MAYO CLINIC LABORATORIES

Test Definition: 7AC4

7AC4, Bile Acid Synthesis, Serum

Overview

Useful For
Screening for bile acid malabsorption in patients with irritable bowel syndrome with diarrhea

Testing Algorithm
For more information see Ordering Guide: Bile Acid-Associated Tests.

Special Instructions
- Bile Acid-Associated Tests Ordering Guide

Highlights
This test should be used for screening for bile acid malabsorption, a condition in which excess bile acids are found in the stool that is one cause of chronic diarrhea.

Method Name
Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required
Patient Preparation:
1. **Fasting: 12 hours, required**; Fasting morning specimen is preferred.
2. Patient should not be taking bile acid sequestrants for 24 hours prior to collection or statins for 5 days prior to collection.

Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL
Collection Instructions:
1. Centrifuge and aliquot 1 mL of serum into a plastic vial.
2. Send specimen frozen.

Forms

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

Specimen Minimum Volume

0.5 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	90 days	
	Ambient	24 hours	
	Refrigerated	72 hours	

Clinical & Interpretive

Clinical Information

Bile acids are synthesized from cholesterol in the liver and released into the digestive tract where they function to emulsify dietary fats and facilitate lipid absorption in the small intestine. More than 95% of bile acids are then reabsorbed primarily by active uptake in the distal ileum, while less than 5% are excreted in stool. The synthesis of bile acids in the liver is regulated by a negative feedback mechanism from the bile acids reabsorbed from the intestine. 7 Alpha-hydroxy-4-cholesten-3-one (7aC4) is an intermediate in the biosynthesis pathway of cholesterol to bile acids. The concentration of 7aC4 in serum is a surrogate for the amount of bile acid synthesis in the liver. There is some diurnal variation in 7aC4 serum concentrations, so measurement should be performed on a fasting morning sample.

Patients with increased bile acid in their stool suffer from chronic diarrhea termed bile acid diarrhea (BAD). Approximately 10% to 33% of patients with irritable bowel syndrome with diarrhea have BAD. Additionally, BAD has been identified as a contributor of diarrhea in other conditions such as irritable bowel disease (IBD), Celiac disease, microscopic colitis, and neuroendocrine tumors.(1) Identifying patients with BAD can be done by measuring total and fractionated bile acids in stool. The increased bile acids in feces can be caused by an inability to reabsorb bile acids in the terminal ileum (bile acid malabsorption: BAM). If the intestinal reabsorption if BA is decreased, this leads to increase synthesis of bile acids in the liver. Recent studies have shown that serum concentrations of 7aC4 are elevated in patients with BAD. Several intestinal diseases or functional abnormalities can lead to BAD.

The definitive test in the United States for BAD is the 48-hour stool bile acids test (BA48F / Bile Acids, Bowel Dysfunction, 48 Hour, Feces). However, given the challenge of a 48-hour specimen collection, a random stool collection can be used in combination with the results from serum 7aC4 testing. From a random stool collection, only the percentage of primary bile acids can be reported. Internal studies have shown that a combination of serum 7aC4 result above 52.5 ng/mL and primary fecal bile acid result above 10% is 66% sensitive and 95% specific for BAD.(2)

Identification of these patients can influence treatment decisions that could include the use of bile acid sequestrants. Conversely, patients with irritable bowel syndrome with constipation may have lower circulating 7aC4 as compared to

healthy individuals.

Reference Values

> or =18 years: 2.5-63.2 ng/mL

Reference values have not been established for patients who are <18 years of age.

Interpretation

In patients with irritable bowel syndrome with diarrhea, elevated 7alpha-hydroxy-4-cholesten-3-one (7aC4) is consistent with bile acid diarrhea (BAD). A result of 17.6 ng/mL or greater is 83% sensitive and 53% specific for BAD. In these cases, a confirmatory 48-hour fecal bile acid test could be considered. A result above 52.5 ng/mL is 40% sensitive and 85% specific for BAD.

Interpretation of 7aC4 results in patients with chronic diarrhea (bile acid malabsorption: BAM):

Below 17.6	17.6 or above	Above 52.5
BAM unlikely, consider other conditions	BAM indeterminate, consider confirmatory fecal bile acids test or trial of bile acid sequestrant	BAM likely, consider bile acid sequestrant therapy

Serum 7aC4 can be used in combination with a random (single collection) stool bile acid assessment for increased sensitivity and specificity for BAM detection. See BAMRP / Bile Acids Malborption Panel, Serum and Feces.

Cautions

Testing should not be performed on individuals with liver disease or dysfunction.

Supportive Data

In an internal study of 55 patients with irritable bowel syndrome with diarrhea, a fasting serum 7 alpha-hydroxy-4-cholesten-3-one (7aC4) result of 17.6 ng/mL or above was 83% sensitive and 53% specific for identifying patients with elevated fecal bile acids (eg, patient with bile acid diarrhea).(3) In another study, a result above 52.5 ng/mL resulted in 40% sensitivity and 85% specificity for BAD.(4)

Additional internal studies have shown that a combination of serum 7aC4 above 52.5 ng/mL and primary fecal bile acids above 10% is 66% sensitive and 95% specific for BAD.(2)

Clinical Reference

1. Vijayvargiya P, Gonzalez Izundegui D, Calderon G, et al: Increased fecal bile acid excretion in a significant subset of patients with other inflammatory diarrheal diseases. Dig Dis Sci. 2022 Jun;67(6):2413-2419

2. Camilleri M, Nadeau A, Tremaine WJ, et al: Measurement of serum 7 alpha-hydroxy-4-cholesten-3-one (or 7AC4), a surrogate test for bile acid malabsorption in health, ileal disease and irritable bowel syndrome using liquid chromatography-tandem mass spectrometry. Neurogastroenterol Motil. 2009;21(7):734-743

3. Vijayvargiya P, Camilleri M, Carlson P, et al: Performance characteristics of serum C4 and FGF19 measurements to exclude the diagnosis of bile acid diarrhoea in IBS-diarrhoea and functional diarrhoea. Aliment Pharmacol Ther. 2017;46(6):581-588. doi: 10.1111/apt.14214

4. Vijayvargiya P, Camilleri M, Shin A, et al: Methods for diagnosis of bile acid malabsorption in clinical practice. Clin Gastroenterol Hepatol. 2013;11(10):1232-1239

5. Vijayvargiya P, Camilleri M, Taylor A, et al: Combined fasting serum C4 and primary bile acids from a single stool sample to diagnose bile acid diarrhea. Gastroenterology. 2020 Nov;159(5):1952-1954.e23.

6. Wong BS, Camilleri M, Carlson P, et al: Increased bile acid biosynthesis is associated with irritable bowel syndrome with diarrhea. Clin Gastroenterol Hepatol. 2012 Sep;10(9):1009-1015.e3

Performance

Method Description

7 Alpha-hydroxy-cholesten-3-one (7aC4) is extracted from the sample. After addition of a deuterium-labeled 7aC4 internal standard, 7aC4 is measured by liquid chromatography tandem mass spectrometry. (Donato LJ, Lueke A, Kenyon SM, Meeusen JW, Camilleri M: Description of analytical method and clinical utility of measuring serum 7-alpha-hydroxy-4-cholesten-3-one (7aC4) by mass spectrometry. Clin Biochem. 2018;52:106-111)

PDF Report

No

Day(s) Performed

Monday, Thursday

Report Available

5 days

Specimen Retention Time

14 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

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

82542

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value

7AC4	7AC4, Bile Acid Synthesis, S	94866-1

Result ID	Test Result Name	Result LOINC® Value
65504	7AC4, Bile Acid Synthesis, S	94866-1