

# The Effects of Metabolic Surgery on Fatty Liver Disease and Nonalcoholic Steatohepatitis



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## KEYWORDS

• Fatty liver disease • NAFLD • NASH • Bariatric surgery

## KEY POINTS

- Nonalcoholic fatty liver disease (NAFLD) is a severe and under-recognized hepatic manifestation of insulin resistance and the metabolic syndrome.
- NAFLD is typically asymptomatic, even in the setting of nonalcoholic steatohepatitis (NASH) and high-grade fibrosis.
- A significant number of retrospective and prospective observational cohort studies have demonstrated bariatric surgery to be effective for improving and even completely resolving NAFLD.
- Bariatric surgery acts on NAFLD not only by inducing rapid and substantial weight loss but also through a host of other indirect effects that improve liver steatosis and steatohepatitis.

## INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is a drastically underappreciated consequence of morbid obesity. Fatty liver disease represents a spectrum of disease from simple fat deposition in hepatic steatosis to inflammation and fibrosis in nonalcoholic steatohepatitis (NASH) with potential progression to cirrhosis.<sup>1</sup> This process is thought to develop through complex interactions of obesity, insulin resistance, and inflammation. Over the last 20 years, NAFLD has become the most common liver disease in the western world, surpassing both alcoholic and viral liver disease.<sup>2</sup>

In samples of nonobese patients, the prevalence of NAFLD is very low, generally less than 3%.<sup>3</sup> However, fatty liver disease in the obese and morbidly obese

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populations is significant. Large studies suggest that NAFLD affects greater than 80% of morbidly obese patients.<sup>4</sup> Even more significant is that nearly 15% of obese patients demonstrate severe liver disease, including NASH or fibrosis, on histologic review.<sup>4</sup> Today, 70% of American adults are overweight and 35% are classified as obese, putting most of the US population at risk for developing fatty liver disease or worse.<sup>5</sup> Increased recognition and understanding has led to the realization that fatty liver disease is also present in the pediatric population.<sup>6</sup> As the obesity epidemic continues, NAFLD will likely affect more than half of the United States population in the years to come. This surge in liver disease would predispose the population to unprecedented levels of cirrhosis, cancer risk, and the morbidity and mortality associated with these syndromes.

NAFLD is a sinister disease process. Although many patients are asymptomatic, NAFLD has the potential to progress to NASH, cirrhosis, and even end-stage liver disease. Additionally, most patients with NAFLD have normal liver enzymes even in the setting of NASH or cirrhosis.<sup>4,7</sup> These factors make it challenging to determine which patients are at risk for developing progressive fatty liver disease. It is important to accurately classify these patients because those with NAFLD have an increased mortality compared with those with normal liver disease, even when controlling for other patient comorbidities.<sup>8,9</sup> It is now recognized that many individuals previously diagnosed with cryptogenic cirrhosis actually suffered from progressive NASH.<sup>10</sup> It is not surprising that NASH is rapidly growing as an indication for liver transplantation and may even overtake viral hepatitis as the primary indication for liver transplant before 2030.<sup>11</sup>

Comorbidities such as diabetes and coronary artery disease are well known to be associated with obesity. These conditions also increase in severity and prevalence as BMI increases.<sup>12</sup> However, only recently has pathophysiology of NAFLD begun to be understood. Although NAFLD is associated with obesity, unlike other comorbidities associated with the metabolic syndrome, the severity of obesity does not seem to affect the severity or prevalence of NAFLD.<sup>4</sup> Fatty liver disease has also been independently associated with insulin resistance and dyslipidemia. Although there can be severe consequences from the development of NAFLD, most patients will not develop progressive liver disease. Nevertheless, a sizable minority of patients will progress to severe liver disease, which can significantly shorten life. Scoring systems have been developed to estimate the risk of disease presence and progression.<sup>13</sup> Unfortunately, these scoring systems lack sensitivity and specificity to accurately and effectively dichotomize patients. As a result, both the duration of quiescence and the factors for disease progression remain largely unknown.

NAFLD and even NASH have potential for improvement and even reversibility with weight loss.<sup>14</sup> Importantly, repeat liver biopsies have shown recovery of even high-grade steatosis and steatohepatitis after significant weight loss.<sup>15</sup> The unique ability of the liver to regenerate in the setting of severe disease has significant implications for the workup and treatment of NAFLD. This is especially important concerning the use of bariatric surgery in these patients.

Bariatric surgery and liver disease have a long history together. Elevated liver enzymes were commonly observed after certain types of early bariatric surgery, especially the jejunoileal bypass procedure. Early reports and anecdotal evidence suggested that this procedure may even lead to steatohepatitis and subsequent hepatic failure.<sup>16–18</sup> These reports raised concerns on the safety of bariatric surgery. It also simultaneously drew increased attention to the risks of fatty liver disease, and the relationship between NAFLD and bariatric surgery. For a comprehensive understanding of the effects of bariatric surgery, this article reviews the biologic development and progression of NAFLD and discusses treatment options that are currently available.

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