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Bariatric Surgery Before and After Kidney Transplantation: Long-Term Weight Loss and Allograft Outcomes

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Abstract

Background: Severe obesity is frequently a barrier to kidney transplantation, and kidney transplant recipients often have significant weight gain following transplantation.

Objectives: The goals of this study were to evaluate the long-term risks and benefits of bariatric surgery before and after kidney transplantation.

Setting: University Hospital, United States

Methods: We performed a retrospective cohort study of 43 patients who had pre-transplantation bariatric surgery and 21 patients who had post-transplantation bariatric surgery from 1994–2017, with 10:1 propensity score matching to identify matched controls using national registry data.

Results: Body mass index at the time of transplantation was similar in patients who underwent bariatric surgery before versus after transplantation (32 vs 34 kg/m², p=0.172). There was no significant difference in body mass index in the 5 years after bariatric surgery among patients who underwent bariatric surgery before versus after kidney transplantation (36 vs 32 kg/m², p=0.814). Compared to matched controls, bariatric surgery before (n=38) and after kidney transplantation (n=18) was associated with a decreased risk of allograft failure (hazard ratio 0.31, 95% confidence interval 0.29–0.33 and 0.85, 95% confidence interval 0.85–0.86 for pre and post-transplant,

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CONFLICTS OF INTEREST STATEMENT

The authors declare no conflicts of interest

respectively) and mortality (hazard ratio 0.57, 95% confidence interval 0.53–0.61 and 0.80, 95% confidence interval 0.79–0.82 for pre and post-transplant, respectively).

Conclusions: Bariatric surgery before and after kidney transplantation results in similar maintenance of weight loss and improved long-term allograft survival compared to matched controls. Bariatric surgery appears to be a safe and reasonable approach to weight loss both before and after transplantation.

Keywords

Kidney transplantation; bariatric surgery; weight loss surgery; weight gain; obesity; body mass index

INTRODUCTION

Obesity, defined as a body mass index (BMI) ≥ 30 kg/m², is a critical public health problem affecting >35% of adults in the United States (US) ⁽¹⁾ and >30% of all US kidney transplant candidates and recipients ⁽²⁾. In kidney transplant recipients, obesity has been associated with longer hospital stays, increased perioperative 30-day mortality, poor wound healing, delayed graft function, increased incidence of post-transplant diabetes, and worse allograft outcomes ⁽³⁻⁷⁾. Possibly because of these adverse events, obese patients have reduced access to kidney transplantation compared to non-obese patients ^(8, 9), despite studies showing survival benefit of kidney transplantation in obese patients compared to remaining on the wait-list ^(10, 11). In fact, extreme obesity (BMI ≥ 40 kg/m²) is a contraindication to kidney transplantation in most US transplant centers.

In non-transplant patients with severe obesity (BMI of ≥ 35 kg/m²), bariatric surgery is considered the most effective therapy for sustained weight loss ⁽¹²⁾. However, with limited evidence of the safety and efficacy of bariatric surgery in transplantation, there exists ongoing unease in counseling transplant candidates and recipients to pursue bariatric surgery. Small single-center case series of patients who underwent bariatric surgery before or after kidney transplantation reported sustained short-term weight loss ⁽¹³⁻¹⁶⁾, stable allograft function ^(15, 17), and improvement in diabetes, hypertension, and dyslipidemia ⁽¹⁵⁾ at one-year post-bariatric surgery. One of the largest existing studies, which identified bariatric surgery cases using Medicare billing claims within the US Renal Data System registry (1991–2004) ⁽¹⁸⁾, demonstrated higher post-bariatric surgery BMI among patients who underwent bariatric surgery post-transplant compared to those who underwent bariatric surgery pre-transplant (40.2 and 35.1 kg/m², respectively). To our knowledge, no previous studies have reported kidney allograft outcomes beyond one-year post-bariatric surgery in patients who had post-transplant bariatric surgery, nor allograft outcomes beyond one-year post-transplant in patients who had pre-transplant bariatric surgery.

The current study was performed with the objectives of evaluating if bariatric surgery, performed before or after kidney transplantation, is associated with sustained weight loss, and how long-term allograft and patient survival in these patients compares to matched controls. In the setting of limited preexisting longitudinal outcomes data, we hypothesized that bariatric surgery is safe and effective both before and after transplantation.

MATERIALS AND METHODS

Overview of the Study Design

We performed a retrospective chart review of patients who underwent bariatric surgery either before or after kidney transplantation, whose medical care took place at our center. We then performed 10:1 propensity-score matching using national registry data to compare allograft and patient outcomes to individuals who did not undergo bariatric surgery. The study was approved by the Institutional Review Board at our institution and adheres to the Declaration of Helsinki.

Study Population

For individual chart review, patients were required to have undergone both bariatric surgery and kidney transplantation and to be ≥18 years of age at the time of transplantation. Matched controls were identified using the Organ Procurement and Transplantation Network (OPTN), which includes data on all donor, wait-listed candidates, and transplant recipients in the US, submitted by the members of the OPTN. The Health Resources and Services Administration (HRSA), US Department of Health and Human Services provides oversight to the activities of the OPTN contractor.

Data Collection (see Supplemental Methods)

Patient and donor characteristics at the time of transplant and subsequent follow-up were collected by chart review. Recipient body mass index (BMI) was collected at the time of transplant, time of bariatric surgery, and in one-year intervals following each procedure, up to five years. Missing outcomes data, including death and allograft failure among patients who were not seen at our center in ≥18 months, were addressed using OPTN data and National Death Index data.

Statistical Analysis

Statistical analyses were performed using STATA version 15.0 (Statacorp LP, College Station, TX, USA). All analyses used 2-sided hypothesis testing and required a p-value of <0.05 to establish statistical significance. We performed 10:1 propensity score matching using a national kidney transplantation registry to identify controls based on the likelihood of undergoing bariatric surgery⁽¹⁹⁻²²⁾; refer to the Supplemental Methods for additional details related to the analyses and to Supplemental Tables S1-S3 for balance tables demonstrating variable distribution in each of the matched groups. All individuals who underwent pre-transplantation (with long-term follow-up data, n=38) and post-transplantation bariatric surgery (with a functioning allograft, n=18) were matched to non-bariatric surgery controls based on age, sex, race, transplant year, dialysis vintage, sensitization, donor type, and diabetes status^(23, 24). Post-transplantation bariatric surgery patients were also matched based on post-transplant follow-up time with a functioning allograft to address immortal time bias⁽²⁵⁾. In addition to the variables listed above, individuals who underwent pre-transplantation and post-transplantation bariatric surgery were matched with non-bariatric surgery controls based on BMI at the time of transplant; a

separate set of controls for individuals who underwent pre-transplantation bariatric surgery were matched using pre-bariatric surgery BMI.

Cox proportional hazards regression was used to compare the risk of the primary outcomes, 1) all-cause allograft failure and 2) mortality, across individuals who underwent bariatric surgery versus matched controls who did not. In those individuals who had bariatric surgery pre-transplantation, multivariable logistic regression was also used to estimate the odds of the secondary outcomes, 1) delayed graft function and 2) treated acute rejection within one-year post-transplant.

RESULTS

Recipient Characteristics (see Supplemental Results)

Among the 64 patients who met eligibility criteria, there were 43 patients who had bariatric surgery pre-transplantation and 21 patients who had post-kidney transplantation bariatric surgery, spanning from 1994–2017 (see Figure S1 for timeline). Patients who had bariatric surgery pre-transplantation were older (Table 1, Table S4; median 50 vs 41 years, $p=0.002$) and transplanted more recently (median year 2012 vs 2004, $p<0.001$) compared to patients who had bariatric surgery post-transplantation. Median BMI at the time of transplantation was similar in the patients who underwent pre- versus post-transplant bariatric surgery (32 vs 34 kg/m², $p=0.172$). There was also no significant difference in median BMI at the time of bariatric surgery in patients who underwent pre- versus post-transplant bariatric surgery (43 vs. 41 kg/m², $p=0.704$).

Pre-transplant bariatric surgery patients had a median post-transplant follow-up time of 43 (interquartile range 20–89) months. One in 43 patients who had pre-transplant bariatric surgery died from lymphoma with a functioning graft. At a median post-transplant follow-up time of 130 (interquartile range 74–194) months, seven of 21 patients with post-transplant bariatric surgery experienced allograft failure (consistent with the national average during that time period⁽²⁶⁾). Three patients experienced transplant-related complications associated with post-transplant bariatric surgery: one patient had progressive allograft failure and resumed dialysis six months post-bariatric surgery (no clear cause was documented), another had erratic tacrolimus levels, and the last one had multiple episodes of acute kidney injury post-operatively. The last two patients had stable graft function at most recent follow-up.

Long-Term Weight Outcomes

In the first five years post-kidney transplantation, median BMI was lower in patients who had pre- versus post-transplant bariatric surgery (Figure 1A, Figure S2; 33 vs 38 kg/m², $p=0.020$). There was no significant difference in median BMI during the first five years post-bariatric surgery (Figure 1B, Figure S3; 36 vs 32 kg/m², $p=0.814$). Among patients who underwent bariatric surgery before compared to after transplant, there was no significant difference in excess weight loss at one-year (51% vs. 59%, $p=0.872$) or two years (69% vs. 71%, $p=0.870$) following bariatric surgery. There was also no significant difference in total weight loss (22% vs. 26% based on the last collected weight, $p=0.235$).

Allograft and Patient Outcomes

Compared to controls matched on pre-bariatric surgery BMI, pre-transplant bariatric surgery (with available follow-up data, n=38) was associated with an increased risk of acute rejection at one-year (Table 2, Table S2; aOR 1.19, 95% CI 1.07–1.33), and a decreased risk of delayed graft function (aOR 0.53, 95% CI 0.42–0.68), all-cause allograft failure (aHR 0.31, 95% CI 0.29–0.33), and mortality (aHR 0.57, 95% CI 0.53–0.61). Compared to matched controls, post-transplant bariatric surgery (n=18) was associated with a decreased risk of all-cause allograft failure (Table 2, Table S3; aHR 0.85, 95% CI 0.85–0.86) and mortality (aHR 0.80, 95% CI 0.79–0.82).

DISCUSSION

In this study, we present the results of one of the largest cohorts evaluating obese kidney transplant patients who underwent bariatric surgery, either before or after transplantation. Our detailed chart review allowed comprehensive assessment of longitudinal graft function, peri-bariatric surgery complications, and longer term weight loss outcomes than previously reported. We demonstrated that bariatric surgery, performed at any time, seems to result in sustained weight loss and improved patient and allograft survival. While bariatric surgery before transplant was associated with increased risk of acute rejection, long-term allograft and patient survival were better compared to controls with similar BMIs to our patients' pre-bariatric surgery BMIs. Post-transplant bariatric surgery was associated with overall improved allograft and patient survival compared to matched controls.

Among patients who underwent bariatric surgery before transplantation, we suspect these patients benefitted from lower rates of post-transplant weight gain, likely contributing to improved allograft outcomes. Although the overall allograft outcomes in patients who had post-transplant bariatric surgery are reassuring, our chart review suggests that bariatric surgery post-transplant has the potential to be associated with allograft complications, including acute kidney injury and erratic tacrolimus levels. Thus, close monitoring of transplant recipients after bariatric surgery, focusing on volume status, allograft function, and immunosuppression levels, remains imperative.

Alterations in immunosuppressive pharmacokinetics have been observed in patients who underwent Roux-en-Y gastric bypass ⁽²⁷⁾. This is thought to be largely due to the characteristics of the procedure, which is associated with gastric restriction and a degree of malabsorption. In contrast, immunosuppressive pharmacokinetic alterations were not demonstrated in kidney transplant candidates who underwent sleeve gastrectomy (which is only restrictive) ⁽²⁸⁾. In the current study, we were not able to accurately assess stability of immunosuppression regimens following bariatric surgery; the data were not collected prospectively, and we were unable to distinguish between true trough levels and erroneous readings. We were also unable to obtain detailed immunosuppressant data for the national controls. We observed higher rates of acute rejection in patients who underwent bariatric surgery before transplantation compared to matched controls, suggesting possible instability of immunosuppression absorption. This may in part be because individuals who had bariatric surgery before transplantation in our cohort were slightly more likely to have had the Roux-en-Y procedure.

Although previous small studies demonstrated sustained weight loss following bariatric surgery in transplant recipients, follow-up was mostly limited to one to two years after bariatric surgery (13-15, 17, 18). To our knowledge, post-transplant BMIs in patients who had bariatric surgery pre-transplant have not been reported. In our cohort of patients who had bariatric surgery before transplant, even with weight gain, the median BMI was still <40 kg/m² at five years post-transplant. The median BMI for patients in both groups were comparable at five years post-bariatric surgery.

While the study was strengthened by detailed data available through individual chart review, there were a number of important limitations. Individuals who underwent bariatric surgery before, as opposed to after transplant, were fundamentally quite different; patients who underwent post-transplant bariatric surgery represent a group of patients who gained substantial weight only after initiation of immunosuppression and resolution of uremia. Transplantation year was also different between groups, leading to differences in duration of follow up, immunosuppression, and type of surgery, which can alter metabolic risk profiles; (29) there was insufficient power to assess for differences by era and type of surgery. Additionally, while the national data provided important comparison groups, bariatric surgery history is not recorded in the OPTN dataset, and it is possible that some controls underwent bariatric surgery. Furthermore, we suspect there is confounding by indication for bariatric surgery; patients who elect to undergo bariatric surgery may be more motivated and adherent compared to otherwise similar patients who choose not to. Additionally, post-transplant and post-bariatric surgery BMIs and measures of glycemic control were not systematically obtained, and were only intermittently captured in many patients in our electronic health record. Given the small sample size, we were able to graphically demonstrate the available BMI data points for each individual (Figures S1-S2), helping to support the conclusion that bariatric surgery, at any time point, seems to be associated with sustained weight loss.

CONCLUSIONS

In conclusion, bariatric surgery appears to be a safe and reasonable approach to weight loss, both before and after transplantation. The issues of obesity, weight loss, and timing of the transplant should be discussed in detail with all obese transplant candidates when they are seen for transplant evaluation. Having a kidney transplant should not be a contraindication to bariatric surgery; however, because of the possibility of kidney-related complications, close monitoring of allograft function and calcineurin-inhibitor levels is recommended. Absent larger, multi-center, prospective studies focusing on obese transplant candidates and recipients, we recommend candidates with a BMI ≥ 35 to be directed to weight loss programs for more detailed information and education. Pre-transplant bariatric surgery does not seem to significantly delay access to transplantation based on the results of the current study, and should be considered for this group of patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Median body mass index during A) the first five years post-kidney transplantation and B) the first five years post-bariatric surgery

A black outline encircling a point indicates statistically significant difference in median BMIs across the two groups at that time point

Table 1.

Characteristics of Kidney Transplant Recipients who Underwent Bariatric Surgery Before vs. After Transplant

	Bariatric Surgery Before Transplant N=43	Bariatric Surgery After Transplant N=21	P-value
Recipient Characteristics			
Median age at kidney transplant, years (IQR)	50 (43-59)	41 (26-49)	0.002
Male gender, n (%)	23 (59%)	6 (30%)	0.035
Race/Ethnicity, n (%)			0.127
White	24 (56%)	7 (33%)	
Black	12 (28%)	12 (57%)	
Hispanic	2 (5%)	0 (0%)	
Asian	1 (2%)	0 (0%)	
American Indian/Alaskan Native	0 (0%)	1 (5%)	
Mixed race, other, or missing	4 (9%)	1 (5%)	
Median body mass index at the time of transplant, kg/m ² (IQR)	32 (28-36)	34 (33-37)	0.172
Diabetes mellitus, n (%)	19 (44%)	8 (38%)	0.708
Cause of end stage kidney disease, n (%)			0.217
Diabetes	10 (23%)	6 (29%)	
Hypertension	5 (12%)	4 (19%)	
Cystic disease	5 (12%)	0 (0%)	
Glomerular disease	2 (5%)	4 (19%)	
Other or missing	21 (48%)	7 (33%)	
Median dialysis vintage at the time of transplant, days (IQR)	500 (0-1387)	382 (0-1723)	0.658
Private insurance, n (%)	23 (53%)	7 (33%)	0.263
Functional status requiring assistance, n (%)	4 (9%)	4 (14%)	0.329
Bariatric Surgery Characteristics			
Median body mass index at the time of bariatric surgery, kg/m ² (IQR)	43 (38-48)	41 (39-44)	0.704
Type of bariatric surgery, n (%)			0.394
Gastric bypass	27 (63%)	6 (28%)	
Sleeve gastrectomy	9 (21%)	10 (48%)	
Laparoscopic adjustable gastric banding	6 (14%)	4 (19%)	
Vertical banded gastroplasty	0 (0%)	1 (5%)	
Unspecified	1 (2%)	0 (0%)	
On hemodialysis at the time of bariatric surgery	8 (16%)	1 (5%)	0.184
On peritoneal dialysis at the time of bariatric surgery	1 (2%)	1 (5%)	0.612
Immunosuppression Characteristics			
Lymphocyte-depleting induction immunosuppression, n (%)	33 (77%)	11 (52%)	0.008
Calcineurin inhibitor, n (%)			0.005
Tacrolimus	41 (95%)	14 (67%)	

	Bariatric Surgery Before Transplant N=43	Bariatric Surgery After Transplant N=21	P-value
Cyclosporine	0 (0%)	3 (14%)	
Both	1 (2%)	0 (0%)	
Steroid maintenance therapy, n (%)	42 (98%)	17 (94%)	0.518
Patient Outcome Characteristics			
Median duration of follow-up post-transplant, months (IQR)	43 (20-89)	139 (74-194)	<0.001
Cause of death, n (%)			0.572
Infection	1 (33%)	0 (0%)	
Cardiovascular	1 (33%)	1 (33%)	
Malignancy	1 (33%)	1 (33%)	
Other or unknown	0 (0%)	1 (33%)	
Cause of graft failure, n (%)			0.156
Recurrent disease	0 (0%)	1 (14%)	
Chronic rejection	0 (0%)	3 (42%)	
Potential bariatric surgical complication	0 (0%)	1 (14%)	
Chronic urologic complication	0 (0%)	1 (14%)	
Malignancy	1 (100%)	0 (0%)	
Other or unknown	0 (0%)	1 (14%)	

Abbreviation: IQR = interquartile range

Table 2.

Allograft and patient outcomes of kidney transplant recipients who underwent bariatric surgery before or after kidney transplantation *

	Adjusted Risk	95% CI	P-Value
Bariatric surgery before transplant (n=38) compared to national controls (n=380), matched by pre-bariatric surgery BMI			
Delayed graft function, aOR	0.53	0.42-0.68	<0.001
Acute rejection at one year post-transplant, aOR	1.19	1.07-1.33	0.001
All-cause allograft failure, aHR	0.31	0.29-0.33	<0.001
Mortality, aHR	0.57	0.53-0.61	<0.001
Bariatric surgery before transplant (n=38) compared to national controls (n=380), matched by BMI at the time of transplant			
Delayed graft function, aOR	1.16	1.13-1.18	<0.001
Acute rejection at one year post-transplant, aOR	1.75	1.62-1.88	<0.001
All-cause allograft failure, aHR	0.52	0.50-0.54	<0.001
Mortality, aHR	0.99	0.91-1.07	0.742
Bariatric surgery after transplant with a functioning allograft (n=18) compared to national controls (n=180), matched by BMI at the time of transplant[†]			
All-cause allograft failure, aHR	0.85	0.85-0.86	<0.001
Mortality, aHR	0.80	0.79-0.82	<0.001

Abbreviations: CI = confidence interval; aOR = adjusted odds ratio; aHR = adjusted hazard ratio

* Matched controls were determined using Organ Procurement and Transplantation Network national data. All matched variables had a standardized difference of <10%, with an overall Rubin's B = 25% and Rubin's R 0.5-2 (see Supplemental Tables S1-3 for balance tables). All models were matched by age, BMI, gender, race, transplant year, dialysis vintage, and diabetes status

[†] Also matched by duration of post-transplant follow-up prior to bariatric surgery