Noninvasive assessment of hepatic fibrosis: Ultrasound-based elastography

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INTRODUCTION

Liver disease is an important problem worldwide. Accurately diagnosing liver fibrosis is the most important factor for determining the stage of the disease, assessing the patient's prognosis, and predicting treatment responses [1-6]. This is true for a wide range of disorders, including viral hepatitis, alcohol- and nonalcohol-associated fatty liver disease, drug-induced liver injury, primary biliary cholangitis, and autoimmune hepatitis. Ultrasound-based elastography provides noninvasive approaches for assessing hepatic fibrosis.

This topic will review the use of ultrasound-based elastography for assessing liver fibrosis. Other methods for assessing liver fibrosis, including liver biopsy, magnetic resonance elastography, and serologic testing, are discussed separately. (See "Approach to liver biopsy" and "Histologic scoring systems for chronic liver disease" and "Noninvasive assessment of hepatic fibrosis: Overview of serologic tests and imaging examinations".)

ROLE OF ULTRASOUND-BASED ELASTOGRAPHY

Ultrasound-based elastography is primarily used as an alternative to liver biopsy for the assessment of hepatic fibrosis. It can also be used to predict complications in patients with cirrhosis. Society guidelines on the use of ultrasound elastography of the liver are available [7-10].

Ultrasound-based elastography has been studied for the evaluation of focal liver lesions, but because of limitations, such as limited depth of penetration and overlap of values, it is not generally recommended for this application.

Assessing hepatic fibrosis — Assessing hepatic fibrosis has traditionally been done with liver biopsy but clinical practice has been changing because liver biopsy has several disadvantages: it is invasive; it is associated with rare but serious complications; and it can only sample a small portion of the liver parenchyma, making it susceptible to sampling variation [11]. To overcome these problems, alternative noninvasive serologic and radiographic methods have been developed to assess hepatic fibrosis (table 1). One of the more commonly used ultrasound-based techniques for assessing hepatic fibrosis is transient elastography, a shear wave elastography technique. Other ultrasound-based techniques include acoustic radiation force impulse (ARFI) techniques (eg, point-shear wave elastography [SWE], two-dimensional-SWE). (See 'Shear wave speed measurements using acoustic radiation force impulse (ARFI)' below.)

Predicting complications — In patients with cirrhosis, elastography can be used to predict complications (including the development of large varices and hepatocellular carcinoma) and mortality. (See 'Efficacy of transient elastography' below.)

Evaluation and detection of focal liver lesions — Ultrasound-based elastography methods have been studied for the detection and characterization of focal liver lesions (image 1 and image 2 and image 3) [12-14]. Because most focal liver lesions are stiffer than the surrounding liver parenchyma, ultrasound-based elastography may provide reliable quantitative stiffness information of focal liver lesions, however, it cannot yet reliably differentiate benign from malignant lesions [12,15]. Focal nodular hyperplasia is the stiffest benign lesion [16,17]. For patients with hepatocellular carcinoma, stiffness values measured in the liver parenchyma at more than 2 cm from the lesion are more reliable than measurements closer to the lesion [18]. In addition, the limited depth of penetration limits the ability of ultrasound-based elastography to detect lesions. The main limitation is the overlap of values. As a result, ultrasound-based elastography is not yet recommended for the differentiation of benign from malignant liver lesions. Ultrasound-based elastography can be considered in patients with newly detected focal liver lesions to determine stiffness of the liver parenchyma and, therefore, if the patient is at risk. The analysis of liver viscosity parameters may provide additional viscoelastic information about focal liver lesions before surgical intervention [19].

DETERMINANTS OF LIVER STIFFNESS

Liver stiffness (elasticity and viscosity) depends on many factors. Fibrosis is an important factor contributing to liver stiffness and is often the factor focused on in studies [20-25]. However, other factors also influence liver stiffness, including:

- Inflammation from causes such as acute or chronic liver failure, acute hepatitis, acute-on-chronic hepatitis, and chronic viral hepatitis [26-29]
- Blood volume
- Liver perfusion
- Possibly fatty infiltration [30-37].
- Cholestasis [38]
- Heart failure (acute or chronic)/central venous pressure [39]
- Whether the patient has eaten [28,40-44]

Because of the influence of heart failure/central venous pressure and eating on liver stiffness, cardiopulmonary disease should be excluded prior to performing ultrasound-based elastography and patients undergoing ultrasound-based elastography should be fasting.

PRINCIPLES BEHIND ULTRASOUND-BASED ELASTOGRAPHY

There are two primary ultrasound-based elastography techniques used in clinical practice for evaluating liver stiffness: shear wave elastography (SWE) and strain elastography. Both use mechanical excitation of the hepatic parenchyma with monitoring of the resulting tissue response. Fibrotic tissue differs from healthy tissue in the way it responds to excitation (shear waves propagate faster in fibrotic tissue, and fibrotic tissue when compressed shows less strain displacement than healthy tissue).

SWE and strain elastography differ in the way the external mechanical excitation is applied and what quantity is measured [45-47]. SWE is able to quantify elasticity and has been described as a dynamic method. Strain elastography is semiquantitative and does not directly measure elasticity but rather determines elasticity relative to other structures. It has been described as a quasistatic method. For both techniques, colored elastograms are superimposed on conventional ultrasound B-mode images.

Shear wave elastography — Shear waves can be generated from external pressure and transducer derived vibration and from acoustic radiation force impulse (ARFI). Shear waves propagate in any solid medium, including biologic tissue. They can be generated in tissues when a directional force is applied to the tissue, causing shear deformation [48]. Liver stiffness measurements are based on shear wave propagation speed and the density of the material the

shear wave is travelling through [48-50]. The shear wave speed is related to the liver parenchyma stiffness, with faster wave progression seen in stiffer tissue [51,52].

There are several methods for performing SWE, including transient elastography [53-56], point-SWE [57-59], and two-dimensional (2D)-SWE [60-62]. The methods differ in how the shear wave is generated and in what measurements are taken. In transient elastography, the shear waves are generated by a mechanical piston with a single-element ultrasound transducer. It is used to lightly push the skin over an intercostal space, resulting in a shear wave that travels through the liver. Measurements are then taken along the direction of the ultrasound beam. Point-SWE and 2D-SWE use ARFI to generate shear waves. ARFI uses focused acoustic radiation force "push" pulses to deform tissue and generate shear waves of low amplitude [63,64]. The resulting shear waves are tracked, and the distribution of displacement or its normalized value is displayed [48-50]. Shear wave speed measurements are taken either from one small area (usually 5 by 10 mm, point-SWE) or from sequential measurement points (2D-SWE) [7,48,52].

Strain elastography — For strain elastography, the external mechanical excitation force is applied by compressing the liver (by transducer, cardiovascular pulsation, or respiratory motion). Tissue displacement is measured and is converted to a strain image that is the percentage of displacement [48]. Fibrous tissue displaces less than normal parenchyma and strain images from fibrotic tissue will indicate less strain relative to normal tissue (image 2).

TRANSIENT ELASTOGRAPHY

Transient elastography is performed using transducer-induced vibrations at a low frequency (50 Hz) and amplitudes. The transmitted shear waves propagate through the liver parenchyma. Pulse-echo ultrasound acquisition is used to follow the propagation of the shear wave and to measure its average speed (image 4) [45]. Results are expressed in kPa and can range from 2.5 to 75 kPa [51]. Cutoff values for diagnosing significant fibrosis (F≥2) or cirrhosis (F4) vary depending on the underlying liver disease. However, commonly used cutoffs in clinical settings are >7 kPa for significant fibrosis (F2 to F4) and >11 to 14 kPa for cirrhosis. Transient elastography does not allow differentiation between the contiguous stages of liver fibrosis [65-67].

Optimal cutoff values for diagnosing cirrhosis appear to be lower for patients with chronic hepatitis B virus (HBV) than for patients with hepatitis C virus (HCV). Studies in patients with chronic HCV report optimal cutoff values of 11 to 14 kPa for cirrhosis [50,68,69]. In patients with chronic HBV, the cutoff values for diagnosing cirrhosis are between 9.0 and 10 kPa, based on studies performed primarily in Asian populations [70-74]. The diagnostic accuracy of transient

elastography for identifying liver fibrosis in patients with chronic hepatitis B was also demonstrated in several meta-analyses [75-77].

Measurements are taken from the right lobe of the liver via the 9th, 10th, or 11th intercostal space [78]. Transient elastography measurements are taken from representative cylindrical areas approximately 10 mm wide and 40 mm long. Transient elastography is performed with a standard M probe, an XL probe (for patients with obesity [79]), or an S probe (for children and patients with narrow intercostal spaces) [48-50,79-83].

Efficacy of transient elastography — Transient elastography has primarily been evaluated in patients with chronic HCV and in predominantly Asian populations with chronic HBV and other liver diseases. Overall, for diagnosing significant fibrosis (F≥2), it has an estimated sensitivity of 70 percent and an estimated specificity of 84 percent [53]. For diagnosing cirrhosis, the sensitivity and specificity are estimated to be 87 and 91 percent, respectively. Several studies have been performed in patients with NAFLD [37,84,85], and guidelines on the use of elastography for patients with other etiologies of liver disease have been published [10].

Multiple studies have described test characteristics of transient elastography. At least four meta-analyses have been published [53,55,86,87]. One meta-analysis that included 50 studies estimated test characteristics by reporting the area under the receiver operator characteristic (ROC) curve [55]:

- The mean areas under the ROC curves for the diagnosis of significant fibrosis (F≥2), severe fibrosis (F≥3), and cirrhosis (F4) were 0.84, 0.89, and 0.94, respectively (with a value of 1 corresponding to a perfect test).
- Estimates for diagnosis of significant fibrosis were influenced by the type of underlying liver disease and the cutoff level for diagnosing cirrhosis. The most consistent findings were in patients with HCV.

An earlier meta-analysis of nine studies provided summary estimates in terms of sensitivity and specificity [53].

- For diagnosing significant fibrosis (F≥2), the sensitivity was 70 percent and the specificity was 84 percent.
- For diagnosing cirrhosis, the sensitivity was 87 percent and the specificity was 91 percent.

Transient elastography has good inter- and intraobserver agreement in patients without obesity [78,88-91]. As an example, in a study with 200 patients with various liver diseases examined by two operators, reproducibility was high, with intraclass correlation coefficients (ICCs) of 0.98 for

inter- and intraobserver agreement; however, interobserver agreement was lower in patients with mild fibrosis, steatosis, or an increased body mass index (BMI >25 kg/m^2) [78].

Liver stiffness values may also be associated with complications and prognosis [92-97]. In a meta-analysis of 17 studies with 7058 patients with chronic liver disease, baseline liver stiffness was associated with the risk of hepatic decompensation (relative risk [RR] 1.07, 95% CI 1.03-1.11), hepatocellular carcinoma development (RR 1.11, 95% CI 1.05-1.18), and death (RR 1.22, 95% CI 1.05-1.43) [92]. Examples of individual studies that have looked at the association of liver stiffness with prognosis include:

- A study of 239 patients coinfected with human immunodeficiency virus (HIV) and HCV [93]. Cirrhosis was defined by a liver stiffness of >14 kPa. During a median follow-up of 20 months, patients with liver stiffness values ≥40 kPa were more likely to develop decompensation than those with values <40 kPa (29 versus 8 percent). On multivariable analysis, liver stiffness was a predictor of decompensation during follow-up (for each kPa increase, the hazard ratio was 1.03, 95% CI 1.01-1.05).

- A study of 92 patients undergoing hepatectomy for hepatocellular carcinoma [94]. A liver stiffness of >15.7 kPa was a risk factor for postoperative liver failure (sensitivity 96 percent, specificity 69 percent).

- A study of 1000 patients with cirrhosis [96]. Mean liver stiffness values were higher in patients with grade 2 or 3 varices compared with patients without esophageal varices or with grade 1 varices (45 versus 26 kPa). Among patients with esophageal varices, mean liver stiffness values were higher among those with a history of variceal bleeding compared with those who had never bled (52 versus 35 kPa).

Limitations of transient elastography — Limitations of transient elastography include lack of anatomic orientation, limited depth of penetration, and specific requirements for patient positioning [36,78]. In addition, fluid and adipose tissue attenuate shear wave propagation [36,39]. These limitations may result in failed examinations in patients with obesity, patients with anatomic distortions, patients with ascites, and patients with elevated central venous pressures [88].

A total failure rate of 3.1 percent was reported in a series of 13,369 transient elastography examinations [36]. In addition, results were deemed unreliable in an additional 16 percent of examinations. Factors associated with unreliable results included BMI >30 kg/m^2, age >52 years, female sex, operator inexperience, and type 2 diabetes mellitus. Hepatic inflammation may also reduce the accuracy of the test [28,98-101]. Finally, hepatic steatosis may decrease the accuracy of transient elastography [99,102]. In a study of 253 patients with nonalcoholic fatty liver

disease (NAFLD), the degree of fibrosis was often overestimated in patients with severe steatosis (≥66 percent), however, these results were not confirmed in other studies [37,102].

Special probes have been developed in an attempt to improve accuracy in assessing the degree of liver fibrosis in overweight patients (XL probe) and children (S probe) [7,30,31,103].

SHEAR WAVE SPEED MEASUREMENTS USING ACOUSTIC RADIATION FORCE IMPULSE (ARFI)

Shear wave speed measurement using ARFI is an alternative to transient elastography. An advantage of the ARFI technique (point-shear wave elastography [SWE] and two-dimensional [2D]-SWE) compared with transient elastography is that ARFI technique combines conventional ultrasound with liver stiffness measurements. In addition, methods that use ARFI can obtain liver stiffness values in patients with ascites [104] and may be less influenced by obesity than transient elastography [105]. In one study with 23 patients with a mean body mass index >44 kg/m^2 who underwent point-SWE, valid liver stiffness measurements were obtained in all 23 patients [106].

Point-shear wave elastography — Point-shear wave elastography simultaneously displays the shear wave speed and conventional ultrasound images (image 5). The liver stiffness measurement is guided by conventional grayscale ultrasound. The same transducer is used to generate the shear waves and to assess their propagation. The sensitivity of point-SWE for the diagnosis of significant (F≥2) fibrosis is approximately 75 percent, and for diagnosing cirrhosis (F4) is approximately 90 percent [107,108]. Approximate specificities are 85 and 87 percent, respectively. Similar to other elastography techniques, point-SWE does not allow differentiation between the contiguous stages of liver fibrosis [50].

A right intercostal approach is preferred when performing point-SWE, similar to the transient elastography examination technique. Minimal transducer pressure and a short breath hold in the mid-respiratory position (avoiding breath hold in deep inspiration) are recommended to improve the reproducibility of measurements. Liver stiffness is reported as an average value within a region of interest (point measurement). The values are reported as either shear wave speed (m/s) or converted to kPa (elastic modulus). In general, the measured speed may be converted into stiffness values: velocity squared and multiplied by three. The shear wave propagation speed is proportional to the square root of the tissue elasticity divided by three.

Efficacy of point-shear wave elastography — Point-SWE has been shown to be useful for diagnosing hepatic fibrosis in patients with chronic hepatitis C virus infection [22,58,109-112],

chronic hepatitis B virus infection [113,114], nonalcoholic fatty liver disease [115,116], and alcoholic liver disease [117].

A meta-analysis that included nine studies with a total of 518 patients with chronic liver disease evaluated the overall diagnostic performance of point-SWE for staging liver fibrosis [108]. Optimal cutoff values for diagnosing liver fibrosis with their respective sensitivities and specificities were:

- F≥2: 1.34 m/s, sensitivity 79 percent, specificity 85 percent
- F≥3: 1.55 m/s, sensitivity 86 percent, specificity 86 percent
- F4: 1.80 m/s, sensitivity 92 percent, specificity 86 percent

Point-SWE permits comparison of measurements at different sites in the right and left lobes of the liver. Higher values are often noted in the left lobe of the liver (table 2), but the accuracy of point-SWE appears to be higher in the right lobe of the liver compared with the left lobe [49,118-120].

Comparison with transient elastography — A meta-analysis of 13 studies with 1163 patients with chronic liver disease compared point-SWE with transient elastography, using liver biopsy as a gold standard [107]. It found that point-SWE had a lower failure rate than transient elastography (2.1 versus 6.6 percent). The sensitivities of point-SWE and transient elastography were similar for diagnosing significant fibrosis (F≥2; 74 and 78 percent, respectively) and cirrhosis (87 and 89 percent, respectively), as were the specificities (F≥2: 83 and 84 percent, respectively; cirrhosis: 87 percent for both modalities).

Limitations of point-shear wave elastography — The limitations associated with conventional ultrasound also apply to point-SWE (eg, operator dependent). Another limitation is that necroinflammatory activity (reflected by elevated aminotransferase levels) has been associated with overestimation of hepatic fibrosis [24,58]. The same is true for all SWE techniques.

Two-dimensional shear wave elastography — Two-dimensional (2D)-SWE produces an image of the liver which is color-coded, using several ARFI lines to capture the propagation of the resulting shear waves in real time (image 6) [121,122]. Like point-SWE, 2D-SWE can be used in patients with ascites [49]. Studies suggest that the sensitivity for diagnosing significant fibrosis (F≥2) is 77 to 83 percent, with a specificity of 82 to 83 percent [123-125]. The sensitivity for diagnosing cirrhosis is 81 to 85 percent, with a specificity of 61 to 83 percent.

2D-SWE examination is performed under conventional ultrasound guidance using a conventional ultrasound probe. The right intercostal approach is preferred, similar to the

transient elastography examination technique. However, unlike transient elastography, other approaches may also be used. The patient lies down in the supine position, with the right arm in maximum abduction. This makes the right hypochondrium accessible. The probe must be placed parallel to the intercostal window to avoid shadowing from the ribs. A breath suspension in the mid-respiratory phase (avoiding breath hold in deep inspiration) improves the reproducibility of measurements. The shear wave elastography map should be moved to an area that is free of blood vessels with a uniform image on B-mode, at least 2 cm below the liver capsule. The region of interest is placed in the central area of the shear wave elastography map, over an area of relative homogeneous elasticity (which is true also for point-SWE).

Efficacy of 2D-shear wave elastography — The optimal cutoff values for diagnosing liver fibrosis with their respective sensitivities and specificities were estimated in a series of 383 patients who underwent 2D-SWE [123]:

- F≥1: 7.1 kPa, sensitivity 75 percent, specificity 78 percent
- F≥2: 7.8 kPa, sensitivity 77 percent, specificity 83 percent
- F≥3: 8.0 kPa, sensitivity 92 percent, specificity 76 percent
- F4: 11.5 kPa, sensitivity 81 percent, specificity 61 percent

Similar results were seen in a second study that included 336 patients who underwent 2D-SWE [124]:

- F≥1: 7.8 kPa, sensitivity 68 percent, specificity 100 percent
- F≥2: 8.0 kPa, sensitivity 83 percent, specificity 82 percent
- F≥3: 8.9 kPa, sensitivity 90 percent, specificity 81 percent
- F4: 10.7 kPa, sensitivity 85 percent, specificity 83 percent

The study also compared the accuracy of 2D-SWE with point-SWE and transient elastography. The accuracy of 2D-SWE was higher than that of transient elastography for diagnosing severe fibrosis (F≥3) and higher than that of point-SWE for diagnosing significant fibrosis (F≥2). There were no significant differences among the three techniques for the diagnosis of mild fibrosis or cirrhosis. Studies suggest that interobserver agreement for 2D-SWE is good [126].

A technical guide to performing SWE of the liver has been published [127,128].

Limitations of 2D-shear wave elastography — The limitations of 2D-SWE are likely similar to those seen with point-SWE. (See 'Limitations of point-shear wave elastography' above.)

STRAIN ELASTOGRAPHY

Strain elastography (also referred to as quasistatic imaging, strain imaging, or real-time tissue elastography) measures the strain response of tissue to stress, such as manual compression or cardiovascular pulsation, and is a relative measurement of tissue elasticity [45,129]. While strain elastography has been used successfully to evaluate lesions in the breast [130-132], thyroid [133], pancreas [134,135], and lymph nodes [134,136], its role in the assessment of liver fibrosis is unclear because experience with it in this setting is limited, it is a nonquantitative technique, and there is a lack of standardization [48-50,137-141].

Strain elastography analyzes the strain profile generated along the ultrasound beam as a result of external compression caused by a transducer or the movement of the surrounding tissue (eg, by pulsation of the aorta). Because the liver is deeply located, compression applied at the body surface may not be readily transmitted, making it difficult to elicit strain from the body surface. Therefore, strain induced by cardiovascular pulsation is typically used for evaluation of liver fibrosis [140]. Results are displayed as a color-coded overlay of the grayscale (B-mode) image (image 7). The distribution of strain values can be displayed as a histogram and measurements such as mean strain, standard deviation from the mean, and percentage of blue pixels can be made and have been shown to correlate with increasing degrees of liver fibrosis [140,141].

Strain elastography is performed during a normal liver ultrasound examination. The transducer is placed in a right intercostal space for assessing the right lobe of the liver and in the epigastric region for the left lobe [142]. Where to obtain measurements varies in published studies, but the area must not contain large blood vessels [143]. Different methods for recording and analysis of the data have been published [137,140]; however, none are well established.

Efficacy of strain elastography — Strain elastography has been studied in the liver primarily for assessing liver fibrosis and investigating liver tumors. Several different elasticity score methods have been published [137,138,144]. In a meta-analysis of 15 studies with 1626 patients, the sensitivities of strain elastography for significant fibrosis (F≥2), severe fibrosis (F≥3), and cirrhosis (F4) were 79, 82, and 74 percent, respectively [145]. Specificities were 76, 81, and 84 percent, respectively. However, the authors noted that the sensitivity and specificity may have been overestimated because there were signs of publication bias.

In a study that compared strain elastography with point-shear wave elastography (SWE) and transient elastography, there was no significant difference among the three techniques for the diagnosis of cirrhosis, but point-SWE and transient elastography performed better than strain elastography in predicting significant fibrosis [146].

Initially reported intraobserver variability and interobserver agreement for the assessment of liver fibrosis were relatively low [141,147,148]. More recently, the elastic ratio of measurements obtained from four separate locations between two operators showed better agreement (kappa = 0.84) [149].

Limitations of strain elastography — The biggest limitations of strain elastography are that it is a nonquantitative technique and it is not standardized. However, variability among examiners with proper training is reportedly low [149]. Although elastography images can be obtained in patients with ascites, in this setting strain elastography may depict the liver as hard, irrespective of its elasticity because of the influence of the surrounding ascites [147]. In addition, strain elastography may incorrectly display areas of the liver near the ribs or near the liver's surface as hard.

SUMMARY

- Disadvantages of liver biopsy include the fact that it is invasive, it is associated with rare but serious complications, and it can only sample a small portion of the liver parenchyma, making it susceptible to sampling variation. To overcome these problems, alternative noninvasive methods such as ultrasound-based elastography have been developed to assess hepatic fibrosis (table 1). (See 'Role of ultrasound-based elastography' above and "Noninvasive assessment of hepatic fibrosis: Overview of serologic tests and imaging examinations".)

- While ultrasound-based elastography is primarily used to assess hepatic fibrosis, it can also be used to predict complications in patients with cirrhosis. Ultrasound-based elastography has been studied for the evaluation of focal liver lesions, but because of limitations such as limited depth of penetration, it is not recommended for this application. (See 'Role of ultrasound-based elastography' above.)

- The ultrasound-based elastography technique used in clinical practice for evaluation of liver stiffness is shear wave elastography (SWE). Fibrotic tissue differs from healthy tissue in the way it responds to excitation (ie, shear waves propagate faster in fibrotic tissue). (See 'Principles behind ultrasound-based elastography' above.)

- There are several methods for performing SWE, including transient elastography, point-SWE, and two-dimensional (2D)-SWE. The methods differ in how the shear wave is generated and in what measurements are taken. (See 'Shear wave elastography' above.)

- In transient elastography, the shear waves are generated by a mechanical piston with a single-element ultrasound transducer. It is used to lightly push the skin over an intercostal space, resulting in a shear wave that travels through the liver. Measurements are then taken along the direction of the ultrasound beam. (See 'Transient elastography' above.)

- Point-SWE and 2D-SWE use acoustic radiation force impulse (ARFI) to generate shear waves. ARFI uses focused acoustic radiation force "push" pulses to deform tissue and generate shear waves of low amplitude. The resulting shear waves are tracked and the distribution of displacement or its normalized value is displayed. Shear wave speed measurements are taken either from one small area (usually 5 by 10 mm, point-SWE) or from sequential measurement points (2D-SWE). (See 'Shear wave speed measurements using acoustic radiation force impulse (ARFI)' above and 'Point-shear wave elastography' above and 'Two-dimensional shear wave elastography' above.)

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Topic 96717 Version 13.0

GRAPHICS

Advantages and disadvantages of noninvasive methods to evaluate liver fibrosis

Parameters	Transient elastography	pARFI	2D-SWE	MR elastography	Serum biomarke
Advantages	High accuracy, rapid results	High accuracy, rapid results	High accuracy, rapid results	High accuracy	Availability
	Reproducibility	Reproducibility	Reproducibility	Reproducibility	Reproducibilit
	Very easy to learn	Easy to learn	Easy to learn, larger measurement area than other ultrasound techniques	Examination of the whole liver	
		Conventional ultrasound images are also obtained	Conventional ultrasound images are also obtained	Conventional MR images are also obtained	
		Obesity and ascites are not limiting	Ascites is not limiting	Obesity and ascites are not limiting	
Disadvantages	Technical requirements (elastography equipment)	Technical requirements (ultrasound equipment)	Technical requirements (ultrasound equipment)	Technical requirements (MR imaging equipment)	Nonspecific (e hyperbilirubin hemolysis, inflammation)
	Intermediate cost	Intermediate cost	Intermediate cost	High cost, time-consuming	Relatively high cost, limited availability (pa
	Limited recognition of intermediate stages of fibrosis	Limited recognition of intermediate stages of fibrosis	Limited recognition of intermediate stages of fibrosis	Limited recognition of intermediate stages of fibrosis	Limited recogı of intermediat stages of fibrc
	Blind selection of measurement area			Not applicable in case of iron deposition	Results not immediately available

	Restricted value in obese patients and patients with ascites	Narrow range of values, small measurement area			
	False positive values in patients with acute hepatitis, cholestasis, and heart failure	Quality criteria not well-defined	Quality criteria not well-defined		

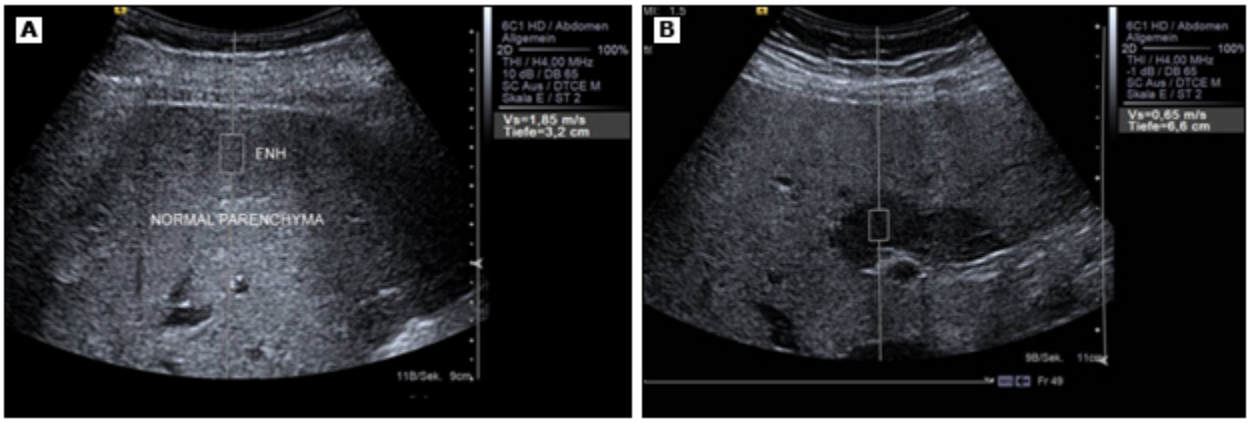
pARFI: point-shear wave elastography using acoustic radiation force impulse; 2D-SWE: two-dimensional shear wave elastography; MR: magnetic resonance.

Reference:

1. *Cui XW, Friedrich-Rust M, De Molo C, et al. Liver elastography, comments on EFSUMB elastography guidelines 2013. World J Gastroenterol 2013; 19:6329.*

Graphic 97043 Version 1.0

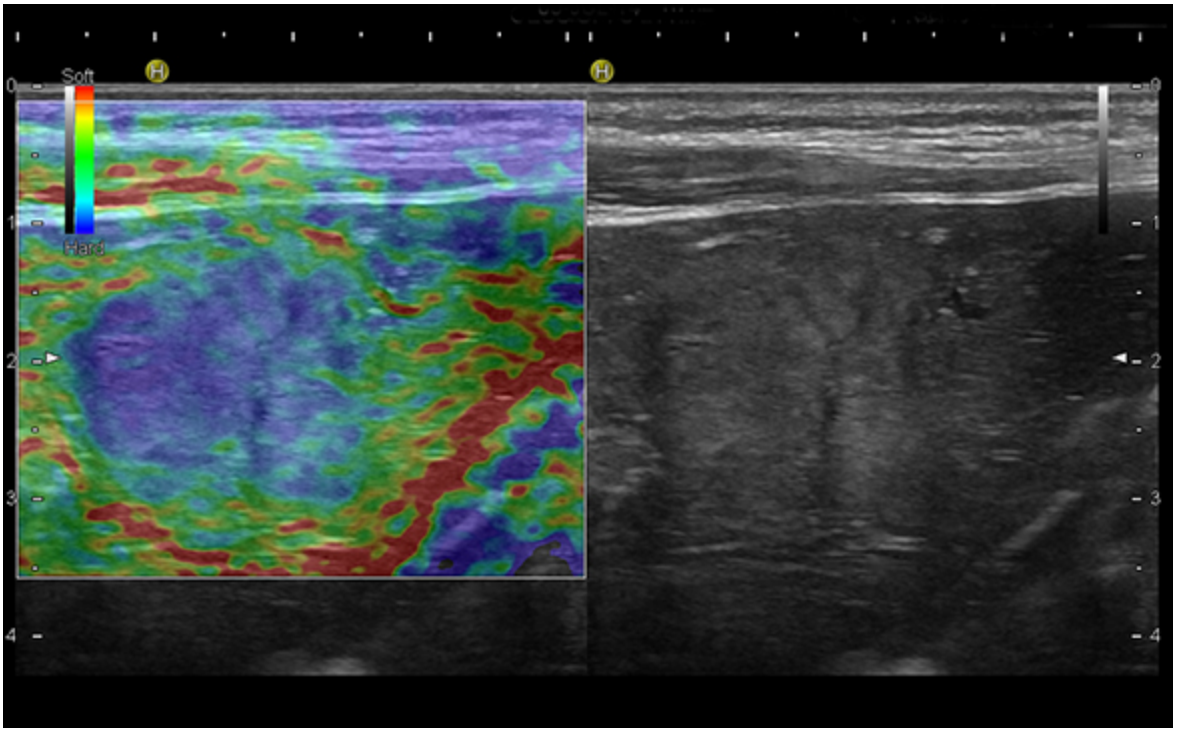
Point-shear wave elastography of focal liver lesions



Point-shear wave elastography for evaluation of focal nodular hyperplasia (A) and focal fatty lesion of liver (B). Almost all focal liver lesions are stiffer than the surrounding hepatic parenchyma except focal fatty sparing.

Graphic 97052 Version 1.0

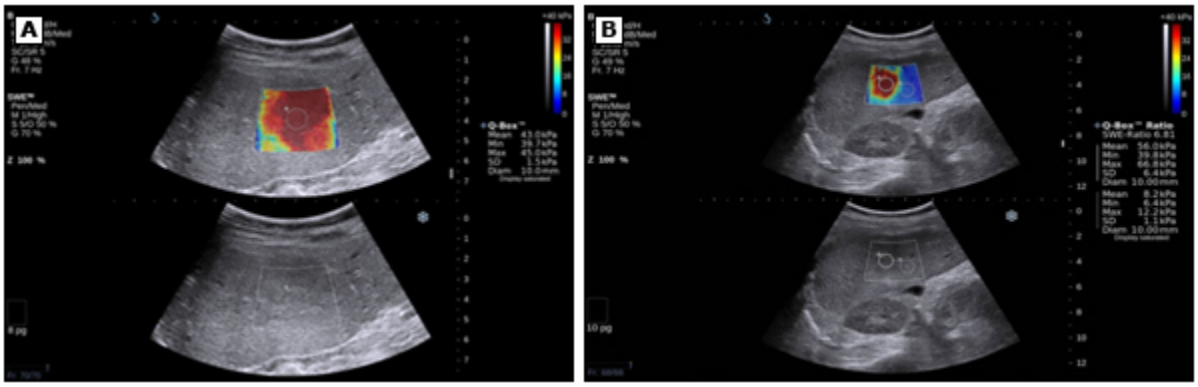
Strain elastography of focal nodular hyperplasia



Strain elastography image of a small focal nodular hyperplasia (blue). Almost all liver neoplasias are stiffer than the surrounding hepatic parenchyma.

Graphic 97054 Version 1.0

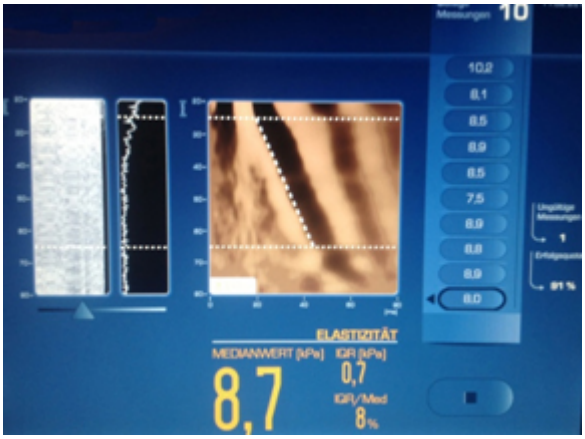
Two-dimensional shear wave elastography of focal liver lesions



Two-dimensional shear wave elastography for evaluation of hemangioma (A) and hepatocellular carcinoma (B). Almost all liver neoplasias show higher shear wave velocities compared with the surrounding hepatic parenchyma.

Graphic 97053 Version 1.0

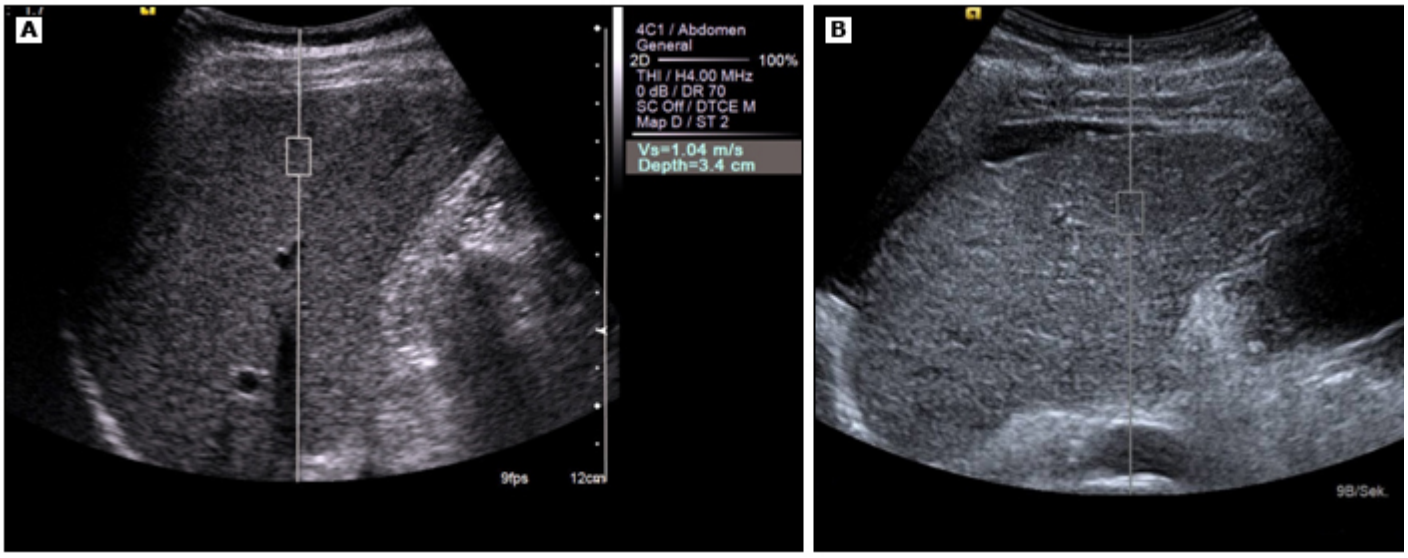
Transient elastography of the liver



Transient elastography showing the measurement of liver stiffness in kilopascals (kPa) along the left side of the screen. An A-mode image is displayed to assist the operator in selecting the measurement zone. On the right side, the values of 10 measurements are shown with the mean value depicted at the bottom of the screen.

Graphic 97037 Version 1.0

Point-shear wave elastography of the liver



Point-shear wave elastography using acoustic radiation force impulse in healthy liver parenchyma (A) and cc cirrhosis (B). The shear wave speed and the depth of the region of interest (rectangular box) are shown on tl the image.

Graphic 97038 Version 1.0

Mean shear wave velocities of the left and right liver lobes on point-shear wave elastography using acoustic radiation force impulse

Author	N	Subjects	Left lobe (m/s)	Right lobe (m/s)	Ref
Karlas T, et al	50	Healthy individuals	1.28 ± 0.19	1.15 ± 0.17	[1]
Karlas T, et al	23	Patients with F1 or F2 fibrosis	2.1 ± 0.72	1.75 ± 0.89	[1]
Toshima T, et al	103	24 healthy volunteers, 79 patients with chronic liver disease	1.90 ± 0.68	1.61 ± 0.51	[2]
Piscaglia F, et al	14	Healthy individuals	1.29 (1.00 to 1.60)	1.15 (0.80 to 1.74)	[3]
Piscaglia F, et al	114	Patients with chronic liver disease	1.79 (0.80 to 4.00)	1.67 (0.45 to 3.76)	[3]

Ref: reference; N: number of patients studied.

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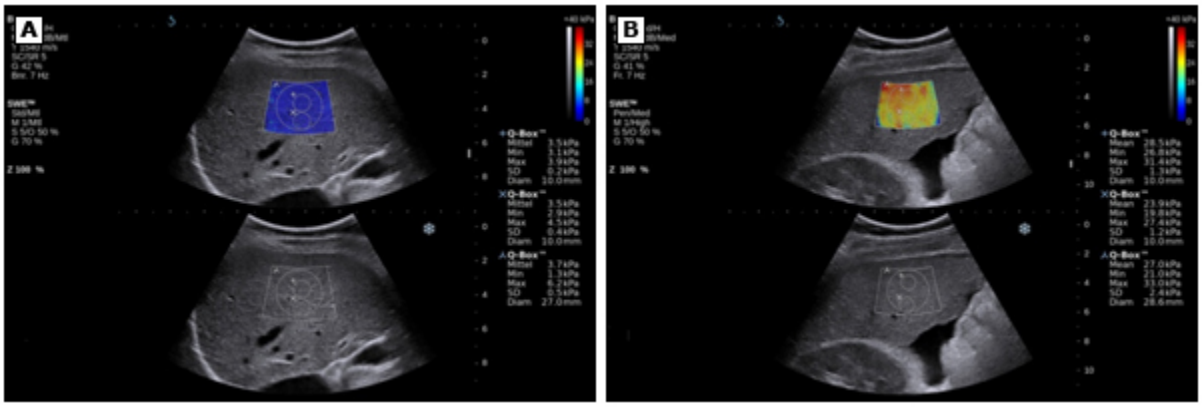
2. *Toshima T, Shirabe K, Takeishi K, et al. New method for assessing liver fibrosis based on acoustic radiation force impulse: a special reference to the difference between right and left liver. J Gastroenterol 2011; 46:705.*
3. *Piscaglia F, Salvatore V, Di Donato R, et al. Accuracy of VirtualTouch Acoustic Radiation Force Impulse (ARFI) imaging for the diagnosis of cirrhosis during liver ultrasonography. Ultraschall Med 2011; 32:167.*

Graphic 97040 Version 1.0

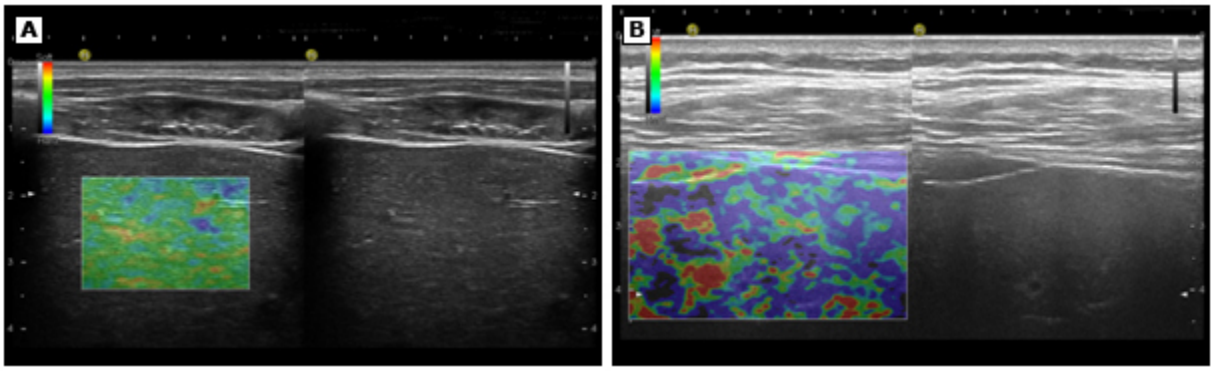
Two-dimensional shear wave elastography of the liver



Two-dimensional shear wave elastography in a patient with healthy liver parenchyma (A) and a patient with liver cirrhosis (B). The color indicates the stiffness of the liver: blue means soft, and red means hard. At least one box can be drawn within the area being evaluated; the value of the shear wave speed is shown on the right side of the image either in m/s (top) or in kPa (bottom).

Graphic 97041 Version 1.0

Strain elastography of the liver



Strain elastography showing healthy liver parenchyma (A) and liver cirrhosis (B).

Graphic 97042 Version 1.0

Contributor Disclosures

Christoph F Dietrich, MD, MBA No relevant financial relationship(s) with ineligible companies to disclose. **Jonathan B Kruskal, MD, PhD** No relevant financial relationship(s) with ineligible companies to disclose. **Kristen M Robson, MD, MBA, FACG** No relevant financial relationship(s) with ineligible companies to disclose.

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