Nonalcoholic Steatohepatitis (NASH): Focus on Oxidized LDL

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NAFLD and NASH overview

Nonalcoholic fatty liver disease (NAFLD) is considered a manifestation of metabolic syndrome within the liver and is associated with obesity, type 2 diabetes, and dyslipidemia, as well as increased risk of cardiovascular disease and cancer.[1,2] An estimated 25% of the global population has NAFLD, and as many as 33-66% of people with type 2 diabetes are estimated to have NAFLD.[3]

Nonalcoholic steatohepatitis (NASH) is the progressive form of NAFLD and is associated with greater risk of liver-related events.[4] Between 1.5% and 6.45% of the general population are estimated to have NASH.[3]

NAFLD can progress to NASH and even cirrhosis with nonspecific symptoms, making detection difficult.[5] However, if NAFLD is identified, its progress can be reversed, even after liver fibrosis has developed.[3]

NASH pathogenesis and oxLDL

The pathogenesis of NASH is complex, with many mechanisms involved. As metabolic dysfunction occurs, the liver's capacity to handle carbohydrates and fatty acids is overwhelmed, leading to lipotoxicity, which injures the hepatocytes.[4] Oxidative stress adds to the hepatocyte injury. The hepatocyte injury in the form of ballooning and the resulting inflammatory response together form NASH.

Oxidized low-density lipoprotein (oxLDL) is formed when oxidative stress leads to modification of the LDL cholesterol particle, and its presence can induce further oxidative stress and inflammation. OxLDL levels serve as a marker of oxidative stress and metabolic risk.[6,7]

OxLDL linked to NASH

An abstract presented in 2019 at the European Association for the Study of the Liver reported the finding that "oxLDL levels were associated to NASH but not to liver fibrosis. These data may reinforce the role of oxidative stress in NASH, independently of obesity and diabetes, and highlights the interesting role of this molecule linking NASH and cardiovascular risk."[8]

NASH testing options

The FIB-4 index (calculated from AST, ALT, platelet count, and patient age) is a useful and recommended tool for identifying individuals with a high or low likelihood of advanced liver fibrosis (stages F3-F4) due to NASH.[3] In patients with NAFLD, FIB-4 index scores >2.67 are associated with presence of advanced liver fibrosis, and scores <1.30 are associated with absence of advanced liver fibrosis. However, scores of 1.30 to 2.67 are indeterminate for risk of advanced liver fibrosis.[9]

There is a need for biomarker testing options beyond the FIB-4 index to identify patients who have NASH but have not progressed to advanced liver fibrosis.

Given the role of oxidative stress in the pathophysiology of NASH and in light of the association found between elevated oxLDL levels and NASH, oxLDL may have utility to identify patients with NASH activity in the absence of advanced liver fibrosis.

Test details

Test Code	Test Name	Clinical Use
30555	**Liver Fibrosis, Fibrosis-4 (FIB-4) Index Panel** *Includes AST (822), ALT (823), and Platelet Count (723)*	• Identify patients with high or low likelihood of advanced liver fibrosis
30710	**Liver Fibrosis, Hepatic Function Panel with Fibrosis-4 (FIB-4) Index** *Includes Hepatic Function Panel (10256) [components: Total Protein (754), Albumin (223), Globulin (calculated), Albumin/Globulin Ratio (calculated), Total Bilirubin (287), Direct Bilirubin (285), Indirect Bilirubin (calculated), Alkaline Phosphatase (234), AST (822), ALT (823)] and Platelet Count (723)*	• Identify patients with high or low likelihood of advanced liver fibrosis • Assess other aspects of liver function
92769	**OxLDL**	• Identify oxidative stress and metabolic risk

Components of panels can be ordered separately. Healthcare providers should use their clinical discretion, based on patient exams and presenting symptomology, to guide appropriate diagnostic testing.

For more information, go to **QuestDiagnostics.com/NAFLD**

References

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