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Liver Transplantation in the Obese Cirrhotic Patient

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Abstract

Despite the rapidly increasing prevalence of obesity in the transplant population, the optimal management of obese liver transplant candidates remains undefined. Setting strict body mass index cutoffs for transplant candidacy remains controversial, with limited data to guide this practice. Body mass index is an imperfect measure of surgical risk in this population, partly due to volume overload and variable visceral adiposity. Weight loss before transplantation may be beneficial, but it remains important to avoid protein calorie malnutrition and sarcopenia. Intensive lifestyle modifications appear to be successful in achieving weight loss, though the durability of these interventions is not known. Pretransplant and intraoperative bariatric surgeries have been performed, but large randomized controlled trials are lacking. Traditional cardiovascular comorbidities are more prevalent in obese individuals and remain the basis for pretransplant cardiovascular evaluation and risk stratification. The recent US liver transplant experience demonstrates comparable patient and graft survival between obese and nonobese liver transplant recipients, but obesity presents important medical and surgical challenges during and after transplant. Specifically, obesity is associated with an increased incidence of wound infections, wound dehiscence, biliary complications and overall infection, and confers a higher risk of posttransplant obesity and metabolic syndrome-related complications. In this review, we examine current practices in the obese liver transplant population, offer recommendations based on the currently available data, and highlight areas where additional research is needed.

The number of obese patients undergoing liver transplantation (LT) is rising in parallel with the current obesity epidemic in the United States[1,2] and in the world. Obese patients made up 20% of LT recipients between 1988 and 1996[3] compared with 33% between 2001 and 2011.[4] Obesity presents challenges before and after LT, due to high rates of obesity-related comorbidities and unique challenges with perioperative and postoperative care (Figure 1). Clear guidelines regarding the workup and management of obese patients before, during, and after transplant are lacking. Consequently, we examined the current literature to synthesize available data, highlight limitations in our knowledge, and provide practical recommendations for patient evaluation and care. We also outline potential areas for future improvement and investigation in this growing field.

PRETRANSPLANT CONSIDERATIONS

Defining Obesity in End-stage Liver Disease

Obesity is generally defined as a body mass index (BMI) ≥30. However, the categorization of obesity is more difficult in patients with end-stage liver disease (ESLD) in part due to variable volume status. One study found that correcting BMI for ascites moved 11% to 20%

of patients into lower BMI classes.[5] In fact, pretransplant BMI did not correlate with posttransplant BMI or dry weight.[6] Even if BMI is corrected for ascites, it may not provide a useful measure of obesity-related risk in this population. The distribution of fat deposition, which is not accounted for in BMI, appears to have a more significant effect on morbidity and mortality in patients with cirrhosis, both pre and posttransplantation. Among 384 LT recipients, visceral adiposity—but not peripheral adiposity—was associated with increased mortality after LT.[7] This was particularly apparent among patients with lower lean muscle mass (sarcopenia) as measured by psoas muscle mass.[7] Sarcopenic obesity, severe muscle depletion in the setting of obesity, is reported in 30% to 42% of obese patients with cirrhosis[8–10] and is associated with increased risk of pre-LT mortality.[9,11,12] Unfortunately, studies evaluating waitlist and post-LT outcomes do not use unified criteria for defining obesity or sarcopenia in this unique population, which may lead to discrepant results. Given the many limitations of BMI as a measure of obesity-related risk in liver transplant candidates, we recommend against its use as the sole measure of obesity in this population. Rather than use BMI as a nonspecific surrogate for obesity-related risk factors, we advocate that centers quantify visceral adiposity, assess sarcopenia and frailty, and determine the number and severity of comorbid conditions, such as diabetes and coronary artery disease (CAD), that can affect transplant outcomes. Although several studies suggest ways to measure sarcopenia, frailty and visceral adiposity, we recognize the current lack of standardization of these measurements. Accordingly, as with all aspects of the liver transplant candidate evaluation, we advise centers to use these data to help determine risk for patients, rather than to permit or exclude listing based on specific threshold values. Future research should focus on identifying a reproducible, quantifiable test of these risk factors and standardizing the obesity-related assessment with the greatest predictive value. A tool that could be utilized in the clinic or through a readily available modality, such as ultrasound, computed tomography (CT) or magnetic resonance imaging would allow near universal use and standardization in transplant centers. Current measures under investigation include single slice abdominal CT, psoas muscle CT, axial DEXA scan, and combinations of hip-to-waist ratio measurements with quadriceps strength testing.

Recommendation—Given the challenges of an accurate calculation of BMI in patients with significant ascites, we advise against the isolated reliance on BMI for assessment of obesity in LT candidates. We also advocate against the use of BMI as a surrogate for obesity-related comorbidities.

Areas for Future Study—Frailty, sarcopenia, and visceral adiposity quantification represent 3 promising predictors of health outcomes in obese cirrhotic patients who undergo LT. Prospective validation of these measures and evaluation of their value in predicting LT outcomes are needed.

Pre-LT Cardiac Evaluation in Obese Patients

The American Association for the Study of Liver Diseases recommends an evaluation for CAD in LT candidates who have a history of diabetes, chronic tobacco use, or a personal or family history of CAD.[13] Although there are no specific screening recommendations for obese LT candidates, it is known that obesity is strongly associated with diabetes mellitus

and CAD,[14] leading to more frequent screening in this population. However, the accuracy of noninvasive CAD screening tests (eg, exercise or pharmacologic cardiac stress tests) and the prognostic value of these screening test results are uncertain in patients with cirrhosis.[15] This may be further limited in the obese patient with cirrhosis due to chronotropic incompetence or compromised ventricular stress response.[16] The pre-LT cardiac workup in patients with cirrhosis varies significantly from center to center, with no single algorithm being universally accepted. Given the lack of clear evidence in favor of an alternative screening modality, we recommend that centers follow their standard protocol when evaluating obese LT candidates, which is typically driven by the number of known CAD risk factors. Coronary angiography has an acceptable safety profile in LT candidates, although the post-LT benefit of current CAD revascularization strategies is uncertain in both obese and nonobese LT patients.[17]

Recommendation—When evaluating obese LT candidates, transplant centers should follow their standard protocol for cardiac evaluation, which should be driven by the number of known CAD risk factors.

Coronary angiography has an acceptable safety profile in LT candidates and may be the most reliable modality for cardiac risk assessment in obese patients who have multiple risk factors for CAD.

Areas of Future Study—Additional research is needed to determine the sensitivity, specificity, positive and negative predictive values of nuclear myocardial perfusion scan and dobutamine stress echocardiogram in obese patients with cirrhosis.

Pre-LT Weight Loss

Weight reduction before LT remains a common goal in patients with obesity, although there is no sconsensus on how best to achieve this. One prospective cohort study evaluated the effectiveness of a multidisciplinary, intensive weight loss program for patients listed for LT with BMI of 35 or greater.[18] Of the 44 patients referred for LT with a median BMI of 40 (interquartile range, 36–46), 37 patients (84%) achieved a target BMI less than 35 without bariatric surgery. Although this study is small, it demonstrates that lifestyle interventions can effectively achieve weight loss in listed patients if implemented in the right setting. Because many centers do not have the resources to perform a similar multidisciplinary intervention, creation of a technology-driven approach is an appealing area for research initiatives. When recommending pretransplant lifestyle interventions, we suggest separating patients into 2 categories: patients with compensated cirrhosis and patients with decompensated cirrhosis. Patients with compensated cirrhosis can follow traditional lifestyle modifications, as long as very low calorie diets (<1000 calories daily) are avoided. For patients with decompensated cirrhosis, we recommend focusing on improvements in nutrition and muscle mass, rather than weight loss. These patients are at high risk of sarcopenia, frailty, and malnutrition, which may be worsened with many diets, particularly lower calorie diets. Even short periods without calorie intake can lead to development of a starvation state that can increase catabolism, muscle breakdown, and fatty acid oxidation. For these patients, frequent high-protein, high-nutrient meals with a nighttime snack may be more beneficial than traditional

dieting. Advising patients to avoid high-calorie, low-nutrient foods may be beneficial. Patients should maintain caloric intake with higher-protein, nutrient-rich foods. Encouraging frequent low-impact exercise may help preserve muscle mass, decrease bone loss, and improve rehabilitation efforts post-LT.

For compensated cirrhotic patients with class III obesity (BMI ≥35) who are unable to reach an acceptable weight, bariatric surgery may be an option for weight loss to achieve LT candidacy. Although the studies evaluating the outcomes of bariatric surgery in the LT population are small and predominantly retrospective, these studies are reviewed (Table 1) to show that such interventions may be a viable option in the near future and are an important area of continued research.

When considering bariatric surgery in obese patients with compensated cirrhosis, there are 2 major issues: the timing and the type of bariatric surgery. Ideally, bariatric surgery in patients with cirrhosis should be performed before the development of portal hypertensive complications, with the intent of reducing potential obesity-related perioperative and posttransplant morbidity. A retrospective study of 20 patients who underwent laparoscopic sleeve gastrectomy (SG) while listed for LT showed a mean of 50% of excess body weight was lost within 12 months, with a mean time from SG to LT of 17 months in the 7 patients who ultimately underwent LT.[19] All patients achieved the institution's BMI cutoff for LT less than 35 kg/m^2 by 12 months, with no procedure-associated mortality.[19]

Other small retrospective studies examining bariatric surgery performed at the time of LT (8 with SG, 1 with gastric band) showed favorable short- and medium-term outcomes, with effective weight loss and reduced incidence of post-LT diabetes, with no reported graft loss.[18,24,25] The only reported complications were 1 gastric staple line leak and 1 patient with excessive weight loss.[18] No studies have evaluated whether transjugular intrahepatic portosystemic shunts can safely be used to reduce morbidity with bariatric surgery. There are also no direct comparisons of different bariatric procedures in the LT population. Gastric banding is a less effective weight loss modality in the noncirrhotic population,[26] and is not a preferred bariatric surgical modality in the obese LT population. Its use in obese cirrhotic patients with portal hypertension precludes access to potential gastric varices distal to the band, and its presence after LT may increase the risk of foreign-body associated infection.

For patients with decompensated cirrhosis, bariatric surgery is associated with poor outcomes. In a study comparing outcomes after bariatric surgery performed in 3888 compensated cirrhotic patients and 62 decompensated cirrhotic patients from the Nationwide Inpatient Sample registry, patients with decompensated cirrhosis had an unacceptably high postoperative mortality rate of 16.3%, as compared with 0.9% for patients with compensated cirrhosis or 0.3% for patients without cirrhosis ($P < 0.001$).[27]

Recommendation—Patients with compensated cirrhosis should follow traditional lifestyle modifications, but very low calorie diets (<1000 calories daily) should be avoided.

Given the relative simplicity of the procedure, low rate of complications, and preservation of biliary access post-LT, SG is the preferred surgical procedure for weight reduction in obese

patients with compensated cirrhosis who are unable to achieve desired weight loss with nonsurgical therapies alone. Given the limited data at this time, we recommend this intervention be considered with caution and only in transplant centers that have expertise in bariatric surgery.

We advise against pre-LT bariatric surgery in patients with decompensated cirrhosis, given the high risk-to-benefit in this population.

Areas for Future Study—The optimal timing of bariatric surgery relative to LT remains unknown. Larger prospective trials are needed to help clarify the best way to select LT candidates for bariatric procedures and inform the decisions on timing and type of surgery that is most effective and least morbid.

Waitlist Mortality

Three United Network for Organ Sharing (UNOS) Registry studies have evaluated waitlist mortality in obese patients. Among waitlisted candidates from 2001 to 2004, there was a trend toward increased adjusted mortality in patients with BMI between 35 and 40 (hazards ratio [HR], 0.89; 95% confidence interval [CI], 0.79–1.01; $P = 0.05$), but not in those with BMI of 40 or greater (HR, 1.01; 95% CI, 0.87–1.17; $P = 0.93$), when compared to nonobese patients (BMI, 20 to <25).[28] In a separate analysis of US waitlisted candidates from 2002 to 2006, adjusted rates of LT were 11% lower in patients with a BMI 35 to less than 40 kg/m^2 (95% CI, 3–19%; $P < 0.01$) and 29% lower in patients with a BMI of 40 kg/m^2 or greater (95% CI, 10–45%; $P < 0.01$) when compared with nonobese candidates (BMI, 18.5 to <30 kg/m^2).[29] In the largest and most contemporary cohort including patients from 2005 to 2014, waitlist mortality was significantly higher for LT candidates with BMI of 40 kg/m^2 or greater as compared with those with a BMI less than 30 kg/m^2 (HR, 1.16; 95% CI, 1.08–1.26) with a cumulative incidence of waitlist mortality of 17% versus 13% at 1 year and 26% versus 21% at 3 years.[30] Although the reasons underlying these differential rates is not definitively known, the authors of these articles speculated that the increased waitlist mortality rates observed in obese LT candidates was due to a lower probability of receiving model for ESLD exception points, a higher rate of organ turndown, as well as faster disease progression among obese versus nonobese patients.[29,30]

Recommendation—LT candidates with class II or III obesity may be counseled on their increased risk of waitlist mortality and lower transplant rates to facilitate discussions regarding willingness to accept livers from donors designated as higher risk.

Area for Future Study—Studies are needed to identify modifiable factors that contribute to higher waitlist mortality and decreased access to transplant among obese LT candidates.

PERITRANSPLANT CONSIDERATIONS

Intraoperative Outcomes

Mean operative time has been reported to be longer in recipients with BMI > 40 kg/m^2 compared with recipients with BMI less than 25 kg/m^2 (8.2 vs 7.2 hours; $P = 0.003$).[31]

There appears to be no significantly increased need for intraoperative packed red blood cell transfusions in obese versus nonobese recipients.[32–34]

Morbidity Immediately After LT

Studies reporting morbidity after LT in obese versus nonobese patients are conflicting, likely in part due to the heterogeneity of obesity definitions and center-specific effects. The major studies evaluating posttransplant morbidity that include patients transplanted after 2000 are summarized in Table 2. Evaluating the studies in aggregate, rates of primary graft nonfunction, acute rejection, vascular complications, and need for reoperation within the immediate postoperative period were similar between patients with BMI of 35 kg/m^2 or greater and nonobese (BMI < 25 kg/m^2) LT recipients. Rates of wound infection, wound dehiscence, and overall infections were significantly higher among the patients with class II to III obesity (Table 2). One study found that nonoperative biliary complications occurred more frequently in the obese recipients, but the authors did not find a difference in biliary complications requiring surgical revision.[31] This raises the possibility that obese patients with biliary complications were more likely to receive nonoperative intervention due to technical challenges of reoperation. Alternatively, the obese patients may have had biliary complications that were less severe and more amenable to nonsurgical therapies. Although rates of postoperative respiratory infections were similar between the 2 groups,[38] postoperative respiratory failure occurred more commonly among obese versus nonobese recipients (23% vs 3%; $P = 0.009$).[32]

Length of Stay

Multiple single-center studies have demonstrated obesity to be associated with longer ICU and hospital lengths of stay (LOS) in the immediate posttransplant period.[31,38,40,41] In the largest single-center cohort that included a total of 1325 LT recipients from 1994 to 2009, both ICU LOS (4.7 vs 3.2 days; $P = 0.03$) and total hospital LOS (22.4 vs 18.0 days; $P = 0.047$) were significantly higher among the 73 recipients with BMI of 35 or greater compared with the 643 recipients with BMI of 18.5 to 24.9.[38] These findings were confirmed in an analysis of the Scientific Registry of Transplant Recipients (SRTR) data. Among 12 445 LT recipients, 416 (3%) of whom had a BMI of 40 or greater (class III obesity) ICU days (mean [SD], 3 [6] vs 3 [4]; $P < 0.001$) and hospital days (11 [10] vs 9 [8]; $P < 0.001$) were both significantly higher in recipients with a BMI of 40 or greater compared with those with a BMI less than 40.[41] In addition, obese recipients with a BMI of 40 or greater were more likely to be discharged to a skilled nursing facility or rehabilitation center after LT as compared with recipients with a BMI less than 40 (23% vs 15%; $P < 0.001$).[41]

Recommendation—Although causation has not been demonstrated, optimization of nutrition, management of metabolic comorbidities such as diabetes before and immediately after LT, and judicious use of antimicrobial coverage to prevent wound infections in obese LT recipients may mitigate their increased risk of immediate postoperative complications.

Area for Future Study—A multicenter study with granular data on immediate postoperative complications is needed to identify specific contributors to increased LOS in obese LT recipients.

POSTTRANSPLANT CONSIDERATIONS

Immunosuppressive Regimen and Weight Gain

No studies have established superiority of 1 immunosuppressive regimen over another with respect to weight gain posttransplant. In a trial of 39 patients randomized to a corticosteroid-containing (n = 20) versus corticosteroid-free regimen (n = 19), rates of obesity after 2 years were not significantly different.[42] In a European review of 296 recipients, the type of immunosuppressive drug had no effect on waist circumference or BMI post-LT.[43] A recent retrospective review of 455 recipients similarly showed no significant association between immunosuppression type and prevalence of obesity at 1 year after LT: tacrolimus versus other (odds ratio [OR], 1.18; $P = 0.702$), cyclosporine (CSA) versus other (OR, 0.78; $P = 0.651$), and tacrolimus versus CSA (OR, 1.58; $P = 0.347$).[44] Although sirolimus-based immunosuppression was associated with less weight gain posttransplant in a large renal transplant population, no data are available in LT.[45] At this time, we do not suggest making any changes to the standard immunosuppression regimen based on recipient BMI.

Long-term Weight Gain and the Development of Metabolic Syndrome

One of the greatest concerns for long-term complications in obese LT recipients is the development and management of posttransplant metabolic syndrome.[46] Up to 46% of patients will develop post-LT metabolic syndrome, with the greatest risk seen in those with BMI of 30 kg/m^2 or greater pre-LT.[43,44,46] Pretransplant obesity has been shown to be a strong risk factor for posttransplant weight gain[47,48]). Even among 37 obese cirrhotic patients enrolled in an intensive pretransplant weight loss program (and who achieved target BMI <35 kg/m^2), 60% gained weight to a BMI greater than 35 kg/m^2 after LT.[18] Posttransplant obesity (class II or greater) increases the risk of posttransplant diabetes, a strong predictor of decreased survival after LT,[49,50] as well as post-LT nonalcoholic steatohepatitis.[47] The risk of new onset DM may be further heightened by corticosteroids and/or calcineurin-inhibitor use.[51] We recommend early dietary intervention and/or referral to weight management specialist in all patients with BMI greater than 35 after LT. Close monitoring of blood sugar in all patients, with particular focus on patients with pretransplant obesity, remains an important part of post-LT care.

Weight Loss Posttransplantation

Although there are no large studies evaluating the efficacy of weight loss programs after LT, lifestyle modifications including regular exercise are recommended for all LT recipients. Orlistat (Xenical), a reversible inhibitor of pancreatic lipase that prevents absorption of triglycerides resulting in modest weight loss, was used in an underpowered study of 15 post-LT patients for a total of 24 weeks. This resulted in a significant reduction in waist circumference (mean reduction of 13 cm from 110 cm at the start to 97 cm posttreatment; $P < 0.01$) but did not lead to a significant weight loss at 6 months (−9.8 kg [2.7]) or 12 months (−9.2 kg [5.5]).[52] At least 9 patients demonstrated a reduction in CSA troughs by approximately 50% while on Orlistat, despite spacing out the medications as recommended by the package insert.[53–56] Therefore, the use of Orlistat to manage obesity is currently limited to clinical trials, and we do not recommend its use outside this setting.

Several studies have evaluated bariatric surgery after LT, all reporting successful weight reduction (Table 1). A systematic review on bariatric surgery in LT recipients consisted only of case reports and series with great heterogeneity. Among 22 patients, SG was performed in 11 patients, Roux-en-Y gastric bypass in 10, and biliopancreatic diversion in 1, within 0.8 to 5.9 years of LT using open, laparoscopic or robotic techniques. Patients' mean BMI was 44.5, and weight loss ranged from 41% to 64.7% of excess weight in 6 to 36 months or longer of follow-up. There was a 33% reoperation rate reported by Lin et al,[21] and a 13.6% 1-year postoperative all-cause mortality rate, thought to be unrelated to surgery.[22] SG was a preferred procedure, due to the preservation of endoscopic access to the biliary system and absorptive capacity of immunosuppressive medications. Indeed, dose and serum levels of immunosuppressive agents remained stable after SG.[57] However, the effect of SG on the absorption of medications that are affected by pH and partial gastric absorption, such as mycophenolate mofetil, are unknown. Larger prospective studies are needed before post-LT bariatric procedures can be routinely recommended.

Long-term Patient and Graft Survival in Obese LT Recipients

Data regarding the association between class III obesity and posttransplant outcomes are conflicting. In a UNOS Registry study evaluating all U.S. LT from 1987 to 2007, recipients with BMI of 40 kg/m^2 or greater experienced higher rates of death compared with those with a BMI of 18.5 to 39.9 kg/m^2.[58] In contrast, 3 UNOS-based studies evaluating the more contemporary LT experience through 2014 refuted the association between class III obesity and posttransplant survival (Table 3).[4,30,60] One-year patient and graft survival for recipients with BMI of 40 kg/m^2 or greater ranged from 88% and 83% versus 88% and 85% for recipients with BMI of 18.5 to 30 kg/m^2 (P = NS), and there was no significantly association between BMI of 40 kg/m^2 or greater and model for ESLD at transplant.[4] LT also conferred overall survival benefit in ESLD patients with class III obesity, with an 85% decreased adjusted relative risk of death after LT compared with remaining waitlisted.[28]

Posttransplant death from cardiovascular disease (13% vs 12%), graft failure (15% vs 15%), and cerebrovascular disease (3% vs 3%) were similar between recipients with BMI of 40 kg/m^2 or greater (class III obesity) compared with recipients with BMI 18.5 to 39.9 kg/m^2.[58] However, some differences in causes of death after transplant have been identified among LT recipients with class III obesity, who experienced higher rates of death from infections (26% vs 22%; P = 0.02) and lower rates of death from malignancy (8% vs. 12%; P = 0.004).[58]

Recommendation—Taking these studies in aggregate, we recommend against using BMI greater than 40 as a strict contraindication to LT. Rather, patients with BMI greater than 40 should be evaluated for obesity-associated comorbidities, such as CAD and diabetes, which are known to be associated with adverse post-LT outcomes.

There are not sufficient data to support a particular immunosuppressive regimen in obese LT recipients, so immunosuppression in obese LT recipients should be managed similarly as in the nonobese LT recipient.

Early and aggressive interventions for weight management and close monitoring and proactive management of metabolic complications are recommended in this population.

Area for Future Study—The optimal dosing of the common immunosuppressants in obese LT recipients, including those who have undergone bariatric surgery, remains unknown. Whether certain immunosuppressive agents/regimens can reduce the development of metabolic syndrome in this population warrants future study.

CONCLUSIONS

Despite the rapidly growing population of obese patients with ESLD, there remains limited evidence-based recommendations to guide LT evaluation and management. in this cohort. Although each transplant program must develop their own guidelines when caring for this unique population, it is important that the decisions be made with current limitations in mind. After extensive review of the literature, we have concluded that there are not good data to support that patients with class II and II obesity have inferior LT outcomes when compared to patients with a normal BMI. Although current available data are retrospective in nature, and susceptible to patient selection bias, the apparently similar outcomes make limiting access to transplant based on BMI alone a difficult policy to support. Although recent studies suggest equivalent graft and patient survival in obese LT recipients, long-term outcomes are still being investigated. By understanding the current limitations in our knowledge and focusing research efforts accordingly, the LT community can continue to adapt and achieve excellent outcomes in our ever-increasing obese population.

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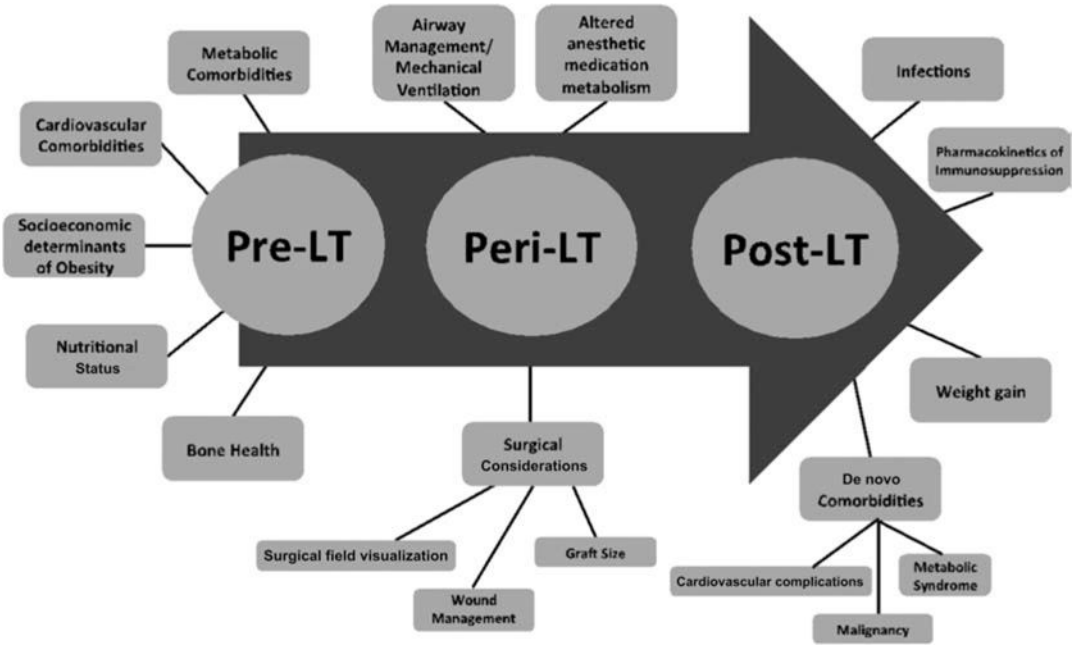

FIGURE 1.

Conceptual diagram of the pretransplant, peritransplant and posttransplant challenges in the obese liver transplant patient.

TABLE 1

Studies of bariatric surgery in patients before, during, and after liver transplant

Timing of surgery	Author, year	N	Type	Mean BMI kg/m^2 Pre → postsurgery[c]	Deaths	Complications
Pretransplant	Lin et al, 2013[19]	20[a]	SG	48 → 34	0	Wound infections (n = 2) Staple line leak (n = 1) Bleeding (n = 1) Transient encephalopathy (n = 1) Renal insufficiency (n = 1)
	Takata et al 2008[20]	6	SG	50 → 40	0	Bleeding and ascites (n = 1) UTI and encephalopathy (n = 1)
During transplant	Heimbach et al, 2012[18]	7	SG	48 → 29	0	Steroid-resistant rejection (n = 1) Excess weight loss, late HAT (n = 1) Leak from gastric staple line and early graft dysfunction (n = 1)
After transplant	Lin et al, 2012[21]	9	SG	41 → n/a	0	Mesh dehiscence (n = 1) Bile leak (n = 1) Dysphagia that required reoperation (n = 1)
	Al-Nowaylati et al, 2013[22]	7	RYGB	44 → 26 (mean, 42 mo)	1[b]	Wound complications (n = 3) Incisional hernias (n = 2) Malnutrition and ulcer requiring reversal of surgery (n = 1)
	Khoraki et al, 2016[23]	5	SG	47 → 35	0	Intraoperative bleeding and PVT (n = 1)

[a] 20 with cirrhosis, 6 who went on to LT; BMI decrease also includes 6 patients with renal disease undergoing renal transplant because data were presented for all patients.

[b] 2 patients in the series died, 1 was from metastatic esophageal carcinoma, the other from multisystem organ failure.

[c] Mean BMI before obesity surgery to mean BMI after surgery; change at 12 months unless specified.

BPD, biliopancreatic diversion; JIB, jejunoileal bypass; PVT, portal vein thrombosis; RYGB, Roux-en-Y gastric bypass.

TABLE 2

Perioperative morbidity in obese liver transplant recipients (including patients 2000 to present)

Complications	Study, year	Study period	Total n	BMI categories (kg/m^2): n	Rates	P^a
Primary graft nonfunction	LaMattina et al, 2012[31]	1997–2008	813	BMI, 18–25: n = 216	0%	0.32
				BMI, >35 to 40: n = 83	0%	
				BMI, >40: n = 47	2.1%	
	Mathur et al, 2013[35]	1996–2008	159	BMI, <25: n = 47	2%	NS
				BMI, ≥30: n = 58	3%	
Acute graft rejection	Fujikawa et al, 2006[36]	1990–2005	700	BMI, <25: n = 288	46%	NS
				BMI, ≥30: n = 167	40%	
	Conzen et al, 2014[33]	2002–2012	785	BMI, 18–24.9: n = 210	24%	NS
				BMI, 35.1–40: n = 77	27%	
				BMI, >40: n = 26	27%	
Biliary complications	Fujikawa et al, 2006[36]	1990–2005	700	BMI, <25: n = 288	23%	NS
				BMI, ≥30: n = 167	27%	
	LaMattina et al, 2012[31]	1997–2008	813	BMI, 18–25: n = 216	Operative: 6%	Operative: 0.82
					Nonoperative: 19%	Nonoperative: <0.001
				BMI, >35 to 40: n = 83	Operative: 8%	
					Nonoperative: 34%	
				BMI, >40: n = 47	Operative: 4%	
					Nonoperative: 30%	
Wound infection	Schaeffer et al, 2009[37]	1999–2003	167	BMI, <30: n = 143	4%	<0.001
				BMI, >35: n = 10	20%	
	Hakeem et al, 2013[38]	1994–2009	1325	BMI, 18.5–24.9: n = 643	20%	0.43
				BMI ≥35: n = 35	15%	
	LaMattina et al, 2012[31]	1997–2008	813	BMI, 18–25: n = 216	Reference	—
				BMI, >35 to 40: n = 83	HR, 4.0 (95% CI, 1.9–8.8)	<0.001
				BMI, >40: n = 47	HR, 6.3 (95% CI, 2.8–14.0)	<0.001
Wound dehiscence	Schaeffer et al, 2009[37]	1999–2003	167	BMI, <30: n = 143	1%	<0.001
				BMI, >35: n = 10	40%	
Vascular complications	Fujikawa et al, 2006[36]	1990–2005	700	BMI, <25: n = 288	9%	NS

Complications	Study, year	Study period	Total n	BMI categories (kg/m^2): n	Rates	P^a
				BMI, ≥30: n = 167	7%	
	LaMattina et al, 2012[31]	1997–2008	813	BMI, 18–25: n = 216	HAT: 3%	HAT: 0.75
					PVT: 5%	PVT: 0.31
				BMI, >35 to 40: n = 83	HAT: 7%	
					PVT: 10%	
				BMI, >40: n = 47	HAT: 4%	
					PVT: 6%	
	Tanaka et al, 2013[39]	2000–2006	507	BMI, 18.5–25: n = 162	5%	NS
				BMI, 35.1–40: n = 30	7%	
				BMI, >40: n = 14	8%	
	Hakeem et al, 2013[38]	1994–2009	1325	BMI, 18.5–24.9: n = 643	5%	0.24
				BMI, ≥35: n = 35	1%	
Reoperation	Conzen et al, 2014[33]	2002–2012	785	BMI, 18–24.9: n = 210	7%	0.47
				BMI, 35.1–40: n = 77	13%	
				BMI, >40: n = 26	8%	
	Nair et al, 2009[3]	2005–2007	93	BMI, ≤30: n = 125	10%	NS
				BMI, 35–39.9: n = 19	5%	
				BMI, ≥35: n = 8	25%	
Overall infections	Hillingso et al, 2005[34]	1990–2003	40	BMI, <30: n = 20	20%	NS
				BMI, ≥30: n = 20	40%	
	Hakeem et al, 2013[38]	1994–2009	1325	BMI, 18.5–24.9: n = 643	50%	0.047
				BMI, ≥35: n = 35	63%	

[a] Actual *P* values shown when reported in the study.

IQR, interquartile range; HAT, hepatic artery thrombosis; DVT, deep venous thrombosis; OLT, orthotopic liver transplantation; HCC, hepatocellular carcinoma.

TABLE 3

Posttransplant mortality and causes of death among obese liver transplant recipients (including patients transplanted from 2000 to present)

Study, year	Study period	Total (N)	BMI categories (kg/m^2), n	Mortality rates	*P*
Hillingso et al, 2005[34]	1990–2002	40	BMI, < 30: n = 20	65% (13/20)	0.01
			BMI, > 30: n = 20	30% (6/20)	
Fujikawa et al, 2006[36]	1990–2005	700		**1 y patient survival**	
			BMI, < 25: n = 288	82%	NS
			BMI, 25–30: n = 245	87%	NS
			BMI, ≥ 30: n = 167	86%	NS
			BMI, ≥ 35: n = 37	n/a)	NS
				5 y patient survival	
			BMI, < 25: n = 288	67%	NS
			BMI, 25–30: n = 245	73%	NS
			BMI, ≥ 30: n = 167	71%	NS
			BMI, ≥ 35: n = 37	n/a	NS
Pelletier et al, 2007[28]	2001–2004	4488		**HR**	
			BMI, <20: n = 181	1.28	0.15
			BMI, 20 to <25: n = 1161	1.00 (reference)	Ref
			BMI, 25 to <30: n = 1648	0.92	0.35
			BMI, 30 to <35: n = 944	0.84	0.10
			BMI, 35 to <40: n = 402	1.04	0.78
			BMI, ≥ 40: n = 152	1.16	0.43
Leonard et al, 2008[5]	1998–2006	1313	**Corrected for ascites**	**1 y Mortality—11%**	0.79
		NIDDK - 704	BMI, <18: n = 67	11%	
		Mayo - 609	BMI, 18.5–25: n = 561	11%	
			BMI, 25.1–30: n = 405	11%	
			BMI, 30.1–35: n = 178	8%	
			BMI, 35.1–40: n = 69	10%	
			BMI, >40: n = 33	3%	
				5 y Mortality—31%	0.79
			BMI, <18: n = 67	31%	

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Study, year	Study period	Total (N)	BMI categories (kg/m^2), n	Mortality rates	P
			BMI, 18.5–25: n = 561	20%	
			BMI, 25.1–30: n = 405	23%	
			BMI, 30.1–35: n = 178	12%	
			BMI, 35.1–40: n = 69	18%	
			BMI, >40: n = 33	20	
Dick et al, 2009[58]	1987–2007	71 446	BMI, 18.5 to <40: n = 68 172	36%	0.02
			BMI, ≥40: n = 1447	39%	
				Mortality 1 y post-LT	NS
Bambha et al, 2015[4]	2002–2011	45 551:	BMI, 18.5 to 24.9: n = 13262	12%	
			BMI, 25–29.9: n = 16329	11%	
			BMI, 30 to 34.9: n = 9639	11%	
			BMI, 35–39.9: n = 4062	12%	
			BMI, ≥40: n = 1396	12%	
Saab et al, 2014[59]	1990–2013	74 487	BMI, <30: n = 72 212		0.66
			BMI, >30: n = 2275		
				5 y Mortality	
Schlansky et al, 2016[30]	2005–2014	80 221	BMI, < 30: n = 49 969	21.2%	0.45
			BMI, 30–35: n = 18 793	20.5%	
			BMI, 35.1–40: n = 8.356	21.5%	
			BMI, ≥40: n = 3103	21%	