Clinical Policy Title: Liver elastography

Clinical Policy Number: CCP.1118

Effective Date: October 1, 2014
Initial Review Date: June 18, 2014
Most Recent Review Date: August 7, 2018
Next Review Date: August 2019

Related policies:

CCP.1079 Serum biomarkers for liver fibrosis in chronic hepatitis

ABOUT THIS POLICY: Select Health of South Carolina has developed clinical policies to assist with making coverage determinations. Select Health of South Carolina’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Select Health of South Carolina when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Select Health of South Carolina’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Select Health of South Carolina’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Select Health of South Carolina will update its clinical policies as necessary. Select Health of South Carolina’s clinical policies are not guarantees of payment.

Coverage policy

Select Health of South Carolina considers the use of liver elastography (FibroScan®, Echosens SA, Paris, France) to be clinically proven and, therefore, medically necessary for members with (American Association for the Study of Liver Diseases and the Infectious Diseases Society of America, 2018; Lim, 2017; Terrault, 2016):

- Chronic liver diseases to distinguish hepatic cirrhosis from non-cirrhosis.
- Suspected compensated cirrhosis to assess the need for esophagogastroduodenoscopy to identify high-risk esophageal varices.
- Suspected chronic liver disease undergoing elective non-hepatic surgery to detect clinically significant portal hypertension and inform preoperative care.
- Suspected recurrent fibrosis after liver transplantation (Bhat, 2017).

Select Health of South Carolina considers the use of acoustic radiation force impulse imaging to be clinically proven and, therefore, medically necessary for distinguishing hepatic cirrhosis from non-cirrhosis in members with chronic liver diseases (Hu, 2017).
Select Health of South Carolina considers the use of magnetic resonance elastography to be clinically proven and, therefore, medically necessary for distinguishing hepatic cirrhosis from non-cirrhosis in members with non-alcoholic fatty liver disease at high risk of cirrhosis (Lim, 2017).

Limitations:

All other uses of liver elastography are not medically necessary.

Alternative covered services:

- Liver-directed physical exam (normal in most patients).
- Routine blood tests (e.g., alanine transaminase, aspartate aminotransferase, albumin, bilirubin, international normalized ratio, and complete blood count with platelet count).
- Liver imaging (e.g., ultrasound or computed tomography scan).
- Liver biopsy.

Background

Liver fibrosis and chronic cirrhosis represent the pathological results of chronic liver injury. This may be the result of infection with one of the viral etiologies such as hepatitis B, C, or E, or of toxins such as alcohol. Hepatitis C virus is the most viral cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma, and an estimated 3.5 million Americans live with hepatitis C infection (Centers for Disease Control and Prevention, 2018).

The majority of hepatitis C infections are asymptomatic with low risk of disease progression. Current treatment recommendations focus on proper patient selection, including those with advanced fibrosis or cirrhosis (i.e., METAVIR Stage F3 or F4). Liver biopsy is the standard for staging hepatic pathology but is associated with complications ranging from pain to perforation of internal organs, and sampling errors may occur (Regev, 2002). There are several noninvasive alternatives to liver biopsy, and most are rapidly evolving.

Liver elastography:

Certain diseases can alter the elastic properties of the liver. Elastography exploits the elastic properties of the liver by inducing a distortion in the tissue and observing the tissue’s response, from which the mechanical properties of the tissue can be mapped. Elastography has the advantage of depicting diffuse disease, which a biopsy can easily miss.

The main elastographic methods for assessing liver fibrosis apply ultrasonography or magnetic resonance imaging (Barr, 2016):

- Transient elastography applies vibration-controlled ultrasonography to track and quantify shear wave speed, which correlates with liver elasticity, to produce a one-dimensional image of tissue
stiffness. The U.S. Food and Drug Administration (2017) granted 510(k) approval for FibroScan as a commercially available transient elastography unit, citing the high degree of reliability of measurement. It can be used at the point of care.

- Acoustic radiation force impulse exploits the propagation of acoustic waves from a focused ultrasonographic beam to create a qualitative two-dimensional map of tissue stiffness. It can be used independently or as an add-on during liver ultrasonography.

- Magnetic resonance elastography acquires a sequence of measurements of shear wave velocity to produce a color-scaled, quantitative, three-dimensional image depicting tissue stiffness in units of kilopascals. It uses standardized shear wave driver systems, processing algorithms, and display conventions that allow for direct comparison between magnetic resonance elastography systems. It can be added to an abdominal magnetic resonance imaging examination or be used as a stand-alone test.

**Searches**

Select Health of South Carolina searched PubMed and the databases of:
- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality Guideline Clearinghouse and evidence-based practice centers.
- The Centers for Medicare & Medicaid Services.

We conducted searches on June 1, 2018. Search terms were: “Elasticity Imaging Techniques” (MeSH), “noninvasive liver,” “imaging liver,” and “noninvasive hepatitis.”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.

- **Guidelines based on systematic reviews.**

- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

Wilder (2014) and Foucher (2006) illustrate the importance of the etiology of both hepatic fibrosis and cirrhosis and differences in optimal elastography cutoffs used to define the stage of liver fibrosis when interpreting test results. Wilder (2014) pointed to the high degree of accuracy of FibroScan for patients with cirrhosis but also a higher error rate at METAVIR stage F2 or less.

**Policy updates:**
Crossan (2015) reviewed the cost effectiveness of treating patients in the absence of liver biopsy using a variety of statistical models and generally found FibroScan to be the most cost-effective test.

In 2016, we identified four new systematic reviews and meta-analyses (Houot, 2016; Li, 2016; Liu, 2015; Singh, 2015) and two guideline updates (American Association for the Study of Liver Diseases and Infectious Disease Society of America, 2016; Terrault, 2016) for this policy. The systematic reviews and meta-analyses confirmed earlier findings that noninvasive tests, such as FibroScan or acoustic radiation force impulse, may be useful in ruling out cirrhosis, but are less accurate in predicting presence of significant fibrosis (F2 or higher) across a range of etiologies.

Current guidelines recommend that all persons with hepatitis C virus or hepatitis B virus infection undergo an evaluation for advanced fibrosis using liver biopsy or noninvasive techniques to facilitate an appropriate decision regarding treatment strategy and management of cirrhosis (American Association for the Study of Liver Diseases and Infectious Disease Society of America, 2017; Terrault, 2016). While none of the noninvasive tests is as diagnostic as liver biopsy, transient elastography is a reliable and easily repeated tool for following the progression of liver fibrosis toward cirrhosis.

Insufficient, low-quality evidence supports magnetic resonance elastography for measuring liver stiffness as a surrogate marker of liver disease and fibrosis. The evidence suggests moderate diagnostic performance that improves with disease severity, but prospective studies are needed to confirm these findings before wide application (Singh, 2015). These new findings would not alter the conclusions of the initial policy; therefore, no policy changes are warranted.

In 2017, we added three systematic reviews/meta-analyses (Kim, 2017; Njei, 2016; Singh, 2016) and professional guidance from the Society of Radiologists in Ultrasound (Barr, 2016) and the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (Vos, 2017). Portal hypertension is a consequence of chronic liver disease, and its severity is associated with a poor prognosis. Kim (2017) found transient elastography could be a reliable noninvasive alternative to the hepatic venous pressure gradient for diagnosing the severity of portal hypertension, but the results require confirmation in prospective research before more widespread clinical application.

In patients with human immunodeficiency virus-hepatitis C virus coinfection, transient elastography is highly accurate for detecting cirrhosis but less accurate for detecting less severe fibrosis (Njei, 2016). Studies of transient elastography generally exclude persons with a mean body mass index greater than 30 kg/m², but Singh (2016) found neither body mass index nor inflammation affected the high diagnostic performance of magnetic resonance elastography in persons with non-alcoholic fatty liver disease. Nonetheless, the current evidence base for magnetic resonance elastography is less established than that for transient elastography and acoustic radiation force impulse. It consists of retrospective studies, has a high potential for spectrum and referral bias, and lacks established cutoffs for classifying disease severity, which could lower its diagnostic performance in other populations.
Noninvasive detection of liver fibrosis is particularly appealing for children, but the limitations in the evidence base for all modalities of elastography are magnified in this population. The need for larger prospective studies representing a spectrum of disease severity calls for cautious use in pediatric populations (Vos, 2017). The Society of Radiologists in Ultrasound supports noninvasive measurement of liver fibrosis using transient elastography, acoustic radiation force impulse, or magnetic resonance elastography to distinguish patients with no or minimal (METAVIR stages F0 and F1) fibrosis who could avoid liver biopsy and unnecessary treatment from patients with severe fibrosis or cirrhosis who would require additional follow-up and treatment (Barr, 2016). These results are consistent with previous findings, and no policy changes are warranted.

In 2018, we added two meta-analyses (Bhat, 2017; Hu, 2017) and updated guidelines from the American Gastroenterological Association (Lim, 2017) and American Association for the Study of Liver Diseases and the Infectious Diseases Society of America (2018). The evidence supports noninvasive evaluation of recurrent fibrosis after liver transplantation, representing a new indication for transient elastography (Bhat, 2017). The results of the other meta-analysis confirm previous findings in this policy for assessing chronic hepatitis B- and C-related fibrosis using acoustic radiation force impulse elastography (Hu, 2017).

The American Gastroenterological Association (Lim, 2017) issued recommendations based on a comprehensive evidence review (Singh, 2017). Three recommendations result in changes to this policy:

- Magnetic resonance elastography is preferred to transient elastography for its higher accuracy in evaluating non-alcoholic fatty liver disease in patients at high risk of cirrhosis.
- Transient elastography is indicated to assess the need for esophagogastroduodenoscopy in persons with suspected compensated cirrhosis to identify high-risk esophageal varices.
- Transient elastography is indicated for persons with suspected chronic liver disease undergoing elective non-hepatic surgery to detect clinically significant portal hypertension and inform preoperative care.

Policy name changed from Non-invasive assessment of hepatic fibrosis to Liver elastography. Policy ID changed from CP# 08.01.03 to CCP.1118.

**Summary of clinical evidence:**

<table>
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<tr>
<th>Citation</th>
<th>Comments, Methods, Recommendations</th>
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| American Association for the Study of Liver Diseases and the Infectious Diseases Society of America (2018) | **Key points:**
| | • The most efficient approach (avoiding unnecessary liver biopsy) to fibrosis assessment is to combine direct biomarkers and vibration-controlled transient liver elastography; consider a biopsy for discordant results between the two modalities that would affect clinical decision-making.
| | • For transient elastography, children require specialized probes and cutoff values for advanced fibrosis/cirrhosis that differ from those used in adults, but this approach appears promising for monitoring children with chronic hepatitis C infection.
<p>| | • Individuals with clinically evident cirrhosis do not require additional staging (biopsy or noninvasive assessment). |</p>
<table>
<thead>
<tr>
<th>Citation</th>
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<tbody>
<tr>
<td>Bhat (2017)</td>
<td><strong>Key points:</strong>&lt;br&gt;  - Meta-analysis of eight studies of aspartate aminotransferase-to-platelet ratio index, four studies of fibrosis score-4, and 12 studies of transient elastography, all compared to biopsy as the reference standard. Studies included a variety of etiologies.&lt;br&gt;  - Transient elastography performed best to diagnose recurrent fibrosis, but the aspartate aminotransferase-to-platelet ratio index and fibrosis score-4 can be used if transient elastography is not available.&lt;br&gt;  - Longitudinal assessment of fibrosis by means of these noninvasive tests may reduce the need for liver biopsy.</td>
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<td>Hu (2017)</td>
<td><strong>Key points:</strong>&lt;br&gt;  - Meta-analysis of 21 articles (2,691 total adult patients in different stages of hepatic fibrosis) comparing acoustic radiation force impulse elastography to liver biopsy.&lt;br&gt;  - Overall quality: moderate to high with a low or unclear risk of bias.&lt;br&gt;  - Acoustic radiation force impulse elastography is accurate and reliable in the diagnosis of chronic hepatitis B- and C-induced liver fibrosis and is especially suitable for the evaluation of stages F ≥ 3 and F = 4.&lt;br&gt;  - Patients with chronic hepatitis C manifest higher acoustic radiation force impulse values than patients with chronic hepatitis B especially in the F3 stage.</td>
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<td>Lim (2017) for the American Gastroenterological Association Institute</td>
<td><strong>Key points:</strong>&lt;br&gt; Recommendations (strength of recommendation, strength of evidence):&lt;br&gt;  - Chronic hepatitis C — transient elastography preferred over noninvasive serum tests to detect cirrhosis (strong, moderate) and magnetic resonance elastography (conditional, very low); cutoff of 12.5 kPa to obviate need for biopsy (conditional, low).&lt;br&gt;  - Chronic hepatitis B — transient elastography preferred over noninvasive serum tests to detect cirrhosis (conditional, low); cutoff of 11.0 kPa to detect cirrhosis (conditional, low).&lt;br&gt;  - Non-alcoholic fatty liver disease — no recommendation for or against transient elastography; magnetic resonance elastography is preferred for patients at high risk of cirrhosis.&lt;br&gt;  - Chronic alcoholic liver disease — transient elastography cutoff of 12.5 kPa to detect cirrhosis (conditional, low).&lt;br&gt;  - Suspected compensated cirrhosis — transient elastography cutoff of 19.5 kPa to assess the need for esophagogastroduodenoscopy to identify high-risk esophageal varices (conditional, low).&lt;br&gt;  - Suspected chronic liver disease undergoing elective non-hepatic surgery — transient elastography cutoff of 17.0 kPa to detect clinically significant portal hypertension to inform preoperative care (conditional, low).</td>
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| Kim (2017) Transient elastography versus hepatic venous pressure gradient for diagnosing portal hypertension | **Key points:**  
  - Systematic review and meta-analysis of eight studies (1,356 total patients).  
  - Overall quality: low with inconsistent patient characteristics, cirrhosis etiologies, and diagnostic thresholds.  
  - For the detection of portal hypertension (hepatic venous pressure gradient $\geq 6$ mmHg), sensitivity 0.88 (95% confidence interval [CI] 0.86 to 0.90) and specificity 0.74 (95% CI 0.67 to 0.81).  
  - For clinically significant portal hypertension (hepatic venous pressure gradient $\geq 10$ mmHg), sensitivity 0.85 (95% CI 0.63 to 0.97) and specificity 0.71 (95% CI 0.50 to 0.93).  
  - High correlation between transient elastography and hepatic venous pressure gradient (0.75, 95% CI 0.65 to 0.82, $P < 0.0001$).  
  - Promising, but additional rigorous research is needed. |
| Vos (2017) for North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition Guideline: diagnosis and treatment of non-alcoholic fatty liver disease in children | **Key points:**  
  - Acoustic radiation force impulse, transient elastography, and magnetic resonance elastography are mostly assessed in adults; pediatric literature is characterized by small sample size, and particularly small numbers of patients with clinically significant fibrosis ($\geq F2$).  
  - Research needed to determine optimal cut-points and track fibrosis over time in children. |
| Liu (2015) Acoustic radiation force impulse in non-alcoholic fatty liver disease | **Key points:**  
  - Systematic review and meta-analysis of seven studies (723 total patients with fibrosis stage F2–F4).  
  - Modest test performance: sensitivity 80%, specificity 85%, area under the receiver operating characteristic curve 0.898.  
  - Head-to-head comparison of acoustic radiation force impulse and other elastographic imaging is needed. |

**References**

**Professional society guidelines/other:**


**Peer reviewed references:**


**Center for Medicare & Medicaid Services National Coverage Determinations:**

No National Coverage Determinations identified as of the writing of this policy.

A54953 Independent Diagnostic Testing Facilities- physician supervision and technician requirements.

**Local Coverage Determinations:**

Add-on code 0346T listed as a non-covered service in the following:

L33392 Category III CPT® Codes.
L36219 Non Covered services.

L34555 Non-Covered Category III CPT Codes.

L33777 Noncovered services.

L35008 Non-Covered services.

L35094 Services That Are Not Reasonable and Necessary.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
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<tr>
<td>91200</td>
<td>Liver elastography, mechanically induced shear wave (e.g., vibration, without imaging with interpretation and report)</td>
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<tr>
<td>0346T</td>
<td>Add-on code; ultrasound elastography</td>
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<tr>
<td>B17.10</td>
<td>Acute hepatitis C without hepatic coma</td>
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<tr>
<td>B17.11</td>
<td>Acute hepatitis C with hepatic coma</td>
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<tr>
<td>B18.2</td>
<td>Chronic viral hepatitis C</td>
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<tr>
<td>B19.20</td>
<td>Unspecified viral hepatitis C without hepatic coma</td>
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<tr>
<td>K71.7</td>
<td>Toxic liver disease with fibrosis and cirrhosis of liver</td>
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<tr>
<td>K74.0</td>
<td>Hepatic fibrosis</td>
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<tr>
<td>K74.60 &amp; K74.69</td>
<td>Other and unspecified cirrhosis of liver</td>
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<tr>
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