness and spleen stiffness, or platelets count, have been proposed (59).

In a multicenter study in which liver stiffness and spleen stiffness were available in 109 patients undergoing hepatic venous pressure gradient measurement, liver stiffness of 16.0 kPa (2.3 m/sec) or less and spleen stiffness of 21.7 kPa (2.7 m/sec) or less were able to help rule out CSPH, whereas liver stiffness values greater than 29.5 kPa (3.2 m/sec) and spleen stiffness values greater than 35.6 kPa (3.5 m/sec) were able to help rule in CSPH (specificity, >92%). In patients with liver stiffness of 38.0 kPa (3.6 m/sec) or less, a splenic stiffness greater than 27.9 kPa (3.2 m/sec) ruled in CSPH. This algorithm had a sensitivity of 89.2% and a specificity of 91.4% to rule in CSPH (41). However, in a series of 191 patients (60), this algorithm has not been validated: Specificity and positive predictive value were 52% and 83%, respectively.

Interestingly, it has been reported that patients with hepatis C virus hepatitis successfully treated with antiviral drugs show a rapid decline of liver stiffness but not of spleen stiffness because there is not an immediate effect on portal hypertension. Spleen stiffness is more accurate in assessing portal hypertension in this setting. Therefore, the risk of variceal hemorrhage remains in the short term (61).

Table 4: Summary of Recommendations

Protocol for acquisition: As reported in Table 1, the most important criterion is IQR/M ≤30% for values in kilopascals and 15% for values in meters per second. In pediatric patients, the same protocol must be used
Protocol for 2D SWE acquisition in children who are unable to hold their breath: The consensus panel suggests recording a 2D SWE cine loop for up to 30 seconds if real-time 2D SWE is available, reviewing it, and choosing the image that demonstrates the most stable pattern for the stiffness measurement. No more than one image should be chosen in each recorded cine loop
Cut-off values: "rule of four" (5, 9, 13, 17 kPa) for the ARFI techniques for viral causes and NAFLD (Table 2)
NAFLD and rare diseases in pediatric patients: The number of published pediatric studies of NAFLD remains low, and the cutoff values for staging liver fibrosis varies between studies. It is expert opinion that each patient becomes his or her own control, using the stiffness delta changes over time to evaluate the efficacy of the treatment or the progression of disease—remembering that the measurement reflects stiffness and not fibrosis
Follow-up: The use the delta changes of LS values over time should be used instead of the absolute values. In patients with chronic viral hepatitis who are successfully treated, the baseline LS stiffness should be that obtained after viral eradication or suppression. A clinically significant change should be considered when the delta change is greater than 10%. Applying this rule, LS assessment can be suitable for evaluating all clinical conditions leading to an increase of LS, independent of the disease cause including nonfibrotic causes of LS increase (eg, congestive heart failure)
Spleen stiffness: It appears that spleen stiffness is better correlated with portal pressure than LS. However, there are differences in cut-off values between studies and the level of evidence is still low to recommend spleen stiffness in the diagnostic work-up of patients with cirrhosis
Reporting: The report should include the system vendor name, the SWE technique (pSWE or 2D SWE), the probe used, the number of acquisitions, the IQR/M, and conclusions (Fig 5)

Note.—ARFI = acoustic radiation force impulse, IQR/M = interquartile range–to-median ratio, LS = liver stiffness, NAFLD = non-alcoholic fatty liver disease, pSWE = point SWE, SWE = shear-wave elastography, 2D = two-dimensional.

Pediatric Patients

The use of a noninvasive technique for staging liver fibrosis is of great interest because it may avoid liver biopsy, which, in addition to its well-known complications, is particularly stressful for pediatric patients. In the pediatric age group, NAFLD is the most common cause of chronic liver disease. A 2015 meta-analysis (62) determined that the pooled mean prevalence of NAFLD in the United States was 7.6% in the general U.S. pediatric population and that it reached 34.2% in obese children. In one study of 347 children suspected of having NAFLD who were identified through screening in primary care and referral to pediatric gastroenterology, advanced fibrosis was present in 17% of 193 children diagnosed with NAFLD at liver biopsy. Conversely, in 242 consecutive adolescents undergoing bariatric surgery, the prevalence of NAFLD was 58.8%, and 6% of the cohort had definite nonalcoholic steatohepatitis. Fibrosis was mild: 81% had none, while 18% had stage 1 or 2 fibrosis (63,64).

The use of noninvasive techniques in this population is particularly appealing. However, the number of published pediatric studies of NAFLD to date remains low and the cut-off values for staging liver fibrosis vary between studies (65).

For liver stiffness assessment, the procedure used for adults should be adopted. In children who are unable to hold their breath, the consensus panel suggests recording a 2D SWE cine loop for up to 30 seconds if real-time 2D SWE is available, reviewing it, and choosing the image demonstrating the most stable pattern for the stiffness measurement. No more than one image should be chosen in each recorded cine loop.

For ARFI-based techniques, most published studies have shown that age has no significant influence on liver stiffness values (66–68). However, there is not enough literature at this time for the panel to recommend the rule of four for NAFLD in pediatric patients.

The mean normal shear-wave velocity value ranges from 1.07 to 1.16 m/sec (66–68).

For liver disease associated with cystic fibrosis, autoimmune hepatitis, biliary atresia and the Kasai procedure, or congenital heart disease with Fontan surgery or even NAFLD or viral hepatitis, it is expert opinion that each patient becomes his or her own control, using the stiffness delta changes over time to evaluate the efficacy of the treatment or the progression of disease—remembering that the measurement reflects stiffness and not fibrosis. Results must always be interpreted considering transaminase values and clinical condition.

Steatosis Assessment

Liver fat content has also been evaluated by using US-based methods. Several studies have demonstrated proof of concept. Although there is insufficient evidence at this time to provide recommendations regarding the use of US-based methods in this setting, early work suggests that these methods will be clinically useful (69–73).

Artifacts

Artifacts are common in ARFI-based techniques and can significantly change the liver stiffness value. It is important to recognize and avoid these artifacts (eg, liver capsule reverberation artifact [Fig 2], ARFI push artifacts, artifacts from blood vessels [Fig 3], and the artifact that occurs when the transducer is not parallel to the liver capsule [Fig 4]). Most systems now have a confidence map or quality map that helps identify most artifacts. However, none of the confidence maps or quality maps depict all artifacts and knowledge of artifacts is crucial for obtaining accurate liver stiffness values. Although a detailed discussion of artifacts is beyond the scope of this article, it is available elsewhere (74–77).

Reporting

The report should include the system vendor name, the SWE technique (pSWE or 2D SWE), the probe used, the number of acquisitions, the IQR/M, and conclusions. Conclusions should use the rule of four detailed earlier (Table 2). An example of a report is shown in Figure 5. A summary of recommendations is given in Table 4.

Future Directions

The development of new US techniques that will provide a measurement of liver steatosis and dispersion imaging (ie, evaluating the change in stiffness values by varying the ARFI frequency) are also being evaluated as a method to assess inflammation. This is extremely important to differentiate simple steatosis, a benign condition, from nonalcoholic steatohepatitis. However, evidence available for these techniques is not yet at a level where recommendations can be given. Other US techniques that do not use vibration-controlled transient elastography or ARFI technology techniques are being evaluated for liver stiffness evaluation (78).

Future Research Questions

Basic Questions

1. What are the sources of variability between commercial SWE systems? In particular, how does the ARFI frequency component affect measures of stiffness?
2. Should we measure in more than one location?
3. What are appropriate tissue-mimicking phantom materials for the liver?
4. Will liver dispersion be helpful in evaluating inflammation and/or steatosis?

Clinical Questions

1. How different are cut-offs depending on the cause of chronic liver disease?
2. How can US elastography complement hepatic venous pressure measurements in the assessment of portal hypertension and in the assessment of changes in portal venous pressure in patients with liver disease?
3. Inflammation and congestion are important processes to document in the evolution of liver disease. Histologic assessment of biopsy specimens can only be used to identify the cellular component of inflammation and is essentially blind to the fluid component. Quantitative elastography, conversely, seems to be sensitive to the effects of the fluid component of inflammation. How can this capability be exploited for diagnostic purposes?
4. Can we use elastography and measures of loss modulus to differentiate nonalcoholic or alcoholic steatohepatitis from simple steatosis?

Follow-up of Patients

1. What is a minimal clinically important difference in stiffness measurements over time? How often should these measures be obtained?
2. How should the use of elastography change the screening interval in patients at risk for hepatocellular carcinoma?

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