

The Use of Liver Biopsy in Nonalcoholic Fatty Liver Disease: When to Biopsy and in Whom



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KEYWORDS

- Nonalcoholic fatty liver disease • Nonalcoholic steatohepatitis • Liver biopsy
- Elastography

KEY POINTS

- Liver biopsy remains the gold standard for the diagnosis of nonalcoholic fatty liver and is currently the only modality that can reliably differentiate benign fatty liver from nonalcoholic steatohepatitis.
- Liver biopsy remains a valuable tool for the assessment of liver disease progression or regression in patients with nonalcoholic steatohepatitis.
- Liver biopsy is the only tool that can correctly differentiate which process may be causing liver injury in patients with clinical features of the metabolic syndrome and serologic markers of another liver disorder.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of liver disease worldwide.¹ NAFLD is most commonly observed in persons with obesity and the metabolic syndrome. In the United States, approximately one-third of persons are obese, approximately one-third of obese persons have NAFLD, and approximately one-third of persons with NAFLD have nonalcoholic steatohepatitis (NASH). This amount represents about 100, 33, and 11 million persons, respectively. NAFLD is

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suspected in persons with elevated liver transaminases when imaging (either ultrasound, computerized tomography [CT], or MRI) suggests fatty liver, serologic studies for all other causes of chronic liver disease are negative, patients have features of metabolic syndrome, and the clinical history suggests patients do not consume excessive amounts of alcohol.² However, the diagnosis of NAFLD, and especially that of NASH, can only be confirmed by histologic assessment of liver tissue. NAFLD is present when there is greater than 5% steatosis in the liver histologic specimen in the absence of excessive alcohol consumption.³ NASH requires the presence of steatosis, inflammation, and ballooning of hepatocytes by steatosis.⁴

Noninvasive testing can be useful in predicting that patients suspected of having NAFLD have significant fibrosis and, therefore, NASH. These tests include scoring systems that are based on clinical findings and readily available biochemical tests.^{5,6} Vibration controlled transient elastography (VCTE) with the controlled attenuation parameter (CAP) or shear wave elastography can assess liver stiffness and suggest this is due to NAFLD.⁷⁻¹⁰ Imaging modalities, such as ultrasound and CT scan can suggest that patients have fatty liver; MRI can quantitate steatosis; and magnetic resonance (MR) elastography can assess liver stiffness, which in most situations reflects hepatic fibrosis.^{4,11-14} However, neither ultrasound nor CT can determine if patients actually have NASH. In addition, the various scoring systems, elastography, and MRI techniques that attempt to diagnose NASH base this distinction on the assessment of fibrosis and presume that patients with suspected NAFLD and fibrosis have NASH. In reality, none of these tests can determine if liver injury and fibrosis is really due to NAFLD or to another coexistent liver disorder.

When to perform a liver biopsy in patients with suspected fatty liver remains controversial because no medication is available now to treat NAFLD when it is identified. Clinical guidelines suggest that only those patients who are suspected of having NASH based on clinical features, noninvasive testing, and imaging should undergo liver biopsy.^{15,16} Clinicians are, therefore, often left debating the need for biopsy with their patients because, in the absence of enrolling in a clinical trial, the only treatment of NAFLD is dietary modification and weight reduction; clearly, patients do not need to undergo a liver biopsy in order to diet or lose weight.

This article discusses the role of liver biopsy in the management of patients with NAFLD and identifies which patients with NAFLD might benefit from liver biopsy and why. The role of noninvasive testing in patients suspected of having NAFLD and how these tests can be used to select patients who may benefit from biopsy are discussed. Finally, the pros, cons, and limitations of liver biopsy are also reviewed.

NATURAL HISTORY AND CLINICAL FEATURES OF NONALCOHOLIC FATTY LIVER DISEASE

NAFLD can be divided into 2 categories: benign steatosis, also referred to as isolated fatty liver or NAFL, and NASH. NAFL is present in about 66% to 80% of patients with NAFLD.^{1,2,4} Long-term studies have demonstrated that patients with NAFL have less than a 1% chance of developing fibrosis progression to cirrhosis or liver-related mortality over 15 years.¹⁷⁻²¹ Long-term survival is similar to that of the general population. In contrast, 20% to 33% of patients with NAFLD have NASH.^{1,2,4} Patients with NASH have an 11% risk of developing progressive fibrosis, cirrhosis, hepatic decompensation, and liver cancer and a 7% risk of both liver-related and all-cause mortality over 15 years from the time of diagnosis.¹⁷⁻²¹ The presence of fibrosis in patients with NAFLD is also associated with increased mortality regardless of whether or not patients have other histologic features of NASH. Given the increased risk of both

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