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Obesity, transplantation, and bariatric surgery: An evolving solution for a growing epidemic

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The increasing obesity epidemic has major implications in the realm of transplantation. Patients with obesity face barriers in access to transplant and unique challenges in perioperative and postoperative outcomes. Because of comorbidities associated with obesity, along with the underlying end-stage organ disease leading to transplant candidacy, these patients may not even be referred for transplant evaluation, much less be waitlisted or actually undergo transplant. However, the use of bariatric surgery in this population can help optimize the transplant candidacy of patients with obesity and end-stage organ disease and improve perioperative and postoperative outcomes. We review the impact of obesity on kidney, liver, and cardiothoracic transplant candidates and recipients and explore potential interventions to address obesity in these populations.

KEYWORDS
clinical decision-making, clinical research/practice, obesity, organ transplantation in general, recipient selection

1 | INTRODUCTION

Obesity is a worldwide epidemic. In 2005, 25% of the world population was overweight (as defined by body mass index [BMI] 25-29.9 kg/m^2) and 10% was obese (BMI > 30 kg/m^2).[1] By 2030, the prevalence is projected to reach 38% overweight and 20% obese. In the United States, the rates of obesity in 2014 were 35% of men and 40% of women.[2] The health-related ramifications of obesity have been well documented, including but not limited to cardiovascular disease, diabetes mellitus (DM), and cancer.[3-5] In patients with end-organ disease, obesity-related comorbidities can influence access to transplant, technical aspects of the transplant operations, and posttransplant outcome. Although class 1 obesity (BMI 30-34.9 kg/m^2) is not typically a contraindication, class 2 (BMI 35-39.9 kg/m^2) and class 3 (BMI > 40 kg/m^2) obesity can be relative or absolute contraindications to transplant. Findings from a survey of American Society of Transplant Surgeons (ASTS) members administered by our task force showed

that for kidney transplant (KT) candidates, the average BMI cutoff considered to be a relative and absolute contraindication was 38 and 41 kg/m^2, respectively. For liver transplant (LT) candidates, these cutoffs were 40 and 45 kg/m^2, and for thoracic transplant candidates, they were 35 and 38 kg/m^2.

Optimal posttransplant outcomes are desirable for the individual recipient and from the perspective of responsible stewardship of limited donor organs. Studies examining the impact of obesity on transplant outcomes are limited by a lack of consensus not only of a commonly accepted definition of obesity but also of a standard approach to assessment of obesity. Despite these limitations, known comorbidities associated with obesity, such as DM, cardiovascular disease, obstructive sleep apnea, metabolic syndrome, and impaired pulmonary function, can affect transplant outcomes. These cardiometabolic risks are compounded by the increased incidence of hyperlipidemia, hypertension, and DM observed with immunosuppressive drugs. Other considerations include the challenges of dosing immunosuppressive and other medications, especially lipophilic agents that are affected by the variability in the volume of distribution in patients with obesity.

Given the impact of obesity on transplant outcomes, many transplant centers have incorporated interventions that target obesity in their transplant candidates. Dietary education and interventions can be helpful but are resource intensive for a relatively modest level of impact.[6] For those failing nutritional intervention and medical therapy, bariatric surgery can be helpful. Currently, the 2 predominant procedures are laparoscopic sleeve gastrectomy (LSG) and laparoscopic Roux-en-Y gastric bypass (LRYGB). Although both procedures achieve 60%-80% excess body weight loss (%EBWL) within 18-24 months, the mechanism differs insofar as LSG is a restrictive procedure involving resection of the greater curve of the stomach and LRYGB is a restrictive/malabsorptive procedure that entails the creation of a gastric pouch and formation of a Roux-en-Y gastrojejunostomy.

The literature on patients with end-stage renal disease (ESRD) and concurrent obesity has generally shown bariatric surgery to have a positive impact on access to KT as well as posttransplant outcomes, but uncertainties remain regarding the optimal timing of bariatric surgery, either pretransplant or posttransplant. For KT candidates, 62.3% of transplant surgeons surveyed preferred bariatric surgery pretransplant, whereas 23.6% preferred posttransplant bariatric surgery. For LT candidates, however, only 29.0% and 30.3% of surgeons preferred bariatric surgery either pretransplant or posttransplant, respectively. This likely reflects the less robust evidence base for bariatric surgery in this patient population, with questions remaining regarding overall impact on transplant outcomes as well as appropriate timing of bariatric surgery. For cardiothoracic transplant candidates, the literature is more limited regarding the use of bariatric surgery, as evidence is only beginning to emerge in this population. One potential benefit for early bariatric surgery, particularly for patients with chronic organ disease, is the potential for weight loss to prevent progression to end-stage organ failure.[7] However, the focus of this report is that of patients who already have end-stage organ failure, and we do not cover the scope of chronic disease before organ failure.

With the pervasiveness of obesity in potential transplant candidates, there is a need for increased awareness and further education of all providers who care for this patient population. Of all ASTS members surveyed, only 64.2% of respondents expressed interest in attending a course to learn more about bariatric surgery and how to set up a bariatric transplant center. Here, we review the impact of obesity on KT, LT, and cardiothoracic transplant candidates and recipients and explore potential interventions to address obesity in these populations.

2 | KIDNEY TRANSPLANT

2.1 | Access to KT

Like the rest of the US population, the ESRD population is becoming progressively more obese.[8] Obesity-related comorbidities including cardiovascular disease, DM, and cancer can all affect progression of chronic kidney disease (CKD) as well as morbidity preventing potential listing for kidney transplant (KT).[3-5] However, there is an "obesity paradox" for patients on hemodialysis. There are data suggesting that patients with higher BMIs (>27 to 27.8 kg/m^2) have better outcomes on dialysis compared with patients with lower BMIs (<21.8 to 23.1 kg/m^2).[9,10] In ESRD patients, higher BMI associated with visceral fat or abdominal obesity (potential indicators of metabolic syndrome) increases the risk of DM and cardiovascular disease, whereas higher BMI with normal to high muscle mass or favorable waist circumference may confer some protection.[4,11-17] Further complicating the picture, it has been suggested that subcutaneous fat may be a marker of nutritional status in patients receiving hemodialysis, whereas visceral fat may be associated with a more inflammatory state.[18,19]

Despite the potential protective effect of obesity in patients on dialysis, KT still provides a clear survival advantage over dialysis.[20] Given these interacting factors, a more nuanced approach to the management of obesity is desirable to increase access to transplant, as well as increase the likelihood of operative technical success and long-term posttransplant outcomes. The use of weight assessment, often using BMI, is common, although controversial, and can occur even at the referral level.[21-23]

Once listed, patients with obesity continue to face lower rates of transplant and higher likelihood of organ offer bypass, and this is further compounded by sex-related differences, with women less likely to be transplanted with BMI > 25 kg/m^2.[8,24] Paradoxically, programs that have become "more conservative" after receiving a low-performance Scientific Registry of Transplant Recipients (SRTR) report are more likely to remove patients with BMI ≤ 24 kg/m^2, rather than higher-BMI patients, suggesting an underlying appreciation for reasonable outcomes in patients with obesity who are otherwise considered good surgical candidates.[25]

2.2 | Graft and patient outcomes

The survival benefit of transplant over dialysis for patients with obesity has been established (Figure 1), although the benefit is lower at higher BMIs, particularly BMIs > 40 kg/m^2, and there are suggestions that certain subgroups have inferior outcomes.[20,26,27] It is similarly well established that graft and patient survival rates in patients with obesity are inferior.[28] This pattern follows a U-shaped distribution, as patients with either lower or higher than normal range BMI (either ≤20 or ≥26 kg/m^2) have worse outcomes following transplant.[6,29] These results are likely due to some combination of visceral fat effect, lean muscle mass or sarcopenia, frailty, propensity for diabetes, and other obesity-related comorbidities.[30,31] Interestingly, significant posttransplant weight gain (>20% in the first year or 10% in the second year) or weight loss (>5%) has been associated with decreased patient survival, suggesting that unintentional nutritional or metabolic states that result in large swings in weight are deleterious.[32] Preexisting DM before transplant has also been associated with increased mortality in the first 10 years after transplant.[33]

Consistent with the model of obesity as an inflammatory state, obesity has been associated with increased biopsy-proven rejection, as well as delayed graft function.[34-37] Posttransplant obesity or visceral adiposity is further associated with the development of cardiovascular disease, hypertension, and posttransplant DM.[38,39] Many of these comorbidities have an inflammatory component, which may be partially mitigated by controlled weight management. Complicating this issue, obesity can also affect immunosuppression, with tacrolimus overdosing more common among patients with obesity.[40]

There are technical aspects to KT that can be more difficult with obesity. Some techniques, such as caval extensions in deceased donor right kidneys, have been developed to address these issues. However, particularly for those with obesity and significant iliac arterial disease, the operation is technically more challenging and occasionally prohibitive. Morbidity is affected—recipients with BMI values > 30 kg/m^2 may have up to a 4-fold increase in surgical site infections (SSIs) and a nearly 3-fold increase in hernias.[41] The incidence of SSIs has been reported to range from 20% to 40% in recipients with BMI values > 40 kg/m^2.[42] Despite these complication risks, overall physical quality of life is similar for those who are overweight or obese following transplant, although costs are higher for those with BMI values > 40 kg/m^2.[43,44] Nonetheless, it is important to note that the presence of SSIs correlates with worse graft survival.[45]

The application of minimally invasive techniques to KT, such as robotic surgery, has shown promising results compared with open KT.[46] Robot-assisted KT (RAKT) has resulted in statistically significant reduction in SSIs in a cohort of recipients with obesity.[47,48] Additionally, a matched-pair cohort study comparing recipients of robotic KT and a historical open KT cohort (28 patients each arm) found comparable patient and graft survival rates.[46] RAKT seems to be a safe approach with a reduced complication rate in patients with obesity.

2.3 | Treatment options for KT patients with obesity

Weight loss is difficult, particularly for those with ESRD. For patients with obesity and CKD, particularly if on dialysis, pharmacological options are limited and usually ineffective. Traditionally, bariatric surgery has been thought to be risky for patients with CKD.[49] However, as the preferred approach has migrated from LRYGB to LSG,[50] there has been increased interest, particularly for patients requiring dialysis.[51] For those patients with CKD who are predialysis, bariatric surgery may also improve effective renal function, with acceptable morbidity and mortality.[52,53] Furthermore, pretransplant LSG increases access to the transplant waitlist and improves posttransplant outcomes (Figure 2).[54-56] Granular studies on posttransplant bariatric surgery are small, but the
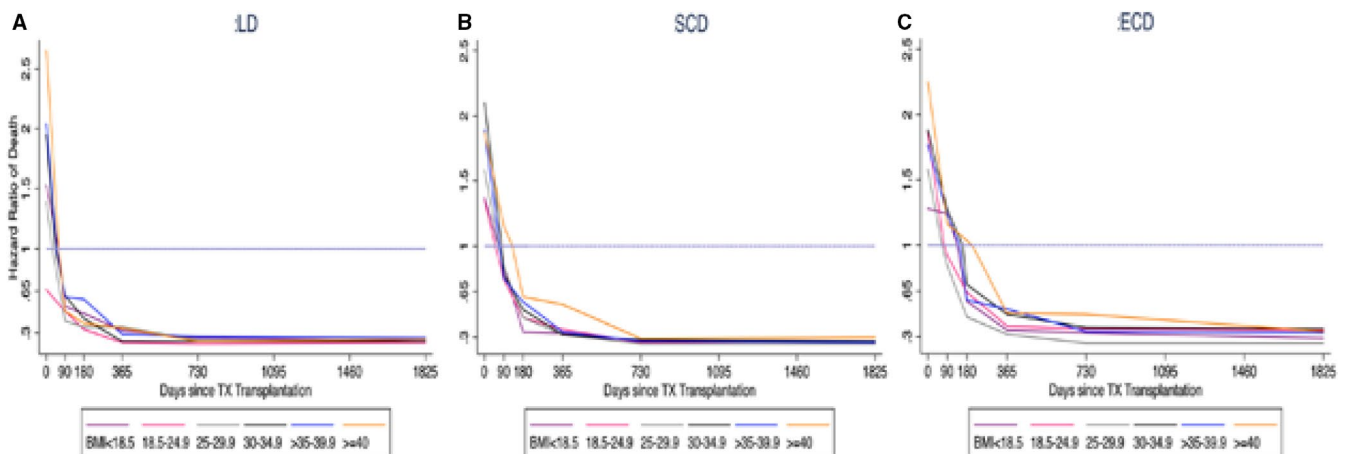
FIGURE 1 The survival benefit of kidney transplant in obese patients. The figure shows the multivariate adjusted hazard ratio for death in recipients of a living donor (LD; A), standard criteria deceased donor (SCD; B), and expanded criteria deceased donor (ECD; C) grouped by BMI compared with patients of the same BMI who had been on dialysis for equal lengths of time but had not yet received a kidney transplant (reference group denoted in blue with as relative risk of 1.0 in each figure). Reproduced from original publication Gill JS, et al. *Am J Transplant*. 2013;13(8):2083-90. Reproduced with permission from Wiley Publishing Co [Color figure can be viewed at wileyonlinelibrary.com]

A

B

FIGURE 2 A, Short-term outcomes in recipients of kidney transplant after undergoing laparoscopic sleeve gastrectomy (LSG) compared with controls (recipients of kidney transplants with similar BMI who did not undergo LSG). MI, myocardial infarction; CVA, cerebrovascular accident; TIA, transient ischemic attack. Reproduced fro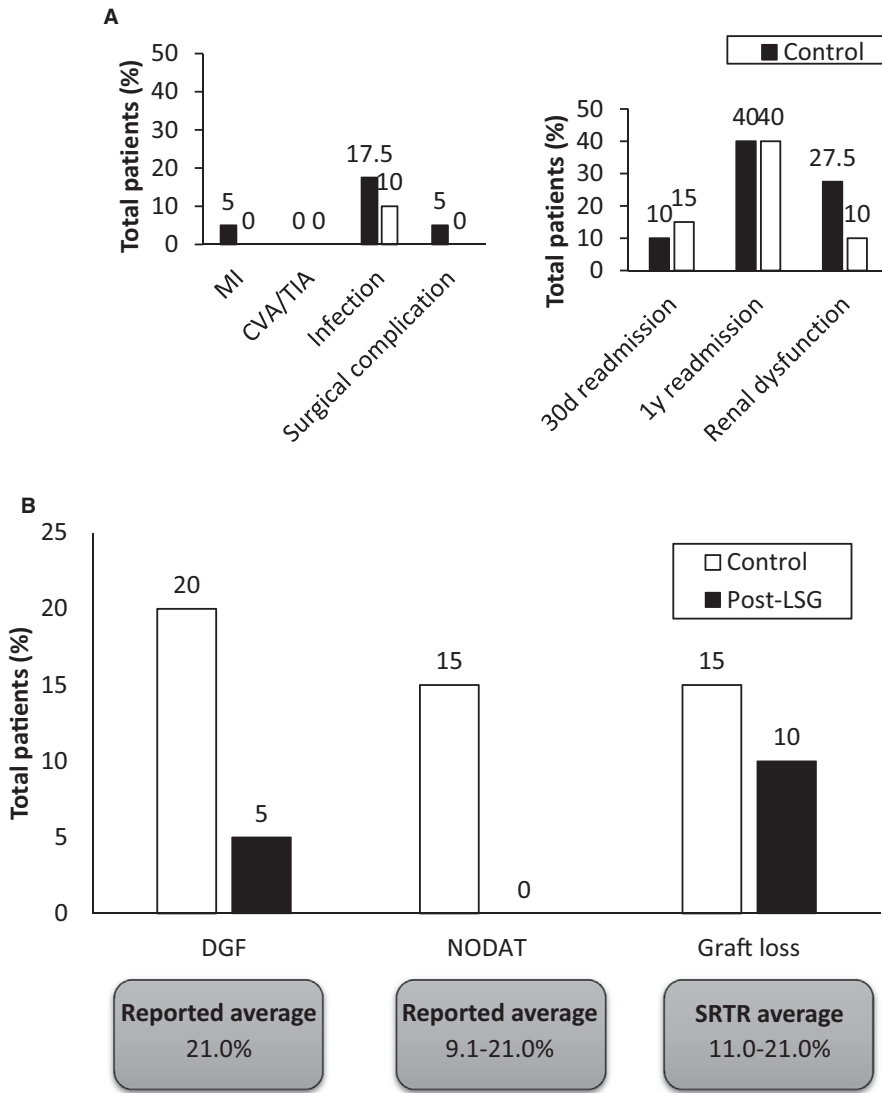m original publication Kim Y, et al. *Am J Transplant*. 2018;18(2):410-416. B, Long-term outcomes in recipients of kidney transplant after undergoing laparoscopic sleeve gastrectomy (LSG) compared with controls (recipients of kidney transplants with similar BMI who did not undergo LSG). Abbrev. DGF: delayed graft function, NODAT: new-onset diabetes after transplant, SRTR: Scientific Registry of Transplant Recipients. Reproduced from original publication Kim Y, et al. *Am J Transplant*. 2018;18(2):410-416

risk profile appears to be acceptable, with similar improvement in co-morbidities seen in solid organ transplant recipients as compared with the general population.[57] A retrospective study evaluating bariatric surgery before and after KT compared with propensity-matched nonbariatric surgery controls from the OPTN database found that those who underwent bariatric surgery (either before or after KT) had significantly decreased allograft failure and mortality.[58] However, the risks of complications and mortality after bariatric surgery in solid organ transplant recipients remain unclear and need further investigation.

2.4 | Conclusions and Recommendations

- KT results in a survival benefit compared with dialysis or wait-listed patients in all classes of obesity.
- Patient and graft survival after KT exhibit a U-shaped phenomenon, where those at either extreme of BMIs have impaired outcomes, although survival benefit is still maintained.
- Pretransplant sleeve gastrectomy and Roux-en-Y gastric bypass have been shown to be safe and efficacious, in addition to increasing access to the transplant waitlist and improving post-transplant outcomes.

- As the survival benefit of KT exists across BMIs, timing of KT relative to obesity intervention may be influenced by anticipated time on the transplant waitlist (or availability of living donors). For candidates with shorter anticipated wait times, proceeding with transplant followed by bariatric surgery is reasonable, but with longer anticipated wait times, the candidate may benefit from bariatric surgery first.

3 | LIVER TRANSPLANT

3.1 | Access to LT

The US obesity epidemic has led to a dramatic rise in obesity-related liver disease and the number of patients who require LT for decompensated nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), or associated hepatocellular carcinoma.[59] While only a minority of patients with obesity-related liver disease

(4% of NAFLD and 20% of NASH) will progress to cirrhosis and potential consideration for LT, the vast number of patients affected by obesity drives the increased demand.[60,61] In fact, NAFLD has become the second most common indication for listing and the third most common indication for transplant.[62,63]

Despite the increased incidence of NAFLD and resultant need for transplant, an analysis of waiting list outcomes from 2002 to 2006 demonstrated that patients with obesity were less likely to be listed for or undergo transplant.[64] More detailed analysis demonstrated that this was at least partly due to fewer Model for End-Stage Liver Disease (MELD) exceptions being granted, along with a higher likelihood of offer rejections, resulting in a nearly 30% lower transplant rate.[64] The reluctance to consider patients with obesity for transplant may have been driven in part by initial SRTR data, which indicated reduced posttransplant survival for LT recipients with obesity.[65] Importantly though, this study had a relatively small proportion of patients in the higher BMI cohorts (5% with BMI 35-40 kg/m^2 and 2% with BMI > 40 kg/m^2), with no adjustment for ascites. Subsequent analyses also using SRTR data based on a more contemporary data set, as well as a multicenter prospective database, demonstrated similar outcomes for both patient and graft survival for transplant recipients with and without obesity.[26,66-68]

3.2 | Graft and patient outcomes

Patients with obesity tend to gain weight after transplant and a significant proportion develop metabolic syndrome.[69] LT recipients who develop posttransplant metabolic syndrome have higher risk of vascular events (stroke, transient ischemic attacks, myocardial infarction, acute coronary syndrome, and sudden cardiac death).[70] The increased incidence of posttransplant DM is also associated with decreased survival rate after LT.[71]

Surgical complications, including wound infections, dehiscence, biliary complications, and overall infection rate after LT are increased (in some studies 4- to 6-fold) in patients with BMI > 35 kg/m^2.[72,73] A number of studies have reported longer ICU and hospital lengths of stay (LOSs), as well as increased rates of discharge to a skilled nursing or rehabilitation facility in LT recipients with obesity.[65,72,74,75] Other studies have shown mixed outcomes in terms of both short-term morbidity and long-term survival.[65,68,76-78] Regardless of these varied results, recent cohorts suggest similar posttransplant survival between recipients with and without obesity.[73,79] Furthermore, a survival benefit with LT is observed in candidates with all categories of obesity.[26]

Patients with obesity and NASH are reported by some groups to have equivalent graft and patient survival compared with those with other causes of liver disease.[80,81] However, NASH recipients also had increased operative time, blood loss, and hospital LOS.[81] Another study noted that mortality within 4 months of LT was twice as high in patients with NASH compared with those without and that patients with obesity and NASH, along with a high-risk phenotype

(age >60 years, BMI > 30 kg/m^2, concomitant hypertension, and DM), had lower 5-year survival rates compared with NASH recipients without the phenotype.[82]

Future directions for research to guide patient selection and interventions to optimize short- and long-term outcomes after LT in patients with obesity may benefit from a consensus conference to establish uniform (1) categories of obesity, (2) approaches to measure type (visceral/peripheral) and degree of obesity in patients with end-stage liver disease (ESLD), (3) assessment of key comorbidities associated with obesity and liver disease, (4) pretransplant and posttransplant interventions to enhance muscle mass and mitigate metabolic syndrome including recurrent disease posttransplant, and (5) criteria to measure postintervention success.

3.3 | Treatment options for LT patients with obesity

Currently, options for managing obesity in the transplant population similar to the nontransplant population and includes diet, exercise, and bariatric surgery. Given the effect of obesity on perioperative and postoperative outcomes, weight loss is likely beneficial for LT recipients. However, optimal times for weight loss interventions and best method(s) remain unclear (Table 1).[83]

3.3.1 | Pretransplant obesity management

Certainly, management of obesity before transplant is beneficial as it can improve candidacy for transplant and reduce both the technical challenges of operating in patients with obesity and the attendant perioperative complications. While there is limited information regarding the effects of diet and exercise on pretransplant weight loss, a few studies have demonstrated the beneficial effect of both aerobic exercise and caloric restriction in patients with compensated cirrhosis vis-à-vis improved insulin resistance and liver enzymes, as well as decreased body fat and BMI.[84-87] Two separate studies showed a loss of 10% total body weight to be associated with a reduction in fibrosis.[88,89]

Bariatric surgery may be feasible for patients with compensated cirrhosis, though it is less commonly an option for waitlisted patients given the risk of elective surgery for patients with decompensated liver disease. LSG has advantages over LRYGB in patients with compensated cirrhosis given (1) the technical ease of the procedure and therefore shorter operative time and (2) preservation of the gastrointestinal tract for creation of a possible Roux-limb as part of an LT or maintenance of access for potential future therapeutic endoscopic interventions.[55] Studies have shown the safety and efficacy of LSG in patients with ESLD.[55,90] Short-term complications included bleeding, wound infections, staple line leak, and hepatic encephalopathy, though there were not associated 30-day mortalities. The percent EBWL was 50%-62% at 1 year post LSG, and for those who underwent LT, this weight loss was maintained up to 1 year post LT, suggesting a protective effect of pretransplant LSG on posttransplant weight gain.

TABLE 1 Bariatric surgery and liver transplant case series, including those with pretransplant, simultaneous with transplant, and posttransplant bariatric surgery

Author	Time range	Cohort (n)	Bariatric procedure done	Timing of bariatric procedure to transplant	Endpoints and notable findings
Lin et al[55]	2006-2012	SG pre–liver (n = 20) and kidney (n = 6) transplant	SG	Pretransplant	7/20 transplanted, all met weight criteria. 1 staple line leak, 2 patients with transient hepatic decompensation
Safwan et al[121]	2007-2017	Patients currently undergoing LT with remote history of prior bariatric surgery Roux en Y (9) Sleeve gastrectomy (1) Jejunoileal bypass (1)	LRYGB SG Jejunoileal bypass	Pretransplant	30 d re-op rate, biliary complications, patient and graft survival at 1 and 2 y. No comparison group for complications, but similar patient/graft survival to those without bariatric surgery
Takata et al[90]	2004-2007	Patients with cirrhosis (n = 6) who underwent SG	SG	Pretransplant	Complications, excess weight loss, obesity-related comorbidities, transplant candidacy. Excellent weight loss noted, though short follow-up. No major complications but transient hepatic decompensation noted peri-operatively
Heimbach et al[87]	2006-2012	Obese patients undergoing LT who had a combined LT and SG (n = 7) and who had LT with no SG (N = 37)	SG	Simultaneous	Death, graft loss, operative complications were similar in two groups. Post LT metabolic outcomes superior in the combined group
Tariciotti et al[93]	2016	N = 1 obese patient with NAFLD and HCC undergoing combined LT + SG	SG	Simultaneous	Weight loss robust, no significant complications, follow-up only 5 mo, no comparison group
Nesher et al[92]	Not stated	LT and simultaneous SG (n = 3)	SG	Simultaneous	Normal allograft function, robust weight loss at 13 mo. No comparison group
Lin et al[55]	2007-2011	SG post LT (n = 8)	SG	Posttransplant	30-d complications include 3 re-ops. Weight loss robust, allograft function normal, improved metabolic parameters
Osseis et al[96]	2008-2015	SG post LT (N = 6)	SG	Posttransplant	Surgical outcomes, liver and kidney function tests, outcomes of obesity-related complications, excess weight loss
Tsamalaidze et al[122]	2010-2016	SG after LT (n = 12) and SG with no previous transplant (n = 36)	SG	Posttransplant	Case-control noted similar postoperative events, long-term weight loss, comorbidity resolution. Slightly longer hospital stay in those with prior LT
Elli et al[98]	2008-2014	Post solid organ transplant recipients undergoing sleeve gastrectomy and nontransplant patients undergoing sleeveb gastrectomy Kidney transplant (n = 6) Liver transplant (n = 2) Pancreas transplant (n = 2)	SG	Posttransplant	Percentage excess weight loss, perioperative and postoperative complications
Khoraki et al[97]	2008-2014	Post solid organ transplant patients undergoing SG Liver (n = 5) Also heart and kidney patients reported (total 10)	SG	Posttransplant	Robust weight loss, resolution or improvement of obesity-related co morbidities, normal allograft function. Splenectomy required in LT recipient due to bleeding, with subsequent PV thrombosis and need for TIPS

(Continues)

TABLE 1 (Continued)

Author	Time range	Cohort (n)	Bariatric procedure done	Timing of bariatric procedure to transplant	Endpoints and notable findings
Al-Nowaylati et al[95]	2001-2009	Patient who underwent open RYGB after OLT (n = 7)	RYGB	Posttransplant	Robust weight loss, improved glycemic control and Dyslipidemia control. One death and one reversal due to complications related to surgery

3.3.2 | Perioperative obesity management

Simultaneous bariatric surgery and LT (S-LT) is another approach to managing obesity in this patient population. The advantage of this approach includes addressing both obesity and liver disease in one operation, with potentially less patient discomfort and lower costs. The disadvantage lies in the fact that combining both surgeries creates a more complicated procedure. To examine this, Heimbach et al[87] compared outcomes between LT candidates who lost weight preoperatively using lifestyle modification (n = 37) to those patients who underwent S-LT (n = 7) due to failure of lifestyle modification. Their results demonstrated that the cohort who had S-LT had noninferior perioperative outcomes despite having a significantly higher preoperative BMI. Specifically, in patients undergoing the combined procedures, there were no deaths or graft losses. Complications included 1 leak from the gastric staple line and 1 patient with excess weight loss. There were no patients who developed posttransplant DM or steatosis, and all patients maintained substantial weight loss out to an average of 17 months (Figure 3). Taken together, this study suggests a role for bariatric surgery at the time of LT in carefully selected patients. A recent report from the same group reported on longer-term outcomes for 29 patients who underwent S-LT, including 13 patients more than 3 years out, demonstrating efficacy for achieving and maintaining weight loss as well as favorable metabolic profiles for those who underwent S-LT.[91] Two additional case reports of S-LT also supported safety and efficacy of the procedure.[92,93] The first reported case of simultaneous SG with a living donor LT recipient was described in 2017, resulting in post-transplant weight loss to BMI < 30 kg/m^2 within 2 months, as well as cure of DM.[94]

3.3.3 | Posttransplant obesity management

A noninvasive, structured multidisciplinary weight loss program remains the foundation of obesity management even in the posttransplant setting. If not successful, which is more likely for patients with severe obesity, delayed bariatric surgery after LT (D-LT) may be considered. In a series of RYGB after LT (n = 7), Al-Nowaylati et al[95] reported effective weight loss but concerning results included 1 death and 1 reversal due to complications of bariatric surgery. A matched case-control series of LSG in patients with (n = 12) vs without prior LT (n = 36) noted similar operative times and postoperative morbidity with no conversion to open surgery, though with a longer hospital LOS in those with a prior LT.[96] Other smaller series of D-LT note similar efficacy with weight loss and metabolic complications, though adhesions, bleeding issues, and longer operative time were described.[55,96-98]

3.4 | Conclusions and recommendations

- Obesity-related liver disease is projected to become the leading indication for LT in the next decade in the United States.
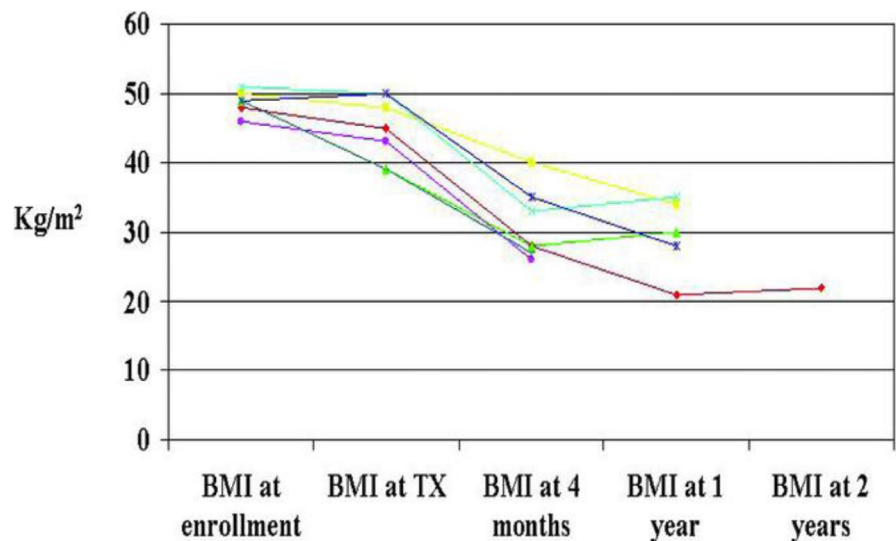- LT results in a survival benefit in all classes of obesity.

FIGURE 3 BMI trends for those patients who underwent combined liver transplant plus sleeve gastrectomy (N = 7). Mean follow-up is 17 mo. Reproduced from original publication Heimbach JK, et al. *Am J Transplant*. 2013;13(2):363-368 [Color figure can be viewed at wileyonlinelibrary.com]

- Recommendations based on low-to-moderate grade evidence suggest sleeve gastrectomy as the preferred bariatric surgical technique in LT candidates or recipients.
- Future studies should investigate comparative effectiveness of bariatric surgery timing in the LT population between S-LT and D-LT.

4 | CARDIOTHORACIC TRANSPLANT

4.1 | Access to cardiothoracic transplant

As all healthcare providers know, obesity is an epidemic worldwide, and this is no different in thoracic transplant. In a recent survey of thoracic transplant surgeons (2018 Obesity in Transplantation Task Force Survey), 60% of programs have a BMI threshold with 33% being an absolute and 50% a relative contraindication. Of survey responders, 75% have intervention programs for obesity, spanning the spectrum of interventions from dietary and lifestyle modifications to medical and surgical interventions. The presence of obesity thresholds, as well as the hesitancy of certain centers to surgically intervene on patients with both obesity and end-stage cardiopulmonary failure, significantly inhibits access to life-saving transplant therapies. If patients are able to be transplanted, their wait-time can be increased and access to suitable organs limited.[99]

4.2 | Graft and patient outcomes

As with other transplants, there is a tendency of patients to gain weight post cardiothoracic transplant,[100] and this can confound mobilization and infections. Functional status of patients with morbid obesity coupled with a risk for hidden sarcopenia drives a large portion of the concern. These patients with obesity have an increased risk for impaired sternal wound healing, with sternal nonunion/dehiscence,[101-103] which is a problem even without the added burden of immunosuppression. In patients with left ventricular assist devices (LVADs), obesity is correlated with driveline infections[104] which can also influence recovery after heart transplant.

The impact of obesity on outcomes posttransplant is not limited to the morbidity of wound healing but on survival as well.[105] Obesity predisposes recipients to increased cardiac allograft vasculopathy, cardiovascular diseases, and metabolic syndrome after heart transplant.[106] Patients with obesity are also at a higher risk of posttransplant mortality in both heart and lung transplant.[107-110] These outcomes are accentuated in patients with idiopathic pulmonary fibrosis where the risk of 90-day mortality is 1.71-fold higher with obesity, and this can significantly affect overall center performance.[107,108] Additionally, in LT recipients, obesity is associated with a significant 2-fold increase risk of primary graft dysfunction (PGD)[111] within 72 hours posttransplant and there is an increased risk of 40% occurrence of PGD for each additional 5-kg/m² increase in BMI.[111]

4.3 | Treatment options for cardiothoracic transplant patients with obesity

Treatment options for the patient with morbid obesity have relative pros and cons. Dietary, supplementation, and lifestyle modifications were used by all respondents in the ASTS Taskforce Survey. These approaches have some benefit, though the overall impact on the patient with end-stage cardiopulmonary failure can be limited. The relative sedentary nature of the disease courses, the impact on oxygen delivery, and limited mobility can hinder increased caloric expenditure (i.e., exercise). Socioeconomic impacts compound the issues. For many patients, the time-sensitive nature of their disease means that the likelihood of losing meaningful weight before becoming transplant ineligible is prohibitive. Pre–lung transplant weight loss significantly improves survival and decreases days on the ventilator,[112] so any intervention resulting in weight loss can have significant impacts on outcomes and survival. Patients with morbid obesity who are able to undergo LSG can facilitate weight loss and improve eligibility for transplant.[113,114] In patients with end-stage lung disease, select patients with obesity undergoing bariatric surgery can have improvement of their lung disease and function, as well as pulmonary hypertension, through the weight loss.[115,116]

In summary, obesity has significant negative impact on access to thoracic transplant. Furthermore, obesity negatively affects perioperative morbidity and mortality. When appropriate and feasible, LSG provides a strategy to facilitate weight loss and improvement in pretransplant symptoms and function as well as enhancing access.

## 4.4 | Conclusions and recommendations

- Bariatric surgery before thoracic transplant may lead to improved pulmonary function, access to transplant, and posttransplant outcomes.

5 | FINANCIAL CONSIDERATIONS FOR OBESITY INTERVENTION

The ASTS has previously shared the high cost of patients on the transplant waitlist. For example, the cost of maintenance pretransplant hemodialysis can easily be as high as $260 000 per year per covered life.[117] Even after transplant, average Medicare payments in the following 3 years after KT increase with higher BMI (Figure 4). LSG can have a significant positive financial and clinical impact in the KT population. Using LSG in a patient with obesity and advanced CKD or early ESRD can potentially allow these patients to be listed for a deceased donor KT or, even better, to receive a preemptive living donor KT. Additionally, small studies have shown that performing S-LT for patients with NASH prevents disease recurrence, thus avoiding the high cost

FIGURE 4 A, Average accumulated Medicare payments as a function of body mass index for select sample of deceased donor recipients who are alive with functioning graphs 3-y post–kidney transplant. Unpublished data, courtesy of Leah Crow, PharmD, and TS Diwan. B, Average accumulated Medicare payments as a function of body mass index for select sample of living donor recipients who are alive with functioning graphs 3-y post–kidney transplant. Unpublished data, courtesy of Leah Crow, PharmD, and TS Diwan [Color figure can be viewed at wileyonlinelibrary.com]

A

Average 3-Year Payments: Deceased Donor Recipient (n=8663)
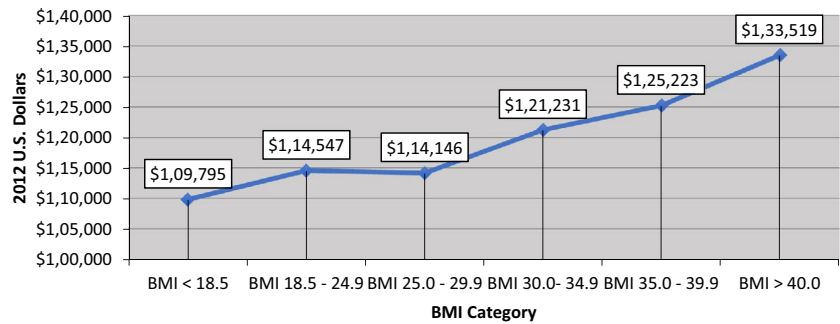
Mean 3-year Payments	N	Mean	Std. Dev	Std. Error	95% CI for Mean	
					Lower Bound	Upper Bound
BMI < 18.5	196	$109,795	$60,324	$4,309	$101,297	$118,293
BMI 18.5 - 24.9	2758	$114,547	$92,517	$1,762	$111,093	$118,002
BMI 25.0 - 29.9	3014	$114,146	$67,433	$1,228	$111,737	$116,554
BMI 30.0- 34.9	1824	$121,231	$75,451	$1,767	$117,766	$124,696
BMI 35.0 - 39.9	667	$125,223	$75,893	$2,939	$119,453	$130,993
BMI > 40.0	204	$133,519	$78,385	$5,488	$122,698	$144,340
Total	8663	$116,976	$78,704	$846	$115,319	$118,634

B

Average 3-Year Payments (n=3188)
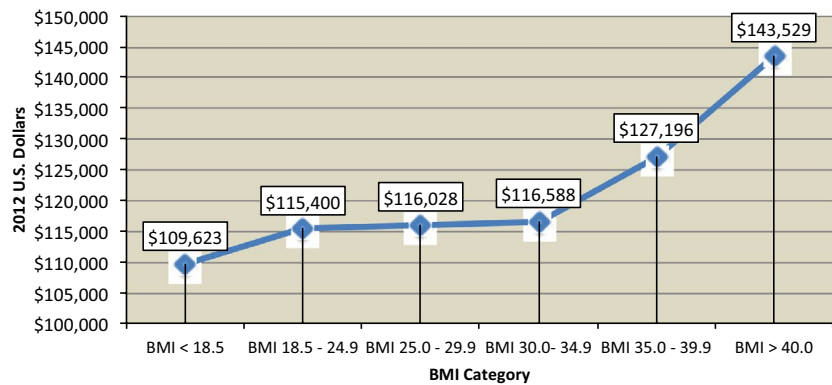
Mean 3-year Payments	N	Mean	Std. Deviation	Std. Error	95% CI for Mean	
					Lower Bound	Upper Bound
BMI < 18.5	94	$109,623	$42,770	$4,411	$100,863	$118,383
BMI 18.5 - 24.9	1127	$115,400	$50,487	$1,504	$112,449	$118,351
BMI 25.0 - 29.9	1072	$116,028	$50,887	$1,554	$112,978	$119,077
BMI 30.0- 34.9	635	$116,588	$49,965	$1,983	$112,694	$120,481
BMI 35.0 - 39.9	194	$127,196	$53,589	$3,847	$119,607	$134,784
BMI > 40.0	66	$143,529	$74,969	$9,228	$125,099	$161,959
Total	3188	$116,977	$51,314	$909	$115,195	$118,759

of potential graft failure and retransplant, with the 1-year additional cost of liver graft failure >$150 000.[91] In summary, consideration of bariatric surgery in the transplant population has early potential to positively affect the transplant process financially. However, there is a need for well-designed clinical trials as well as cost-effectiveness studies to support broader payor coverage of bariatric surgery before, or even during, transplant surgery.

6 | PHARMACOLOGY/ PHARMACOKINETICS

Bariatric surgery may result in altered absorption of medications, including immunosuppressive agents that are crucial in the posttransplant setting. RYGB in KT candidates and recipients has been shown to result in higher requirements of cyclosporine as well as significant differences in pharmacokinetics of tacrolimus, sirolimus, mycophenolic

acid, and mycophenolic acid glucuronide compared with nonbypass patients.[118,119] KT candidates who underwent LSG did not appear to have significantly different pharmacokinetics of tacrolimus (immediate or extended release) or mycophenolic acid, suggesting that post-LSG patients may not require dose modification out of the norm for transplant recipients.[120] However, a larger series demonstrated that both RYGB and LSG could be performed without requiring significant dosage adjustments of tacrolimus, mycophenolic acid, or prednisone, and indeed, stability of blood trough levels increased after bariatric surgery.[57] Therefore, with appropriate monitoring, immunosuppression may be well maintained in recipients of both RYGB and LSG.

7 | CONCLUSIONS AND FUTURE DIRECTIONS

Patients with obesity and concurrent end-stage organ failure face significant challenges in access to transplant as well as negative impacts on outcomes after solid organ transplant. Addressing obesity in select patients with bariatric surgery before transplant may improve access, facilitate an easier operation, as well as improve benefits of transplant. Bariatric surgery after transplant may also help to enhance the benefits from transplant under certain situations. Further investigation is needed to clarify optimal timing of bariatric surgery relative to transplant, as well as to evaluate the role of bariatric surgery for chronic organ disease before development of end-stage organ failure, and to assess the role of bariatric surgery for potential living donors with obesity.

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Kelly T, Yang W, Chen CS, Reynolds K, He J. Global burden of obesity in 2005 and projections to 2030. *Int J Obes (Lond)*. 2008;32(9):1431-1437.
2. Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD, Ogden CL. Trends in obesity among adults in the United States, 2005 to 2014. *JAMA*. 2016;315(21):2284-2291.
3. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation*. 1983;67(5):968-977.
4. Bray GA, Jablonski KA, Fujimoto WY, et al. Relation of central adiposity and body mass index to the development of

5. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. *Lancet*. 2008;371(9612):569-578.
6. DiCecco SR, Francisco-Ziller N. Obesity and organ transplantation: successes, failures, and opportunities. *Nutr Clin Pract*. 2014;29(2):171-191.
7. Ristow B, Rabkin J, Haeusslein E. Improvement in dilated cardiomyopathy after bariatric surgery. *J Card Fail*. 2008;14(3):198-202.
8. Segev DL, Simpkins CE, Thompson RE, Locke JE, Warren DS, Montgomery RA. Obesity impacts access to kidney transplantation. *J Am Soc Nephrol*. 2008;19(2):349-355.
9. Wolfe RA, Ashby VB, Daugirdas JT, Agodoa LY, Jones CA, Port FK. Body size, dose of hemodialysis, and mortality. *Am J Kidney Dis*. 2000;35(1):80-88.
10. Port FK, Ashby VB, Dhingra RK, Roys EC, Wolfe RA. Dialysis dose and body mass index are strongly associated with survival in hemodialysis patients. *J Am Soc Nephrol*. 2002;13(4):1061-1066.
11. Postorino M, Marino C, Tripepi G, Zoccali C; CREDIT (Calabria Registry of Dialysis and Transplantation) Working Group. Abdominal obesity and all-cause and cardiovascular mortality in end-stage renal disease. *J Am Coll Cardiol*. 2009;53(15):1265-1272.
12. Stefan N, Artunc F, Heyne N, Machann J, Schleicher ED, Haring HU. Obesity and renal disease: not all fat is created equal and not all obesity is harmful to the kidneys. *Nephrol Dial Transplant*. 2016;31(5):726-730.
13. Stefansson VTN, Schei J, Solbu MD, Jenssen TG, Melsom T, Eriksen BO. Metabolic syndrome but not obesity measures are risk factors for accelerated age-related glomerular filtration rate decline in the general population. *Kidney Int*. 2018;93(5):1183-1190.
14. Cerhan JR, Moore SC, Jacobs EJ, et al. A pooled analysis of waist circumference and mortality in 650,000 adults. *Mayo Clin Proc*. 2014;89(3):335-345.
15. Beddhu S, Pappas LM, Ramkumar N, Samore M. Effects of body size and body composition on survival in hemodialysis patients. *J Am Soc Nephrol*. 2003;14(9):2366-2372.
16. Kovesdy CP, Czira ME, Rudas A, et al. Body mass index, waist circumference and mortality in kidney transplant recipients. *Am J Transplant*. 2010;10(12):2644-2651.
17. Molnar MZ, Streja E, Kovesdy CP, et al. Associations of body mass index and weight loss with mortality in transplant-waitlisted maintenance hemodialysis patients. *Am J Transplant*. 2011;11(4):725-736.
18. Delgado C, Chertow GM, Kaysen GA, et al. Associations of body mass index and body fat with markers of inflammation and nutrition among patients receiving hemodialysis. *Am J Kidney Dis*. 2017;70(6):817-825.
19. Stenvinkel P, Gillespie IA, Tunks J, et al. Inflammation modifies the paradoxical association between body mass index and mortality in hemodialysis patients. *J Am Soc Nephrol*. 2016;27(5):1479-1486.
20. Gill JS, Lan J, Dong J, et al. The survival benefit of kidney transplantation in obese patients. *Am J Transplant*. 2013;13(8):2083-2090.
21. Lentine KL, Delos Santos R, Axelrod D, Schnitzler MA, Brennan DC, Tuttle-Newhall JE. Obesity and kidney transplant candidates: how big is too big for transplantation? *Am J Nephrol*. 2012;36(6):575-586.
22. Chan G, Soucisse M. Survey of Canadian Kidney Transplant specialists on the management of morbid obesity and the transplant waiting list. *Can J Kidney Health Dis*. 2016;3:2054358116675344.
23. Stenvinkel P, Ikizler TA, Mallamaci F, Zoccali C. Obesity and nephrology: results of a knowledge and practice pattern survey. *Nephrol Dial Transplant*. 2013;28(Suppl 4):iv99-iv104.

24. Gill JS, Hendren E, Dong J, Johnston O, Gill J. Differential association of body mass index with access to kidney transplantation in men and women. *Clin J Am Soc Nephrol*. 2014;9(5):951-959.

25. Schold JD, Buccini LD, Poggio ED, Flechner SM, Goldfarb DA. Association of candidate removals from the kidney transplant waiting list and center performance oversight. *Am J Transplant*. 2016;16(4):1276-1284.

26. Pelletier SJ, Maraschio MA, Schaubel DE, et al. Survival benefit of kidney and liver transplantation for obese patients on the waiting list. *Clin Transpl*. 2003;17:77-88.

27. Krishnan N, Higgins R, Short A, et al. Kidney transplantation significantly improves patient and graft survival irrespective of BMI: a cohort study. *Am J Transplant*. 2015;15(9):2378-2386.

28. Hoogeveen EK, Aalten J, Rothman KJ, et al. Effect of obesity on the outcome of kidney transplantation: a 20-year follow-up. *Transplantation*. 2011;91(8):869-874.

29. Meier-Kriesche HU, Arndorfer JA, Kaplan B. The impact of body mass index on renal transplant outcomes: a significant independent risk factor for graft failure and patient death. *Transplantation*. 2002;73(1):70-74.

30. Terjimanian MN, Underwood PW, Cron DC, et al. Morphometric age and survival following kidney transplantation. *Clin Transplant*. 2017;31(10). https://doi.org/10.1111/ctr.13066.

31. Chang SH, Coates PT, McDonald SP. Effects of body mass index at transplant on outcomes of kidney transplantation. *Transplantation*. 2007;84(8):981-987.

32. Chang SH, McDonald SP. Post-kidney transplant weight change as marker of poor survival outcomes. *Transplantation*. 2008;85(10):1443-1448.

33. Lim WH, Wong G, Pilmore HL, McDonald SP, Chadban SJ. Long-term outcomes of kidney transplantation in people with type 2 diabetes: a population cohort study. *Lancet Diabetes Endocrinol*. 2017;5(1):26-33.

34. Wu D, Dawson NA, Levings MK. Obesity-associated adipose tissue inflammation and transplantation. *Am J Transplant*. 2016;16(3):743-750.

35. Cannon RM, Jones CM, Hughes MG, Eng M, Marvin MR. The impact of recipient obesity on outcomes after renal transplantation. *Ann Surg*. 2013;257(5):978-984.

36. Nicoletto BB, Fonseca NK, Manfro RC, Goncalves LF, Leitao CB, Souza GC. Effects of obesity on kidney transplantation outcomes: a systematic review and meta-analysis. *Transplantation*. 2014;98(2):167-176.

37. Gore JL, Pham PT, Danovitch GM, et al. Obesity and outcome following renal transplantation. *Am J Transplant*. 2006;6(2):357-363.

38. el-Agroudy AE, Wafa EW, Gheith OE, Shehab el-Dein AB, Ghoneim MA. Weight gain after renal transplantation is a risk factor for patient and graft outcome. *Transplantation*. 2004;77(9):1381-1385.

39. Cron DC, Noon KA, Cote DR, et al. Using analytic morphomics to describe body composition associated with post-kidney transplantation diabetes mellitus. *Clin Transplant*. 2017;31(9):e13040.

40. Andrews LM, de Winter BCM, Tang J-T, et al. Overweight kidney transplant recipients are at risk of being overdosed following standard bodyweight-based tacrolimus starting dose. *Transplant Direct*. 2017;3(2):e129.

41. Humar A, Ramcharan T, Denny R, Gillingham KJ, Payne WD, Matas AJ. Are wound complications after a kidney transplant more common with modern immunosuppression? *Transplantation*. 2001;72(12):1920-1923.

42. Lynch RJ, Ranney DN, Shijie C, Lee DS, Samala N, Englesbe MJ. Obesity, surgical site infection, and outcome following renal transplantation. *Ann Surg*. 2009;250(6):1014-1020.

43. Zaydfudim V, Feurer ID, Moore DR, Moore DE, Pinson CW, Shaffer D. Pre-transplant overweight and obesity do not affect physical quality of life after kidney transplantation. *J Am Coll Surg*. 2010;210(3):336-344.

44. Kim Y, Chang AL, Wima K, et al. The impact of morbid obesity on resource utilization after renal transplantation. *Surgery*. 2016;160(6):1544-1550.

45. Sood A, Hakim DN, Hakim NS. Consequences of recipient obesity on postoperative outcomes in a renal transplant: a systematic review and meta-analysis. *Exp Clin Transplant*. 2016;14(2):121-128.

46. Oberholzer J, Giulianotti P, Danielson KK, et al. Minimally invasive robotic kidney transplantation for obese patients previously denied access to transplantation. *Am J Transplant*. 2013;13(3):721-728.

47. Tzvetanov I, D'Amico G, Benedetti E. Robotic-assisted kidney transplantation: our experience and literature review. *Curr Transplant Rep*. 2015;2(2):122-126.

48. Modi P, Pal B, Modi J, et al. Retroperitoneoscopic living-donor nephrectomy and laparoscopic kidney transplantation: experience of initial 72 cases. *Transplantation*. 2013;95(1):100-105.

49. Modanlou KA, Muthyala U, Xiao H, et al. Bariatric surgery among kidney transplant candidates and recipients: analysis of the United States renal data system and literature review. *Transplantation*. 2009;87(8):1167-1173.

50. Sheetz KH, Woodside KJ, Shahinian VB, Dimick JB, Montgomery JR, Waits SA. Trends in bariatric surgery procedures among patients with ESKD in the United States. *Clin J Am Soc Nephrol*. 2019;14(8):1193-1199.

51. Mozer AB, Pender JR, Chapman WHH, Sippey ME, Pories WJ, Spaniolas K. Bariatric surgery in patients with dialysis-dependent renal failure. *Obes Surg*. 2015;25(11):2088-2092.

52. Kassam A-F, Mirza A, Kim Y, et al. Long-term outcomes in patients with obesity and renal disease after sleeve gastrectomy. *Am J Transplant*. 2019. https://doi.org/10.1111/ajt.15650.

53. Friedman AN, Wahed AS, Wang J, et al. Effect of bariatric surgery on CKD risk. *J Am Soc Nephrol*. 2018;29(4):1289-1300.

54. Freeman CM, Woodle ES, Shi J, et al. Addressing morbid obesity as a barrier to renal transplantation with laparoscopic sleeve gastrectomy. *Am J Transplant*. 2015;15(5):1360-1368.

55. Lin MYC, Mehdi Tavakol M, Sarin A, et al. Laparoscopic sleeve gastrectomy is safe and efficacious for pretransplant candidates. *Surg Obes Relat Dis*. 2013;9(5):653-658.

56. Kim Y, Jung AD, Dhar VK, et al. Laparoscopic sleeve gastrectomy improves renal transplant candidacy and posttransplant outcomes in morbidly obese patients. *Am J Transplant*. 2018;18(2):410-416.

57. Yemini R, Nesher E, Winkler J, et al. Bariatric surgery in solid organ transplant patients: Long-term follow-up results of outcome, safety, and effect on immunosuppression. *Am J Transplant*. 2018;18(11):2772-2780.

58. Cohen JB, Lim MA, Tewksbury CM, et al. Bariatric surgery before and after kidney transplantation: long-term weight loss and allograft outcomes. *Surg Obes Relat Dis*. 2019;15(6):935-941.

59. Ascha MS, Hanouneh IA, Lopez R, Tamimi TA, Feldstein AF, Zein NN. The incidence and risk factors of hepatocellular carcinoma in patients with nonalcoholic steatohepatitis. *Hepatology*. 2010;51(6):1972-1978.

60. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice guideline by the American Gastroenterological Association, American Association for the Study of Liver Diseases, and American College of Gastroenterology. *Gastroenterology*. 2012;142(7):1592-1609.

61. Rinella ME. Nonalcoholic fatty liver disease: a systematic review. *JAMA*. 2015;313(22):2263-2273.

62. Wong RJ, Aguilar M, Cheung R, et al. Nonalcoholic steatohepatitis is the second leading etiology of liver disease among adults awaiting liver transplantation in the United States. *Gastroenterology*. 2015;148(3):547-555.

63. Singal AK, Guturu P, Hmoud B, Kuo YF, Salameh H, Wiesner RH. Evolving frequency and outcomes of liver transplantation based on etiology of liver disease. *Transplantation*. 2013;95(5):755-760.

64. Segev DL, Thompson RE, Locke JE, et al. Prolonged waiting times for liver transplantation in obese patients. *Ann Surg.* 2008;248(5):863-870.

65. Nair S, Verma S, Thuluvath PJ. Obesity and its effect on survival in patients undergoing orthotopic liver transplantation in the United States. *Hepatology.* 2002;35(1):105-109.

66. Leonard J, Heimbach JK, Malinchoc M, Watt K, Charlton M. The impact of obesity on long-term outcomes in liver transplant recipients-results of the NIDDK liver transplant database. *Am J Transplant.* 2008;8(3):667-672.

67. Dick AAS, Spitzer AL, Seifert CF, et al. Liver transplantation at the extremes of the body mass index. *Liver Transpl.* 2009;15(8):968-977.

68. Orci LA, Majno PE, Berney T, Morel P, Mentha G, Toso C. The impact of wait list body mass index changes on the outcome after liver transplantation. *Transpl Int.* 2013;26(2):170-176.

69. Pagadala M, Dasarathy S, Eghtesad B, McCullough AJ. Posttransplant metabolic syndrome: an epidemic waiting to happen. *Liver Transpl.* 2009;15(12):1662-1670.

70. Laryea M, Watt KD, Molinari M, et al. Metabolic syndrome in liver transplant recipients: prevalence and association with major vascular events. *Liver Transpl.* 2007;13(8):1109-1114.

71. Watt KD, Pedersen RA, Kremers WK, Heimbach JK, Charlton MR. Evolution of causes and risk factors for mortality post-liver transplant: results of the NIDDK long-term follow-up study. *Am J Transplant.* 2010;10(6):1420-1427.

72. LaMattina JC, Foley DP, Fernandez LA, et al. Complications associated with liver transplantation in the obese recipient. *Clin Transplant.* 2012;26(6):910-918.

73. Spengler EK, O'Leary JG, Te HS, et al. Liver transplantation in the obese cirrhotic patient. *Transplantation.* 2017;101(10):2288-2296.

74. Hakeem AR, Cockbain AJ, Raza SS, et al. Increased morbidity in overweight and obese liver transplant recipients: a single-center experience of 1325 patients from the United Kingdom. *Liver Transpl.* 2013;19(5):551-562.

75. Singhal A, Wilson GC, Wima K, et al. Impact of recipient morbid obesity on outcomes after liver transplantation. *Transpl Int.* 2015;28(2):148-155.

76. Sawyer RG, Pelletier SJ, Pruett TL. Increased early morbidity and mortality with acceptable long-term function in severely obese patients undergoing liver transplantation. *Clin Transplant.* 1999;13(1 Pt 2):126-130.

77. Bambha KM, Dodge JL, Gralla J, Sprague D, Biggins SW. Low, rather than high, body mass index confers increased risk for post-liver transplant death and graft loss: risk modulated by model for end-stage liver disease. *Liver Transpl.* 2015;21(10):1286-1294.

78. Schlansky B, Naugler WE, Orloff SL, Enestvedt CK. Higher mortality and survival benefit in obese patients awaiting liver transplantation. *Transplantation.* 2016;100(12):2648-2655.

79. Saab S, Lalezari D, Pruthi P, Alper T, Tong MJ. The impact of obesity on patient survival in liver transplant recipients: a meta-analysis. *Liver Int.* 2015;35(1):164-170.

80. Quillin RC, Wilson GC, Sutton JM, et al. Increasing prevalence of nonalcoholic steatohepatitis as an indication for liver transplantation. *Surgery.* 2014;156(4):1049-1056.

81. Agopian VG, Kaldas FM, Hong JC, et al. Liver transplantation for nonalcoholic steatohepatitis: the new epidemic. *Ann Surg.* 2012;256(4):624-633.

82. Kennedy C, Redden D, Gray S, et al. Equivalent survival following liver transplantation in patients with non-alcoholic steatohepatitis compared with patients with other liver diseases. *HPB (Oxford).* 2012;14(9):625-634.

83. Diwan TS, Rice TC, Heimbach JK, Schauer DP. Liver transplantation and bariatric surgery: timing and outcomes. *Liver Transpl.* 2018;24(9):1280-1287.

84. Hayashi F, Matsumoto Y, Momoki C, et al. Physical inactivity and insufficient dietary intake are associated with the frequency of sarcopenia in patients with compensated viral liver cirrhosis. *Hepatol Res.* 2013;43(12):1264-1275.

85. Hickman IJ, Jonsson JR, Prins JB, et al. Modest weight loss and physical activity in overweight patients with chronic liver disease results in sustained improvements in alanine aminotransferase, fasting insulin, and quality of life. *Gut.* 2004;53(3):413-419.

86. Konishi I, Hiasa Y, Tokumoto Y, et al. Aerobic exercise improves insulin resistance and decreases body fat and serum levels of leptin in patients with hepatitis C virus. *Hepatol Res.* 2011;41(10):928-935.

87. Heimbach JK, Watt KDS, Poterucha JJ, et al. Combined liver transplantation and gastric sleeve resection for patients with medically complicated obesity and end-stage liver disease. *Am J Transplant.* 2013;13(2):363-368.

88. Glass LM, Dickson RC, Anderson JC, et al. Total body weight loss of >/= 10 % is associated with improved hepatic fibrosis in patients with nonalcoholic steatohepatitis. *Dig Dis Sci.* 2015;60(4):1024-1030.

89. Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, et al. Weight loss through lifestyle modification significantly reduces features of nonalcoholic steatohepatitis. *Gastroenterology.* 2015;149(2):367-378.e5; quiz e314–365.

90. Takata MC, Campos GM, Ciovica R, et al. Laparoscopic bariatric surgery improves candidacy in morbidly obese patients awaiting transplantation. *Surg Obes Relat Dis.* 2008;4(2):159-164; discussion 164–155.

91. Zamora-Valdes D, Watt KD, Kellogg TA, et al. Long-term outcomes of patients undergoing simultaneous liver transplantation and sleeve gastrectomy. *Hepatology.* 2018;68(2):485-495.

92. Nesher E, Mor E, Shlomai A, et al. Simultaneous liver transplantation and sleeve gastrectomy: prohibitive combination or a necessity? *Obes Surg.* 2017;27(5):1387-1390.

93. Tariciotti L, D'Ugo S, Manzia TM, et al. Combined liver transplantation and sleeve gastrectomy for end-stage liver disease in a bariatric patient: first european case-report. *Int J Surg Case Rep.* 2016;28:38-41.

94. Kumar S, Khandelwal N, Kumar A, et al. Simultaneous living donor liver transplant with sleeve gastrectomy for metabolic syndrome and NASH-related ESLD-First report from India. *Indian J Gastroenterol.* 2017;36(3):243-247.

95. Al-Nowaylati A-R, Al-Haddad BJS, Dorman RB, et al. Gastric bypass after liver transplantation. *Liver Transpl.* 2013;19(12):1324-1329.

96. Osseis M, Lazzati A, Salloum C, et al. Sleeve gastrectomy after liver transplantation: feasibility and outcomes. *Obes Surg.* 2018;28(1):242-248.

97. Khoraki J, Katz MG, Funk LM, Greenberg JA, Fernandez LA, Campos GM. Feasibility and outcomes of laparoscopic sleeve gastrectomy after solid organ transplantation. *Surg Obes Relat Dis.* 2016;12(1):75-83.

98. Elli EF, Gonzalez-Heredia R, Sanchez-Johnsen L, Patel N, Garcia-Roca R, Oberholzer J. Sleeve gastrectomy surgery in obese patients post-organ transplantation. *Surg Obes Relat Dis.* 2016;12(3):528-534.

99. Weiss ES, Allen JG, Russell SD, Shah AS, Conte JV. Impact of recipient body mass index on organ allocation and mortality in orthotopic heart transplantation. *J Heart Lung Transplant.* 2009;28(11):1150-1157.

100. Baker AM, Levine TB, Goldberg AD, Levine AB. Natural history and predictors of obesity after orthotopic heart transplantation. *J Heart Lung Transplant.* 1992;11(6):1156-1159.

101. Heilmann C, Stahl R, Schneider C, et al. Wound complications after median sternotomy: a single-centre study. *Interact Cardiovasc Thorac Surg.* 2013;16(5):643-648.

102. Landes G, Harris PG, Sampalis JS, et al. Outcomes in the management of sternal dehiscence by plastic surgery: a ten-year review in one university center. *Ann Plast Surg*. 2007;59(6):659-666.

103. Olbrecht VA, Barreiro CJ, Bonde PN, et al. Clinical outcomes of noninfectious sternal dehiscence after median sternotomy. *Ann Thorac Surg*. 2006;82(3):902-907.

104. Akay MH, Nathan SS, Radovancevic R, et al. Obesity is associated with driveline infection of left ventricular assist devices. *ASAIO J*. 2019;65(7):678-682.

105. Kilic A, Conte JV, Shah AS, Yuh DD. Orthotopic heart transplantation in patients with metabolic risk factors. *Ann Thorac Surg*. 2012;93(3):718-724.

106. Milaniak I, Przybylowski P, Wierzbicki K, Sadowski J. Post-transplantation body mass index in heart transplant recipients: determinants and consequences. *Transplant Proc*. 2014;46(8):2844-2847.

107. Allen JG, Arnaoutakis GJ, Weiss ES, Merlo CA, Conte JV, Shah AS. The impact of recipient body mass index on survival after lung transplantation. *J Heart Lung Transplant*. 2010;29(9):1026-1033.

108. Gries CJ, Bhadriraju S, Edelman JD, Goss CH, Raghu G, Mulligan MS. Obese patients with idiopathic pulmonary fibrosis have a higher 90-day mortality risk with bilateral lung transplantation. *J Heart Lung Transplant*. 2015;34(2):241-246.

109. Russo MJ, Hong KN, Davies RR, et al. The effect of body mass index on survival following heart transplantation: do outcomes support consensus guidelines? *Ann Surg*. 2010;251(1):144-152.

110. Upala S, Panichsillapakit T, Wijarnpreecha K, Jaruvongvanich V, Sanguankeo A. Underweight and obesity increase the risk of mortality after lung transplantation: a systematic review and meta-analysis. *Transpl Int*. 2016;29(3):285-296.

111. Lederer DJ, Kawut SM, Wickersham N, et al. Obesity and primary graft dysfunction after lung transplantation: the Lung Transplant Outcomes Group Obesity Study. *Am J Respir Crit Care Med*. 2011;184(9):1055-1061.

112. Chandrashekaran S, Keller CA, Kremers WK, Peters SG, Hathcock MA, Kennedy CC. Weight loss prior to lung transplantation is associated with improved survival. *J Heart Lung Transplant*. 2015;34(5):651-657.

113. Chaudhry UI, Kanji A, Sai-Sudhakar CB, Higgins RS, Needleman BJ. Laparoscopic sleeve gastrectomy in morbidly obese patients with end-stage heart failure and left ventricular assist device: medium-term results. *Surg Obes Relat Dis*. 2015;11(1):88-93.

114. Hawkins RB, Go K, Raymond SL, Ayzengart A, Friedman J. Laparoscopic sleeve gastrectomy in patients with heart failure and left ventricular assist devices as a bridge to transplant. *Surg Obes Relat Dis*. 2018;14(9):1269-1273.

115. Ardila-Gatas J, Sharma G, Nor Hanipah Z, et al. Bariatric surgery in patients with interstitial lung disease. *Surg Endosc*. 2019;33(6):1952-1958.

116. Sheu EG, Channick R, Gee DW. Improvement in severe pulmonary hypertension in obese patients after laparoscopic gastric bypass or sleeve gastrectomy. *Surg Endosc*. 2016;30(2):633-637.

117. Levitsky J, Formica RN, Bloom RD, et al. The American Society of Transplantation Consensus Conference on the use of hepatitis C viremic donors in solid organ transplantation. *Am J Transplant*. 2017;17(11):2790-2802.

118. Marterre WF, Hariharan S, First MR, Alexander JW. Gastric bypass in morbidly obese kidney transplant recipients. *Clin Transplant*. 1996;10(5):414-419.

119. Rogers CC, Alloway RR, Alexander JW, Cardi M, Trofe J, Vinks AA. Pharmacokinetics of mycophenolic acid, tacrolimus and sirolimus after gastric bypass surgery in end-stage renal disease and transplant patients: a pilot study. *Clin Transplant*. 2008;22(3):281-291.

120. Diwan TS, Lichvar AB, Leino AD, et al. Pharmacokinetic and pharmacogenetic analysis of immunosuppressive agents after laparoscopic sleeve gastrectomy. *Clin Transplant*. 2017;31(6). https://doi.org/10.1111/ctr.12975.

121. Safwan M, Collins KM, Abouljoud MS, Salgia R. Outcome of liver transplantation in patients with prior bariatric surgery. *Liver Transpl*. 2017;23(11):1415–1421.

122. Tsamalaidze L, Stauffer JA, Arasi LC, et al. Laparoscopic sleeve gastrectomy for morbid obesity in patients after orthotopic liver transplant: a matched case-control study. *Obes Surg*. 2018;28(2):444–450.