# Management and Risks Before, During, and After Liver Transplant in Individuals With Obesity

Saleh A. Alqahtani, MD,[1,2] and Robert S. Brown Jr, MD, MPH[3]

[1]Liver Transplant Center, King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia

[2]Division of Gastroenterology and Hepatology, Johns Hopkins University, Baltimore, Maryland

[3]Division of Gastroenterology and Hepatology, Department of Medicine, Weill Cornell Medicine, New York, New York

Corresponding author:
Dr Robert S. Brown Jr
Weill Cornell Medical College
1305 York Avenue
New York, NY 10021
E-mail: rsb2005@med.cornell.edu

**Abstract:** Obesity has become a global epidemic, adding to the burden of chronic diseases and disabilities. Metabolic syndrome, especially obesity, is a significant risk factor for nonalcoholic fatty liver disease, which is the most common indication for liver transplant (LT). The prevalence of obesity among the LT population is growing. Obesity increases the necessity of LT by playing a role in the development of nonalcoholic fatty liver disease, decompensated cirrhosis, and hepatocellular carcinoma, and it can also coexist with other diseases requiring LT. Therefore, LT teams must identify key aspects required to manage this high-risk population, but there are currently no defined recommendations for managing obesity in LT candidates. Although body mass index is often used to assess the weight of patients and classify them as overweight or obese, this measure may be inaccurate to use in patients with decompensated cirrhosis, as fluid overload or ascites can significantly add to the weight of patients. Diet and exercise remain the cornerstone of obesity management. Supervised weight loss before LT, without worsening frailty and sarcopenia, may be beneficial in reducing surgical risks and improving long-term LT outcomes. Bariatric surgery is another effective treatment for obesity, with sleeve gastrectomy currently conferring the best outcomes in LT recipients. However, evidence supporting the timing of bariatric surgery is lacking. Long-term patient and graft survival data in individuals with obesity following LT are scarce. Class 3 obesity (body mass index ≥40) further complicates the treatment of this patient population. This article discusses the impact of obesity on the outcome of LT.

**Keywords**
Obesity, liver transplant, waitlist mortality, obesity management, bariatric surgery, transplant outcomes

Obesity prevalence has reached epidemic status, contributing to the global burden of chronic diseases and disabilities. During the past 4 decades, obesity rates have increased more than 3-fold in North America.[1,2] Currently, almost 40% of the US population is obese, defined by a body mass index (BMI) of greater than 30.[3] Subsequently, the number of individuals with obesity referred and evaluated for liver transplant (LT) has also increased.[4] According to the

**Table 1.** Interventions in Patients With Obesity in the Pretransplant Setting

| Intervention | Pre–Liver Transplant | Considerations |
|---|---|---|
| Diet | • For patients with obesity, daily caloric intake must be targeted to 25 kcal/kg of ideal body weight and protein at 2.0-2.5 g/kg of ideal body weight.<br>• To prevent the risk of malnutrition and sarcopenia, diets <1000 kcal per day must be avoided.<br>• Focus should be placed on improving nutrition and muscle mass, instead of weight loss, for individuals with decompensated cirrhosis. | • Malnutrition<br>• Limited efficacy |
| Physical activity | • Nutrition should be optimized before initiating physical activity.<br>• Exercise under supervision is safe in patients with cirrhosis.<br>• Additional caution is warranted in patients with ascites and intense stimulation of renin-aldosterone and sympathetic nervous systems because both may impair renal dysfunction. | • Concerns of portal pressure and variceal bleeding with exercise |
| Pharmacologic treatment | • Liraglutide appears to be safe in patients with hepatic impairment. | • Studies of obesity medications in patients with cirrhosis are limited. |
| Bariatric surgery | • In early cirrhosis with a compensated liver, bariatric surgery may be helpful for weight loss. | • Worsening of sarcopenia and malnourishment |

kcal, kilocalorie.

2018 Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients, 34.6% of adult patients receiving LT were obese (BMI >30), with 13.9% having a BMI of greater than 35.[5]

Nonalcoholic fatty liver disease (NAFLD), which is estimated to affect up to 25% of the global population, is a spectrum of illnesses ranging from simple steatosis to more progressive nonalcoholic steatohepatitis (NASH), decompensated cirrhosis, and other associated liver complications, including hepatocellular carcinoma (HCC). Metabolic syndrome, especially obesity, is a major risk factor for developing NAFLD. Almost 80% of individuals with NAFLD have some degree of obesity.[4,6] NASH is the leading cause of liver-related mortality and morbidity, resulting in end-stage liver disease (ESLD) and the subsequent need for LT.[7,8] In the United States, cirrhosis owing to NASH is the leading indication for LT and the fastest-growing cause of HCC among waitlisted candidates.[9,10] LT remains the only therapeutic option, offering the best treatment for patients with ESLD. The prevalence of obesity in the LT population is growing because it increases the risk of NAFLD and subsequent severe liver damage requiring LT, and it can coexist with other diseases requiring LT, such as cirrhosis from viral hepatitis or autoimmune hepatitis. This growing prevalence is a concern for a number of reasons. First, individuals with obesity are more likely to have other comorbidities, such as type 2 diabetes, cardiovascular disease, and other metabolic complications, which may impact the selection process for LT.[11] Second, if the patient undergoes LT, obesity can make the surgery challenging and increase the risk for perioperative complications.[12] Finally, after LT, obesity can lead to hepatic steatosis and negatively impact the patient's quality of life.[13]

This article discusses the impact of obesity on the outcome of LT and the management of this condition using therapeutics and lifestyle modifications.

## Obesity Before Liver Transplant

### *Assessment of Obesity in End-Stage Liver Disease*

In patients with ESLD, the definition of obesity (BMI >30) may not apply because of variable volume status owing to ascites and fluid retention, which may exaggerate BMI measurements. The American Association for the Study of Liver Diseases guidelines indicate class 3 obesity (BMI ≥40), previously referred to as morbid obesity, as a contraindication for LT.[14] However, these recommendations were based on moderate-quality evidence, and recent studies raise concerns about using perioperative BMI as a parameter to predict LT outcomes. A prospective analysis showed that adjusting BMI for ascites shifted 11% to 20% of patients into the lower BMI classes.[15] Further, no correlation was observed between pre- and posttransplant BMI.[16] BMI alone cannot be used to predict risks because it ignores factors such as fat

distribution and loss of muscle mass, which both appear to be closely related to pre- and post-LT morbidity and mortality. For example, in patients with cirrhosis, visceral adiposity is linked to higher mortality following LT compared with peripheral adiposity.[17] Moreover, patients with cirrhosis and sarcopenic obesity (characterized by a loss of muscle mass or strength[18,19]) demonstrated a worse prognosis and a higher risk of pre- and post-LT mortality.[18,20-23] Given these limitations, BMI alone is not appropriate for assessing obesity and obesity-related risk factors in patients awaiting LT.[24] Rather, a comprehensive assessment of visceral adiposity, sarcopenia, and the severity of other comorbidities, including diabetes and cardiovascular diseases, should be used to determine potential LT outcomes in individuals with obesity and cirrhosis.[24]

Furthermore, after adjusting for age, race, sex, ascites, etiology, and the Model for End-Stage Liver Disease (MELD) score, a retrospective study found no difference in mortality between overweight individuals (BMI 25-29.9) or individuals with obesity (BMI ≥30) and those with normal weight (BMI 18.5-24.9) after LT.[4] Similarly, although a univariate analysis showed an association among BMI, decompensated cirrhosis, and mortality, no such association was observed after adjusting for diabetes and insulin resistance (in patients with advanced fibrosis and compensated cirrhosis),[25] highlighting that cumulative comorbidities determine LT outcomes in a patient. Thus, class 3 obesity should not be considered an independent contraindication for LT; instead, rigorous assessment and screening may facilitate the selection of eligible recipients (Table 1).[26]

### *Influence of Obesity and Cardiovascular Diseases on Liver Transplant Assessment*

Given the association between obesity and cardiovascular diseases, screening for cardiovascular risks in patients with obesity on the LT waitlist is imperative. The American Association for the Study of Liver Diseases recommends cardiac evaluation for patients with a history of diabetes, smoking, or family or personal history of coronary artery disease, or for patients above 60 years of age. Obesity is not included as a factor for this recommendation.[14] Noninvasive cardiac evaluation is not always possible in patients with obesity and liver failure owing to the challenges of complying with standard exercise testing protocols; in such cases, pharmacologic stress tests may be applied. However, the accuracy and the predictive value of these tests are not validated in patients with ESLD and are further limited in patients with obesity because of chronotropic incompetence or reduced ventricular stress response.[27-29] Coronary angiography is invasive but has an acceptable safety profile for highly selected patients as part of pre-LT evaluation. However, the benefits of coronary angiography on post-LT survival are uncertain in patients with or without obesity.[30] Currently, there are no specific cardiac screening recommendations for candidates with obesity who undergo LT. For this reason, one review suggested following the individual LT center's protocols when evaluating a patient based on the number of known coronary disease risk factors.[24]

In addition, the requirement for a large-sized graft to reach the necessary allograft size and weight indicated by the graft-to-recipient weight ratio complicates living donor LT in individuals with obesity. To achieve an adequate graft-to-recipient weight ratio, patients with obesity may require livers from donors with higher BMIs. However, donors with high BMIs may not be suitable candidates because of underlying NAFLD.[31]

### *Waitlist Mortality*

Candidates with obesity approved for LT have higher mortality and dropout risks while on the waitlist, especially among patients with class 3 obesity.[32,33] Owing to a multitude of reasons, patients with class 3 obesity may not be considered for LT.[34]

Between 2001 and 2004, waitlist candidates with a BMI of 35 to 40 demonstrated higher adjusted mortality (hazard ratio [HR], 0.89; 95% CI, 0.79-1.01; $P$=.05) than waitlist candidates with a normal BMI of 20 to 25, but patients with a BMI of 40 or greater showed no increase in adjusted mortality risk (HR, 1.01; 95% CI, 0.87-1.17; $P$=.93), which might be owing to limited power.[1] However, a more recent, large cohort study including 80,221 waitlisted patients between 2005 and 2014 showed that candidates with a BMI of 40 or greater had significantly higher waitlist mortality rates than those with a BMI of less than 30 (HR, 1.16; 95% CI, 1.08-1.26).[33] The cumulative incidence of waitlist mortality was 17% vs 13% at 1 year and 26% vs 21% at 3 years for candidates with a BMI of 40 or greater and a BMI of less than 30, respectively. Another study showed that, between 2002 and 2006, the adjusted LT rate was 11% lower in candidates with a BMI between 35 and 40 (95% CI, 3-19; $P$<.01) and 29% lower in candidates with a BMI of 40 or greater (95% CI, 10-45; $P$<.01) than those with a BMI of 18.5 to 30.[35] This study also reported that patients with class 3 obesity are less likely to have a MELD exception score, and are more likely to be declined for LT.

Although some LT centers consider class 3 obesity a contraindication for LT, multiple studies have confirmed that all subgroups of LT patients (including patients with obesity) have a significant survival benefit, again highlighting that BMI should not be used as a contraindication for LT.[4,34]

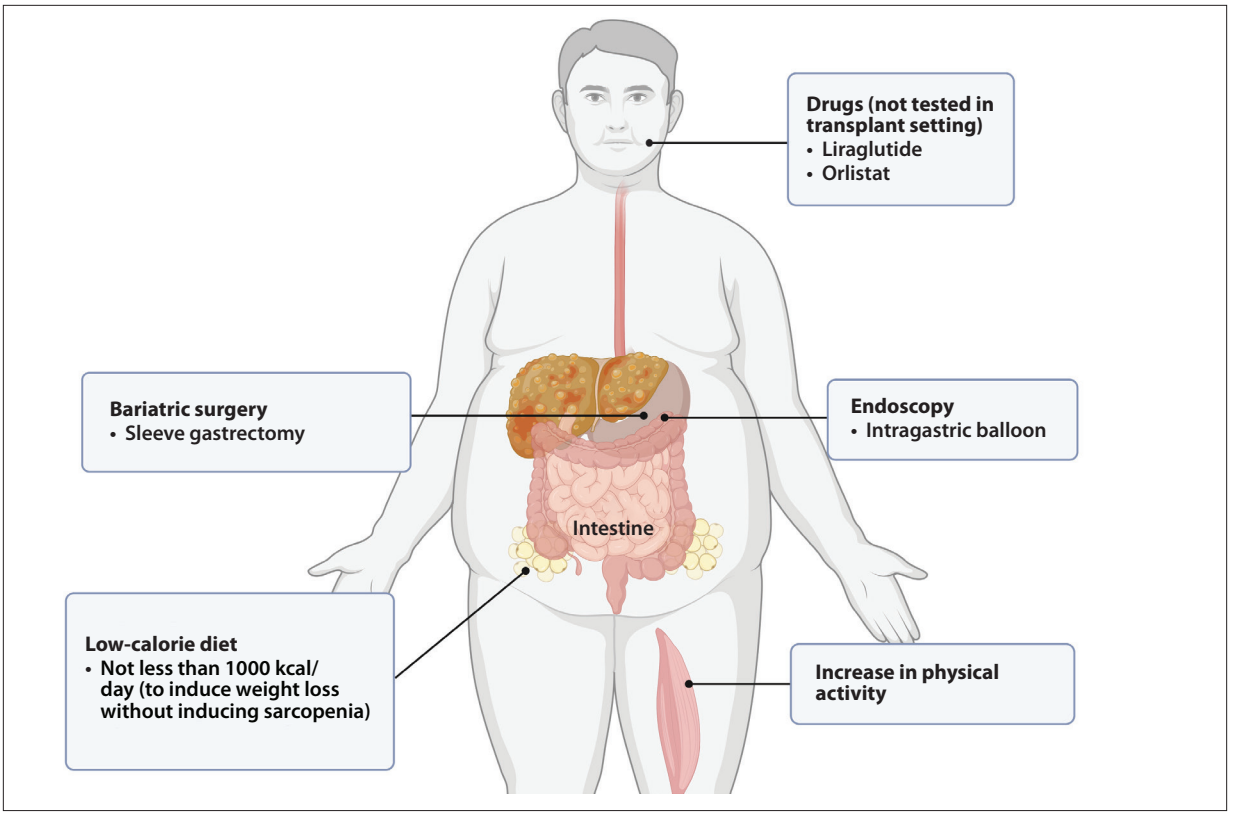


**Figure.** Strategies for weight loss in patients waitlisted for liver transplant without decompensated cirrhosis.

kcal, kilocalorie.

### *Strategies for Obesity Management in Waitlisted Patients*

**Diet and Lifestyle Modifications** Weight gain after a solid organ transplant is common, and patients who are obese at the time of transplant are more likely to gain even more weight than leaner patients.[36] The long-term effect of obesity on post-LT outcomes includes an increased risk of NASH as well as increased risks of diabetes, heart disease, and cancer, which remain the leading causes of morbidity and mortality post-LT.[37] Because of these increased risks, weight loss before LT remains a goal for patients with obesity (Figure). Weight loss can be achieved by lifestyle modifications (eg, diet, exercise) and surgical procedures (eg, bariatric surgery).[36,37] Although lifestyle modifications can result in a significant amount of weight loss (>10%) before LT, weight regain post-LT is common.[36] Further, very-low-calorie diets containing less than 1000 kilocalories (kcal) per day should be avoided to prevent protein-energy malnutrition and sarcopenia.[37] Because patients with decompensated cirrhosis are at an even higher risk for malnutrition, improving nutrition and muscle mass should be emphasized instead of weight loss in those patients.[24,28] For patients with obesity, the 2020 European Society for Clinical Nutrition and Metabolism practical guidelines recommend a high-protein, hypocaloric diet of 25 kcal/kg/day and 2.0 g/kg/day to 2.5 g/kg/day of protein (using ideal body weight) in order to promote fat loss and reduce insulin resistance while preserving muscle mass.[38]

Exercise is an integral part of the lifestyle change in a patient with obesity who undergoes LT, as moderate weight loss (<5%) without exercise is insufficient to improve hepatic fat accumulation.[38] However, patients with cirrhosis are less likely to exercise than healthy individuals.[39,40] One reason is that moderate physical activity in patients with cirrhosis was previously thought to increase portal pressure and risk of variceal bleeding in patients without proper β-blockade therapy.[41] More recent research shows that patients with compensated cirrhosis can safely exercise under supervision (with proper β-blockade therapy), and that exercise may decrease hepatic venous pressure gradient and improve physical fitness, nutritional status, and ammonia metabolism.[42] Exercise under supervision was also shown to result in increased muscle mass, improved exercise capacity, and even reduced fatigue in patients with cirrhosis.[43,44] The

benefit of tailored nutritional intervention and a supervised exercise program was shown in a 16-week intervention study in which 52% of patients with obesity and compensated cirrhosis lost at least 5% of body weight, and 40% of patients reduced their hepatic venous pressure gradient by at least 10%.[45] If patients are unable to participate in supervised exercise programs, some research suggests that walking 5000 steps or more per day can help lower the incidence of sarcopenia, which is associated with increased mortality rates in patients with cirrhosis.[39] Because patients with decompensated cirrhosis are at an increased risk for protein and energy malnutrition (and related risks such as sarcopenia) and the benefits of exercise in this population are not clear, unsupervised exercise should be avoided.[46] Additional caution is warranted in patients with ascites and intense stimulation of renin-aldosterone and sympathetic nervous systems because both may impair renal dysfunction following exercise.[47] More research is warranted to determine the benefits and risks of physical activity in these patient populations.

**Pharmacologic Treatments** Studies on the efficacy and safety of obesity medications in patients with cirrhosis are limited. Currently, the US Food and Drug Administration has approved 4 weight loss medications to treat obesity: orlistat, phentermine-topiramate, naltrexone-bupropion, and liraglutide (Table 1). Of these, only orlistat and liraglutide have been studied in the context of hepatic impairment. Because orlistat has been associated with drug-induced liver injury and fat-soluble vitamin deficiency (which are already prevalent in patients with cirrhosis), it may not be suitable for this population.[48] Liraglutide appears to be safe in patients with hepatic impairment (specifically NASH) owing to acceptable pharmacokinetics.[49,50] Although the use of phentermine-topiramate has not been investigated in patients with chronic liver disease, it has been shown to successfully help patients with obesity lose more than 10% of their total body weight in clinical trials.[51,52] Owing to its limited hepatic metabolism, a reduced dose of phentermine-topiramate can be used to help patients with Child-Pugh class B disease lose weight. However, phentermine-topiramate is to be avoided in patients with Child-Pugh class C disease.[53] To date, no evidence supports the use of these medications in patients with decompensated cirrhosis.

**Bariatric Surgery Before Liver Transplant** Because patients with obesity are less likely to be accepted for LT[33] and because surgical treatment of obesity can provide more sustainable results,[36] bariatric surgery prior to transplant may improve not only the accessibility to LT but also both short- and long-term LT outcomes. In general, the research suggests that patients with early cirrhosis and a well-compensated liver can safely achieve weight loss after bariatric surgery.[54-56] In patients with compensated cirrhosis, bariatric surgery before LT offers several benefits, including improved liver function and a lower risk of postsurgical complications associated with obesity.[54,57] However, the risks associated with bariatric surgery before LT include worsening sarcopenia and malnourishment,[58] with patients with decompensated cirrhosis more likely to experience pronounced adverse postsurgical outcomes.[59] Therefore, pre-LT bariatric surgery is indicated only in patients with compensated cirrhosis. Moreover, a recent case-control series of waitlisted patients with and without prior bariatric surgery reported that those with prior bariatric surgery were more likely to be delisted or die while on the waitlist.[60] There are also multiple reports demonstrating higher perioperative mortality rates in patients with cirrhosis who undergo bariatric surgery.[59,61]

Roux-en-Y gastric bypass is a commonly performed surgery in patients with obesity alone. However, for patients with obesity and cirrhosis, a laparoscopic sleeve gastrectomy is usually more acceptable because its mechanism of action is restrictive rather than restrictive and malabsorptive, which may benefit these patients (Table 1).[13,55,57] In a cohort study of 32 LT candidates with class 3 obesity who had failed to lose adequate weight with a medically supervised weight loss intervention program, sleeve gastrectomy was beneficial in achieving weight loss with low perioperative risks.[57] A median weight loss of 22 kg and 31 kg was achieved at 6 and 12 months postsurgery, respectively. Within 6 months post–sleeve gastrectomy, 88% of candidates were deemed eligible for LT, but none were removed completely from the waitlist. Reduced perioperative and malnutrition risks, endoscopic access to the biliary tree, lack of interference with corticosteroid pharmacokinetics, and easier access to the stomach in the event of gastric variceal bleeding are all advantages of sleeve gastrectomy.

**Endoscopic Interventions** Intragastric balloon implantation is a minimally invasive weight loss procedure that has been shown to be effective in patients with class 3 obesity; however, it has not been extensively studied in patients with chronic liver disease. Weak evidence suggests that an intragastric balloon may be a viable weight loss approach for patients with class 3 obesity and decompensated cirrhosis who are ineligible for LT owing to high BMI. Choudhary and colleagues reported a weight loss of 24 kg (BMI reduced from 48.3 to 39.2) at 6 months post–intragastric balloon placement in a 61-year-old patient with decompensated cirrhosis.[62] The authors later published a small study involving 8 patients with decompensated cirrhosis, where they reported successful LT in

**Table 2.** Intervention in Patients With Obesity in the Peri-LT Setting

| Intervention | Peri-LT | Considerations |
|---|---|---|
| Bariatric surgery | • Simultaneous bariatric surgery and LT procedures are preferred owing to the single recovery and potentially fewer complications.<br>• Patients who underwent both sleeve gastrectomy and LT showed significant weight loss at 2 years postsurgery compared with patients who underwent LT alone.<br>• Combined sleeve gastrectomy and LT demonstrated an acceptable safety profile. | • Complications include gastric staple line leaks and excessive weight loss.<br>• Limited evidence<br>• Not suitable for decompensated cirrhosis |

LT, liver transplant.

5 patients after weight loss through intragastric balloon placement.[63] The authors emphasized the benefits of an intragastric balloon as an innovative modality for short-term weight loss in this high-risk population, thereby facilitating access to LT and reducing perioperative morbidity and mortality. However, more research is needed in this area to confirm these findings and potential benefits over other interventions.

## Obesity During Liver Transplant

### *Perioperative Mortality and Morbidity*

The impact of obesity on perioperative morbidity and mortality risks is contradictory, with research indicating both increased and decreased risks, which could be attributable to varying definitions of obesity and center-specific protocols. Moreover, the presence of comorbid conditions such as diabetes may also influence surgical outcomes. A retrospective analysis evaluating the additive risks of pre-LT obesity, diabetes, and cardiovascular risk factors reported obesity and concomitant diabetes to be the strongest predictors of postsurgical complications such as infections (eg, bacteremia, wound infection, pneumonia), respiratory complications, and cardiovascular complications (eg, arrhythmia, myocardial infarction),[64] resulting in extended hospital stays.[64,65] Additionally, a meta-analysis assessing post-LT complications found that patients with class 1 obesity (BMI 30-34.9) experienced an extended hospital stay, cardiopulmonary complications, and higher 30-day mortality.[66] Some of these risks may be further exacerbated by hyperglycemia (from new-onset diabetes after LT) owing to the use of corticosteroids, which are typically administered in higher doses during the perioperative phase.[67]

Another risk is the occurrence of biliary complications in recipients with obesity. It is hypothesized that this complication may be owing to an increased risk of small vessel disease, which may render the biliary tree of the donor liver more susceptible to ischemia-reperfusion injury from the transplant procedure.[68]

### *Perioperative Bariatric Surgery*

Some research focuses on the benefits of simultaneous bariatric surgery for weight loss and LT, as this limits the number of surgical procedures, requires only a single recovery, and potentially evokes fewer complications (Table 2). For example, in 1 small study, patients undergoing simultaneous sleeve gastrectomy and LT reported no deaths or graft losses.[69] However, complications included gastric staple line leaks in 1 patient and excessive weight loss in 1 patient. Among the patients who underwent LT alone, weight regain and complications such as posttransplant diabetes and steatosis were common. In addition, at 3 years postsurgery, 29.4% of patients who received LT alone maintained greater than 10% total body weight loss compared with 100% of patients who received LT plus sleeve gastrectomy.[36,69] Overall, although these were small studies and the evidence is currently limited, combined sleeve gastrectomy and LT may be a safe and effective method to help patients maintain weight loss post-LT.[36,53,69]

## Obesity After Liver Transplant

### *Posttransplant Outcomes in Recipients of Liver Transplant With Obesity*

Studies on the association between post-LT survival outcomes and recipients with class 3 obesity are conflicting.[4,11,33,70-72] Higher mortality risks observed in patients with obesity are likely confounded by concomitant comorbidities, especially diabetes and cardiovascular risks, because studies adjusting for concomitant diabetes through multivariate analysis found no independent association between obesity and patient outcomes.[65,68,73-75] Three separate United Network for Organ Sharing–based studies assessing LT outcomes reported no association between class 3 obesity and posttransplant survival.[33,73,76] Further, LT offered overall survival benefits in patients with class 3 obesity and ESLD, with 85% reduced adjusted relative risk of mortality post-LT compared with other waitlisted candidates.[1] As a result, using a BMI

**Table 3.** Intervention in Patients With Obesity in the Post-LT Setting

| Intervention | Post-LT | Consideration |
|---|---|---|
| Bariatric surgery | • Bariatric surgery after LT is challenging, but could be the only option for patients who gain substantial weight after transplant.<br>• Sleeve gastrectomy is generally considered safe with limited complications, but the need for reoperation warrants caution. | • Sleeve gastrectomy has no effect on the pharmacokinetics of immunosuppressive agents. |

LT, liver transplant.

greater than 40 as a contraindication to LT may not be ideal. Instead, carefully assessing patients with class 3 obesity for concomitant comorbidities may help identify eligible patients suitable for LT.

### *Immunosuppressive Regimen and Weight Gain*

Although corticosteroids have been found to increase the risk of metabolic syndrome, especially for diabetes and hypertension after LT,[77,78] several studies showed no association between corticosteroid use and obesity, and the type of immunosuppressant did not impact the waist circumference or BMI after LT.[79,80] For example, a retrospective analysis of 455 consecutive recipients of LT between 1999 and 2004 reported no significant association between the type of immunosuppressive agent used and obesity after 1 year posttransplant (tacrolimus vs no calcineurin inhibitors [odds ratio, 1.18; *P*=.702], cyclosporine vs no calcineurin inhibitors [odds ratio, 0.78; *P*=.651], and tacrolimus vs cyclosporine [odds ratio, 1.58; *P*=.347]).[81] A randomized controlled study reported attenuated weight gain at 1 and 2 years following LT among patients treated with the immunosuppressant everolimus, with reduced exposure to tacrolimus compared with patients treated with regular tacrolimus dosing.[82] Although immunosuppressants do not appear to affect weight gain, limiting corticosteroid use or switching to a corticosteroid-free immunosuppressive regimen following LT has been shown to reduce the risk of metabolic disorders such as new-onset diabetes.[79,83,84]

### *Metabolic Disorders After Liver Transplant*

One of the biggest challenges following LT in patients with obesity is the management of posttransplant metabolic diseases (including metabolic syndrome, new-onset diabetes, and NAFLD, which is one of the hepatic manifestations of metabolic syndrome). Nearly 46% of patients developed metabolic syndrome following LT.[80,81,85-87] Various factors increase this risk, including pretransplant BMI and weight gain after LT, and several studies reported pretransplant obesity as the most substantial risk factor for posttransplant weight gain.[88,89] In addition, posttransplant obesity (BMI ≥35) increases the risk of posttransplant diabetes, which is the strongest predictor of mortality after LT.[74,75]

Evidence regarding the risk of cardiovascular events in recipients with obesity after LT is unclear. In general, cardiovascular risks are high across all populations after LT, with a cardiovascular event incidence rate of 12.8% 30 days post-LT and 11.8% after 6 months.[90,91] Patients transplanted for NASH had a higher risk for post-LT cardiovascular outcomes,[92] and pre-LT diabetes was a consolidated independent risk factor for post-LT cardiovascular outcomes.[93,94] However, there is no clear evidence of BMI as an independent risk factor for post-LT cardiovascular outcomes, and a retrospective study of 170 LT recipients showed no significant difference in the occurrence of cardiovascular events between recipients with obesity and normal weight at 5 years posttransplant.[95]

NAFLD and NASH are the hepatic manifestations of metabolic syndrome, and LT recipients have a 20% to 40% and 10% risk of developing new-onset NAFLD and NASH, respectively.[96,97] New-onset obesity and diabetes may increase the risk of steatosis in the graft following transplant.[98] At 10 years post-LT, a study evaluating histologic changes in 271 LT recipients found new-onset obesity to significantly worsen steatosis grades, inflammation, and fibrosis stages.[98] The rates of new-onset obesity and type 2 diabetes were 30.9% and 24.4%, respectively, after LT, and a post hoc analysis of 370 recipients reported twice the risk for mortality in patients with obesity 1 year after LT.[99] Therefore, interventional strategies and surgery are required to improve long-term survival outcomes following LT in high-risk patients.

### *Weight Loss After Liver Transplant*

There have been few studies on the effectiveness of weight loss programs after LT, and it is generally accepted that lifestyle changes in both diet and physical activity should be encouraged.[38]

**Bariatric Surgery Post–Liver Transplant** Bariatric surgery after LT is challenging, but it can be an option for patients who gain substantial weight after transplant (Table 3). The outcomes of bariatric surgery after LT have

been described in several small studies, with most of the studies performing sleeve gastrectomy at least 2 years posttransplant.[100-107] Sleeve gastrectomy is generally considered safe with limited complications, but the need for reoperation warrants caution (Table 3).[102,105] Moreover, sleeve gastrectomy has no effect on the pharmacokinetics of immunosuppressive agents (mycophenolic acid or tacrolimus). In contrast, despite yielding targeted weight loss in recipients of LT, Roux-en-Y has a considerable impact on the pharmacokinetics of mycophenolic acid, sirolimus, and tacrolimus, necessitating higher doses, and carries a relatively higher risk for additional complications.[101,108,109]

## Conclusion

Despite the growing prevalence of ESLD in patients with obesity, no clear guidelines or evidence-based recommendations exist to advise the evaluation and treatment of patients with obesity for LT. Patients with ESLD and class 3 obesity are at a disadvantage owing to stringent BMI cutoffs for LT, although evidence does not support inferior LT outcomes in these patients compared with patients with a normal-range BMI. However, short- and long-term complications can arise in patients with obesity, and thus weight loss strategies are essential for minimizing morbidity and mortality risks before, during, and after LT. Caution is warranted in managing obesity in patients with decompensated cirrhosis because weight loss strategies may worsen sarcopenia and frailty. With limited data supporting pharmacologic treatments, bariatric surgery (especially sleeve gastrectomy) may be a viable option for sustainable weight loss.

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