Bariatric Surgery and Liver Transplantation

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Keywords
Liver transplantation, bariatric surgery, cirrhosis, liver disease, obesity

Abstract: Obesity is an important public health and medical concern in the United States. The rate of obesity has steadily risen for the past several decades. Obesity is associated with the development of nonalcoholic steatohepatitis, which is one of the leading indications for liver transplantation. After liver transplantation, recipients tend to gain weight and develop recurrent fatty liver. Over time, recurrent fatty liver may impact patient and graft survival. A bariatric surgical approach may be beneficial in select patients.

Obesity is a significant medical and public health concern in the United States. The prevalence of obesity has doubled in the past several decades and is currently approximately 35%.[1,2] Children in the United States are significantly impacted, as one-third are overweight.[3] Major complications of obesity include the development of nonalcoholic steatohepatitis (NASH) and subsequent cirrhosis.[4-7] Not only can obesity cause liver disease but also accelerate disease progression of other causes of cirrhosis.[8,9] The impact of fatty liver disease is becoming realized in clinical practice. NASH is now one of the most common causes of liver disease in the United States and the second most common indication for liver transplantation.[10,11]

Obesity increases the perioperative and long-term complications of liver transplant recipients.[12-14] Moreover, a body mass index (BMI) greater than 40 has been associated with high rates of mortality following liver transplantation.[15,16] Specifically, obesity is more common among patients transplanted for NASH than for other indications.[16] However, the impact of obesity on the development of recurrent cirrhosis is not clear.[17-19] Over long-term follow-up, obese patients have an increased likelihood of developing progressive liver disease, particularly patients who were transplanted for NASH.[20]

The purpose of this article is to evaluate surgical options for the treatment of obesity in patients with chronic liver disease, particularly those undergoing liver transplantation. The criteria for bariatric surgery, at least in the general population, include a BMI of at least 40 or a BMI of at least 35 with 1 or more obesity-related

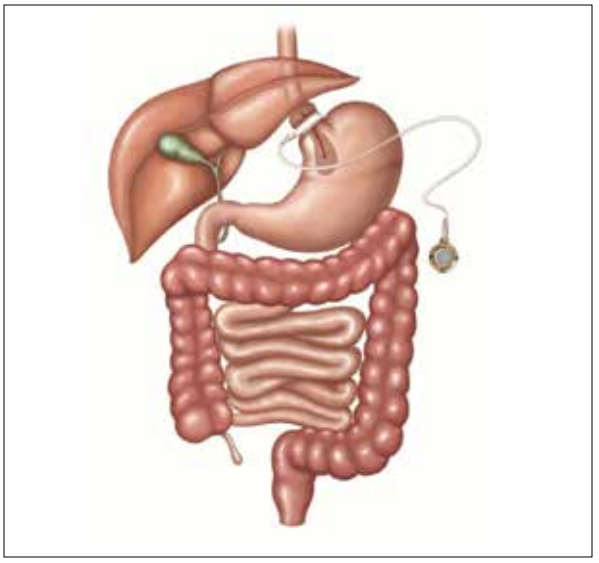

Figure 1. An adjustable gastric band. The arrow shows the direction of food.

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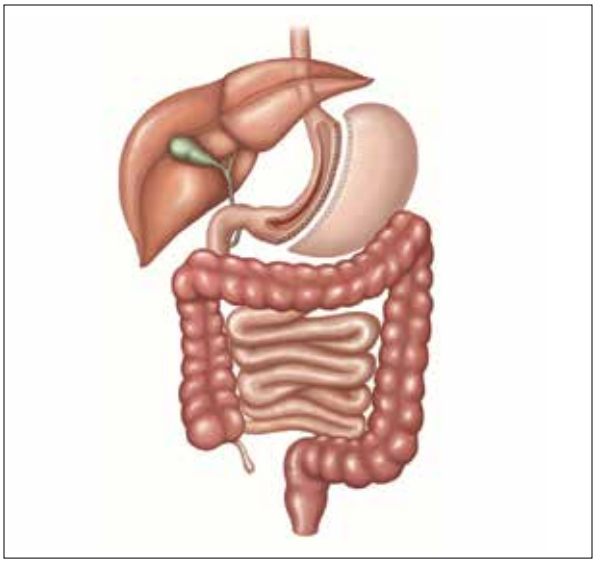

Figure 2. A sleeve gastrectomy. The arrow shows the direction of food.

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comorbidities in carefully screened patients.[21] The mechanism through which bariatric surgery leads to weight loss is controversial. Although it is well accepted that bariatric surgery functions through a restrictive or malabsorptive process, there is increasing evidence for the potential role of neurohormonal exposure.[22-24] Bariatric surgery has been shown to be more effective in achieving weight loss and in the management of obesity-associated comorbidities than intensive medical therapy alone.[21,25] Particularly in liver transplant recipients, bariatric surgery may decrease the likelihood of developing NASH and improve graft function.[26,27] The 3 most common types of bariatric surgery, which this article will focus on, include the gastric band, sleeve gastrectomy, and Roux-en-Y gastric bypass.

Types of Bariatric Surgery

The gastric band is an adjustable band placed in the proximal portion of the stomach to create a restrictive pouch (Figure 1).[28,29] The diameter of the band can be adjusted through an inflatable cuff accessible by a subcutaneous port. A mean weight loss of 45% to 65% can be obtained after the procedure.[30-32] Complications are not uncommon and include band erosion, band infection, band slippage, esophagitis, esophageal dilation, and port problems.[30,31,33] Although technically less difficult than other types of bariatric surgery, the adjustable gastric band has high reoperation rates and weight loss is less than that described with other surgical procedures. Thus, the gastric band is no longer recommended.

Sleeve gastrectomy is the permanent removal of the majority of the gastric body and fundus (Figure 2).[29,34] The mechanism through which patients lose weight is hypothesized to be the reduction of gastric volume and alteration of neurohormonal pathways.[35] For instance, ghrelin is secreted by the stomach and its levels decrease after sleeve gastrectomy, therefore reducing the sensation of hunger.[35] A mean excess weight loss of 40% to 70% is typically achieved 12 months after the procedure.[35-37] Patients may develop nausea and emesis from overeating.

Roux-en-Y gastric bypass is thought to result in significant weight loss through multiple pathways, including restrictive, malabsorptive, and neurohormonal means (Figure 3).[29,38-43] The procedure involves the creation of a small gastric pouch, typically 30 cm in size, by segmentation of the stomach.[44] The proximal jejunum is then divided approximately 30 cm below the ligament of Treitz with the proximal end joining the small bowel approximately 100 cm below the point of division and the distal end brought up to form a gastroenterostomy.

While the data on the use of bariatric surgery in the liver transplant setting are limited, it has become clear that the adjustable gastric band can no longer be recommended due to poor efficacy and a high rate of complications requiring reoperation.[30,31,33] Although Roux-en-Y gastric bypass achieves greater weight loss and possibly greater resolution of obesity-associated comorbidities than sleeve gastrectomy, nutritional deficiencies (eg, involving calcium, vitamin B1, vitamin B12, and iron)

Figure 3. A Roux-en-Y gastric bypass. The red arrows show the direction of food, and the green arrows show the direction of bile.

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with Roux-en-Y gastric bypass make sleeve gastrectomy more attractive in liver transplant patients.[29,45-47]

Bariatric Surgery in Patients With Cirrhosis

Currently, there are no clear guidelines on the use of bariatric surgery in patients with cirrhosis or consensus on which bariatric modality is best for patients with cirrhosis.[48,49] One retrospective study found that there was an increase in mortality in patients with compensated and decompensated cirrhosis undergoing bariatric surgery when compared with patients without cirrhosis.[50] Shimizu and colleagues conducted a database review to assess outcomes of bariatric surgery in patients with cirrhosis and found that laparoscopic Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy can be performed safely in these patients.[51] Previous studies have found similar results supporting the use of laparoscopic bariatric surgery in patients with compensated cirrhosis.[52,53] Although there is no consensus on the specific Model for End-Stage Liver Disease or Child-Pugh score threshold, pursuing bariatric surgery in patients with compensated cirrhosis is reasonable in select patients. Bariatric surgery should not be pursued in patients with decompensated liver cirrhosis with manifestations of portal hypertension. It is often recommended that screening esophagogastroduodenoscopy and abdominal ultrasound be used to evaluate patients for portal hypertension prior to pursuing bariatric surgery. Patients with any evidence of portal hypertension should be excluded from bariatric surgery. Acute liver failure has been described in patients undergoing bariatric surgery even up to close to a year after the procedure, generally associated with jejunoileal bypass.[26,54-57] Thus, patients who undergo bariatric surgery require close follow-up to continue even after the immediate postoperative period.

The evaluation of cirrhotic patients for bariatric surgery can have further challenges, as some of these patients have cognitive impairment owing to hepatic encephalopathy. Obesity alone has also been associated with cognitive dysfunction, and its effects on bariatric surgery evaluation have been well documented.[58-60] It is vital to use a multidisciplinary team and neuropsychological and cognitive testing to carefully evaluate cirrhotic patients who are cognitively impaired. The use of a bioethicist to help determine a patient's ability to assent to a proposed treatment plan is highly recommended.[61] It is generally not recommended to pursue bariatric surgery in patients living alone with intellectual disability who have limited support.

Bariatric Surgery in Liver Transplant Candidates

Bariatric surgery prior to transplantation aims to ameliorate obesity-associated medical conditions before the patient receives the organ. However, attempting bariatric surgery prior to liver transplantation may delay receipt of the organ while the patient awaits adequate BMI response and addresses potential complications from bariatric surgery. Lin and colleagues conducted a retrospective analysis of 20 patients with end-stage liver disease and 6 patients with end-stage renal disease who underwent laparoscopic sleeve gastrectomy as a weight loss method prior to liver or kidney transplantation.[62] At 1, 3, and 12 months, the mean percentage of excess body weight loss (defined as the percentage of weight exceeding a BMI of 25 that was lost) was 17%, 26%, and 50%, respectively. Six patients (23%) experienced postoperative complications, compared with a complication rate of 1% to 5% in the general population. Complications included infections, staple line leak, bleeding, and kidney injury. There was no perioperative mortality. All patients reached BMI goals for liver transplantation within 1 year, with a mean time from gastrectomy to liver transplant of 16.6 months. Takata and colleagues evaluated the safety and efficacy of laparoscopic Roux-en-Y gastric bypass in 7 patients with end-stage renal disease and laparoscopic sleeve gastrectomy in 6 patients with cirrhosis and 2 patients with end-stage lung disease.[63] The mean percentage of excess weight loss at 9 months was 61% in end-stage renal disease patients, 33% in patients with cirrhosis, and 61.5% in patients with end-stage lung disease. Obesity-associated comorbidities

Table. Liver Disease and Candidacy for Bariatric Surgery

Type of Patient	Bariatric Surgery Candidate
Compensated cirrhotic without portal hypertension	Yes
Compensated cirrhotic with portal hypertension	No
Decompensated cirrhotic	No
Liver transplant recipient (<1 year posttransplant)	No
Liver transplant recipient (≥1 year posttransplant)	Yes

improved or resolved in all patients. Fourteen of the 15 patients (93%) achieved their BMI goal for transplantation. A recent case report highlighted successful sleeve gastrectomy prior to liver transplantation.[64]

Bariatric Surgery During Liver Transplantation

Other benefits of performing simultaneous bariatric surgery and liver transplantation include decreased hospital stay, reduced cost, and decreased stress and pain. Heimbach and colleagues compared noninvasive pretransplant weight loss with weight loss achieved by sleeve gastrectomy that was performed during liver transplantation.[65] A total of 37 patients achieved weight loss and underwent liver transplant alone, and 7 patients underwent transplantation combined with sleeve gastrectomy. In those who were enrolled in the noninvasive weight loss program alone, weight gain to a BMI greater than 35 was seen in 62% (21/34), post–liver transplant diabetes in 35% (12/34), and steatosis in 21% (7/34); in addition, there were 3 deaths and 3 graft losses (2 because of early graft dysfunction and 1 because of chronic rejection). In patients who underwent sleeve gastrectomy, there was substantial weight loss, with a mean BMI of 29. No patients developed post–liver transplant diabetes or steatosis, and there were no deaths or graft losses. One patient developed a leak from the gastric staple line, and 1 had excessive weight loss, with a BMI of 20.

Bariatric Surgery After Liver Transplantation

The goal of performing bariatric surgery after liver transplantation is to improve survival by reducing obesity-related comorbidities as well as reducing the incidence of recurrent NASH. A serious drawback in performing bariatric surgery in liver transplant recipients is the increased risk of wound complications and dehiscence due to the use of corticosteroids and other immunosuppressant medications, such as mechanistic target of rapamycin inhibitors. In fact, chronic and active use of corticosteroid or immunosuppressant medications has been shown to be a strong predictor of 30-day postoperative morbidity and mortality following primary bariatric surgery.[66] In addition, major adhesions can make laparoscopic bariatric surgery technically difficult in patients who have undergone liver transplantation.[67] Lin and colleagues performed sleeve gastrectomy in 9 obese liver transplant recipients with the goal of improving diabetes and steatohepatitis.[62] The mean time between liver transplant and bariatric surgery was 5.9 (±2.4) years. At 6 months, mean excess body weight loss was 55.5%. Three patients had complications of mesh dehiscence after synchronous incisional hernia repair, bile leak from the liver surface requiring laparoscopic drainage, and postoperative dysphagia that required reoperation. There were no episodes of graft rejection, and hepatic and renal functions were not impacted. Furthermore, calcineurin inhibitor levels remained stable with no need for dose adjustments.

Conclusion

A goal in liver transplant candidates is to lower BMI so that patients may meet weight-listing requirements and reduce the risk of perioperative transplant morbidity and mortality. The potential benefits of meeting listing requirements by performing bariatric surgery are offset by the risk of hepatic decompensation in patients with portal hypertension. Moreover, bariatric surgery performed at the time of liver transplantation may be associated with high preoperative risks. Thus, the ideal time to perform bariatric surgery in patients with cirrhosis is before portal hypertension develops or at least a year after liver transplantation to minimize the risk of rejection from interruptions in immunosuppressant therapy (Table).

The authors have no relevant conflicts of interest to disclose.

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