Liver Fibrosis, Fibrosis-4 (FIB-4) Index Panel

**Test Code:** 30555, 30710

**Specimen Requirements:** Refrigerated serum (1 mL in serum separator tube [SST®], 0.5 mL minimum); and room-temperature whole blood (full EDTA lavender-top tube, 1 mL minimum; or full EDTA lavender Microtainer®, 0.5 mL minimum)

**CPT Codes**: 84450; 84460; 85049

**CLINICAL USE**
- Assess likelihood of advanced liver fibrosis in patients with nonalcoholic fatty liver disease (NAFLD), hepatitis B, or hepatitis C

**CLINICAL BACKGROUND**
NAFLD, hepatitis B, and hepatitis C are liver diseases that can result in abnormal development of scar tissue (ie, fibrosis). NAFLD is considered a manifestation of metabolic syndrome within the liver and is associated with type 2 diabetes and cardiovascular disease, whereas hepatitis B and C are caused by infection with the hepatitis B (HBV) and C (HCV) viruses, respectively. Many patients with these liver diseases have a mild clinical presentation. However, chronic disease progression can lead to the development of fibrosis, cirrhosis, and associated complications such as hepatocellular carcinoma.

Management of NAFLD, hepatitis B, and hepatitis C depends, in part, on liver disease severity that is characterized by the presence of inflammation and/or advanced fibrosis. Tests for advanced fibrosis are of particular interest owing to the strong association of fibrosis stage with mortality in NAFLD and management implications for hepatitis B and hepatitis C. A biopsy is the gold standard for assessing liver disease severity, including the presence of fibrosis, but the procedure is highly invasive and involves safety risks. Biopsies are also susceptible to sampling error (ie, a representative tissue sample is not collected). Thus, noninvasive tests that assess for advanced fibrosis have been developed.

One such noninvasive test, the FIB-4 index, uses a combination of routine blood tests to indicate whether a patient has a high or low probability of advanced fibrosis. The FIB-4 index formula yields a single score by combining patient age with measurements of 3 biomarkers: aspartate aminotransferase (AST), alanine aminotransferase (ALT), and platelet count.

The FIB-4 index has clinical utility for management of NAFLD, hepatitis B, and hepatitis C, and is included in respective clinical practice guidance:
- For NAFLD, the American Association for the Study of Liver Diseases (AASLD) recommends the FIB-4 index as an option for noninvasive testing to identify patients with high likelihood of advanced fibrosis; patients with an elevated FIB-4 index are recommended to consider further evaluation with a biopsy. The FIB-4 index has a high negative predictive value (≥90%) in patients with NAFLD, which makes this test particularly useful for ruling out advanced fibrosis and thereby avoiding unnecessary biopsies. In addition, this test is useful in a primary care setting to determine whether a patient with NAFLD requires referral to a specialist for further evaluation.
- For hepatitis B, AASLD guidance includes the FIB-4 index as an alternative to biopsy for assessing disease severity; this assessment helps guide treatment decisions for patients with chronic HBV infection, including identification of appropriate candidates for antiviral therapy and determination of therapy duration.
- For hepatitis C, a joint panel from AASLD and the Infectious Diseases Society of America recommends the FIB-4 index to be evidence of cirrhosis, which, in turn, determines treatment strategy selection and indicates additional surveillance for associated complications.

Quest Diagnostics offers the Liver Fibrosis, Fibrosis-4 (FIB-4) Index Panel (test code 30555), which includes tests for AST, ALT, and platelet count, plus calculation of the FIB-4 index. Quest also offers the Liver Fibrosis, Hepatic Function Panel with Fibrosis-4 (FIB-4) Index (test code 30710), which includes the FIB-4 index in conjunction with additional tests for liver function: total protein, albumin, globulin, albumin/ globulin ratio, bilirubin (total, direct, and indirect), and alkaline phosphatase.
INDIVIDUALS SUITABLE FOR TESTING

- Individuals with NAFLD who are undergoing risk stratification and will potentially be considered for a liver biopsy
- Individuals with chronic HBV infection who are being considered for, or receiving, antiviral therapy
- Individuals with HCV infection

METHOD

- AST and ALT measured using spectrophotometry
- Platelet count measured using electronic cell sizing and counting/cytometry/microscopy
- The FIB-4 index calculated with a formula using AST, ALT, platelet count, and patient age

INTERPRETIVE INFORMATION

The Table contains information useful in interpreting FIB-4 index values for NAFLD, hepatitis B, and hepatitis C. For all testing indications, an elevated FIB-4 index is consistent with the presence of advanced fibrosis, whereas a low FIB-4 index is consistent with the absence of advanced fibrosis. Patient characteristics and clinical features should guide interpretation. Consider additional assessment for patients with an indeterminate result.

<table>
<thead>
<tr>
<th>Indication for testing</th>
<th>Compatible with the absence of advanced fibrosisa</th>
<th>Compatible with the presence of advanced fibrosisa</th>
<th>Indeterminate result</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAFLD</td>
<td>&lt;1.30</td>
<td>&gt;2.67</td>
<td>1.30-2.67</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>&lt;1.00</td>
<td>&gt;2.65</td>
<td>1.00-2.65</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>&lt;1.45</td>
<td>&gt;3.25</td>
<td>1.45-3.25</td>
</tr>
</tbody>
</table>

NAFLD, nonalcoholic fatty liver disease.
a Advanced fibrosis is defined as stage 3 or stage 4.


*The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

References