



**SANDHILLS
CENTER**



Liver elastography

Clinical Policy ID: CCP.1118

Recent review date: 10/2021

Next review date: 2/2023

Policy contains: Acoustic radiation force impulse imaging; hepatic fibrosis; liver elastography; magnetic resonance elastography.

This policy is a Sandhills Center Clinical Coverage Policy adopted from AmeriHealth Caritas of North Carolina. These clinical policies are used to assist with making coverage determinations. Sandhills Center'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 Sandhills Center 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. Sandhills Center 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. Sandhills Center's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Sandhills Center will update its clinical policies as necessary. Sandhills Center clinical policies are not guarantees of payment.

Coverage policy

Liver shear wave elastography (FibroScan®, Echosens SA, Paris, France) is clinically proven and, therefore, medically necessary for members with any of the following (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).

Acoustic radiation force impulse imaging is clinically proven and, therefore, medically necessary for distinguishing hepatic cirrhosis from non-cirrhosis in members with chronic liver diseases (Hu, 2017).

Magnetic resonance elastography is 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).
- Initial diagnosis and staging of liver fibrosis in members with chronic liver disease (American College of Radiology, 2019; Dong, 2021; Liang, 2020; Selvaraj, 2021).

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; toxins such as alcohol; or nonalcoholic fatty liver disease. Hepatitis C virus is the most viral cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma, and an estimated 2.4 million Americans live with hepatitis C infection (Centers for Disease Control and Prevention, 2020).

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. There are several evolving noninvasive alternatives to liver biopsy.

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 (2013) 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 sequential 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.

Findings

Wilder (2014) illustrates 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.

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. Invasive measurement of the hepatic venous pressure gradient is used to determine severity. 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.

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

In 2019, we revised the list of Local Coverage Determinations. No other new publications were identified.

In 2020, we added updated guidance from the American College of Radiology (2019) with no policy changes warranted.

In 2021, we updated the references and added one meta-analysis comparing the diagnostic performance of artificial intelligence-assisted ultrasonography, elastography, computed tomography, and magnetic resonance imaging for diagnosing liver fibrosis and steatosis (Decharatanachart, 2021). Preliminary findings suggest the potential value of artificial intelligence technology to aid in the diagnosis of fibrosis and non-alcoholic fatty liver disease, but the results require validation compared to conventional diagnostic methods in real-world clinical settings.

We added four systematic reviews and meta-analyses examining magnetic resonance elastography and other imaging modalities for staging liver fibrosis in patients with chronic hepatitis B infection (Dong, 2021, 24 studies, n = 5,126 patients) and non-alcoholic fatty liver disease (Liang, 2020, 12 studies, n = 910 patients; Selvaraj, 2021, n = 82 studies (14,609 patients), and for detecting portal hypertension (Singh, 2021, 14 studies). The new findings suggest a staging role for magnetic resonance elastography in different populations at risk for liver cirrhosis, but its diagnostic performance overlaps with other noninvasive modalities without a clear advantage of one modality over another.

The American College of Radiology (2019) recommends transient elastography or magnetic resonance elastography of the abdomen as “usually appropriate” as the initial imaging for diagnosis and staging of liver fibrosis in patients with chronic liver disease, but they listed elastography methods as “usually not appropriate” for screening or post-treatment monitoring for hepatocellular carcinoma. The policy was changed to reflect the new staging indication for magnetic resonance elastography.

References

On July 15, 2021, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “Elasticity Imaging Techniques” (MeSH), “noninvasive liver,” “imaging liver,” and “noninvasive hepatitis.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

6/2014: initial review date and clinical policy effective date: 10/2014

7/2015: Policy references updated.

7/2016: Policy references updated.

7/2017: Policy references updated.

10/2018: Policy references updated. Changes to coverage, policy title, and policy ID.

10/2019: Policy references updated.

10/2020: Policy references updated.

10/2021: Policy references updated. Coverage modified.