LabCorp Facets

HCV FibroSure™

Introduction

Liver biopsies have traditionally been used in the management of hepatitis C patients to provide important information about disease prognosis as well as about the likelihood of response to therapy.[1,2] A baseline biopsy is often used by physicians in determining the urgency for treatment in a given patient. Chronically infected HCV patients with mild hepatitis and limited fibrosis progress slowly or not at all during a 10- to 20-year period, while those with moderate and severe inflammation and fibrosis progress more rapidly to cirrhosis over a similar period.[1,2] Liver biopsy findings may have some usefulness in predicting efficacy of treatment in patients with chronic hepatitis C. Advanced fibrosis or cirrhosis on initial liver biopsy is associated with a decreased likelihood of sustained virologic response to treatment, although the predictive value is not sufficiently strong to withhold therapy for such patients.[1,2] Beyond current assessment and prognosis, the liver biopsy can provide baseline histology for future assessments of response to therapy and/or HCV disease progression.

Liver biopsy is an invasive procedure that is frequently accompanied by transient pain and may occasionally be associated with serious complications including hemorrhage, pneumothorax, or punctured viscera. For some patients, the requirement for a liver biopsy, with its associated expense as well as risks, becomes a barrier to initiation of therapy. Investigators have recently questioned the need for a liver biopsy and have been searching for alternative noninvasive biochemical markers that could be used as surrogate markers for a liver biopsy.[2,3] HCV FibroSure™ (FibroTest–ActiTest), a newly developed six-biochemical marker index, correlates well with liver biopsy findings, as measured by Metavir fibrosis staging and necroinflammatory activity grading.[4,5] It provides an alternative for assessing liver status without the associated risk of an invasive procedure.

Laboratory Method

HCV FibroSure™ is a noninvasive blood test that combines the quantitative results of six serum biochemical markers, α_2-macroglobulin, haptoglobin, apolipoprotein A_1, bilirubin, gamma glutamyl transpeptidase (GGT), and ALT, with a patient's age and gender in a patented artificial intelligence algorithm to generate a measure of fibrosis and necroinflammatory activity in the liver. HCV FibroSure™ is a continuous linear biochemical assessment of fibrosis stage and necroinflammatory activity grade. It provides a numerical quantitative estimate of liver fibrosis ranging from 0.00 to 1.00 corresponding to the well-established Metavir scoring system of stages F0 to F4. (F0 = no fibrosis, F1 = portal fibrosis, F2 = bridging fibrosis with few septa, F3 = bridging fibrosis with many septa, F4 = cirrhosis).[6] In addition, the test provides a numerical quantitative estimate of necroinflammatory activity ranging from 0.00 to 1.00 corresponding to the Metavir scoring system of grades A0 to A3. (A0 = no activity, A1 = minimal activity, A2 = moderate activity, A3 = severe activity).[6]

Clinical Utility

Using a patented algorithm analyzing six serum biochemical markers, HCV FibroSure™ has been shown to lead to a reliable quantitative assessment of fibrogenic and inflammatory activity in the liver of HCV patients.[4,5,8] It provides an accurate measure of bridging fibrosis and/or moderate necroinflammatory activity with AUROC (Area Under Receiver-Operating Characteristic Curve) predictive values between 0.70 and 0.80 when compared with liver biopsy (0.5 being nonpredictive and 1.0 being 100% predictive).[5] Discordance between liver biopsy and Fibrotest/Actitest results were primarily due to sampling errors associated with small biopsies <15mm and/or the presence of hemolysis leading to decreased haptoglobin levels and falsely elevated fibrosis and activity scores.[5,7,8] HCV FibroSure™ AUROC values increased to 0.88 when analysis was limited to samples where biopsy size was >15mm indicating greater concordance when biopsy sampling errors were reduced.[5]

HCV FibroSure™ may be used for

- Assessment of liver status following a diagnosis of HCV
- Baseline determination of liver status before initiating HCV therapy
- Post-treatment assessment of liver status six months after completion of therapy
- Noninvasive assessment of liver status in patients who are at increased risk of complications from a liver biopsy

HCV FIBROSURE™ is not recommended for patients during combined interferon/ribavirin therapy, since ribavirin may induce hemolysis, low haptoglobin levels, and falsely elevated fibrosis and activity scores.[5] HCV FIBROSURE™ is not recommended in Gilbert disease, acute hepatitis, extrahepatic cholestasis, acute sepsis, or transplant patients. Any of the clinical situations mentioned above may lead to inaccurate quantitative predictions of fibrosis and necroinflammatory activity in the liver.

References

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8. Poynard T, Imbert-Bismut F, Ratziu V, et al. An overview of biochemical markers (FibroTest–ActiTest) diagnostic value in chronic liver diseases: A non-invasive alternative to liver biopsy. Boston, Mass: American Association for the Study of Liver Diseases (AASLD); Nov, 2003. Abstract 03.

LabCorp and BioPredictive Inc have entered into an exclusive agreement to offer HCV FIBROSURE™. Published literature that includes data on this test refers to the tests as FibroTest–ActiTest. HCV FIBROSURE™ is a trademarked LabCorp name that combines FibroTest–ActiTest as a single test option.

Hepatitis C Virus (HCV) FibroSure™ 550123

CPT 83883; 83010; 82172; 82977; 82247; 84460

Synonyms HCV FibroSure™; FibroSure™; FibroTest–ActiTest

Test Includes FibroTest (α_2-macroglobulin, haptoglobin, apolipoprotein A_1, bilirubin, gamma glutamyl transpeptidase [GGT]); ActiTest (α_2-macroglobulin, haptoglobin, apolipoprotein A_1, bilirubin, gamma glutamyl transpeptidase [GGT], alanine aminotransferase [ALT])

Specimen Serum

Volume 3 mL

Minimum Volume 3 mL (**Note:** This volume does **not** allow for repeat testing.)

Container Red-stopper tube or serum-separator tube

Collection Separate serum from cells within one hour of collection and refrigerate at 2°C to 8°C. **Protect from light.** Specimen is stable for as long as three days. Freeze if storage longer than 72 hours is needed.

Storage Instructions Refrigerate at 2°C to 8°C for as long as 72 hours; **freeze** if longer storage required.

Patient Preparation Patient should fast at least eight hours.

Causes for Rejection Gross hemolysis; gross lipemia; improperly labeled specimen

Reference Interval

A_2-macroglobulin	110-276 mg/dL
Haptoglobin	34-200 mg/dL
Apolipoprotein A_1	110-205 mg/dL
Bilirubin, total	0.1-1.2 mg/dL
Gamma glutamyl transpeptidase (GGT)	0-65 IU/L (males) 0-60 IU/L (females)
Alanine aminotransferase (ALT)	0-40 IU/L

Metavir scale

Fibrosis Stage (FibroTest)	
F0 - No fibrosis	0.00 - 0.21
F0 - F1	0.21 - 0.27
F1 - Portal fibrosis	0.27 - 0.31
F1 - F2	0.31 - 0.48
F2 - Bridging fibrosis with few septa	0.48 - 0.58
F3 - Bridging fibrosis with many septa	0.58 - 0.72
F3 - F4	0.72 - 0.74
F4 - Cirrhosis	0.74 - 1.00
Activity Grade (ActiTest)	
A0 - No activity	0.00 - 0.17
A0 - A1	0.17 - 0.29
A1 - Minimal activity	0.29 - 0.36
A1 - A2	0.36 - 0.52
A2 - Moderate activity	0.52 - 0.60
A2 - A3	0.60 - 0.63
A3 - Severe activity	0.63 - 1.00

Use Assessment of liver status following a diagnosis of HCV. Baseline determination of liver status before initiating HCV therapy. Post-treatment assessment of liver status six months after completion of therapy. Noninvasive assessment of liver status in patients who are at increased risk of complications from a liver biopsy.

Limitations Because this procedure is new, Medicare and other carriers may not yet recognize it as a covered benefit for patients.

Methodology Patented artificial intelligence algorithm combines patient's age, gender, and the results of six biomarkers to generate a measure of fibrosis and necroinflammatory activity in the liver.

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