Diagnosis and Evaluation of Nonalcoholic Fatty Liver Disease/Nonalcoholic Steatohepatitis, Including Noninvasive Biomarkers and Transient Elastography

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KEYWORDS

• Nonalcoholic fatty liver disease • Steatohepatitis • Noninvasive biomarker
• Transient elastography

KEY POINTS

- Liver biopsy, the current gold standard for diagnosis of nonalcoholic fatty liver disease (NAFLD)/nonalcoholic steatohepatitis (NASH), is not perfect.
- Noninvasive biomarkers are useful in assessing NAFLD/NASH.
- FibroMeter, FIB-4 (Fibrosis-4), and NAFLD fibrosis score have high diagnostic yields in evaluating advanced fibrosis and cirrhosis.
- Transient elastography is very effective and has high accuracy in staging advanced fibrosis and cirrhosis.
- The combination of noninvasive biomarkers and transient elastography improves diagnostic accuracy of NAFLD/NASH.

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of abnormal liver tests in industrial countries. It encompasses the spectrum of liver damage from simple steatosis to nonalcoholic steatohepatitis (NASH) and cirrhosis.[1] NAFLD is associated with insulin resistance and is considered a hepatic manifestation of metabolic syndrome (MetS).[2,3]

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The incidence and prevalence of NAFLD are increasing worldwide in parallel with the obesity and diabetes epidemics.[3,4] In the United States, NAFLD is estimated to affect one-third of the general adult population.[3–5] Persons with only hepatic steatosis are thought to have a benign long-term prognosis. However, 20% to 30% of those with simple steatosis develop NASH (1.5%–6.45% of the general population), which may further progress to cirrhosis.[2,3]

NAFLD with advanced fibrosis or cirrhosis increases the risk of development of hepatocellular carcinoma (HCC), which has poor outcomes and limited therapeutic options.[6,7] NASH is a rapidly growing indication for liver transplant in the United States.[8,9] In data of adults listed for liver transplant extracted from the UNOS (United Network for Organ Sharing) registry in 2015, NASH surpassed chronic hepatitis C as the leading indication for liver transplant among adults.[10]

Screening for NAFLD is not currently recommended in clinical practice because of unclear cost-effectiveness and uncertainties with diagnostic testing and treatments.[11,12] Most patients are asymptomatic until there is significant liver dysfunction. However, because of significant NASH-associated morbidity and mortality, early diagnosis is prudent.[11] Patients with older age, type 2 diabetes mellitus (T2DM), obesity, and MetS are at high risk of developing NAFLD.[13,14] In this subset of high-risk patients, clinicians should maintain high clinical suspicion for the diagnosis of NAFLD, even if liver enzyme levels are normal.

DIAGNOSIS OF NONALCOHOLIC FATTY LIVER DISEASE AND NONALCOHOLIC STEATOHEPATITIS

The initial diagnosis of NAFLD is based on clinical history, biochemical data, and radiographic features. Clinical history requires excluding secondary causes of fatty liver, such as[12]:

- Viral hepatitis (hepatitis C, genotype 3)
- Alcoholic fatty liver disease (>3 drinks/d for men, >2 drinks/d for women)
- Drugs (eg, amiodarone, corticosteroids, methotrexate, tamoxifen, synthetic estrogens, valproic acid, intravenous tetracycline, and highly active antiretroviral drugs)
- Medical conditions (eg, Wilson disease, hemochromatosis, and celiac disease)
- Metabolic abnormalities (eg, inborn errors of metabolism, cholesterol ester storage disease, glycogen storage diseases, abetalipoproteinemia, lysosomal acid lipase deficiency, and Reye syndrome)
- Nutritional status (eg, starvation and parenteral nutrition)

It also includes obtaining clinical history regarding certain risk factors for NAFLD (**Box 1**).

The current gold standard for the diagnosis and staging of NAFLD is liver biopsy. It can determine necroinflammatory activity, degree of steatosis, and extent of fibrosis.[15–18] Liver biopsy has inherent limitations because of sample size and sampling variability. The intraobserver and interobserver variability may also decrease diagnostic accuracy.[18–21] Risks and life-threatening complications render liver biopsy a less-than-ideal gold standard. Potential complications include[22–26]:

- Mortality after percutaneous liver biopsy reported at 0.009% to 0.14%
- Pain
- Intraperitoneal bleeding
- Hemobilia
- Hypotension