Quantitative Elastography Methods in Liver Disease: Current Evidence and Future Directions

Chronic liver diseases often result in the development of liver fibrosis and ultimately, cirrhosis. Treatment strategies and prognosis differ greatly depending on the severity of liver fibrosis, thus liver fibrosis staging is clinically relevant. Traditionally, liver biopsy has been the method of choice for fibrosis evaluation. Because of liver biopsy limitations, noninvasive methods have become a key research interest in the field. Elastography enables the noninvasive measurement of tissue mechanical properties through observation of shear-wave propagation in the tissue of interest. Increasing fibrosis stage is associated with increased liver stiffness, providing a discriminatory feature that can be exploited by elastographic methods. Ultrasonographic (US) and magnetic resonance (MR) imaging elastographic methods are commercially available, each with their respective strengths and limitations. Here, the authors review the technical basis, acquisition techniques, and results and limitations of US- and MR-based elastography techniques. Diagnostic performance in the most common etiologies of chronic liver disease will be presented. Reliability, reproducibility, failure rate, and emerging advances will be discussed.

Online supplemental material is available for this article.
Chronic liver diseases are a major cause of morbidity and mortality in the United States and worldwide. The most prevalent etiologies of chronic liver diseases include chronic hepatitis B virus (HBV) infection, chronic hepatitis C virus (HCV) infection, nonalcoholic fatty liver disease (NAFLD), and alcohol abuse (1). In the United States, chronic liver diseases affect approximately 360 per 100,000 persons and are the 12th leading cause of death, with an estimated mortality of 12 deaths per 100,000 persons (2,3) and a projected financial burden exceeding $100 billion annually, mostly from NAFLD and chronic HCV infection (4,5). Chronic liver diseases can lead to liver fibrosis, which is the result of chronic liver injury (6). The end-stage of liver fibrosis is cirrhosis, which has potential complications including portal hypertension, liver failure, and hepatocellular carcinoma (HCC). There is evidence that when the underlying cause is removed, liver fibrosis may regress or stabilize (7). Accurate staging of liver fibrosis may be beneficial in monitoring treatment efficacy, disease progression, and in establishing prognosis.

Until recently, liver fibrosis was primarily assessed with liver biopsy, which is the reference standard for staging of liver fibrosis and grading of necroinflammatory changes, by using various semiquantitative scoring systems (8–15). The most commonly used scoring systems include the METAVIR score in chronic HBV or HCV infections and the Brunt score in nonalcoholic steatohepatitis (NASH) (8,9). All scoring systems (except the Ishak score) range from F0 to F4, where F0 indicates no fibrosis; F1, mild fibrosis; F2, moderate fibrosis; F3, advanced fibrosis, and F4, cirrhosis. Despite its strengths, liver biopsy has several drawbacks: liver biopsy is relatively invasive and associated with a low rate of complications (approximately 3%) such as pain and bleeding, which reduce patient acceptance and limit its suitability for repeated measurements and disease monitoring. Also, biopsy enables the analysis of only a small portion of the liver, about 1/50,000th of the total parenchyma, introducing sampling variability and possible diagnostic errors (16,17). Inter- and intraobserver variability have also been suggested as limitations to biopsy, which may be linked to the inconsistency in the definition of some pathologic features (8,16,18). Finally, liver biopsy lacks dynamic information about the speed of disease progression. All of these limitations make liver biopsy an imperfect reference standard. An important ramification of these limitations is the difficulty in validating noninvasive tests with use of biopsy as the reference standard, as the inherent flaws of biopsy can cause misinterpretation of results.

Alternative, noninvasive methods of evaluating liver health are being developed, such as serum markers and ultrasonographically (US) and magnetic resonance (MR) imaging-based elastography. Serum markers include simple markers—such as platelet count, aspartate aminotransferase-to-platelet ratio index, or APRI (19), FIB-4 (20)—and more complex, patented composite scores, such as FibroTest/FibroSure (Biopredictive, Paris, France) (21), the enhanced liver fibrosis, or ELF (Siemens Healthineers, Erlangen, Germany), test (22), and FibroMeter (Echosens, Paris, France) (23). Though simple to perform, these tests have limited accuracy in intermediate levels of fibrosis (24), and they are generally considered less accurate than elastographic methods (25).

**Principles of Elastography**

Elastography, first coined by Ophir et al (26), describes the noninvasive assessment of tissue mechanical properties such as elasticity, which describes the resistance to deformation of a tissue to an applied stress. In quantitative elastography methods, the stress is applied via shear-wave propagation, generated transiently, for example, via single mechanical impulse, or dynamically, for example, via continuous application of acoustic waves. US and MR elastographic methods are available clinically and are summarized in Figure 1 and Table 1. A more comprehensive overview of the elastographic methods to be reviewed is included in the Appendix E1 (online).

Quantitative US elastography methods include transient elastography (TE) and acoustic radiation force impulse (ARFI) techniques such as...
techniques use focused US “push” pulses to deform internal tissue and generate shear waves (27). The nomenclature for ARFI elastography in the literature is not standardized. Though pSWE and 2D SWE both utilize ARFI to generate shear waves, pSWE is often referred to as ARFI elastography in published studies. To avoid confusion, in this review we use ARFI to describe the method of wave generation and

point shear-wave elastography (pSWE) and two-dimensional (2D) shear-wave elastography (SWE). The FibroScan system (Echosens, Paris, France) was the first commercially available TE system, introduced in Europe in 2003 and approved in the United States by the Food and Drug Administration in 2013. The FibroScan probe delivers a 50-Hz mechanical impulse to the skin surface and then measures the velocity of the generated shear wave (Figs 1, 2). There are several probes available, with the M probe being used for standard examinations and the XL probe introduced to increase the reliability of TE measurements in overweight patients. The XL probe records the measurement at a greater depth than does the M probe (35–75 mm vs 25–65 mm), with a lower operating frequency (2.5 MHz vs 3.5 MHz). ARFI elastography

Table 1

<table>
<thead>
<tr>
<th>Method</th>
<th>Availability</th>
<th>Cost</th>
<th>Evidence</th>
<th>Liver-sampling Area</th>
<th>Region of Interest Placement</th>
<th>Reported Parameter</th>
<th>Main Reasons for Failure or Unreliable Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient elastography</td>
<td>Widespread</td>
<td>Low</td>
<td>Excellent validation</td>
<td>Small</td>
<td>Restricted, no guidance</td>
<td>Young modulus (kPa)</td>
<td>High body mass index (M probe), ascites</td>
</tr>
<tr>
<td>ARFI</td>
<td>Moderate</td>
<td>Low</td>
<td>Moderate, good validation</td>
<td>Small (pSWE); medium (2D SWE)</td>
<td>Flexible with US guidance; recommended 1 cm below liver capsule and &lt; 5 cm from transducer</td>
<td>Young modulus (kPa) or wave speed (m/sec)</td>
<td>High body mass index</td>
</tr>
<tr>
<td>MR elastography</td>
<td>Limited</td>
<td>High</td>
<td>Limited validation</td>
<td>Large</td>
<td>Large organ coverage</td>
<td>Complex shear modulus (kPa)</td>
<td>Liver iron deposition, large ascites, body mass index* (2D GRE)</td>
</tr>
</tbody>
</table>

* Conflicting evidence reported regarding MR elastography failure in patients with high body mass index.

Figure 1: Illustrations of US elastography techniques, including TE (FibroScan, Echosens), pSWE (Virtual Touch Quantification, Siemens Acuson S2000), 2D SWE (Aixplorer, Supersonic Imagine), and MR elastography. Sampling area for each method is depicted by enclosed green area. TE and pSWE have a fixed sampling area size, though pSWE allows the depth and location to be chosen. Two-dimensional SWE has the ability of pSWE sampling area placement with the additional ability to change the size. MR elastography offers (near) full organ coverage. Corresponding example images for each method are also shown. TE = transient elastography, pSWE = point shear-wave elastography, 2D SWE = two-dimensional shear-wave elastography.
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The speed of a shear wave. In MR elastography, increased wavelength is evident in stiffer tissues. An obstacle to direct comparison between techniques is the frequency dependence of biologic tissue. Higher frequency shear waves produce higher stress and strain rates, resulting in higher stiffness measurements (38). This can be problematic when comparing US elastographic techniques, as TE operates at 50 Hz whereas ARFI methods operate at frequencies of 100–500 Hz (39). Thus, the frequency dependence, method of measurement, and parameter reported (wave speed, E, or G*) should be considered when comparing elastography techniques.

Reliability and Failure Rates of Elastographic Methods

TE Method

Liver fibrosis leads to increased stiffness. As shear waves travel through a tissue, the speed of the wave depends on the tissue stiffness (37). In stiffer tissues, the shear-wave speed is greater, enabling estimation of the degree of liver fibrosis from measuring the speed of a shear wave. In MR elastography, increased wavelength is evident in stiffer tissues. An obstacle to direct comparison between techniques is the frequency dependence of biologic tissue. Higher frequency shear waves produce higher stress and strain rates, resulting in higher stiffness measurements (38). This can be problematic when comparing US elastographic techniques, as TE operates at 50 Hz whereas ARFI methods operate at frequencies of 100–500 Hz (39). Thus, the frequency dependence, method of measurement, and parameter reported (wave speed, E, or G*) should be considered when comparing elastography techniques.

Figure 2

Figure 2: Transient elastography images. Left: image in a 39-year-old woman with chronic hepatitis C virus infection with no fibrosis (stage F0) (liver stiffness, 3.2 kPa; M probe). Middle: image in a 59-year-old man with chronic hepatitis B virus infection with stage F2 fibrosis (liver stiffness, 8.7 kPa; M probe). Right: Image in a 57-year-old man with nonalcoholic fatty liver disease with cirrhosis (liver stiffness, 27.0 kPa; XL probe). Liver stiffness measurement (Young modulus, median value of 10 measurements), interquartile range, and median value percentage are automatically calculated. An elastographic image (red box) shows axial displacement in terms of depth (y-axis) and time (x-axis). In stiffer tissues, the shear wave propagates more quickly and produces a steeper time-depth gradient (arrows).
and/or unreliable measurements. The introduction of the XL probe has improved the reliability of TE in patients with NAFLD (41–46). For example, in a study of 276 patients, reliable measurements were obtained in 73% of patients with the XL probe compared with only 50% of patients with the M probe (41).

Excellent interobserver variability has been reported for TE, with intraclass correlation coefficient (ICC) of 0.98 in a cohort of 188 patients with chronic HCV in whom two measurements were performed by two operators on the same day (47).

**pSWE and 2D SWE Methods**

The reliability of both pSWE and 2D SWE was compared in 79 patients with measurements performed by three radiologists (48). Failure rate was low for both methods (5% for 2D SWE and 1% for pSWE) and intraobserver agreement was higher for pSWE than 2D SWE (0.915 vs 0.829). Scan-rescan repeatability of 2D SWE measurements performed on the same day by the same operator has been shown to be excellent, with ICC of 0.95 and 0.93 for an expert and novice operator, respectively.
Figure 5: MR elastography performed by using a two-dimensional gradient-recalled-echo sequence and a two-dimensional inversion algorithm in a 52-year-old woman with advanced liver fibrosis (stage F3) secondary to nonalcoholic steatohepatitis. A, Transverse magnitude image with intravoxel phase dispersion (arrows) present under the actuator (which is not visible on MR images). B, Transverse image with waves visible in liver parenchyma. C, Transverse colorized wave image shows wave propagation through liver parenchyma. D, Transverse gray-scale elastogram. E, Transverse colorized elastogram (0–8-kPa scale). F, Transverse colorized elastogram (0–8-kPa scale) with 95% confidence grid overlaid highlighting areas of reliable liver stiffness measurement. Liver stiffness was increased (5.3 kPa).

(49). However, intraobserver reproducibility between measurements performed in the same subject on different days revealed ICC values of 0.84 and 0.65 for an expert and novice operator, respectively. There is further evidence to suggest that operator experience has an effect on pSWE measurements (50), thus operators are recommended to be suitably trained. With the introduction of pSWE and 2D SWE into commercial US systems by many manufacturers, interplatform variability may be an issue. The Quantitative Imaging Biomarkers Alliance, or QIBA, has formed a committee tasked with establishing reproducibility across US elastography systems (51).

MR Elastography

The failure rate of MR elastography is low, with the largest series to date reporting a failure rate of only 5.6% when using a 2D GRE sequence (52). The majority of these failures (71%) were attributed to iron deposition. Another large cohort study found a similarly low failure rate at 1.5 T (3.5%); however, at 3T the rate of failure was higher (15.3%) (53). In the same study, failure was also significantly associated with iron deposition, the presence of large ascites, and increased body mass index (see below) (53). The use of MR elastography in children is also reliable, with a recent study reporting a failure rate of 4% with use of the 2D GRE sequence (54). The test-retest reproducibility of MR elastography is high (55–59), with reported ICC of 0.95 (56). A recent meta-analysis of 274 patients concluded that a change in stiffness of 22% or greater measured at the same site by using the same equipment signifies a true change in stiffness with 95% confidence (60). Lee et al (61) showed that a large region of interest representing approximately 70% of the liver, including the greatest part of the liver parenchyma excluding hepatic hilar vessels, increased the interobserver reproducibility, while a placement of a 1-cm region of interest in each liver segment optimized the intraobserver reproducibility. Similarly, with precise definition of region of interest placement, including all the pixels with confidence index higher than 95%, Yasar et al (62) found almost perfect inter- and intraobserver reproducibility, with ICC higher than 0.97 and Bland-Atman limits of agreement range lower than 15.9% and 4.2%, respectively.

To become a widely accepted method for diagnosis and staging of fibrosis, MR elastography must produce consistent results regardless of the MR system used. Good interplatform reproducibility was reported with use of a 2D GRE sequence at 1.5 T, with ICC between 0.82 and 0.99 (62–64). At 3 T, between-vendor ICC was 0.71 for the 2D GRE sequence and 0.69 for the 2D spin-echo echo-planar imaging sequence (64). In the same study, the variance in liver stiffness based on technical factors was reported to be only 0.042 kPa, with corresponding coefficient of variation of 10.7%. The reproducibility of spleen stiffness measurement using MR elastography...
has been less well studied, with a study reporting ICC greater than 0.88 (62). The QIBA has formed a committee (63) dedicated to standardizing MR elastography through identifying bias in measurements and identifying a suitable phantom for characterization of data acquired from different MR elastography systems.

In summary, MR elastography and 2D SWE appear to produce the highest rate of successful measurements; however, the introduction of the XL probe has improved the applicability of TE in overweight patients. Reproducibility is good to excellent among all elastographic techniques.

### Diagnostic Performance of Elastographic Methods for Staging Liver Fibrosis

Diagnostic accuracy for liver fibrosis staging in chronic liver diseases, including chronic HBV or HCV infections, and NAFLD for select publications across Europe, Asia, and the United States, are presented for TE (43,46,66–77) (Table 2), ARFI elastographic methods (46,72,77–83) (Table 3), and MR elastography (38,81,84–94) (Table 4). Publications have been selected on the basis of reporting of diagnostic accuracy, historical primacy, cohort size, and geographic distribution. The TE technique has been thoroughly researched and validated for diagnosis of liver fibrosis in large cohort studies, mostly in Europe.

In the following sections, diagnostic performance of US and MR elastographic methods will be discussed for the major etiologies of liver disease. Summary statements are included to provide condensed conclusions.

### Chronic HBV and HCV Infections

Knowledge of liver fibrosis stage in chronic HBV and HCV infections is beneficial for prognosis, follow-up, and treatment decisions. The combination of powerful direct-acting antivirals recently developed in chronic HCV infection (95) and the recent increased use of noninvasive tests for liver fibrosis...
Table 3

Reported Diagnostic Performance of Prospective pSWE and 2D SWE Studies for Liver Fibrosis Staging in Chronic HBV or HCV and NAFLD

<table>
<thead>
<tr>
<th>First Author and Year</th>
<th>Region</th>
<th>Method</th>
<th>Etiology</th>
<th>No. of Patients</th>
<th>Success (%)</th>
<th>AUC</th>
<th>Cutoff*</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>AUC</th>
<th>Cutoff*</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sporea 2011 (78)</td>
<td>Europe</td>
<td>pSWE</td>
<td>HCV</td>
<td>274</td>
<td>96</td>
<td>0.89</td>
<td>1.21</td>
<td>0.84</td>
<td>0.91</td>
<td>0.91</td>
<td>1.58</td>
<td>0.84</td>
<td>0.94</td>
</tr>
<tr>
<td>Friedrich-Rust 2015 (79)</td>
<td>Europe</td>
<td>pSWE</td>
<td>HCV</td>
<td>235</td>
<td>94†</td>
<td>0.81</td>
<td>1.04</td>
<td>0.90</td>
<td>0.25</td>
<td>0.88</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Ye 2012 (80)</td>
<td>Asia</td>
<td>pSWE</td>
<td>HBV</td>
<td>264</td>
<td>100</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Ferraioli 2012 (82)</td>
<td>Europe</td>
<td>pSWE</td>
<td>HCV</td>
<td>121</td>
<td>98</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Yoneda 2015 (46)</td>
<td>United States</td>
<td>SWE</td>
<td>HBV</td>
<td>102</td>
<td>92†</td>
<td>0.87</td>
<td>7.9</td>
<td>0.73</td>
<td>0.96</td>
<td>0.95</td>
<td>9.3</td>
<td>0.91</td>
<td>0.89</td>
</tr>
<tr>
<td>Leung 2013 (72)</td>
<td>Asia</td>
<td>SWE</td>
<td>HBV</td>
<td>454</td>
<td>98</td>
<td>0.88</td>
<td>7.1</td>
<td>0.85</td>
<td>0.92</td>
<td>0.93</td>
<td>7.9</td>
<td>0.90</td>
<td>0.90</td>
</tr>
<tr>
<td>Zhuang 2016 (83)</td>
<td>Asia</td>
<td>SWE</td>
<td>HBV</td>
<td>549</td>
<td>98</td>
<td>0.97</td>
<td>7.6</td>
<td>0.92</td>
<td>0.90</td>
<td>0.96</td>
<td>9.2</td>
<td>0.92</td>
<td>0.97</td>
</tr>
<tr>
<td>Cassinotto 2016 (77)</td>
<td>Europe</td>
<td>pSWE/pSWE</td>
<td>NAFLD</td>
<td>291</td>
<td>80/81</td>
<td>0.86/0.77</td>
<td>6.3/3.05</td>
<td>0.90/0.90</td>
<td>0.50/0.36</td>
<td>0.89/0.84</td>
<td>8.3/1.15</td>
<td>0.91/0.90</td>
<td>0.71/0.63</td>
</tr>
</tbody>
</table>

Note.— AUC = area under the receiver operating characteristic curve. HBV = hepatitis B virus, HCV = hepatitis C virus, NAFLD = nonalcoholic fatty liver disease, pSWE = point shear-wave elastography, SWE = shear-wave elastography, 2D = two-dimensional.

* Cutoff values in kilopascals for 2D SWE and in meters per second for pSWE. Successful measurements exclude failures and unreliable results.
† Reported for 182.
‡ Combined failure rate for 2D SWE and TE. Two-dimensional SWE only data not available.
§ Reported for 226.
|| Training set (n = 304) results reported. Scheuer scoring system used.

Stage F2–F4 staging as proposed in the most recent European Association for the Study of the Liver, or EASL, guidelines (96) have decreased the use of liver biopsy in chronic HCV infection (97). The American Association for the Study of Liver Diseases, or AASLD, guidelines on chronic HBV infection state that staging of liver disease is important to inform therapy decisions and cite the utility of TE for noninvasive staging of fibrosis, especially in excluding advanced fibrosis (98).
### Table 4

Reported Diagnostic Performance of MR Elastography for Liver Fibrosis Staging in Mixed-Etiology Cohorts, Chronic HBV or HCV, and NAFLD

<table>
<thead>
<tr>
<th>First Author and Year</th>
<th>Region</th>
<th>Manufacturer and Field Sequence</th>
<th>Cutoff Strength</th>
<th>Design</th>
<th>No. of Patients</th>
<th>Success (%)</th>
<th>Stage F2–F4</th>
<th>Stage F3–F4</th>
<th>Stage F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yin 2007 (84)</td>
<td>United States</td>
<td>GE (2D GRE)</td>
<td>1.5 T</td>
<td>P</td>
<td>Mixed</td>
<td>85</td>
<td>98</td>
<td>0.92</td>
<td>4.69</td>
</tr>
<tr>
<td>Huwart 2008 (85)</td>
<td>Europe</td>
<td>Philips (3D SE)</td>
<td>1.5 T</td>
<td>P</td>
<td>Mixed</td>
<td>141</td>
<td>94*</td>
<td>0.99</td>
<td>2.49</td>
</tr>
<tr>
<td>Asbach 2010 (38)</td>
<td>Europe</td>
<td>Siemens (2D SE EPI)</td>
<td>1.5 T</td>
<td>P</td>
<td>Mixed</td>
<td>74</td>
<td>99</td>
<td>0.92</td>
<td>3.18</td>
</tr>
<tr>
<td>Wang 2011 (86)</td>
<td>United States</td>
<td>Siemens (2D GRE)</td>
<td>1.5 T</td>
<td>P</td>
<td>Mixed</td>
<td>78</td>
<td>97</td>
<td>0.98</td>
<td>5.37</td>
</tr>
<tr>
<td>Dyvorne 2016 (87)</td>
<td>United States</td>
<td>GE/S (2D GRE)</td>
<td>1.5 T/3 T</td>
<td>P</td>
<td>Mixed/obese</td>
<td>42</td>
<td>90</td>
<td>0.78</td>
<td>3.9</td>
</tr>
<tr>
<td>Chen 2016 (88)</td>
<td>United States</td>
<td>GE (2D GRE)</td>
<td>1.5 T</td>
<td>P</td>
<td>Mixed/obese</td>
<td>110</td>
<td>96</td>
<td>0.93</td>
<td>3.5</td>
</tr>
<tr>
<td>Ichikawa 2012 (89)</td>
<td>Asia</td>
<td>GE (2D GRE)</td>
<td>1.5 T</td>
<td>R</td>
<td>HCV</td>
<td>119</td>
<td>96</td>
<td>0.99</td>
<td>3.2</td>
</tr>
<tr>
<td>Shi 2014 (90)</td>
<td>India</td>
<td>GE (2D GRE)</td>
<td>3 T</td>
<td>P</td>
<td>HBV</td>
<td>132</td>
<td>91</td>
<td>0.99</td>
<td>4.07</td>
</tr>
<tr>
<td>Cui 2016 (81)</td>
<td>United States</td>
<td>GE (2D GRE)</td>
<td>1.5 T</td>
<td>P</td>
<td>NAFLD</td>
<td>126</td>
<td>99</td>
<td>0.89</td>
<td>3.62</td>
</tr>
</tbody>
</table>

**Note.**—AUC = area under the receiver operating characteristic curve, GE = General Electric, GRE = gradient recalled echo, HBV = hepatitis B virus, HCV = hepatitis C virus, NAFLD = nonalcoholic fatty liver disease, P = prospective, R = retrospective, SE = spin echo, Sens = sensitivity, Spec = specificity, 3D = three-dimensional, 2D = two-dimensional.

* Reported for 96.
† Reported for 270.
lack of studies including validation cohorts (Table 4, Fig 6). From the published studies in chronic HCV or HBV infections (58,89–91,139–144), 2D GRE MR elastography has shown excellent accuracy in diagnosing liver fibrosis or cirrhosis, with AUCs for the diagnosis of fibrosis stages F2–F4, F3–F4, and F4 of 0.95–0.99, 0.94–1, and 0.92–1, respectively (89–91,140–143). A meta-analysis of data from patients with chronic HCV and chronic HBV report accuracy equivalent to, or slightly lower than (in early fibrosis stages), that in published studies, with AUCs for stage F2–F4, F3–F4, and F4 of 0.88, 0.94, and 0.92 in HCV infection and 0.94 (stage F2–F4) and 0.97 (stage F3–F4) in HBV infection (145). Several studies also showed that necroinflammation may increase liver stiffness (90,146,147). Currently, there are limited data on the performance of 2D spin-echo echo-planar imaging and three-dimensional spin-echo echo-planar imaging MR elastography in chronic HBV and HCV; however, similar diagnostic accuracy as that with TE and 2D GRE MR elastography has been reported in a few studies (92,148).

In summary, TE is the most validated technique for diagnosing liver fibrosis and cirrhosis in chronic HCV and HBV infections and has been incorporated in several guidelines for management of chronic HBV and HCV infections. Emerging data suggest that pSWE methods are equivalent to or possibly superior to TE in viral hepatitis, with the integration of pSWE in the National Health Service guidelines in the United Kingdom. Two-dimensional SWE and MR elastography show promising results in chronic HBV and HCV infections; however, the available data are limited. In the case of MR elastography, studies have often included mixed etiologies, with a lack of prospective studies with validation cohorts. All elastographic methods have higher accuracy for diagnosing advanced fibrosis and cirrhosis than lower fibrosis stages.

**NAFLD and NASH**

NASH is becoming a widespread problem in the United States due to the increasing prevalence of obesity and NAFLD (149,150). Liver fibrosis has been shown to be the strongest predictor of complications in NAFLD patients (151), which motivates the need for reliable noninvasive techniques for detection of liver fibrosis and will be of major interest for clinicians and in terms of public health perspective.

**TE Method**

The current EASL guidelines for the management of NAFLD recommend TE as a noninvasive method for liver fibrosis assessment and monitoring, while liver biopsy is still recommended to confirm advanced fibrosis and cirrhosis (152). The use of TE in patients with NAFLD is challenging owing to the poor reliability of the technique in overweight or obese patients when the standard M probe is used. The range of unreliable measures is large, with reported unreliable and/or failed measurements in 3.8%–50% of patients (41,76,153). A meta-analysis of the TE performance using the M probe (n = 854) (154) reported pooled sensitivity and specificity of 79% and 75% for F2–F4, 85% and 82% for F3–F4, and 92% and 92% for stage F4. As in chronic HBV or HCV infections, TE is more accurate in higher fibrosis stages. The introduction of the XL probe has led to more reliable results than with the M probe in overweight or obese patients.
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reported AUCs of 0.90 or greater for the diagnosis of fibrosis stages F3–F4 and F4, with associated cutoffs of 3.77 kPa and 4.09 kPa, respectively. As they were derived from a meta-analysis, these cutoffs are probably the most applicable at this time, but further validation studies are needed. There is also evidence that MR elastography may be able to differentiate NASH and simple steatosis in NAFLD patients (156), with a reported AUC of 0.93, but this needs further confirmation.

Other Etiologies of Liver Disease

TE has also been applied in the study of autoimmune liver disease, with excellent diagnostic performance (166), though several studies have reported that acute inflammation as a result of autoimmune hepatitis may affect liver stiffness (167,168). TE has also been shown to be an accurate method for staging fibrosis in primary biliary cirrhosis (169–171), primary sclerosing...
cholangitis (172,173), and alcoholic liver disease (174–176). pSWE methods have been applied in autoimmune liver disease and alcoholic liver disease in a small number of studies (177–181). Two-dimensional SWE has also been applied in alcoholic liver disease, with similar accuracy to TE reported (176). Excellent diagnostic accuracy of MR elastography has been reported in autoimmune hepatitis (182) and primary sclerosing cholangitis (183); however, the method has not been applied in the study of alcoholic liver disease thus far.

In summary, patients with NAFLD and NASH are more likely to be overweight, which is an important factor to consider for elastography measurements. The TE M probe is prone to unreliable results and/or increased risk of failure in these subjects, and this has been improved with the XL probe. In these subjects, ARFI methods are less susceptible to failure than TE. MR elastography is the most robust technique in overweight or obese patients, with reported high accuracy for fibrosis staging, although published data are still limited.

**Additional and Evolving Applications**

**Assessment of Degree of Portal Hypertension, Risk of Hepatic Decompensation and HCC**

Liver cirrhosis can be further categorized into compensated or decompensated cirrhosis. Decompensated cirrhosis is primarily diagnosed on the basis of the presence of variceal bleeding and ascites and is associated with a significantly increased risk of mortality (184). Recent data suggest that liver and spleen stiffness may represent potential biomarkers for hepatic decompensation and HCC risk.

**TE.—** Many studies have shown the ability of baseline liver stiffness measurement (172,183–199) to help predict hepatic decompensation in patients with chronic liver disease. Two studies also looked at the evolution of liver stiffness values over time (172,197) and found that patients with increasing liver stiffness (1–1.5 kPa per year) were at higher risk of developing complications, with one study estimating a 10-fold increase in complications (172). In a meta-analysis of six studies that reported hepatic decompensation as an outcome, each unit increase in liver stiffness was associated with a 7% increased decompensation risk (200). TE can also help diagnose portal hypertension, with another meta-analysis reporting excellent diagnostic performance of TE for diagnosing the presence of clinically significant portal hypertension (defined by hepatic venous pressure gradient ≥ 10 mm Hg), with an area under the hierarchical summary receiver operating characteristic curve (HSROC) of 0.93 (201). Scores combining liver stiffness with platelet count and spleen diameter at US, referred as LSPS (for liver stiffness-spleen-diameter-to-platelet-ratio score) (202) or portal hypertension risk score (203), have also been proposed to increase the diagnostic accuracy.

The performance of TE in predicting the presence and size of esophageal varices based on liver stiffness measurements is also promising. A meta-analysis of 12 studies (204 patients) (201) found the HSROC of TE to be 0.84 for diagnosing esophageal varices. When evaluating the predictive value of TE for diagnosing large esophageal varices (in nine studies comprising 2168 patients), the HSROC was 0.78. The Baveno VI consensus workshop recommendations (204) state that liver stiffness measured with TE may be useful for classifying patients with portal hypertension. Spleen stiffness has been also suggested as a marker of severity of portal hypertension (205) with a reasonable accuracy (AUC, 0.78–0.90) in predicting the presence of esophageal varices (206–208). However, the measurement of spleen stiffness is difficult with TE and requires concomitant conventional US guidance.

A correlation between liver stiffness measured by TE and the risk of developing HCC has been reported by several longitudinal prospective studies (187,195,209–219). For example, a large prospective Japanese study (n = 866) (214) reported increased cumulative incidence of HCC within 3 years (38.5% among patients with baseline liver stiffness values > 25 kPa, compared with 0.4% among patients with values ≤ 10 kPa).

**pSWE.—** So far, published data show similar prognostic ability between pSWE and TE in predicting hepatic decompensation (220). Due to the integration into conventional US systems, pSWE methods are more suitable for measuring spleen stiffness than is TE. A study of 393 patients with median follow up of 44 months found that liver and spleen stiffness measured with pSWE were associated with decompensation (hazard ratios of 2.53 and 16.58 per unit increase in stiffness, respectively) (221). In patients with chronic HCV infection, pSWE outperformed serum markers in the prediction of esophageal varices (AUC, 0.89 vs 0.73) (222). Diagnostic performance was also excellent for the diagnosis of high-risk esophageal varices, with AUC of 0.87 versus 0.74 for pSWE and serum markers, respectively. Few preliminary studies have evaluated pSWE for the prediction of HCC development (223,224), indicating that liver stiffness measured with pSWE is a significant predictor of HCC development. More studies are needed to validate these results.

**Two-dimensional SWE.—** Liver and spleen stiffness measured with 2D SWE have also been shown to correlate with hepatic venous pressure gradient measurements (225,226). In a cirrhotic population (227), 2D SWE outperformed TE for diagnosing clinically significant portal hypertension (AUC, 0.87 vs 0.78, respectively). Two-dimensional SWE spleen stiffness measurements have been significantly associated with the presence of esophageal varices (228), though a high failure rate in spleen measurements (~30%) is a limitation. There is little published data on the ability of 2D SWE to predict HCC development. In one retrospective study (229), the authors noted significantly higher liver stiffness in patients with HCC than those without; however, prospective studies are required for validation.

**MR elastography.—** To date, few studies have investigated the role of
MR elastography in predicting hepatic decompensation (183, 230, 231). In a retrospective study of 266 patients with primary sclerosing cholangitis, Eaton et al (183) found that liver stiffness was a significant predictor of risk of decompensation (hazard ratio, 1.24–1.30 per unit increase in liver stiffness). MR elastography measurement of predictive markers of portal hypertension is an emerging field of research (232–236). The cross-sectional imaging volume available with MR elastography enables simultaneous acquisition of liver and spleen MR elastography data via the use of an additional actuator placed on the left side (62, 237) and may allow the development of composite diagnostic tests by using both measurements as has been implemented with TE (238). Spleen stiffness measured by means of MR elastography has been associated with the presence of esophageal varices (233, 235) and found to correlate with hepatic venous pressure gradient (15 mmHg) demonstrate elevated liver stiffness (7.5 kPa) and spleen stiffness (9.9 kPa). Though the available data suggest that MR elastography may be beneficial in predicting risk of decompensation and diagnosis of portal hypertension, more studies are required to confirm the findings.

A small number of studies to date have evaluated MR elastography as a predictive tool for the development of HCC, with conflicting data (239, 240). While one retrospective study (240) reported elevated liver stiffness in patients with HCC compared with those without HCC, another study did not (239). Thus, more data are needed to predict risk of HCC with MR elastography.

Monitoring of Chronic HCV Infection after Antiviral Therapy

The introduction of direct-acting antivirals has revolutionized therapy in chronically HCV-infected patients, with excellent cure rates reported in most genotypes (241) and subsequent reduction in liver transplant waiting lists (242). Determination of residual fibrotic burden in patients who have achieved sustained virological response is important for both prognosis and surveillance for complications such as HCC. Several studies have reported reduction in liver stiffness of up to 35% (243) following direct-acting antiviral therapy as measured by TE (243–248) and ARFI methods (249, 250). The clinical significance of reduced liver stiffness following sustained virological response has not been established, as few longitudinal studies incorporating biopsy and noninvasive tests have been performed. One study investigated the longitudinal changes in liver stiffness with paired liver biopsies in HCV/HIV-coinfected patients treated with antiretroviral therapy and anti-HCV drugs (in a portion of the population). Patients with progressing fibrosis were found to have significantly increased liver stiffness at 3 years after baseline, while liver stiffness was unchanged or reduced in stable patients (251). There is no published MR elastography study assessing changes in liver stiffness after antiviral therapy. Further studies are required to establish the utility of noninvasive tests in the longitudinal monitoring of HCV patients undergoing antiviral therapy.

HCC Characterization

Liver lesion characterization is beyond the scope of this review. Briefly, there are some data assessing the role of US and MR elastographic methods in quantifying tumor stiffness for the purpose of liver lesion characterization (252–266), with a trend toward increased stiffness in malignant lesions, such as HCC (Fig 9). A recent study reported higher tumor stiffness values in well or moderately differentiated HCCs compared with poorly differentiated HCCs (267). Another preliminary study has reported a significant correlation between tumor stiffness and degree of tumor necrosis and enhancement in HCC after local-regional therapy (268). A drawback of MR elastography investigation of tumors is the limited spatial resolution and coverage of current 2D MR elastography implementations (209). Nonlinear inversion algorithms (270) paired with threedimensional MR elastography (265) may help to address the problem.

In summary, the available data suggest that elastographic techniques may...
be viable methods for prediction of portal hypertension and hepatic decompensation, although further research is needed to understand how the results should be used to inform patient care. Spleen stiffness appears to be a useful biomarker for portal hypertension and prediction of esophageal varices. Finally, TE has been applied in the monitoring of patients undergoing antiviral therapy in chronic HCV; however, the utility of the technique in this role has yet to be established.

**Comparison of MR Elastography to US Elastography and Other Noninvasive Tests**

A few comparative studies investigating the diagnostic accuracy of MR elastographic and US elastographic methods have been published. Though MR elastography was generally found to be superior to TE in diagnosing fibrosis in mixed cohorts (85,87,271) and NAFLD patients (94,164), other studies have found both techniques to perform similarly (88,148). Less literature on the comparison of MR elastography with ARFI methods is available. A meta-analysis assessing the diagnostic accuracy of pSWE (15 studies, 2128 patients) and MR elastography (11 studies, 982 patients) for staging fibrosis found that MR elastography is more accurate than pSWE, particularly in diagnosing early stages of fibrosis (272). MR elastography has also been compared with 2D SWE in a mixed-etiology cohort (138), with comparable diagnostic accuracy for both techniques in staging fibrosis. A recent study used MR elastography as the reference standard and found the 2D SWE and MR elastography measurements to be well correlated (273). MR elastography has also been shown to outperform serum markers (25,87,89,141,143,162), morphologic features (137), and diffusion measurements (86,87,266,274–276).

When evaluating US elastographic methods alone, a meta-analysis of 13 studies including 1163 patients found that pSWE had a similar predictive value as that of TE for advanced fibrosis and cirrhosis while producing a higher rate of reliable measurements (277). Studies comparing TE to pSWE (278) and 2D SWE (72,82) have found ARFI methods to provide similar or superior diagnostic performance to TE. In comparisons of all three methods, pSWE, 2D SWE, and TE (77,279,280), 2D SWE was the slightly superior method for staging fibrosis (77), with variable reliability compared with pSWE (279,280).

**Limitations of Elastographic Techniques**

Although each elastographic method has its own limitations, some drawbacks apply to all techniques. For example, liver stiffness values increase after meal intake (39,281–286); therefore, elastographic examinations should be performed after fasting for at least 2 hours (110), though fasting for 4–6 hours prior to measurement has also been recommended (39). Similarly, cholestasis has been shown to cause increased liver stiffness in TE (287), pSWE (288), and MR elastography (183). A further difficulty in establishing cutoff values for fibrosis staging is the influence of the underlying etiology of liver disease on measured stiffness values; for example, the cutoffs for predicting esophageal varices in patients with cirrhosis using TE is higher in those with alcoholic cirrhosis than in those with liver cirrhosis of viral etiology (289). The cause of this variance has not been conclusively established. Factors such as alanine aminotransferase levels have been suggested (290); however, the inherent morphologic differences in collagen distribution caused by increases in myofibroblasts, which are associated with the various etiologies of fibrotic liver disease, could also be a reason for the discrepancy in cutoff values, even for livers with the same “stage” of fibrosis (291,292). Also, cutoff values are generally established on the basis of receiver operating characteristic analysis of a single-study population and so are affected by the prevalence and severity of fibrosis and cirrhosis in that population (35). Elastography methods are useful as tools to generally stratify patient risk; however, intermediate fibrosis stages can be difficult to delineate. The Society of Radiologists in Ultrasound consensus report of 2015 (39) highlighted the overlap of pSWE shear-wave speeds at intermediate fibrosis levels (sourced from a meta-analysis [293]) and therefore suggests using thresholds to define population groups, which are unlikely to require follow-up (stage F0–F2), those at high risk (some F3 and F4), and those in between who may require further testing, including MR elastography, to inform treatment decisions.

Breathing motion may also affect US elastography and MR elastography measurements. In US elastography,
taking a deep breath or using the Val- 
salva maneuver can change liver stiff- 
ness (294,295). The 2017 EFSUMB 
guidelines recommend that measure- 
ment be performed during breath hold, 
while avoiding deep inspiration (35). 
Also, it has been recently suggested 
that inspiration statically deforms the 
 liver, which is expected to alter the ob- 
served stiffness due to nonlinearity in 
elasticity of biologic tissues (296). In 
2D GRE MR elastography, a four-sec- 
tion acquisition generally requires four 
breath holds of approximately 15 sec- 
onds each. Three-dimensional MR elas- 
tography acquisitions also require that 
multiple breath holds be performed. 
For accurate determination of liver stiff- 
ess over the liver volume, breath holding should be performed in expi- 
rations to minimize positional changes 
between breath holds.

Because the liver is surrounded by 
a nonelastic envelope (Glisson capsule), 
additional space-occupying tissue ab- 
normals, such as edema, inflammation, 
or congestion, can interfere with 
measurements of liver stiffness, inde- 
pendently of fibrosis. A further con- 
sideration when utilizing elastographic 
methods is the additional cost of the 
examination above standard clinical 
examinations. In the United States, TE 
has recently become a reimbursable 
medical examination with the creation 
of a Current Procedural Terminology 
(CPT) code 91200 for the procedure 
(297). A CPT code 0346T for pSWE 
and 2D SWE methods can be added to 
the regular US code. MR elastography, 
the most expensive method, has not yet 
been granted a CPT code, but its in- 
creasing use may motivate the introduc- 
tion of one. More specific limitations 
for US elastography and MR elastogra- 
yph are discussed below.

Limitations of US Elastography Methods

Two-dimensional SWE and pSWE can be 
performed with one probe in all 
patients, independent of body weight, 
as the region of interest can be posi- 
tioned manually at different depths in 
the liver. As compared with TE, ascites 
is not a limitation for ARFI US 
methods, enabling its performance in 
decompensated liver cirrhosis for prog- 
nostic reasons. TE is not suited for 
spleen measurements owing to the need 
for external guidance from another US 
system. The risk of overestimating liver 
stiffness values has been reported, with 
other confounding factors including 
alanine aminotransferase flares (298– 
300), congestive heart failure (301), 
excessive alcohol intake (302–304), and 
averse viral hepatitis (298,305). Some 
work has been done to establish cut-
offs that account for these confounding 
factors (306), though further validation 
is required. The influence of steatosis 
is still a matter of debate with con- 
flicting results, some studies suggest a 
detrimental effect (307,308), whereas 
that others do not (309,310). In summary, 
US elastographic techniques need to 
be performed by using a standardized 
protocol and with critically interpreted 
results, taking confounding factors into 
account (110).

Limitations of MR Elastography

Although considered a highly accurate 
technique, MR elastography has several 
limitations. The primary drawback of 
 liver MR elastography is the sensitivity 
of 2D GRE sequence to iron deposition. 
The short T2* time of the liver affected 
by iron deposition means that signal- 
to-noise ratio from a standard GRE 
sequence is too low, and thus unable 
to resolve wave propagation (311). This 
has been addressed by the introduction 
of spin-echo and spin-echo echo-planar 
imaging–based sequences, which are 
instead primarily sensitive to T2 relax- 
ation and thus provide higher signal-to-
noise ratio even in slightly longer echo 
times (312) (Fig 10). A study comparing 
2D GRE and spin-echo echo-planar se- 
quences found both sequences produced 
consistent liver stiffness measurements, 
with the spin-echo echo-planar sequence 
producing reliable results in subjects in 
whom the GRE sequence failed due to 
iron deposition and larger reliable re-

gions of interest (311). Another study 
found 2D GRE and spin-echo echo- 
planar MR acquisitions to produce rea-
sonably consistent results at 1.5 T and 
3.0 T with ICCs ranging 0.73–0.9 across 
manufacturers (64).

There is conflicting evidence on 
the effect of body mass index on MR 
elastography measurements: A recent 
study found that body mass index was 
not a contributing factor in failure (88), 
but found waist circumference to be a 
significant factor of failure. In contrast, 
a recent large retrospective study inves-
tigating the cause of MR elastography 
failure using a 2D GRE sequence (312) 
found that body mass index, iron de-
position, massive ascites, and use of 3 
T were significantly associated with MR 
elastography failure (Fig 11). The over-
all failure rate was low (3.5%) at 1.5 
T though it increased to 15.3% at 3 T, 
likely due to increased T2* relaxation 
at higher field strength. Other potential 
causes of failure include poor actuator 
placement, coupling to the body, or 
tube disconnection, which require the 
examination to be repeated, and ab-
normal physiology. MR elastography is 
also costlier and less available than US 
elastography.

New Technical Developments

Measurement of Liver Steatosis with TE

A more recent application of TE is the 
controlled attenuation parameter (CAP) 
(313). CAP, which is available on both 
M and XL probes, estimates the attenu-
ation of the US signal in units of dBm−1 
and is used as a method to grade steato-
sis. A recent meta-analysis of a mixed-
etiology cohort using the M probe (314) 
reported excellent accuracy for detect-
ing steatosis based on histopathologic 
findings. A small pilot study using the XL 
probe (315) found that performance was 
similar between the M and XL probes 
for detecting liver fat. Further validation 
in large cohorts is required to determine 
the performance of CAP, particularly 
with the XL probe. A benefit of MR im-
aging when assessing NAFLD patients is 
the high accuracy of liver fat quantifica-
tion using advanced confounder-correct-
ed chemical shift–encoded methods now 
available with all scanner manufactur-
ers (316), which can be combined with liver 
stiffness measurement for a com-
prehensive examination of liver health (Fig 
6). In the study by Imajo et al (94), the
combination of MR elastography and liver fat quantification outperformed TE and CAP for staging fibrosis and fat quantification, respectively. Further comparison studies are required between MR-based fat quantification and elastography and US-based TE and CAP for combined staging of fibrosis and steatosis.

**Three-dimensional MR Elastography**

Though the acquisition of all three directions of motion is not a new development (317), advances in inversion algorithms and the increasing availability of research three-dimensional MR elastography imaging sequences has made the technique more accessible. Three-dimensional MR elastography enables the determination of additional parameters compared with 2D owing to the acquisition of the full wave field and fewer assumptions about the material model during inversion. These parameters, such as volumetric strain, which has been shown to be sensitive to pressure-related changes (318) and may have applications in the diagnosis of portal hypertension, are still being evaluated to establish clinical benefit. The acquisition of all three motion directions also addresses the issue of artificially increased wavelengths due to oblique 2D waves violating the planar wave assumption (319). Further details on three-dimensional MR elastography are included in the Appendix E1 (online).

A comparison of the diagnostic accuracies of 2D GRE and three-dimensional spin-echo echo-planar imaging MR elastography in 73 patients with chronic liver disease found 2D and three-dimensional sequences to perform similarly (320). However, three-dimensional MR elastography parameter results were significantly lower than those of 2D MR elastography. A similar result was reported from a study of patients with NAFLD performed at 60 Hz and 40 Hz vibration frequencies (163). Diagnostic accuracy for diagnosing F3–F4 fibrosis in 2D and three-dimensional MR elastography at 60 Hz vibration frequency was not significantly different. Three-dimensional MR elastography data acquired at 40 Hz showed improved diagnostic accuracy with a significantly higher AUC than 2D measurements (AUC, 0.98 vs 0.92). Three-dimensional spin-echo echo-planar imaging MR elastography failure rate has been reported as lower than that of 2D GRE MR elastography, as the spin-echo echo-planar imaging sequence is expected to perform better in hepatic iron deposition (92). Spleen stiffness has also been assessed with three-dimensional MR elastography (235), with liver stiffness and spleen stiffness significantly associated with the presence of esophageal varices.

**Multifrequency MR Elastography**

Generally, MR elastography examinations are performed by imaging shear waves at a single frequency (typically...
The stiffness of tissue is dependent on the frequency of the imaged waves, so examinations at a frequency other than 60 Hz will result in a different stiffness measurement. The use of multifrequency MR elastography, where acquisitions acquired at multiple frequencies are performed, may lead to the development of parameters that are independent of frequency through viscoelastic modeling (38,321,322) or via analysis of the regression line of stiffness and frequency (323). Another application of multifrequency data is combining the wave fields from each frequency to improve the resulting elastogram. This is achieved by accounting for areas of low displacement and wave nodes that are present in each wave field, but the location of which varies depending on frequency (324–326). A downside of the acquisition of multiple frequencies is the increased imaging time, as each additional frequency incrementally increases the imaging time limiting clinical adoption, and the associated challenges with increased wave attenuation at higher frequencies. Thus, the diagnostic benefit of multifrequency over single-frequency MR elastography must be established.

**Conclusion**

US and MR elastographic techniques have developed into accurate methods for quantitative, noninvasive diagnosis of liver fibrosis in a wide range of etiologies. Interpretation of results should take into account potential confounding factors of liver stiffness measurements, pitfalls, and technical limitations. MR elastography has equivalent to slightly better diagnostic accuracy than TE and ARFI methods, while providing stiffness measurement over a larger area of the liver; however, the method requires wider validation, and the higher cost and limited availability may limit adoption worldwide. In liver referral centers performing a large number of MR imaging examinations, it is feasible to incorporate MR elastography into the standard imaging protocols to provide a fibrosis-staging tool. The weight of published data on TE has allowed the establishment of measurement cutoffs for most etiologies. ARFI methods have shown similar diagnostic ability to TE, and it is reasonable to assume that once sufficient data have been acquired to fully validate ARFI methods they will also become a recommended noninvasive measurement tool for staging of liver fibrosis. The emergence of advanced techniques such as three-dimensional MR elastography– and US-based controlled attenuation parameter measurement may increase the accuracy of fibrosis and steatosis staging in liver disease, although more data are needed.

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**References**


46. Yoneda M, Thomas E, Schär SN, Grant TT, Schiff EB. Supersonic shear imaging and...
transient elastography with the XL probe accurately detect fibrosis in overweight or obese patients with chronic liver disease. Cln Gastroenterol Hepatol 2015;13(8):1502–1509.e5.


112. Ye XP, Ran HT, Cheng J, et al. Liver and spleen stiffness measured by acoustic radiation force impulse elastography for non-


142. European Association for the Study of the Liver (EASL); European Association for the hepatic fibrosis in chronic hepatitis B. Gut Liver 2017;11(3):401–408.


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254. Ronot M, Di Benzo S, Gregoli B, et al. Characterization of fortuitously discovered focal liver lesions: additional information pro-


