


## ORIGINAL ARTICLE

# Clinical outcome of kidney transplantation after bariatric surgery: A single-center, retrospective cohort study

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## Abstract

Patients with class II and III obesity and end-stage renal disease are often ineligible for kidney transplantation (KTx) due to increased postoperative complications and technically challenging surgery. Bariatric surgery (BS) can be an effective solution for KTx candidates who are considered inoperable. The aim of this study is to evaluate outcomes of KTx after BS and to compare the outcomes to obese recipients (BMI  $\geq 35$  kg/m<sup>2</sup>) without BS. This retrospective, single-center study included patients who received KTx after BS between January 1994 and December 2018. The primary outcome was postoperative complications. The secondary outcomes were graft and patient survival. In total, 156 patients were included, of whom 23 underwent BS prior to KTx. There were no significant differences in postoperative complications. After a median follow-up of 5.1 years, death-censored graft survival, uncensored graft survival, and patient survival were similar to controls (log rank test  $p = .845$ ,  $.659$ , and  $.704$ , respectively). Dialysis pre-transplantation (Hazard Ratio (HR) 2.55; 95%CI 1.03–6.34,  $p = .043$ ) and diabetes (HR 2.41; 95%CI 1.11–5.22,  $p = .027$ ) were independent risk factors for all-cause mortality. A kidney from a deceased donor was an independent risk factor for death-censored graft loss (HR 1.98; 95%CI 1.04–3.79,  $p = .038$ ). Patients who received a KTx after BS have similar outcomes as obese transplant recipients.

## KEYWORDS

bariatric surgery, comorbidity, graft survival, obesity, patient survival, postoperative complications

## 1 | INTRODUCTION

Obesity is worldwide one of the most important causes of preventable deaths and is affecting a large part of patients with end-stage renal disease (ESRD).<sup>1–4</sup> The relative risk of developing ESRD rises

with an increasing body mass index (BMI).<sup>3,5</sup> Ejerblad et al found that obesity class I (BMI  $\geq 30$  kg/m<sup>2</sup>) among men and obesity class II (BMI  $\geq 35$ ) among women anytime during their lifetime was associated with a 3- to 4-time increased risk of chronic kidney disease (CKD).<sup>6</sup> Kidney transplant candidates and recipients are increasingly

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becoming obese.<sup>7,8</sup> Due to the shortage of transplant organs, ESRD patients wait on dialysis, during which they risk gaining even more weight.<sup>9</sup> Paradoxically, patients with obesity are reported to have a longer survival on dialysis compared with lean patients,<sup>9</sup> possibly resulting in an increase in obese transplant candidates. Survival after transplantation, however, is worse in the population with obesity compared with normal weight recipients.<sup>10</sup> In several centers in the Netherlands, a BMI  $\geq 35$  kg/m<sup>2</sup> was considered an absolute contraindication for transplantation. However, guidelines are becoming less strict and there is no consensus on whether or not a patient is ineligible for transplantation based on their weight or BMI.<sup>11</sup> Even with less strict guidelines, patients are more often found ineligible for transplantation based on their BMI.<sup>12</sup> In a multivariate analysis, Lassalle et al found that patients with a BMI  $> 31$  kg/m<sup>2</sup> at the start of dialysis were less likely to receive a kidney transplant.<sup>13</sup> Kidney transplantation in the obese patient is often technically more challenging due to the excess abdominal fat and obesity is associated with more postoperative complications as wound infection, delayed graft function and acute, and chronic rejection.<sup>14-17</sup> In order to reduce these complications after KTx, weight loss resulting in a BMI less than 30 kg/m<sup>2</sup> is recommended.<sup>14</sup> Bariatric surgery (BS) has been proven to be the most effective treatment to achieve long-term weight loss. BS is indicated in patients with a BMI  $\geq 35$  kg/m<sup>2</sup> and at least one obesity-related comorbidity or in patients with a BMI  $\geq 40$  kg/m<sup>2</sup>.<sup>18,19</sup> Andalib et al analyzed 234 patients on dialysis who had undergone primary BS and concluded that the morbidity and mortality is acceptable compared with patients who were not depending on dialysis. Recent studies show that excess weight loss (EWL) in kidney transplant candidates or recipients after BS is comparable to the non-renal disease population.<sup>20,21</sup> A few case studies

report the use of BS to improve eligibility for transplantation after initial rejection based on BMI.<sup>22-24</sup>

In a more recent study, 42 patients underwent KTx after laparoscopic sleeve gastrectomy with a decrease of patients with diabetes, hypertension, and number of antihypertensive medications used.<sup>25</sup> Post-transplantation outcome among these patients were comparable to non-obese patients. This is remarkable considering these patient would have otherwise been ineligible for KTx.

The aim of this study is to compare complications, mortality, graft, and patient survival after kidney transplantation in patients who had BS prior to transplantation with kidney transplant recipients with obesity class II and III (BMI  $\geq 35$ ) without BS.

## 2 | MATERIALS AND METHODS

### 2.1 | Study population

This retrospective, single-center cohort study was conducted at the Erasmus Medical Center in Rotterdam, The Netherlands. The selection process is illustrated in Figure 1. Between January 1994 and December 2018, 2598 adult patients received a kidney transplant. The records of all kidney transplant recipients were screened on a medical history of bariatric surgery. Types of BS that were included were gastric banding (GB), sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB). The WHO classification of weight was used to determine severity of obesity and to established inclusion criteria. Bariatric surgery is indicated in patients with obesity class II (BMI 35.0–39.9) and class III (BMI  $\geq 40$ ) and are therefore included in the control group, the transplant only (TO). Patients who underwent BS

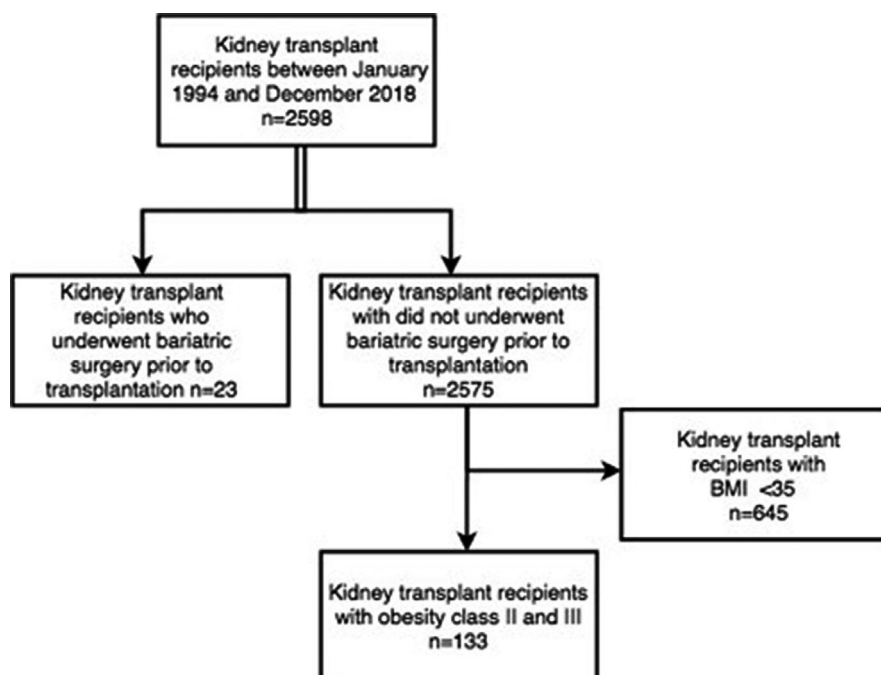


FIGURE 1 Flowchart of inclusion process. BMI, Body mass index

after KTx were included in the control group and censored from the date they underwent BS. All data were obtained from the Electronic Patient Dossier of Erasmus Medical Center until January 1, 2020.

In this center, patients were mainly deemed unsuitable for transplantation based on distribution of the abdominal fat and technical impossibility of performing the implantation in the iliac fossa. From a surgical point of view, subcutaneous abdominal fat is preferred over visceral fat because it can easier—and therefore safer—be manipulated to facilitate kidney transplantation. The immobile visceral fat impairs the view of the surgical field which hinders the implantation of the kidney. Patient eligibility for kidney transplantation was determined by a group of highly experienced surgeons who each performed over 200 kidney transplantations. They based their opinion on whether or not implantation of the transplant is technically possible. The mobility of the abdomen is assessed to determine the accessibility to the iliac artery and vein. The abdomen is mobilized with the hands of the surgeon during physical examination at the outpatient clinic and this simulation is used to determine whether there is sufficient space to transplant a kidney intraoperatively. If the abdomen cannot be mobilized due to the size of the abdomen and/or intra-abdominal fat, surgery is considered impossible and the patient first requires bariatric surgery. Additional imaging was not used to determine eligibility for KTx.

## 2.2 | Outcomes

The primary outcome measure of this study was postoperative complications within 3 months after transplantation in patients who underwent BS prior to transplantation (BSG) compared with patients with obesity class II and III at time of transplantation (TO). Postoperative complications were registered up to 3 months after transplantation. Post-transplant diabetes mellitus (PTDM) was defined as the initiation of any antidiabetic medication after transplantation. Incisional hernia of the Gibson incision after kidney transplantation was recorded up to one year after transplantation. All postoperative complications were recorded, and severity was scored according to the Clavien-Dindo classification. Severe complications were defined as complications with Clavien-Dindo grade IIIa or higher.

For secondary outcomes, graft and patient survival, mortality and early graft loss (EGL) were investigated. Postoperative mortality was defined as mortality during hospital stay or within 90 days after transplantation. Patient survival was calculated from the date of transplantation to the date of an event or the last moment of follow-up. Graft failure was defined as primary non-function (PNF) of the graft, the initiation of renal replacement therapy/dialysis, transplant nephrectomy or re-transplantation. Delayed Graft Function (DGF) was defined as the need of resuming dialysis within 1 week after transplantation. PNF was defined as the failure of a graft without detectable technical or immunological problems within 3 months after transplantation. EGL was defined as the loss of a graft within 30 days of transplantation or primary non-function. Death-censored graft survival was calculated from the date of transplantation to the date of graft loss. Patients who died with a functioning graft and

patients that were lost to follow-up were censored. Uncensored graft survival was calculated from the time of transplantation to the date of graft loss or patient death. Patients who were lost to follow up were censored from the last moment of follow-up.

## 2.3 | Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 24. Baseline characteristics and outcomes were described as counts and percentages for categorical variables. For continuous variables, means and standard deviations (SD) were given for normally distributed variables and medians and interquartile ranges (IQR) for skewed continuous variables. Differences in postoperative complications between groups were compared using the chi-square test or Fisher's exact tests when the expected count was lower than 5. For continuous variables, the Mann-Whitney *U* test was used. Odds ratios and 95% CI were calculated using univariate logistical regression. Propensity scored matching was done to match the two groups to correct for difference in baseline characteristics in a 1:1 ratio. Patients were matched based on time of dialysis treatment, diabetic status, and smoking status. Graft survival and patient survival were estimated with the Kaplan-Meier method, and curves were compared using the log rank test. Multivariable Cox regression analyses were used to identify risk factors for death-censored graft loss and patient death using preselected variables. The enter method was used to test risk factors. A *p*-value < .05 was considered statistically significant.

## 2.4 | Immunosuppression

All KTx recipient receive a standard regimen of immunosuppressive medication consisting of tacrolimus, mycophenolate mofetil (MMF), and prednisone. Normally, prednisone is gradually tapered over the first 3 months followed by complete withdrawal. Blood levels are regularly checked, and dosages are adjusted to optimize blood levels.

## 2.5 | Ethical approval

This study was approved by the Ethics Committee of the Erasmus Medical Center Rotterdam and was conducted in accordance with the provisions of the declaration of Helsinki.

# 3 | RESULTS

## 3.1 | Study population

Of 156 included patients, 23 patients were included in the BSG and 133 patients received a kidney transplant with obesity class II and III (TO). In the group that received a kidney transplant after bariatric

**TABLE 1** Baseline characteristics of kidney transplant recipients with obesity class II and III compared with patients who underwent BS prior to transplantation: overall and propensity score-matched cohort

	Before PSM (n = 156)			After PSM (n = 46)		
	TO (n = 133)	BSG (n = 23)	p-value	TO (n = 23)	BSG (n = 23)	p-value
Age, median (IQR)	53.1 (40.9–63.3)	55.5 (40.4–61.5)	.249	51.4 (38.9–63.5)	55.5 (40.4–61.5)	.974
Male, n (%)	64 (48.1)	7 (30.4)	.088	13 (56.5)	8 (34.7)	.139
BMI (kg/m <sup>2</sup> ) at KTx, median (IQR)	36.7 (35.5–38.8)	33.8 (31.6–34.1)	<.001 <sup>a</sup>	36.8 (36.0–39.3)	33.8 (31.6–34.1)	<.001 <sup>a</sup>
Smokers, n (%)	69 (51.9)	5 (21.7)	<.001 <sup>a</sup>	8 (34.8)	5 (21.7)	.326
Medical history, n (%)						
Diabetes mellitus	52 (39.1)	14 (60.9)	.043 <sup>a</sup>	12 (47.8)	14 (60.9)	.369
Cardiac disease	54 (44.6)	12 (47.8)	.300	10 (43.5)	12 (47.8)	.904
CVA/TIA	8 (6.0)	0 (0.0)	.227	1 (4.3)	0 (0.0)	.500
COPD	8 (6.0)	4 (17.4)	.079	4 (17.4)	4 (17.4)	.000
Thromboembolic events	17 (12.8)	2 (8.7)	.443	6 (26.1)	2 (8.7)	.121
Peripheral arterial disease	11 (8.3)	1 (4.3)	.445	3 (13.0)	1 (4.3)	.304
Dialysis treatment, n (%)	98 (73.7)	17 (73.9)	.603	20 (87.0)	17 (73.9)	.265
Time of dialysis in months, median (IQR)	24 (15–38)	30 (21–61)	.026 <sup>a</sup>	31 (21–50)	30 (21–61)	.806
Type of donor, n (%)						
Living	90 (67.7)	13 (56.5)	.209	11 (47.8)	13 (56.5)	.555
DBD	15 (11.3)	6 (26.0)		5 (21.7)	6 (18.2)	
DCD	27 (20.3)	5 (21.7)		7 (30.1)	5 (15.2)	
Donor age, median (IQR)	52 (40–62)	55 (46–61)	.779	48 (38–59)	55 (46–61)	.442
ECD, n (%)	48 (36.1)	10 (30.3)	.498	4 (17.4)	10 (30.3)	.054
First transplant, n (%)	109 (82.0)	21 (91.3)	.215	16 (70.0)	21 (91.3)	.067
HLA mismatch, n						
0	7	0		3	0	
1–2	28	5		6	5	
3–4	57	12		5	12	
5–6	43	6		8	6	
ABO compatible, n (%)	129 (97.0)	22 (95.7)	.555	21 (91.3)	22 (95.7)	.500
Cause of ESRD, n (%)						
Diabetes mellitus	37 (27.8)	9 (39.1)		9 (39.1)	9 (39.1)	
Hypertension	22 (16.5)	3 (13.0)		3 (13.0)	3 (13.0)	
FSGS	18 (13.5)	5 (21.7)		2 (8.7)	5 (21.7)	
Nephritic syndrome	22 (16.5)	1 (4.3)		1 (4.3)	1 (4.3)	
Polycystic kidney disease	12 (6.0)	2 (8.7)		5 (21.7)	2 (8.7)	
Congenital kidney disease	8 (6.0)	0 (0)		0 (0)	0 (0)	
Other	14 (10.5)	3 (13.0)		3 (13.0)	3 (13.0)	

Abbreviations: BMI, Body mass index; BSG, Bariatric surgery group; COPD, Chronic Obstructive Pulmonary Disease; CVA, Cerebrovascular Accident; DBD, Donation after Brain Death; DCD, Donation after circulatory death; ECD, Extended criteria donor; ESRD, End-stage renal failure; FSGS, Focal segmental glomerulosclerosis; IQR, Interquartile range; KTx, Kidney transplantation; PSM, Propensity Score Matching; TIA, Transient Ischemic Attack; TO, Transplant only.

<sup>a</sup>Statistically significant.

TABLE 2 BS-related outcome

	BS before kidney transplantation (n = 23)
BMI at BS, median (IQR)	42.3 (41.3–47.8)
BMI at KTx, median (IQR)	33.6 (31.4–34.7)
Time between BS and KTx in months, median (IQR)	32.7 (17.2–65.2)
Time of dialysis between BS and KTx in months, median (IQR)	22 (13–37)
Type of BS	
SG, n (%)	11 (47.8)
RYGB, n (%)	9 (39.1)
GB, n (%)	3 (13.0)
Estimated weight loss in kg 1 year after BS, median (IQR)	30.0 (23.0–37.0)
BMI 1 year after BS, median (IQR)	33.9 (31.2–36.5)
%EWL 1 year post BS, median (IQR)	54 (45–64)
%EWL 2 years post BS, median (IQR)	67 (31–76)

Abbreviations: %EWL, percentage excess weight loss; BMI, body mass index; BS, bariatric surgery; GB, gastric banding; IQR, interquartile range; Kg, kilograms; KTx, kidney transplantation; RYGB, Roux-en Y gastric bypass; SG, sleeve gastrectomy.

surgery, 13% of patients had a BMI between 25 and 29.9 ( $n = 3$ ), 65% of patients had a BMI between 30 and 34.9 ( $n = 15$ ), 22% had a BMI between 35 and 39.9 ( $n = 5$ ) and no one had a BMI above 40. In the transplant only group, 89% had a BMI between 35 and 39.9 ( $n = 118$ ) and 11% had a BMI above 40 ( $n = 15$ ). Of the transplant only patients, 15 patients underwent BS after KTx and were censored graft and patient survival from the moment they underwent BS. Table 1 shows baseline characteristics of all patients included. BMI at transplantation was 33.6 kg/m<sup>2</sup> (31.4–34.7) in the BSG compared with 36.7 kg/m<sup>2</sup> (35.5–38.8) in TO. The BSG received a significantly longer period of dialysis treatment compared with the TO, 40 months (22–83) versus 24 months (15–38,  $p = .026$ ). The prevalence of diabetes mellitus was significantly higher in the BSG 60.9% ( $n = 14$ ) versus 39.1% ( $n = 69$ ),  $p = .043$  in the TO. The percentage smokers among TO was significantly higher (51.9% ( $n = 69$ ) vs 21.7% ( $n = 5$ ),  $p < .001$ ).

The baseline characteristics of the propensity scored matched cohort are also shown in Table 1. The BS-related outcomes are presented in Table 2. In the BSG, 48% patients underwent a sleeve gastrectomy ( $n = 11$ ), 39% patients a RYGB ( $n = 9$ ) and 13% patients GB ( $n = 3$ ). The BSG had a median BMI of 42.3 kg/m<sup>2</sup> (41.3–47.8) before BS. BMI 1 year after BS was 33.9 (31.2–36.5).

### 3.2 | Postoperative complications

The incidence of postoperative complications is shown in Table 3. Urinary tract infections (UTI) were more common in the BS (60.9% ( $n = 14$ ) vs 31.6% ( $n = 42$ ), OR 3.37; 95% CI 1.35–8.40;  $p = .007$ ). There were no significant differences between TO patients versus patients after BS in biopsy proven rejections, wound problems, or other complications. There were no significant differences between the matched cohort and the BSG.

Figure 2 shows the percentage of patients with a severe complication divided by Clavien-Dindo grade. There was no significant

difference in the incidence of severe complication between both groups. Table 4 shows an overview of the complications that were included.

### 3.3 | Obesity-related morbidity in BS patients

Prior to bariatric surgery, 16 patients (69.6%) had a history of diabetes. Two of these patient (8.7%) were cured after undergoing bariatric surgery and did not need antidiabetic medication at time of transplantation. At 1 year after transplantation, two patients (8.7%) developed PTDM and started antidiabetic medication. This was similar to the rate of PTDM in the TO, in which 14 patients (10.5%) developed PTDM (OR: 0.82; 95% CI [0.17–3.89],  $p = .578$ ).

One patient (4.3%) discontinued the use of antidiabetic medication and 1 patient (4.3%) did not need insulin anymore and metformin was sufficient. Of the 10 patients who had a follow-up of 5 years, 6 patients (60%) had diabetes.

One year after transplantation, four patients (17.4%) were taken off antihypertensive medication. Four patients (17.4%) switched from combination therapy to monotherapy. Increased use of antihypertensive medication was not observed. In two patient who underwent RYGB, oxalate nephropathy was observed in the kidney transplant during biopsy. In one of these patients, ESRD was initially caused by hyperoxaluria. No transplants were lost to oxalate nephropathy. Table 5 shows the postoperative complications after kidney transplantation in bariatric surgery patient per type of bariatric procedure.

At 1 year post-transplantation, median BMI in TO was 37.2 kg/m<sup>2</sup> (34.7–40.1), which was significantly higher compared with 33.1 kg/m<sup>2</sup> (29.7–35.6) in the BSG ( $p = .000$ ).

Weight gain 1 year post-transplantation was comparable among both groups, 2 kg (–5.5 to 8.5) in the TO and 0.8 kg (–10.1 to 5.5) in the BSG ( $p = .329$ ).

**TABLE 3** Postoperative complications after kidney transplantation in kidney transplant recipients with obesity class II and III (TO) compared with patients who underwent BS prior to transplantation: overall and propensity score-matched cohort

	Before PSM (n = 156)			After PSM (n = 46)			p-value	OR [95% CI]	p-value
	TO (n = 133)	BSG(n = 23)	OR [95% CI]	TO (n = 23)	BSG (n = 23)	OR [95% CI]			
Total operating time in minutes, median (IQR)	139 (116 to 164)	136 (114 to 153)	-	139 (111 to 174)	136 (114 to 153)	-	.449	-	.652
Warm ischemic time in minutes, median (IQR)	22 (19 to 30)	22 (17 to 26)	-	22 (18 to 29)	22 (17 to 26)	-	.414	-	.569
Thrombosis, n (%)	5 (3.8)	1 (4.3)	1.14 [0.13 to 10.20]	2 (8.7)	1 (4.3)	0.48 [0.04 to 5.66]	.455	0.48 [0.04 to 5.66]	.500
Arterial	3	1		2	1				
Venous	2	0		0	0				
Urological problems, n (%)	16 (12.0)	6 (26.1)	2.58 [0.89 to 7.50]	2 (8.7)	6 (26.1)	3.71 [0.66 to 20.77]	.078	3.71 [0.66 to 20.77]	.121
Stenosis, n	16	4		2	4				
Leakage, n	0	2		0	2				
Cardiovascular events, n (%)	23 (17.3)	5 (27.7)	1.33 [0.45 to 3.94]	4 (17.4)	5 (21.7)	1.32 [0.31 to 5.71]	.397	1.32 [0.31 to 5.71]	.500
Ischemia, n	5	1		2	1				
Arrhythmia, n	10	3		1	3				
DVT, n	8	1		1	1				
Pulmonary events, n (%)	7 (5.3)	0 (0)	0.95 [0.91 to 0.99]	1 (4.3)	0 (0)	0.49 [0.36 to 0.66]	.320	0.49 [0.36 to 0.66]	.500
Pneumonia, n	3	0		1	0				
Lung embolism, n	1	0		0	0				
Other, n	3	0		0	0				
Biopsy proven rejection, n (%)	31 (23.3)	6 (26.1)	1.16 [0.42 to 3.20]	5 (21.7)	6 (26.1)	1.27 [0.32 to 4.95]	.477	1.27 [0.32 to 4.95]	.730
Wound problems, n (%)	15 (11.3)	3 (13.0)	1.18 [0.31 to 4.45]	1 (4.3)	3 (13.0)	3.3 [0.32 to 34.35]	.516	3.3 [0.32 to 34.35]	.304
Infection, n	10	3		1	3				
Dehiscence, n	5	0		0	0				
UTI, n (%)	42 (31.6)	14 (60.9)	3.37 [1.35 to 8.40]	10 (43.5)	14 (60.9)	1.42 [0.44 to 4.53]	.007*	1.42 [0.44 to 4.53]	.384
Seroma, n (%)	5 (3.8)	3 (13.0)	3.8 [0.85 to 17.3]	1 (4.3)	3 (13.0)	3.30 [0.32 to 34.35]	.096	3.30 [0.32 to 34.35]	.304
Lymphocele, n (%)	5 (3.8)	2 (8.7)	3.17 [0.73 to 13.7]	1 (4.3)	2 (8.7)	2.10 [0.18 to 24.87]	.262	2.10 [0.18 to 24.87]	.500
DGF, n (%)	37 (27.8)	8 (34.8)	1.38 [0.54 to 3.54]	9 (39.1)	8 (34.8)	0.83 [0.25 to 2.75]	.326	0.83 [0.25 to 2.75]	.500
PNF, n (%)	3 (2.3)	1 (4.3)	0.51 [0.05 to 5.10]	2 (8.7)	1 (4.3)	0.48 [0.04 to 5.66]	.575	0.48 [0.04 to 5.66]	.500
DM one year post-transplantation, n (%)	62 (48.1)	10 (45.5)	0.90 [0.56 to 2.23]	12 (52.2)	10 (45.5)	0.71 [0.22 to 2.25]	.821	0.71 [0.22 to 2.25]	.384

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TABLE 3 (Continued)

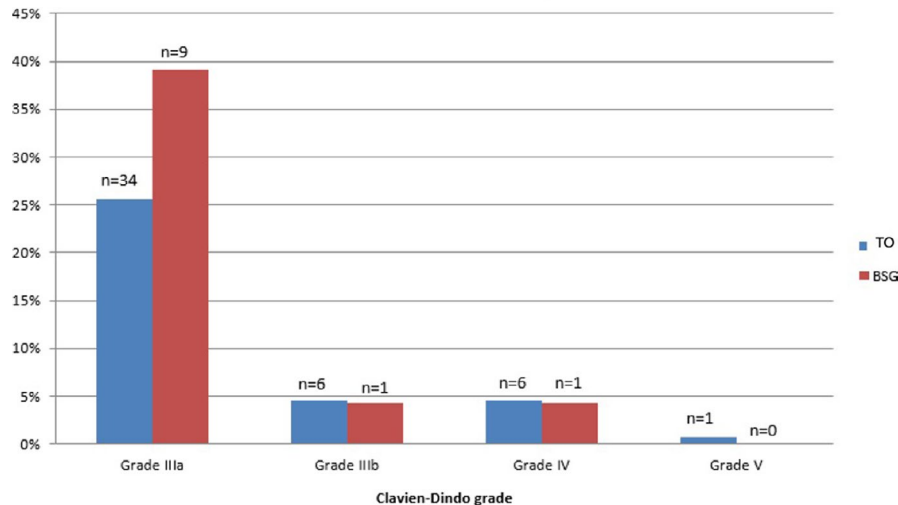
	Before PSM (n = 156)		After PSM (n = 46)		p-value	OR [95% CI]	BSG (n = 23)	TO (n = 23)	OR [95% CI]	p-value
	TO (n = 133)	BSG(n = 23)	TO (n = 23)	BSG (n = 23)						
PTDM, n (%)	14 (10.5)	2 (8.7)	2 (8.7)	2 (8.7)	.578	0.82 [0.17 to 3.89]	2 (8.7)	2 (8.7)	1.00 [0.13 to 7.78]	.696
BMI one year post-transplantation, median (IQR)	37.2 (34.7 to 40.1)	33.1 (29.7 to 35.6)	-	36.2 (34.4 to 37.6)	.000 <sup>a</sup>	-	33.1 (29.7 to 35.6)	36.2 (34.4 to 37.6)	-	.068
Weight gain one year post-transplantation median (IQR)	2 (-5.5 to 8.5)	0.8 (-10.1 to 5.5)	-	0.0 (-7 to 3)	.329	-	0.8 (-10.1 to 5.5)	0.0 (-7 to 3)	-	.991
Incisional herniation, n (%)	6 (4.5)	1 (4.3)	0.82 [0.10 to 6.98]	3 (13.0)	.725	0.82 [0.10 to 6.98]	1 (4.3)	3 (13.0)	0.30 [0.03 to 3.16]	.304
Surgical reintervention, n (%)	15 (11.3)	2 (8.7)	0.75 [0.16 to 3.52]	4 (17.4)	.526	0.75 [0.16 to 3.52]	2 (8.7)	4 (17.4)	0.45 [0.07 to 2.76]	.333
90-day mortality, n (%)	1 (0.8)	0 (0.0)	0.82 [0.10 to 6.98]	1 (4.3)	.853	0.82 [0.10 to 6.98]	0 (0.0)	1 (4.3)	0.49 [0.36 to 0.66]	.500
EGL, n (%)	7 (5.3)	1 (4.3)	1.82 [0.22 to 15.31]	4 (17.4)	.665	1.82 [0.22 to 15.31]	1 (4.3)	4 (17.4)	0.22 [0.02 to 2.10]	.173
Cause of death, <sup>b</sup> n			-		-	-			-	-
Kidney failure	1	0	-	0	-	-	0	0	-	-
Malignancy	4	1	-	1	-	-	1	1	-	-
Infection	6	1	-	2	-	-	1	2	-	-
Cardiovascular	6	0	-	1	-	-	0	1	-	-
Other	6	0	-	0	-	-	0	0	-	-
Cause of death-censored graft loss, n			-		-	-			-	-
Rejection	12	3	-	2	-	-	3	2	-	-
Thrombotic event	2	1	-	1	-	-	1	1	-	-
Recurring UTI's	2	0	-	0	-	-	0	0	-	-
Recurrence of initial disease	2	0	-	1	-	-	0	1	-	-
Other	9	0	-	1	-	-	0	1	-	-

Abbreviation: BSG, Bariatric surgery group; CI, Confidence interval; DGF, delayed graft function; DM, Diabetes mellitus; DVT, Deep vein thrombosis; EGL, Early graft loss; IQR, interquartile range; OR, Odds ratio; PNF, Primary non-function; PSM, Propensity Score Matching; PTDM, Post-transplant diabetes mellitus; TO, Transplant only; UTI, Urinary tract infection.

<sup>a</sup>Statistically significant.

<sup>b</sup>Concerns cause of death during entire follow-up.

### Incidence of severe complications



**FIGURE 2** Incidence of severe postoperative complications according to the Clavien-Dindo classification. BSG, bariatric surgery group; TO, transplant only

**TABLE 4** Overview of complications included in each severe Clavien-Dindo Grade

Clavien-Dindo classification	
Grade IIIa	Ureteral problems treated with only PCN (n = 4) Ureteral problems treated with dotter (n = 6) Arrhythmia treated with cardioversion (n = 3) DGF requiring hemodialysis (n = 30)
Grade IIIb	Ureteral re-implantation (n = 6) Respiratory insufficiency requiring artificial respiration (n = 1)
Grade IV	Myocardial infarct requiring PCI (n = 2) EGL due to rejection (n = 3) EGL due to thrombus (n = 2)
Grade V	Death (n = 1)

Abbreviation: DGF, delayed graft function; EGL, early graft loss; PCI, percutaneous coronary intervention; PCN, percutaneous nephrostomy.

**TABLE 5** Postoperative complications after kidney transplantation in bariatric surgery patient divided by type of bariatric procedure

	SG (n = 11)	RYGB (n = 9)	GB (n = 3)
Myocardial infarct, n (%)	0 (0)	1 (11)	0 (0)
Renal artery thrombosis, n (%)	0 (0)	1 (11)	0 (0)
Biopsy proven rejection, n (%)	2 (18)	3 (33)	1 (33)
Wound infection, n (%)	2 (18)	1 (11)	0 (0)
DVT, n (%)	1 (0)	0 (0)	0 (0)

Abbreviations: DVT, deep vein thrombosis; GB, gastric banding; SG, sleeve gastrectomy; RYGB, Roux-en Y gastric bypass.

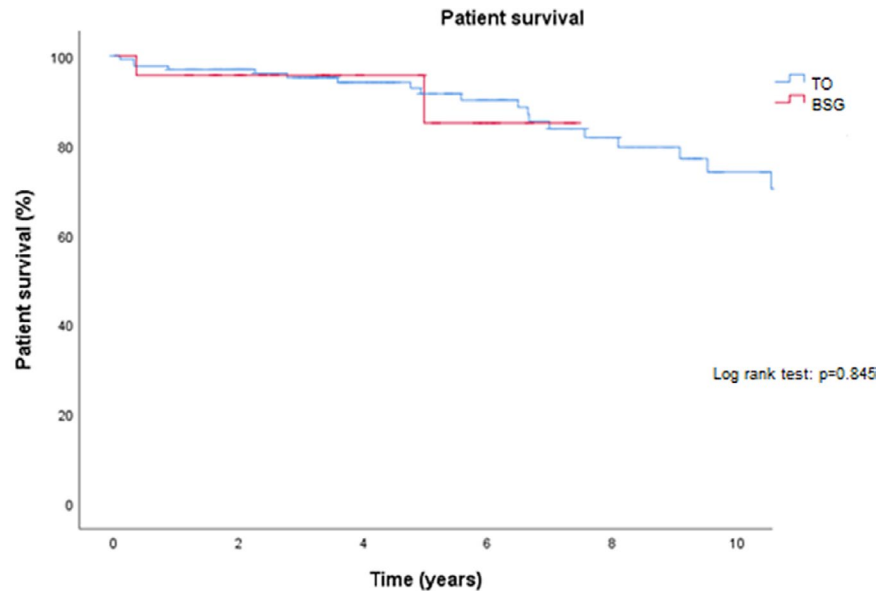
### 3.4 | Patient survival

The minimal follow-up time was 1.2 years, and the maximum follow-up was 21.5 years. The median time between KTx and BS in patients who underwent BS after transplant was 6.87 years (5.37–9.35). Follow-up of these patients was censored after the date of BS. In total, there were 25 (18.8%) deaths in the TO recipients and 2 in the BSG (8.7%). The median follow-up was 5.1 years (2.7–8.1). Eighty-seven patients (56%) had a follow-up time longer than 5 years, 10 in the BSG (43%) and 58% in the TO (n = 77). The 90-day mortality rate was 0.8% (n = 1) in the TO and zero in the BSG (p = .853). The cause of death in that patient was a cardiac arrest. After 5 years, the survival rate of the TO group was 90% compared with 85% of the BSG. There was no significant difference in patient survival between TO and BSG (log rank test: p = .845) (Figure 3). Survival rates were statistically tested in the matched cohort. At 5 years post-transplantation, patient survival rates were 81% in the matched TO cohort and 80% in BSG (log rank test: p = .724). Multivariable analysis was done using preselected variables to identify risk factors for overall death and the effect of each risk factor is shown in Table 6. Bariatric status, diabetes mellitus, and dialysis status were included in Cox proportional hazards multivariable analysis. Independent risk factors for all-cause mortality were dialysis treatment pre-transplantation (HR 2.55; 95% CI 1.03–6.34, p = .043) and having a medical history of diabetes mellitus (HR 2.41; 95% CI 1.11–5.22, p = .027).

### 3.5 | Graft survival

In total, 50 (37.6%) grafts were lost due to either graft failure or patient death in the TO and 6 (26.1%) in the BSG. The incidence of EGL was 6.1% (n = 8) in the TO compared with 4.3% (n = 1) in the BSG (p = .790). Figure 4 shows the death-censored graft survival curve





Numbers at risk:

Year	0	1	2	3	4	5	6	7	8	9	10
TO	133	127	115	100	82	63	50	39	31	22	17
BSG	23	22	18	15	10	8	5	2	0	0	0

FIGURE 3 The patient survival curve post-transplant of recipients with obesity class II and III compared with patients who underwent bariatric surgery. BSG, bariatric surgery group; TO, transplant only

TABLE 6 Multivariable analysis of patient survival using Cox proportional hazards model

	Multivariable analysis HR [95% CI]	p-value
DM	2.41 [1.11-5.22]	.027 <sup>a</sup>
BS	1.57 [0.33-7.42]	.572
Dialysis history	2.55 [1.03-6.34]	.043 <sup>a</sup>

Abbreviations: BMI, Body mass index; BS, Bariatric surgery; CI, confidence interval; DM, diabetes mellitus; HR, hazard ratio.

<sup>a</sup>Statistically significant.

of the two groups. No statistically significant difference was found between the two groups (log rank test:  $p = .659$ ). Death-censored graft survival after 5 years was 78% in TO and 65% in BSG. Death-censored graft survival was statistically tested in the matched cohort. At 5 years post-transplantation, death-censored graft survival was 66% in the matched transplant only cohort and 64% in BSG (log rank test:  $p = .964$ ).

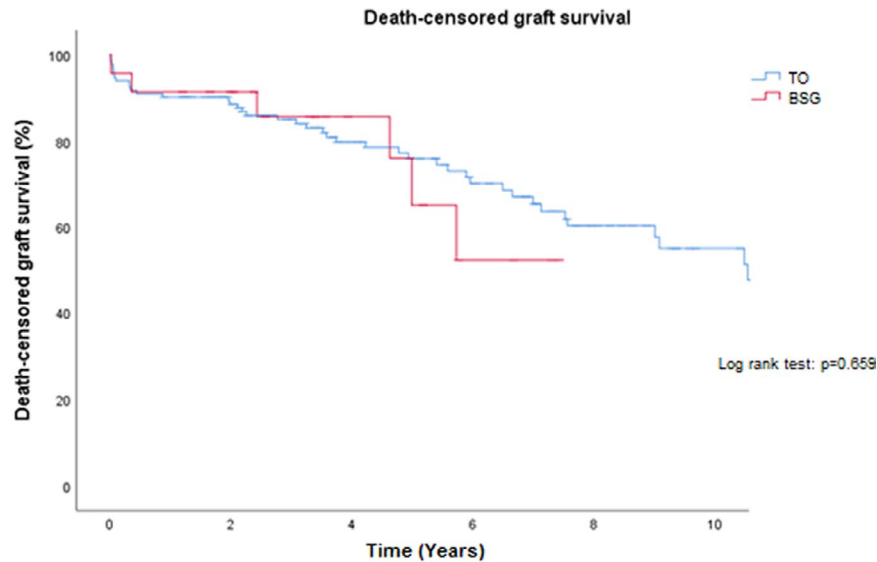
Figure 5 shows the survival curve of the uncensored graft survival. Uncensored graft survival after 5 years was 84% in TO and 80% in BSG. The log rank test showed that there is no significant difference in overall graft survival between the BSG and TO ( $p = .704$ ). Uncensored graft survival was statistically tested in the matched cohort. At 5 years post-transplantation, uncensored graft survival was 70% in the matched TO cohort and 80% in BSG (log rank test:  $p = .869$ ).

Multivariable analysis was done to identify risk factors for death-censored graft loss. The effect of each risk variable is shown in Table 7. Age per year, BMI per point, diabetes, type of donor, and bariatric status were included in the multivariable analysis. Having received a kidney from a deceased donor was an independent risk factor for death-censored graft loss (HR 1.98; 95% CI 1.04-3.79,  $p = .038$ ).

## 4 | DISCUSSION

Patients who became eligible for KTx after BS after initial rejection due to obesity have similar outcome as matched transplant recipients with obesity class II and III. Furthermore, 5-year graft and patient survival after kidney transplantation did not differ between both groups.

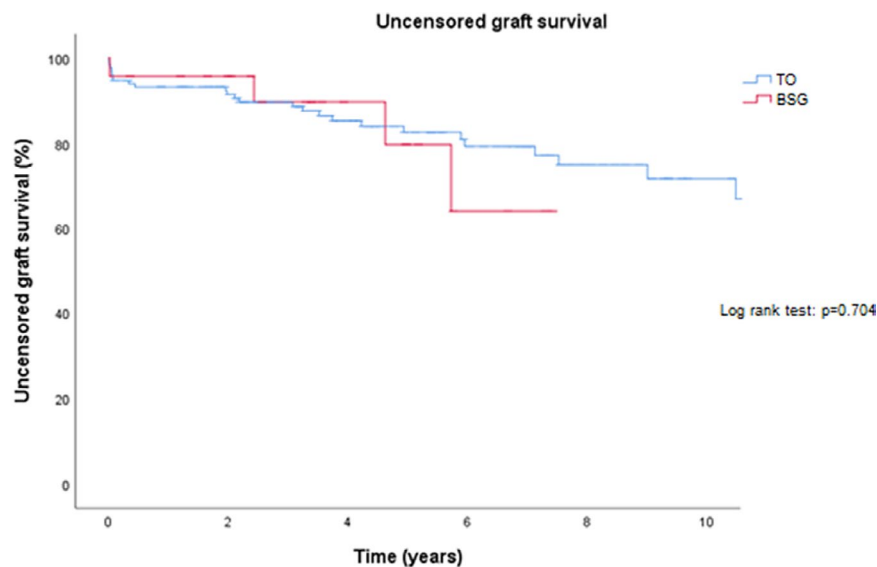
In this cohort, the BSG had a median BMI of 42.3 kg/m<sup>2</sup> before BS and the majority of patients were considered ineligible for transplantation based on the fat distribution. After BS, the median BMI was 33.6 kg/m<sup>2</sup> and all patients were found eligible for transplantation. If patients had not undergone BS, the majority of these patients would have remained on dialysis or would have never been transplanted. This finding is in line with other studies that report the use of BS in helping patients become eligible for KTx.<sup>21-24</sup> In a retrospective study by Modanlou et al,<sup>24</sup> 29 waitlisted patients were referred to undergo BS and 20 of them proceeded with transplantation. Jamal



Numbers at risk:

Year	0	1	2	3	4	5	6	7	8	9	10
TO	133	118	106	90	69	57	48	40	28	23	16
BSG	23	21	18	14	9	6	3	2	1		

**FIGURE 4** The death-censored graft survival curve post-transplant of recipients with obesity class II and III compared with patients who underwent BS prior to transplantation. BSG, bariatric surgery group; TO, transplant only



Numbers at risk:

Year	0	1	2	3	4	5	6	7	8	9	10
TO	133	118	106	90	69	57	48	40	28	23	16
BSG	23	21	18	14	9	6	3	2	1		

**FIGURE 5** The uncensored graft survival curve post-transplant of recipients with obesity class II and III compared with patients who underwent BS prior to transplantation. BSG, bariatric surgery group; TO, transplant only

et al described 21 cases of BS in patients on dialysis of whom 18 had lost sufficient weight and herewith becoming eligible for transplantation. The survival advantage of KTx compared with dialysis stresses the importance of becoming eligible for transplantation.<sup>21</sup>

Gill et al concluded that the survival advantage of KTx compared with dialysis is great across most BMI groups. The only exception were African American women with class III obesity.<sup>26</sup> It is therefore beneficial for the majority of patients with obesity to be transplanted.

**TABLE 7** Multivariable analysis of death-censored graft survival using Cox proportional hazards model

	Multivariable analysis HR [95% CI]	p-value
Age	1.01 [0.99–1.03]	.367
DM	0.92 [0.53–1.59]	.761
BMI	1.08 [0.98–1.18]	.093
BS	1.45 [0.55–3.79]	.761
Deceased donor	1.98 [1.04–3.79]	<b>.038<sup>a</sup></b>

Abbreviations: BMI, body mass index; BS, bariatric surgery; DM, diabetes mellitus; HR, Hazard ratio.

<sup>a</sup>Statistically significant.

As this study shows, having undergone BS was not a risk factor for patient death. Therefore, we can conclude that BS does not render additional risk of morbidity and mortality after KTx compared with the control group.

Patients who became transplantable after BS had similar outcome as matched patients with obesity class II and III. No decrease in complication rates was found in the BSG compared with the TO. This can possibly be explained by the fact that the majority of recipients were still obese (BMI IQR 31.4–34.7 kg/m<sup>2</sup>) at the time of transplantation, even though BS was performed. The main objective of BS in these particular patients is not achieving a healthy weight, but becoming eligible for transplantation by decreasing the amount of intra-abdominal fat. However, considering that the median BMI before BS was 42.3 kg/m<sup>2</sup>, patients did lose a considered amount of excess weight and it can therefore be concluded that BS is feasible in KTx candidates suffering from obesity.

More interestingly, multivariate analysis showed that every increment in BMI adds nearly 8% risk of graft loss (HR 1.08, 95% CI: 0.98–1.18,  $p = .093$ ). As this HR is not statistically significant, it does show a trend toward significance. This suggests that even in the transplant recipients with obesity class II or higher (BMI  $\geq 35$ ) every increment in BMI negatively effects graft survival. Therefore, weight loss should be recommended in every patient with obesity.

Also noteworthy is the high percentage of PNF of 2.3% in the TO and 4.3% in the BSG.

In total, nine grafts were lost in the first 3 months after transplantation. The occurrence of PNF is often attributed to graft characteristics rather than recipient characteristic as it is more prevalent in inferior graft from older donor or deceased donors. Although the percentage of older donors or Extended Criteria donors (ECD) was comparable among groups, the TO more often receive grafts from a living donor (67.7% vs 56.5%).

Another notable matter is the high number of thrombosis in both the TO (3.8%) and BSG (4.3%). This could probably be explained by the fact that obesity a risk factor is for developing thrombosis and obese patients are two to three times more likely to develop renal vein or artery thrombosis.<sup>27,28</sup> As this study only included patient with a BMI  $\geq 35$ , higher numbers of thrombosis are to be expected. Furthermore, in this cohort two graft were lost due to thrombosis,

showing the importance of preventing the development of renal thrombosis. In a study done by Van den Berg et al, the effect of perioperative antithrombotic therapy on the development of renal artery thrombosis was investigated.<sup>28</sup> They concluded that with a stricter antithrombotic therapy, postoperative thromboembolic complications decrease. However, this was associated with higher risk of postoperative bleeding.

This study shows that having undergone bariatric surgery does not increase complications after KTx or negatively effects patient survival and graft survival. Therefore, we can conclude that BS is a safe method to establish long-term weight loss. The policy used by most transplant centers in The Netherlands of withholding KTx until a BMI below 35 kg/m<sup>2</sup> is achieved can result in an extended period of dialysis or in patients not being transplanted at all, as they might never establish the required weight loss. This could eventually lead to higher morbidity and mortality rates than when choosing to perform a transplant in a patient with obesity class II and III obesity. However, benefits of bariatric surgery must weight against the risk of morbidity from extended dialysis prior to kidney transplantation. In our data, BSG received longer dialysis treatment than the TO and although not statistically significant, complications associated with dialysis such as cardiovascular event and wound complications are slightly higher in the BSG. In those patients who do not have a living donor available, BS can be used to bridge the time on the waiting list for a deceased kidney offer. This time can be used to get these patients in optimal condition for KTx.

Wound complications are among the major challenges when performing kidney transplantation in obese patients.<sup>17</sup> In our cohort, the incidence of wound problems was 11.3% among TO recipients and 13% in the BSG. This percentage is higher compared with the incidence of 7% that is reported in the general KTx population.<sup>25</sup> This is probably due to the obesity in both TO and BSG which is known to increase wound problems in kidney transplant recipients.<sup>16,17</sup> As previously mentioned, excessive abdominal fat impairs the view of the surgical field which can hinder the implantation of the kidney. Robot-assisted kidney transplantation (RAKT) can be a feasible alternative in obese kidney transplant recipients, because it provides an enhanced view of the surgical field and can be performed through a smaller incision.<sup>29,30</sup> Tzvetanov et al reviewed six studies about RAKT and concluded that there is a decrease of wound problems in obese recipients after RAKT compared with open surgery.<sup>30</sup> Spaggiari et al performed 28 RAKTs in patients with a BMI above 30 kg/m<sup>2</sup> between 2009 and 2013 and observed no wound infection in patients undergoing RAKT compared with 28.6% in the open surgery group.<sup>31</sup>

In two patients, oxalate nephropathy was observed after RYGB. Oxalate nephropathy is a complication often seen in patients with inflammatory bowel diseases (IBD), ileal resection, and Roux-en-Y gastric bypass (RYGB).<sup>32</sup> Due enteric hyperoxaluria, oxalate accumulates in the kidney and can cause nephrolithiasis and nephrocalcinosis. Literature has shown that even though weight loss after SG is comparable to RYGB, complication rates are much lower.<sup>33</sup> In obese transplant candidates, we have a preference for SG, due to lower complication rates and a lower to no risk of oxalate nephropathy.

This study has several limitations. BS was not considered in kidney transplant candidates up until recently, and therefore, only a small number of patients who had undergone both procedures were included. The present study is a retrospective, single-center analysis. There is a potential for selection bias as the decision for eligibility for KTx is depending on the opinion of a surgeon rather than an objective measure. We hypothesized that obese male candidates would more often require bariatric surgery, as they are more likely to have visceral fat distribution. However, this did not turn out to be the case. In our opinion, it is difficult to establish an objective measure for eligibility through imaging in this group of patients and eligibility based on the physical examinations remains the standard.

It has been shown that recipient obesity influences the outcome of kidney transplantation in the long-term rather than the short-term. This study, to our knowledge, presents the longest follow-up in patients undergoing both kidney transplantation and BS. However, longer follow-up is needed to form a conclusive answer to whether or not successful BS positively influences graft and patient survival in patient with obesity class II and III. The effectiveness of improving eligibility in potential transplant recipients through BS needs to be further determined in order to actively refer patients to BS.

In conclusion, patients who became eligible for KTx after BS after initial rejection due to obesity have similar results of KTx as matched kidney transplant patient with obesity class II and III who were eligible while being obese. Kidney transplantation after BS does not negatively affect the outcome of KTx compared with transplanting patients with obesity class II or higher.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

## AUTHOR CONTRIBUTION

LO, HJANK, JNMIJ, and RCM participated in the research design. LO, HJANK, JNMIJ, JIR, ML, ULB, RAK, JNMIJ, and RCM participated in the writing of the article. LO, HJANK, and RCM participated in the performance of the research and data analysis.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author, RCM. The data are not publicly available due to restrictions, for example, their containing information that could compromise the privacy of research participants.

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