Test Definition: FIBRO

FibroTest-ActiTest, Serum

Overview

Useful For

Evaluating hepatic fibrosis in chronic hepatitis C patients

Diagnosing fibrosis in carriers of chronic hepatitis B virus

Evaluating hepatic fibrosis in co-infected HIV carriers

Providing access to new-generation non-interferon treatment for hepatitis

Evaluating fibrosis in patients suffering from metabolic conditions (nonalcoholic fatty liver disease) and patients who consume excess alcohol

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
INTF	FibroTest-ActiTest, Interpretation	No	Yes
APOAF	Apolipoprotein A1, S	No	Yes
A2MF	Alpha-2-Macroglobulin, S	Yes, (Order A2M)	Yes
HAPTF	Haptoglobin, S	Yes, (Order HAPT)	Yes
ALTF	Alanine Aminotransferase (ALT), S	Yes, (Order ALT)	Yes
GGTF	Gamma Glutamyltransferase (GGT), S	Yes, (Order GGT)	Yes
TBILF	Bilirubin, Total, S	Yes, (Order BILIT)	Yes

Testing Algorithm

This test is a patented test algorithm developed by BioPredictive. FibroTest combines 5 standard biomarkers (gamma-glutamyltransferase, total bilirubin, alpha-2-macroglobulin, apolipoprotein A1, and haptoglobin). The ActiTest adds a marker for inflammatory activity (alanine aminotransferase: ALT). These markers are weighted depending on the patient's age and gender.

Testing is compliant with BioPredictive's technical recommendations and approvals.

Method Name

INTF: Algorithm and Interpretation Provided through BioPredictive
APOAF: Automated Turbidimetric Immunoassay
A2MF, HAPTF: Nephelometry
ALTF: Photometric Rate, L-Alanine with Pyridoxal-5-Phosphate

GGTF: Photometric Rate
TBILF: Photometric, Diazonium Salt

NY State Available
Yes

Specimen

Specimen Type
Serum

Necessary Information
Age and sex are required.

Specimen Required
Supplies: Amber Frosted Tube, 5 mL (T915)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Amber vial
Specimen Volume: 3 mL
Collection Instructions:
1. Centrifuge and aliquot serum into an amber vial within 2 hours of collection.
2. Centrifuged serum must be light protected within 4 hours of collection. It is acceptable to draw the blood and then protect it from light after centrifugation as long as it is within 4 hours of collection.

Forms
If not ordering electronically, complete, print, and send Gastroenterology and Hepatology Test Request (T728) with the specimen

Specimen Minimum Volume
1.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject
Patients <2 years of age	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Ambient	24 hours	LIGHT PROTECTED
	Refrigerated (preferred)	7 days	LIGHT PROTECTED
	Frozen	14 days	LIGHT PROTECTED

Clinical & Interpretive

Clinical Information

Fibrosis and inflammatory activity are the 2 main causes of liver disease.

FibroTest-ActiTest estimates the levels of fibrosis and cirrhosis in the liver as well as the level of necroinflammatory activity. The estimation is made by measuring 6 standard serum biomarkers (gamma-glutamyl transferase, total bilirubin, alpha-2-macroglobulin, apolipoprotein A1, haptoglobin, and alanine aminotransferase). The activity score is a measure of liver inflammation caused by disease. Results from these tests are combined with the patient's age and sex to estimate hepatic fibrosis and inflammatory activity scores.

Hepatic fibrosis is typically compared to a form of scar tissue that progresses throughout the liver. The most serious stage of fibrosis is known as cirrhosis.

Reference Values

FibroTest-ActiTest, Interpretation

FibroTest Score	Stage	Interpretation
0.00-0.21*	F0	No fibrosis
0.21-0.27*	F0-F1	No fibrosis
0.27-0.31*	F1	Minimal fibrosis
0.31-0.48*	F1-F2	Minimal fibrosis
0.48-0.58*	F2	Moderate fibrosis
0.58-0.72*	F3	Advanced fibrosis
0.72-0.74*	F3-F4	Advanced fibrosis
0.74-1.00	F4	Severe fibrosis (Cirrhosis)

*Boundary values can apply to 2 stages based on rounding. For example, a FibroTest score of 0.305 will round up to 0.31 and be staged F1. A FibroTest score of 0.314 will round down to 0.31 and be staged F1-F2.

ActiTest Score	Grade	Interpretation
0.00-0.17*	A0	No activity
0.17-0.29*	A0-A1	No activity
0.29-0.36*	A1	Minimal activity
0.36-0.52*	A1-A2	Minimal activity
0.52-0.60*	A2	Significant activity
0.60-0.62*	A2-A3	Significant activity
0.62-0.100	A3	Severe activity

*Boundary values can apply to 2 grades based on rounding. For example, an ActiTest score of 0.285 will round up to 0.29

and be graded A0-A1. An ActiTest score of 0.294 will round down to 0.29 be graded A1.

ALPHA-2-MACROGLOBULIN
< or =18 years: 178-495 mg/dL
>18 years: 100-280 mg/dL

ALANINE AMINOTRANSFERASE (ALT)
Males
<12 months: Not established
> or =1 year: 7-55 U/L

Females
<12 months: Not established
> or =1 year: 7-45 U/L

APOLIPOPROTEIN A1
Males
<24 months: Not established
2-17 years
Low: <115 mg/dL
Borderline low: 115-120 mg/dL
Acceptable: >120 mg/dL
> or =18 years: > or =120 mg/dL

Females
<24 months: Not established
2-17 years
Low: <115 mg/dL
Borderline low: 115-120 mg/dL
Acceptable: >120 mg/dL
> or =18 years: > or =140 mg/dL

GAMMA-GLUTAMYLTRANSFERASE (GGT)
Males
0-11 months: <178 U/L
12 months-6 years: <21 U/L
7-12 years: <24 U/L
13-17 years: <43 U/L
> or =18 years: 8-61 U/L

Females
0-11 months: <178 U/L
12 months-6 years: <21 U/L
7-12 years: <24 U/L
13-17 years: <26 U/L

> or =18 years: 5-36 U/L

HAPTOGLOBIN
30-200 mg/dL

BILIRUBIN, TOTAL
0-6 days: Refer to www.bilitool.org for information on age-specific (postnatal hour of life) serum bilirubin values.
7-14 days: 0.0-14.9 mg/dL
15 days-17 years: 0.0-1.0mg/dL
> or =18 years: 0.0-1.2 mg/dL

Interpretation

FibroTest-ActiTest provides a score that assesses hepatic fibrosis (F0-F4) and a score that assesses hepatic inflammatory activity (A0-A3). Interpretation of the score is provided in the report. Individual results from the 6 component tests are also provided with institution-specific reference intervals.

Fibrosis is reported relative to a scale ranging from F0-F4 (F0=no fibrosis, F1=minimal fibrosis, F2=moderate fibrosis, F3=advanced fibrosis, F4=severe fibrosis). Fibrosis scores may overlap (eg, F0/F1, F1/F2).

Activity is reported relative to a scale ranging from A0-A3 (A0=no activity, A1=minimal activity, A2=significant activity, A3=severe activity). Activity scores may overlap (eg, A0/A1, A1/A2).

Cautions

Defer the test in transient situations that could modify the components of FibroTest-ActiTest, such as:
-Acute hemolysis, which could decrease haptoglobin and increase unconjugated bilirubin
-Acute hepatitis, whether drug-induced, viral (superinfection by hepatitis A virus: HAV, hepatitis B virus: HBV, Epstein-Barr virus: EBV), or autoimmune. Massive hepatic necrosis leads to a large increase of transaminases and total bilirubin.
-Acute inflammation, as with concomitant bacterial or acute viral infection: bronchopulmonary or urinary tract infection. The large increase of haptoglobin can lead to false-negative results.
-Extrahepatic cholestasis, such as gallstones

The advice of a liver disease specialist should be sought for interpretation in chronic states in which the components of the test could be modified, such as chronic hemolysis, particularly in patients with a cardiac valvular prosthesis; Gilbert disease; protease inhibitors used in HIV treatment, which can increase unconjugated bilirubin (Indinavir, Atazanavir); or gamma glutamyltransferase (GGT) and alanine aminotransferase (Ritonavir).

The interpretation of FibroTest has been validated in renal transplant patients. In patients with renal insufficiency or who are on dialysis, FibroTest had an acceptable diagnostic value, though lower than in transplanted patients.

As a general rule, isolated extreme values of 1 of the 6 components should signal caution in interpreting the results, particularly in the following cases:
-Haptoglobin below 12 mg/dL, in which hemolysis or anhaptoglobinemia (more frequent in western African patients) must be ruled out.
-Haptoglobin above 320 mg/dL, in which acute inflammation must be ruled out.
-Transaminases above 622 IU/L, in which acute hepatitis must be ruled out.

-Bilirubin above 1.75 mg/dL and GGT below 50 IU/L, in which Gilbert syndrome must be suspected.
-Alpha2-macroglobulin above 590 mg/dL

In case of discordance between a biopsy result and a FibroTest result, it is advisable to seek the advice of a liver disease specialist.

Haptoglobin is an acute-phase reactant and increases with inflammation or tissue necrosis. Low haptoglobin is normal for the first 3 to 6 months of life; testing is not performed on patients younger than 2-years old per BioPredictive.

GGT activity is inducible by drugs such as phenytoin and phenobarbital and, therefore, elevations should not be considered indicative of liver disease until drug use is ruled out. Elevations are also seen after ingestion of alcoholic beverages. In very rare cases, gammopathy, in particular, type IgM (Waldenstrom macroglobinemia) may cause unreliable results.

Bilirubin specimens should be protected from light and analyzed as soon as possible. Grossly hemolyzed specimens should be rejected because hemoglobin inhibits the diazo reaction and falsely decreased results may be seen. Compounds that compete for binding sites on serum albumin contribute to lower serum bilirubin levels (eg, penicillin, sulfisoxazole, acetylsalicylic acid).

Clinical Reference

1. BioPredictive. Technical Recommendations for FibroTest and FibroMax assays, Bio Predictive. Accessed September 19, 2023. Available at biopredictive.com/products/fibromax/
2. Halfon P, Bourliere M, Deydier R, et al. Independent prospective mulitcenter validation of biochemical markers (FibroTest-ActiTest) for the prediction of liver fibrosis and activity in patients with chronic hepatitis C: the fibropaca study. Am J Gastroenterol. 2006;101(3):547-555. doi:10.1111/j.1572-0241.2006.00411.x
3. Houot M, Ngo Y, Munteanu M, Marque S, Poynard T. Systematic review with meta-analysis: direct comparisons of biomarkers for the diagnosis of fibrosis in chronic hepatitis C and B. Aliment Pharmacol Thera. 2016;43:16-29. doi:10.1111/apt.13446
4. Anastasiou J, Alisa A, Virtue S, Portmann B, Murray-Lyon I, Williams R. Noninvasive markers of fibrosis and inflammation in clinical practice: prospective comparison with liver biopsy. Eur J Gastroenterol Hepatol. 2010;22(4):474-480. doi:10.1097/MEG.0b013e328332dd0a
5. Martínez SM, Crespo G, Navasa M, Forns X. Noninvasive assessment of liver fibrosis. Hepatology. 2011;53(1):325-335. doi:10.1002/hep.24013

Performance

Method Description

FibroTest-ActiTest, Interpretation:
Proprietary algorithm owned by BioPredictive.

Alpha-2-Macroglobulin and Haptoglobin:
In this method, the light scattered onto the antigen-antibody complexes is measured. The intensity of the measured scattered light is proportional to the amount of antigen-antibody complexes in the sample under certain conditions. If

the antibody volume is kept constant, the signal behaves proportionally to the antigen volume.

A reference curve is generated by a standard with a known antigen content on which the scattered light signals of the samples can be evaluated and calculated as an antigen concentration. Antigen-antibody complexes are formed when a sample containing antigen and the corresponding antiserum are put into a cuvette. A light beam is generated with a light-emitting diode, which is transmitted through the cuvette. The light is scattered onto the immuno-complexes that are present. Antigen and antibody are mixed in the initial measurement, but no complex is formed yet. An antigen-antibody complex is formed in the final measurement.

The result is calculated by subtracting value of the final measurement from the initial measurement. The distribution of intensity of the scattered light depends on the ratio of the particle size of the antigen-antibody complexes to the radiated wavelength.(Unpublished Mayo method; Instruction manual: Siemens Nephelometer II, Siemens, Inc; Version 2.3. 2008; Addendum to the Instruction Manual 2.3, 08/2017)

Alanine Aminotransferase (ALT):
Alanine a minotransferase (ALT) activity is determined by a kinetic method using a coupled enzyme reaction where the rate of NADH consumption is measured at 340 nm. The NADH decrease is directly proportional to the ALT activity.(Package insert: Roche ALT reagent. Roche Diagnostics; 2018)

Apolipoprotein A1:
Anti-apolipoprotein A-1 antibodies react with the antigen in the sample to form antigen/antibody complexes which, following agglutination, can be measured turbidimetrically.(Package insert: Tina-quant Apolipoprotein A-1. Roche Diagnostics; 2019)

Gamma-Glutamyltransferase (GGT):
This is an enzyme colorimetric method (rate method) where gamma-glutamyltransferase (GGT) transfers the gamma-glutamyl group of the substrate (L-gamma-glutamyl-3-carboxy-4-nitroanilide) to glycylglycine. The amount of 5-amino-2-nitrobenzoate liberated is proportional to the GGT activity and can be determined photometrically.(Package insert: Boehringer Mannheim GGT reagent. Boehringer Mannheim; 2017)

Bilirubin, Total:
Total bilirubin, in the presence of a suitable solubilizing agent, is coupled with 3,5-dichlorophenyl diazonium in a strongly acidic medium. The color intensity of the red azo dye formed is directly proportional to the total bilirubin and can be determined photometrically.(Package insert: Bilirubin Total Gen. 3. Roche Diagnostics; 2019)

PDF Report
No

Day(s) Performed
HAPTF, A2MF: Monday through Saturday
ALTF, GGTF, TBILF: Monday through Sunday
APOAF: Monday through Saturday

Report Available
2 to 5 days

Specimen Retention Time
7 days

Performing Laboratory Location
Rochester

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
81596

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
FIBRO	FibroTest-ActiTest, S	48796-7

Result ID	Test Result Name	Result LOINC® Value
TBILF	Bilirubin, Total, S	1975-2
ALTF	Alanine Aminotransferase (ALT), S	1743-4
A2MF	Alpha-2-Macroglobulin, S	1835-8
APOAF	Apolipoprotein A1, S	1869-7
GGTF	Gamma Glutamyltransferase (GGT), S	2324-2
HAPTF	Haptoglobin, S	46127-7
SCRF	FibroTest Score	48795-9
STGF	FibroTest Stage	48794-2
INTEF	FibroTest Interpretation	88447-8
SCRA	ActiTest Score	48792-6
STGA	ActiTest Grade	48793-4
INTEA	ActiTest Interpretation	88448-6
CMMF	FibroTest-ActiTest Comment	48767-8
NUM	BioPredictive Serial Number	74715-4
ERROR	BioPredictive Analyte Error	No LOINC Needed