

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,^{1,2} whereas hepatitis B and C are caused by infection with the hepatitis B (HBV) and C (HCV) viruses, respectively.^{3,4} 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.¹⁻⁴

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.⁵⁻⁷ Tests for advanced fibrosis are of particular interest owing to the strong association of fibrosis stage with mortality in NAFLD⁸ and management implications for hepatitis B and hepatitis C.^{6,7} 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.³⁻⁵ Biopsies are also susceptible to sampling error (ie, a representative tissue sample is not collected).⁵ 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 formula⁹ 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.⁵ The FIB-4 index has a high negative predictive value ($\geq 90\%$) in patients with NAFLD, which makes this test particularly useful for ruling out advanced fibrosis and thereby avoiding unnecessary biopsies.^{10,11} 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.⁶
- For hepatitis C, a joint panel from AASLD and the Infectious Diseases Society of America recommends the FIB-4 index as an option for noninvasive testing to evaluate individuals with HCV infection for advanced fibrosis.⁷ This guidance considers an elevated FIB-4 index to be evidence of cirrhosis, which, in turn, determines treatment strategy selection and indicates additional surveillance for associated complications.⁷

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.

Table. Interpretation Information for the FIB-4 Index, by Testing Indication¹²

Indication for testing	Compatible with the absence of advanced fibrosis ^a	Compatible with the presence of advanced fibrosis ^a	Indeterminate result
NAFLD	<1.30	>2.67	1.30-2.67
Hepatitis B	<1.00	>2.65	1.00-2.65
Hepatitis C	<1.45	>3.25	1.45-3.25

NAFLD, nonalcoholic fatty liver disease.

^aAdvanced fibrosis is defined as stage 3 or stage 4.

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.

References

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