Network Notifications

Massachusetts

WellSense HEALTH PLAN

formerly BMC HealthNet Plan

Date:	October 31, 2023	Number: 249
To:	All WellSense Providers	
From:	WellSense Health Plan	
Subject:	**eviCore Clinical Criteria and Coding Updates**	
Product:	☒ MassHealth ☒ Qualified Health Plans ☒ Senior Care Options	

eviCore Clinical Criteria and Coding Updates

Effective January 1, 2024, eviCore healthcare will be updating the clinical criteria used to determine the medical necessity of laboratory testing that members have requested. There's one material change to the criteria:

- Prior authorization is required due to medical necessity criteria added for the testing of liver fibrosis assessment biomarkers

Updated criteria are available on the eviCore website: Cardiovascular & Radiology Guidelines

Effective January 1, 2024, the CPT codes 81457-81459 and 81462-81464 will require prior authorization by eviCore. These CPT codes represent oncology panels and are additions to the genomic sequencing procedure code set. Industry-wide code updates effective January 1, 2024 will be adopted, including the addition of new service-specific codes and revised code descriptions.

Questions?

If you have questions about this Network Notification, please contact your dedicated Provider Relations Consultant or call the Provider Line at 888-566-0008. You can also send comments about WellSense medical policies to medicalpolicy@wellsense.org . Please include the medical policy title and policy number.

Network Notifications

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All WellSense Health Plan Network Notifications and Reimbursement Policies are available online at wellsense.org.

Liver Fibrosis Assessment Biomarkers

MOL.TS.401.A
v1.0.2024

Introduction

Testing for the assessment of liver fibrosis is addressed by this guideline.

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

Procedure addressed by this guideline	Procedure code
Liver disease, ten biochemical assays (ALT, A2-macroglobulin, apolipoprotein A-1, total bilirubin, GGT, haptoglobin, AST, glucose, total cholesterol and triglycerides) utilizing serum, prognostic algorithm reported as quantitative scores for fibrosis, steatosis and alcoholic steatohepatitis (ASH) (ASH FibroSURE®)	0002M, 82172, 82247, 82465, 82947, 82977, 83010, 83883, 84450, 84460, 84478
Liver disease, ten biochemical assays (ALT, A2-macroglobulin, apolipoprotein A-1, total bilirubin, GGT, haptoglobin, AST, glucose, total cholesterol and triglycerides) utilizing serum, prognostic algorithm reported as quantitative scores for fibrosis, steatosis and nonalcoholic steatohepatitis (NASH) (NASH FibroSURE®)	0003M, 82172, 82247, 82465, 82947, 82977, 83010, 83883, 84450, 84460, 84478
Infectious disease, chronic hepatitis C virus (HCV) infection, six biochemical assays (ALT, A2-macroglobulin, apolipoprotein A-1, total bilirubin, GGT, and haptoglobin) utilizing serum, prognostic algorithm reported as scores for fibrosis and necroinflammatory activity in liver (HCV FibroSURE®/FibroTest™)	81596

What is cirrhosis?

Definition

Cirrhosis refers to permanent, irreversible scarring of the liver, where healthy liver tissue is replaced by fibrosis.[1]

Liver disease has many different causes including autoimmune disease, alcoholism, medications, toxins, genetic diseases such as Wilson's Disease, hereditary hemochromatosis, or alpha-1 anti-trypsin deficiency, and infectious diseases such as hepatitis B and hepatitis C.[2]

Non-alcoholic fatty liver disease (NAFLD) is common, afflicting 25% of the global population.[3] NAFLD is usually diagnosed by ultrasound after abnormal liver enzyme levels are detected. Occasionally it is found incidentally on imaging. Non-alcoholic steatohepatitis (NASH) is a poorer prognosis subset of NAFLD, afflicting 12-14% of patients with NAFLD. NASH is more likely to progress to liver fibrosis and is more likely to result in cirrhosis and liver malignancy. The causes of progressive NAFLD/NASH are not well understood. Risk factors for cases that will progress to a poor outcome include type 2 diabetes, elevated liver enzymes, and metabolic syndrome.[4]

Liver disease is most clinically significant when it progresses. According to the American Liver Foundation:[2]

- "Most liver diseases damage your liver in similar ways and for many, the progression of liver disease looks the same regardless of the underlying disease."

The stages of progression are inflammation, fatty liver, fibrotic liver, cirrhosis, and cancer.[2] Cirrhosis refers to permanent, irreversible scarring of the liver, where healthy liver tissue is replaced by fibrosis.[1] Commonly, there is an overlap between different stages of the progression; for example, a liver can concurrently show signs of inflammation and fatty infiltration, or fatty infiltration and fibrosis. Early identification of liver fibrosis and grading of liver fibrosis may inform the selection of treatments that slow or block progression to cirrhosis.[5]

Test Information

Introduction

The laboratory tests discussed in this guideline have proposed roles in the diagnosis and management of liver fibrosis.

Enhanced liver fibrosis test (ELF test)

Liver disease, analysis of 3 biomarkers (hyaluronic acid [HA], procollagen III amino terminal peptide [PIIINP], tissue inhibitor of metalloproteinase 1 [TIMP-1]), using immunoassays, utilizing serum, prognostic algorithm reported as a risk score and risk of liver fibrosis and liver-related clinical events within 5 years.

The ELF test measures three analytes: hyaluronic acid (HA), Type III procollagen peptide (PIIINP), and tissue inhibitor of matrix metalloproteinase 1 (TIMP-1). An algorithm is then used to calculate a risk score.[6] Specific versions of the test vary regarding the algorithm used to calculate the risk score from the three analyte values. There are two main algorithms in use, the Guha algorithm, and the Siemen algorithm. The results between the two are highly correlated, with an equation being available to convert between the two.[6] Studies vary regarding the suggested decision thresholds for interpreting the risk score.

The ELF test is proposed most frequently for persons with, or at high risk for, NAFLD. The purpose of the test is to assess the risk of disease progression.[3,6]

LIVERFASt

This proprietary test combines the results of ten biochemical assays with gender, age, weight and height to generate a combination of three scores, which are correlated to the degree of liver damage: fibrosis, necroinflammatory activity and steatosis. Each of the three scores are reported on a scale from 0.00-1.00 with a brief interpretation, with interpretive comments such as "significant fibrosis" or "minimal activity."

FibroSpect HCV/NASH

FibroSpect HCV is a non-invasive blood test that aims to assist in the detection, staging, and monitoring of the severity of liver fibrosis in persons with hepatitis C virus (HCV). Test results provide a quantitative fibrosis score as an aid to assess and monitor disease risk based on three different biomarkers (tissue inhibitor of metalloproteinase-1, hyaluronic acid, and α2-macroglobulin). The test is designed to differentiate between F0-F1 and F2-F4 liver fibrosis. The manufacturer suggests that FibroSpect HCV may be beneficial when staging liver fibrosis since initiating treatment in persons with lower-stage fibrosis may augment the benefits of a sustained virologic response (SVR).

FibroSpect NASH is a is a non-invasive blood test, using the same biomarkers as the HCV version, that aims to assist in the detection, staging, and monitoring of liver fibrosis for nonalcoholic steatohepatitis (NASH). The NASH-specific algorithm is proposed to differentiate F0-F2 from F3-F4 liver fibrosis resulting from NASH.

HCV FibroSURE/FibroTest

FibroTest, licensed in the United States as FibroSURE, is intended as a non-invasive alternative to invasive biopsies to diagnose liver fibrosis. It is a combination of five biochemical assays: alpha2-macroglobulin, haptoglobulin, apolipoprotein A1, gamma glutamyl transpeptidase (GGT) and total bilirubin. An additional component – alanine aminotransferase (ALT) – is used to test for necroinflammatory lesions. The results of these assays are combined with a person's age, gender, height and weight to reach an algorithmic score. The score is a range from 0-1, which is proportional to the severity of fibrosis. The scores have been assigned a corresponding METAVIR stage, as well as a Knodell and Ishak stage.

ASH/NASH FibroSURE

This test encompasses the same components as its HCV counterpart, with the algorithm designed for persons suspected of having non-alcoholic fatty liver disease. Separate scores are provided as indicators of the degree of fibrosis, steatosis, and NASH.

Guidelines and Evidence

Introduction

This section includes relevant guidelines and evidence pertaining to liver fibrosis biomarker testing.

Liver biopsy is the gold standard for evaluating the liver including the evaluation of nonalcoholic fatty liver disease (NAFLD) and the stages of liver fibrosis.[3,6-8] The drawbacks to liver biopsy are that it is invasive, is associated with rare but significant side effects, and is subject to variation in pathologist interpretation.

Noninvasive tests, including blood tests and mechanical measurement of liver stiffness, have been developed to assist in the evaluation of liver fibrosis.[3,7] The goal of noninvasive testing is to enhance diagnosis, risk stratification, and monitoring of liver fibrosis, while reducing the number of biopsies. International expert consensus guidelines recommended that whenever NAFLD is suspected, the initial diagnostic workup should include a noninvasive imaging examination (e.g. abdominal ultrasound) to confirm the presence of steatosis, as well as general liver biochemistries.[9]

The guidelines emphasized that liver enzymes or laboratory tests alone are not sensitive enough for screening. The guidelines acknowledged that there is interest in the development of clinical scores of disease severity. However, guidelines stated that noninvasive tests for reliably detecting NASH and distinguishing it from simple steatosis are not yet available and that liver biopsy remains necessary. On the other hand, the American Association for the Study of Liver Diseases (AASLD) guidelines acknowledged the utility of some well-validated scoring tools, such as the NAFLD Fibrosis Score. The AASLD recommended that the NAFLD Fibrosis Score was a "clinically useful tool for identifying NAFLD patients with higher likelihood of having bridging fibrosis (stage 3) or cirrhosis (stage 4)."[10]

The American Gastroenterological Association (AGA) published an evidence-based clinical care pathway to provide "guidance on the screening, diagnosis and treatment of NAFLD."[4] In terms of biomarkers, these guidelines primarily advocated for the use of simple, non-proprietary fibrosis scores (such as Fibrosis-4 [FIB-4] or NAFLD Fibrosis Score) calculated from routine laboratory test results. The FIB-4 score is recommended because of its diagnostic accuracy and correlation with clinical outcomes. The negative predictive value of these non-proprietary scores, along with the wide availability of the test components and their low-cost, limits the applicability of proprietary tests in low-risk populations.

Enhanced liver fibrosis test (ELF)

A guideline on the diagnosis and management of NAFLD was published in 2022 by the AACE in collaboration with the AASLD.[3] The ELF test is included in some of the recommendations in the guideline, albeit with only an intermediate (grade B) level recommendation. The guideline followed the AASLD 2018 guideline, which did not mention the ELF test in the recommendations.[10]

The AACE/AASLD guideline stated that the preferred test for screening is the FIB-4 index.[3] This test is not proprietary and consists of 3 common tests --platelets, AST, ALT —which are input, along with the patient age, into an algorithm that generates a risk score for liver disease progression.[3] However, this recommendation is based on limited supporting evidence. One cited study was retrospective in nature, and less than 16% of study participants had two or more liver biopsies to assess, as a comparator, the ability of a non-invasive test to predict fibrosis stage progression.[11] In a cited systematic review, FIB-4 and other tests demonstrated inconsistent performance in predicting a change in fibrosis stage.[12]

Either an ELF test, or a liver stiffness measurement (LSM), which involves measuring mechanical vibrations from the thoracic wall near the liver, are then used to further characterize persons whose FIB-4 index places them in an indeterminate or high-risk group:[3]

- “Clinicians should consider persons belonging to the "high-risk" groups (as defined under R2.1.1) who have an indeterminate or high FIB-4 score for further workup with an LSM (transient elastography) or ELF test, as available. Grade B; Intermediate Strength of Evidence; BEL 2” [BEL=Best evidence level]
- “Clinicians should further risk stratify persons with T2D, or T1D with cardiometabolic risk factors and/or elevated plasma aminotransferase levels (>30 U/L) using the FIB-4, elastography, and/or ELF test. Grade B; High/Intermediate Strength of Evidence; BEL 2” [T2D=type 2 diabetes; T1D=type 1 diabetes]
- “A combination of the FIB-4 followed by VCTE (description under Q2.3) seems to be the best approach.” [VCTE= vibration-controlled transient elastography]

However, with the following caveat regarding non-invasive tests:

- “...their performance is dependent on the population being studied, with a better performance in hepatology clinics where more people have advanced disease than in primary care settings, where the FIB-4 and other tests have been less well characterized.”

Although the ELF test is not mentioned specifically, the guideline stated that noninvasive tests can be considered as a guide for treatment:[3]

- “R3.3.1b Clinicians must consider treating diabetes with pioglitazone and/or GLP-1 RAs when there is an elevated probability of having NASH based on elevated plasma aminotransferase levels and noninvasive tests. Grade A; High Strength of Evidence; BEL 1”

Like the AACE/AASLD guideline described above, an AGA care pathway[4] suggested using noninvasive fibrosis testing only in groups that are at high-risk for developing significant liver disease. These groups include persons with Type 2 diabetes, elevated transaminases, an incidental finding of fatty infiltration of the liver as shown by imaging, and those with two or more metabolic risk factors. In one cited retrospective study, an elevated ALT in those with steatosis was associated with an increased risk of progression to cirrhosis, but diabetes and dyslipidemia alone were also significant risk factors.[13]

The preferred test for fibrosis screening in the AGA pathway is the FIB-4:[4]

- "We recommend that all individuals in the target risk groups undergo a 2-tier process to assess for clinically significant liver fibrosis. The first tier involves using simple, nonproprietary fibrosis scores. Several proprietary scores are available but might not be cost-effective to use in all clinical situations. The Pathway relies on the FIB-4 score because it has been shown to have the best diagnostic accuracy for advanced fibrosis compared with other noninvasive markers of fibrosis in patients with NAFLD."

One study informing the above recommendation was retrospective in nature, and less than 16% of study participants had two or more liver biopsies to assess, as a comparator, the ability of a non-invasive test to predict fibrosis stage progression.[11] The ELF test was not a method used in that study. In another validity study, 33% of selected participants were excluded from the analysis.[14] A cited retrospective study revealed that a repeat FIB-4 test could not consistently predict liver disease progression.[15]

The preferred test in the AGA pathway for persons with an indeterminate FIB-4 is a liver stiffness measurement (LSM):[4]

- "The remaining 30%-40% of patients with an FIB-4 test would likely have values in the indeterminate range (ie, 1.3–2.67).1 These patients should also undergo LSM, depending on the clinical setting..."

Noninvasive blood tests are only an alternative to be used where LSM is unavailable:[4]

- "We recommend commercially available blood or NITs for patients considered indeterminate or high risk based on FIB-4 score or aspartate transaminase to platelet ratio index where LSM is unavailable" [NITs = noninvasive tests]

The National Institute for Health and Care Excellence (NICE) guideline on NAFLD recommended considering the ELF test, not routine liver function tests, when assessing adults or children with NAFLD:[16]

- "Offer testing for advanced liver fibrosis to people with NAFLD... Consider using the enhanced liver fibrosis (ELF) test in people who have been diagnosed with NAFLD to test for advanced liver fibrosis... Do not use routine liver blood tests to assess for advanced liver fibrosis in people with NAFLD."

The NICE guideline also recommended considering the use of the ELF test to monitor treatment:[16]

- "...Offer to retest people with advanced liver fibrosis 2 years after they start a new pharmacological therapy to assess whether treatment is effective… Consider using the ELF test to assess whether pharmacological therapy is effective…If an adult's ELF test score has risen, stop either vitamin E or pioglitazone and consider switching to the other pharmacological therapy..."

A subsequent Cochrane Review, however, reached the following conclusion regarding vitamin E, and other nutritional supplementation, in those with NAFLD:[17]

- "The evidence indicates considerable uncertainty about effects of nutritional supplementation compared to no additional intervention on all clinical outcomes for people with non-alcohol-related fatty liver disease."

Another Cochrane Review concluded:[18]

- "Due to the very low quality evidence, we are very uncertain about the effectiveness of pharmacological treatments for people with NAFLD including those with steatohepatitis. Further well-designed randomised clinical trials with sufficiently large sample sizes are necessary."

The European Association for Study of Liver (EASL) guidelines regarding noninvasive tests for the evaluation of liver disease severity and prognosis did not recommend using the tests in population screening but did recommend its use in persons with risk factors. EASL also preferred the FIB-4 test, which combines ALT, AST, and platelet count to create a risk score. The guideline stated:[7]

- "Non-invasive fibrosis tests should be preferentially used in patients at risk of advanced liver fibrosis (such as patients with metabolic risk factors and/or harmful use of alcohol) and not in unselected general populations (LoE 2, Strong recommendation)." (LoE 2= Level of Evidence 2)
- "ALT, AST and platelet count should be part of the routine investigations in primary care in patients with suspected liver disease, so that simple non-invasive scores can be readily calculated" (LoE 2, Strong recommendation)"
- "The automatic calculation and systematic reporting of simple non-invasive fibrosis tests such as FIB-4, in populations at risk of liver fibrosis (individuals with metabolic risk factors and/or harmful use of alcohol) in primary care, is recommended in order to improve risk stratification and linkage to care (LoE 2, Strong recommendation)."

To communicate the benefit of a two-tier testing strategy, EASL cited results of one study as follows:[7]

- "In a community, pathways for patients with NAFLD using 2-tier non-invasive testing with FIB-4 followed by ELF™ in patients with indeterminate FIB4 results, improved the detection of advanced fibrosis 4-fold and reduced unnecessary referrals by 88%."

However, the cited study was of a simulation model.[19] While simulation studies are a cost-effective way of generating hypotheses to be tested, the results require confirmation by actual clinical studies.

As for the evaluation of fibrosis in those with alcoholic liver disease, the EASL stated:[7]

- "The most robust evidence involves TE for the diagnosis of advanced fibrosis in patients recruited from secondary and tertiary care centres….FIB-4 and Forns' have good diagnostic accuracies for advanced fibrosis. Their low cost and wide accessibility make them particularly suited to rule-out advanced fibrosis in low prevalence populations…Due to risk of misclassifications, the nonpatented fibrosis scores cannot be recommended to rule-in advanced fibrosis.
- Patented markers have higher diagnostic accuracies than non-patented markers, with AUROCs similar or close to LSM by TE, but cut-offs vary substantially from study to study and would therefore need to be aligned and validated. There is a similar lack of studies investigating combination markers, either in parallel, or sequential. In cases of discrepancy between TE and patented serum markers, TE seems more reliable." [TE= transient elastography]

The North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) guideline regarding NAFLD in children noted that there is a gap in knowledge regarding the role of noninvasive testing for the evaluation of NAFLD and NASH:[8]

- “The emergence of NAFLD has been an important change in the landscape of pediatric liver disease. However, substantial gaps in knowledge remain and are research priorities. These gaps include... Non-invasive detection of NAFLD and NASH and quantification of steatosis, inflammation, hepatocellular injury and fibrosis. Longitudinal studies of imaging and biomarkers are needed to better determine their role in clinical care.”

In a systematic review and meta-analysis, the ELF test had an area under the receiver operator characteristic curve (AUROC) of 0.83 (95% Confidence Interval 0.71-0.90) for detecting advanced fibrosis, which was defined as F ≥ 3 on the fibrosis scale.[6] However, the included studies displayed high heterogeneity with regards to disease severity of study populations, disease prevalence, test result thresholds, and the time interval between biopsy and blood test results; pathologist review was also highly variable. Four studies were scored as having a high risk of bias, and the included studies were predominantly from tertiary centers, limiting external validity of the results.

The authors explored the performance of the ELF test at various points on the ROC curve and concluded that clinicians should carefully choose the ELF decision threshold based on the prevalence of advanced fibrosis in their clinic population.[6] The authors stated:

- “However, as a diagnostic test at high thresholds, the test only achieved specificity and positive predictive value >0.80 in very high prevalence settings (>50%).”

The authors also issued the following cautionary statement:

- “However, it is important to note that the high sensitivity of the test (>0.90) comes at the expense of limited specificity (0.30), which, given the low prevalence, means there will be a substantial number of false positive results. This needs to be

considered, especially when the test is going to be applied in a clinical setting with low prevalence of the disease, as the large number of false positive results might lead patients to have unnecessary invasive and expensive procedures, like biopsy."

The high prevalence requirement to achieve an acceptable PPV limits applicability of the test to those populations for which clinical assessment and the FIB-4 test is likely to be sufficient for evaluation.

Clinical utility of the ELF test has not been demonstrated. The available studies fail to address whether use of the ELF test can reduce the need for liver biopsy, guide therapy, or improve health outcomes.

LIVERFASt

While evidence is growing for other non-invasive liver fibrosis tests, there are insufficient high-quality studies evaluating this specific proprietary test. One study evaluated the use of the LIVERFASt test in persons with metabolic (dysfunction)-associated fatty liver disease (MAFLD).[20] The study found that baseline non-invasive tests (liver stiffness measurement, FIB-4 and LIVERFASt) can predict global and liver-related mortality and morbidity in persons with MAFLD.

HCV FibroSURE/FibroTest

In a systematic review and meta-analysis of 71 studies involving adults with chronic hepatitis B, chronic hepatitis C, or both, FibroTest was essentially equivalent to the FIB-4 index in assessing the presence of F2-F4 fibrosis or cirrhosis.[21] In the study, the pooled AUROC was determined using three different methods, where the pooled difference between FibroTest and FIB-4 was not significant in most of the determinations, even when the results were compared by subgroups.

In a separate meta-analysis of fibrosis (16 studies) or cirrhosis (13 studies) due to chronic hepatitis B and using liver biopsy as the sole comparator, the authors concluded that the accuracy of FibroTest was suboptimal.[22]

The AASLD and IDSA guideline did not recommend a specific fibrosis test for those with hepatitis C:[23]

- "Evaluation for advanced fibrosis using noninvasive markers (or liver biopsy, if required) is recommended for all persons with HCV infection to facilitate an appropriate decision regarding HCV treatment strategy and to determine the need for initiating additional measures for cirrhosis management (e.g., hepatocellular carcinoma [HCC] screening). (I,A)"

The EASL similarly stated:

- "Fibrosis stage can be assessed by non-invasive methods initially, with liver biopsy reserved for cases where there is uncertainty or potential additional aetiologies (A1)" [24]
- " When compared in HCV patients, the different patented tests have similar levels of performance in diagnosing significant fibrosis and cirrhosis (A1)" [25]

With the development of effective therapy for hepatitis C, however, testing for fibrosis may not be necessary. The EASL also stated:[25]

- "...with the availability of highly effective novel antiviral agents significant fibrosis might no longer represent a relevant endpoint in HCV infected patients whereas detection of cirrhosis is still important to guide treatment with novel antiviral agents (A1)"

In a U.K. National Health Service health technology assessment, it was determined that treatment of those with hepatitis C without testing for fibrosis was most cost-effective.[26]

NASH FibroSURE

For those with NAFLD, the EASL stated:[25]

- "In patients patients with NAFLD, detection of cirrhosis represents the most important endpoint. The clinical importance of detecting milder stages of liver fibrosis in NAFLD remains to be defined (A1)"
- "NASH has to be diagnosed by a liver biopsy showing steatosis, hepatocyte ballooning and lobular inflammation (A1)"
- "Monitoring of fibrosis progression in clinical practice may rely on a combination of biomarkers/scores and transient elastography, although this strategy requires validation (C2)"

NICE guidance in regards to fibrosis testing in NAFLD is based predominantly on low quality evidence:[27]

- Do not use routine liver function blood tests to identify advanced liver fibrosis in people with NAFLD. [Based on very low to moderate quality evidence from diagnostic observational studies]
- "Offer testing for advanced liver fibrosis to all people incidentally identified with NAFLD using the ELF blood test. [Based on very low to low quality evidence from diagnostic observational studies]"
- "Diagnose people incidentally identified with NAFLD with advanced liver fibrosis if they have an ELF blood test score or ≥10.51. [Based on very low to low quality evidence from diagnostic observational studies]"
- "Offer retesting for advanced liver fibrosis for people with an ELF blood test score <10.51:
    - Every three years for adults
    - Every two years for children and young people. [Based on very low to moderate quality evidence from observational studies and the experience and opinion of the GDG]" [GDG=Guideline Development Group]

For lean persons with NAFLD, the AGA advised:[28]

- "Serum indices (NAFLD fibrosis score and Fibrosis-4 score) and imaging techniques (transient elastography and magnetic resonance elastography) may be used as alternatives to liver biopsy for fibrosis staging and patient follow-up. These tests can be performed at the time of diagnosis and repeated at intervals of 6 months to 2 years, depending on fibrosis stage and the patient's response to intervention."

In a systematic review and meta-analysis, FibroSURE/FibroTest used in the setting of NAFLD/NASH demonstrated sub-par performance in detecting fibrosis, but was more promising in detecting cirrhosis.[29] The included studies demonstrated a wide range of fibrosis and diabetes prevalence, and some studies were considered to have a high risk of bias.

FibroSpect

This test has been evaluated by several studies of those with hepatitis C or fatty liver disease. A single-center prospective study comparing the result of this test to liver biopsy in a population with hepatitis C and a prevalence of fibrosis of 36% demonstrated a PPV of 60.9% and NPV of 82.3%.[30] A similar multi-center study demonstrated the test to have favorable operating characteristics, however the concordance of histologic assessment was poor, and the prevalence of significant fibrosis was 77%.[31] In a comparison study, this test was reported to improve upon fibrosis assessment by the AST/platelet ratio index (APRI), however a significant number of participants were not evaluated by the latter test.[32] A retrospective study of persons undergoing gastric bypass reported that Fibrospect had a high negative predictive value for F2 or greater fibrosis, but a low positive predictive value in the study population which had a fibrosis prevalence of 30.9%.[33] In a randomized control trial, the Fibrospect score increased in the placebo group but not in those treated with sitagliptin, however MR elastography results were not different between the two groups.[34]

Criteria

Introduction

This guideline outlines coverage criteria for in-vitro testing in the evaluation and management of liver fibrosis.

FibroSURE

CPT 0002M, 0003M, 81596, 82172, 82247, 82465, 82947, 82977, 83010, 83883, 84450, 84460, 84478

Medical Necessity Requirements

FibroSURE testing is investigational and experimental in the screening, diagnosis, or monitoring of liver fibrosis or for any other indication.

Billing and Reimbursement

Introduction

This section outlines the billing requirements for tests addressed in this guideline. These requirements will be enforced during the case review process whenever appropriate. Examples of requirements may include specific coding scenarios, limits on allowable test combinations or frequency and/or information that must be provided on a claim for automated processing. Any claims submitted without the necessary information to allow for automated processing (e.g. ICD code, place of service, etc.) will not be reimbursable as billed. Any claim may require submission of medical records for post service review.

FibroSURE

CPT 0002M, 0003M, 81596, 82172, 82247, 82465, 82947, 82977, 83010, 83883, 84450, 84460, 84478

FibroSURE testing is not reimbursable.

PLA codes and billing of individual tests

PLA codes should be billed in place of CPT codes representing the individual test components of the test which the PLA code represents. Claims containing groups of CPT codes that represent individual test components of test panels for which a PLA code is available are not reimbursable

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Introduction

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