Liver transplantation for nonalcoholic fatty liver disease: role of bariatric surgery for comorbid obesity

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Nonalcoholic fatty liver disease (NAFLD) is an increasingly prevalent form of chronic liver disease throughout the world and is associated with substantial morbidity and mortality related to liver disease and the consequences of metabolic syndrome. NAFLD is projected to become the leading indication for liver transplantation in the United States in the near future, and presents unique challenges due to common comorbidities, particularly obesity. As obesity is often a barrier to transplant, distinctive decision-making and care is needed for this growing population. Bariatric surgery offers a promising option for liver transplant specialists to consider in obese patients with NAFLD cirrhosis. This research highlight reviews the rising burden of NAFLD, concerns regarding obesity and liver transplant, and the potential role of bariatric surgery in the liver transplantation paradigm.

Keywords: NAFLD; Cirrhosis; Obesity; Liver Transplantation; Bariatric Surgery


The disease burden of non-alcoholic fatty liver disease (NAFLD) is increasing throughout the world resulting in substantial health-related consequences and cost. Epidemiological studies estimate the prevalence of this form of chronic liver disease ranging from 25-45% of the general population [1-3]. As the increasingly recognized hepatic manifestation of the metabolic syndrome, NAFLD is defined as the presence of ≥5% hepatic steatosis in the absence of competing liver diseases, such as viral hepatitis and alcoholic liver disease. Though there are still questions regarding the natural history of NAFLD and its histological spectrum, building evidence demonstrates that fibrosis is the strongest predictor of poor outcomes for patients inflicted with this disease [4-6]. The current definitive treatment available for NAFLD patients with cirrhosis that develop end-stage liver disease is liver transplantation. Unsurprisingly, NAFLD is projected to overtake chronic Hepatitis C virus (HCV) infection as the leading indication for liver transplantation in the U.S in the near future [7, 8]. This epidemiological projection is due not only to the increasing prevalence of NAFLD, but also because of the anticipated eventual decline of chronic HCV-related cirrhosis secondary to highly effective direct-acting antiviral medications [7]. As such, NAFLD is becoming a unique focus for liver transplant providers and presents substantial challenges given the burdensome comorbidities of patients with this disease. In particular, obesity appears to be the most influential comorbidity, and often limits transplant candidacy for
NAFLD patients. This healthcare dilemma provides the opportunity for an innovative and unique surgical solution: bariatric surgery in conjunction with liver transplantation.

Evidence suggests a pattern of surgeon reluctance to perform liver transplantation for obese cirrhotic patients. These patients are more likely to be turned down for organ offers (10% higher for severely obese and 16% higher for morbidly obese) and less likely to receive potentially available Model for End Stage Liver Disease (MELD) exception points (8.0% for morbidly obese and 10.3% for severely obese compared to 15.2% for non-obese) [9]. This reluctance may well stem from fear of increased postoperative complications and risk of poor outcomes. Supporting this view, LaMattina noted that obese cirrhotic patients had prolonged operative time, intensive care unit stay, infections, transfusion requirements, biliary complications, and decreased patient survival as compared to non-obese cirrhotic patients [10]. Studies evaluating United Network for Organ Sharing/Organ Procurement and Transplantation Network (UNOS/OPTN) and United Kingdom Transplant data similarly report worse outcomes in obese patients, notably due to increased graft dysfunction, frequency of cardiovascular events, infectious complications, and longer hospital stays [11, 12]. However, conflicting data from Perez-Protto noted no significant differences in perioperative morbidity and mortality in lean (BMI 20-26 kg/m²) versus obese (BMI>38 kg/m²) liver transplant recipients [13]. Nevertheless, given the evidence regarding the negative impact of comorbid obesity, liver transplant providers routinely attempt to address this disease with standard of care approaches including dietary counseling, exercise programs, and behavioral therapies during transplant evaluation and waitlist management. In fact, a comprehensive lifestyle program has been demonstrated in a prospective manner to not only induce weight-loss, but also improve NASH histological outcomes and quality of life [14, 15]. Therefore, NAFLD patients considered for transplant, or on the transplant list, should be especially targeted for these focused approaches given their advanced state of disease. However, medically supervised weight-loss programs have traditionally had low success rates and often do not result in sustained weight loss, leaving more to be desired [16].

Bariatric surgery (BS) represents an opportunity to address comorbid obesity in cirrhotic patients and to improve outcomes of liver transplantation for obese NAFLD patients, as well as possibly for obese patients with other etiologies of end-stage liver disease. BS is well-documented to treat obesity and related metabolic comorbidities such as diabetes mellitus, and has shown promise in regression of NAFLD [17]. Obese NAFLD patients with cirrhosis therefore appear as a logical target population for BS. Potential benefits not only range from pre-transplant listing to better postoperative outcomes, but also to long term graft function and survival potentially from reducing risk of recurrent NAFLD and cardiovascular events. BS has been successfully used before, during, and after liver transplantation for NAFLD, though relatively few studies exist, most published as case series ranging up to 20 patients [18, 19]. There remains a lack of consensus regarding the acceptable degrees of liver dysfunction or portal hypertension that will permit successful bariatric surgery in the pre-transplant/cirrhotic setting. A variety of different types of BS surgeries have been performed on these patients including gastric banding, Roux-en-Y gastric bypass, and the most common, sleeve gastrectomy [18]. Sleeve gastrectomy, in particular, appears to be an attractive option as it does not result in an intestinal bypass (thereby should not affect subsequent absorption of immunosuppression drugs) and does not alter endoscopic access to the biliary tract (given possibility of biliary complications due to liver transplant). The benefit of pre-transplant BS for these patients not only includes improvement in body mass index (BMI) to an acceptable threshold for transplant listing for the morbidly obese, but for further optimization of comorbid conditions such as diabetes mellitus. However, pre-transplant BS would require two separate operations, and BS itself is susceptible to complications such as wound infections, which could result in waitlist dropout. Combined BS and liver transplantation is attractive in that the surgeries are performed during one operation, though the trade-off includes longer operative time and surgical complexity. After transplant BS is particularly attractive in theoretically reducing risk of recurrent NAFLD, although it does require an operation in a post-surgical abdomen with likely increased adhesions and elevated risk of wound complications with use of immunosuppression. At this time, randomized controlled trials addressing the type and timing of BS in relation to liver transplantation have not been conducted, and given the overall paucity of data regarding this endeavor for these patients, firm recommendations regarding these considerations cannot be made. Nevertheless, the potential role for BS in obese NAFLD cirrhotic patients is promising, and several independent authors and institutions have reported successful outcomes demonstrating safety and efficacy in producing sustained weight-loss [19-27].

NAFLD is projected in the near future to become the leading etiology of liver transplantation in the United States. This disease brings unique challenges to liver transplant providers due to prevalent comorbidities that influence eligibility and outcomes, namely obesity. Weight-loss is pivotal for obese NAFLD patients and should be orchestrated through a comprehensive lifestyle program, particularly in those with progressed disease considering transplantation. Early studies show that BS appears to be a safe and effective promising option for this patient population. At this time, further investigation is needed to better define the role of BS and additionally determine optimal surgery type and timing in relation to magnitude of cirrhosis, degree of portal hypertension and transplant.
Conflicting interests

The authors have declared that no conflict of interests exist.

Author contributions

YP was involved in manuscript conception, manuscript preparation, draft revision, final approval for submission. CB was involved in manuscript conception, draft revision, final approval for submission. CM was involved in manuscript conception, draft revision, final approval for submission.

Abbreviations

BS: Bariatric surgery; HCV: Hepatitis C virus; MELD: model for end-stage liver disease; NAFLD: nonalcoholic fatty liver disease; UNOS/OPTN: United Network for Organ Sharing/Organ Procurement and Transplantation Network.

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