

# Bariatric Surgery in Kidney Transplant Candidates and Recipients: Experience at an Asian Center

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**Background:** Kidney transplant (KT) candidates and recipients with obesity experience more frequent complications such as infection, poorer allograft outcomes, diabetes, and mortality, limiting their eligibility for transplantation. Bariatric surgery (BS) is not commonly performed among KT patients given concerns about immunosuppression absorption, wound healing, infections, and graft outcomes. Its role has not been described before in an Asian KT patient setting.

**Methods:** A retrospective review of patients who underwent BS at the largest KT center in Singapore from 2008 to 2020 was conducted. Metabolic outcomes, immunosuppression doses, graft outcomes, and mortality were studied.

**Results:** Seven patients underwent BS and KT (4 underwent BS before KT, 3 underwent BS after KT; 4 underwent sleeve gastrectomy, 3 underwent gastric bypass). Mean total weight losses of 23.8% at 1 year and 18.6% at 5 years post-BS were achieved. Among the five patients with diabetes, glycemic control improved after BS. There were no deaths in the first 90 days or graft loss in the first year after KT and BS. Patients who underwent BS after KT had no significant changes in immunosuppression dose.

**Conclusion:** BS can be safely performed in KT recipients and candidates and results in sustainable weight losses and improvements in metabolic comorbidities. Although no major complications were observed in our study, close monitoring of this complex group of patients is imperative.

**Key words:** Bariatric surgery, Kidney transplantation, Chronic kidney disease

Received November 25, 2021

Reviewed January 25, 2022

Accepted October 26, 2022

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## INTRODUCTION

Obesity is an increasingly common chronic disease associated with multiple complications, including type 2 diabetes mellitus (DM), chronic kidney disease, ischemic heart disease, cancers, and higher mortality.<sup>1</sup> These adverse outcomes are compounded among kidney transplant (KT) recipients, where obesity is associated with peritransplant complications such as poorer allograft outcomes, delayed wound healing, increased incidence of new-onset diabetes after transplantation, and higher mortality.<sup>2</sup> As a result, access to transplantation is limited among patients with obesity, and registry-based

analyses indicate that transplant candidates with obesity are less likely to receive an organ offer than non-obese candidates.<sup>3</sup> Thus, obesity treatment is an important aspect in the care of KT candidates.

Conversely, transplant recipients may also develop obesity following transplantation, driven by the use of glucocorticoids and immunosuppressants.<sup>4</sup> Posttransplant obesity has also been shown to be associated with poorer transplant outcomes. A 20-year follow-up study conducted in the Netherlands showed that a 1-year post-transplant body mass index (BMI) > 30 kg/m<sup>2</sup> was associated with higher mortality and graft failure rates.<sup>5</sup> While supervised

posttransplant exercise training programs are helpful in curbing weight gain, they may not be effective in patients with severe obesity.<sup>6</sup>

For nontransplant patients with severe obesity, bariatric surgery has proven to be effective in prompting long-term weight loss as well as improvements in and resolution of associated medical comorbidities.<sup>7</sup> However, among KT recipients and candidates, the use of bariatric surgery as a treatment option for obesity has not been common. Points of concern include safety outcomes such as rates of postoperative infections in immunosuppressed patients and interference with absorption of immunosuppressants following malabsorptive procedures and suboptimal nutrition.<sup>8</sup>

Retrospective case series of bariatric surgery among transplant candidates and recipients have documented effective weight loss, resulting in overall improved allograft function and survival compared to matched controls.<sup>9-12</sup> However, allograft complications such as acute kidney injury (AKI) and erratic immunosuppression levels have also been described.<sup>12</sup>

With the above safety concerns and lack of prospective longitudinal evidence, access to bariatric surgery among KT recipients and candidates may continue to be limited. Particularly in an Asian setting, evidence is scarce and limited to case reports.<sup>13</sup> Obesity rates in Asia have surged over the past few decades, complicated by obesity-related disorders that typically develop at a younger age in Asians compared to Western populations.<sup>14</sup> Thus, this study aimed to review the outcomes of bariatric surgery performed in KT patients at a tertiary center in Asia in order to address weight loss outcomes as well as possible allograft-related complications.

## METHODS

We performed a retrospective observational review of patients who underwent bariatric surgery at the largest KT center in Singapore from September 2008 to September 2020 (SingHealth Centralised Institutional Review Board, No. 2020/2482). Patients who underwent bariatric surgery either before or after KT were included. Suitability for bariatric surgery was assessed according to the local recommended clinical guidelines (BMI  $\geq 37.5$  kg/m<sup>2</sup> or BMI  $\geq 32.5$  kg/m<sup>2</sup> with  $\geq 1$  obesity-related complication), and surgery was offered to eligible patients.<sup>15</sup>

Patients undergoing KT after bariatric surgery received induction immunosuppression of intravenous steroids and intravenous basiliximab. Maintenance immunosuppression typically consisted of low-dose corticosteroids, an anti-metabolite, and a calcineurin inhibitor (CNI). Maintenance immunosuppression may be altered to include mammalian target of rapamycin (mTOR) inhibitors based on the clinical indication. Transplanted patients were offered bariatric procedures if they had stable graft function and were on stable immunosuppressive therapy in the preceding year. Alternative immunosuppression was prescribed to patients who were on mTOR inhibitors to prevent impairments in wound healing following bariatric surgery.

All bariatric procedures were performed by a team of experienced bariatric surgeons who employed techniques that we have reported on previously for both laparoscopic sleeve gastrectomy (LSG) and Roux-en-Y gastric bypass (RYGB).<sup>16,17</sup> The decision to pursue LSG or RYGB was individualized based on patients' clinical characteristics, risks, and preferences following a discussion with the bariatric team. Patients were managed by a multidisciplinary team involving endocrinologists, bariatric surgeons, transplant nephrologists, dietitians, bariatric nurses, clinical coordinators, exercise physiotherapists, and psychologists.

Data were extracted from a prospective electronic database. Outcomes included metabolic outcomes such as BMI, glycosylated hemoglobin (HbA1c), and diabetes. Kidney outcomes such as serum creatinine level, immunosuppressant doses and levels, graft rejection, and graft loss were collected. Postoperative mortality, defined as mortality during the hospital stay or  $\leq 90$  days after bariatric surgery or transplantation, was also extracted. Outcome data were collected at baseline and annually until 5 years after bariatric surgery.

Statistical analysis was performed using IBM SPSS Statistics ver. 21.0 (IBM Corp., Armonk, NY, USA). Baseline and postoperative descriptive statistics such as mean values were computed. Postoperative outcomes between the two groups were compared using the two-sample Student t-test. A  $P < 0.05$  was considered statistically significant.

## RESULTS

On retrospective chart review, there were seven patients who un-

**Table 1.** Summary of baseline characteristics

Recipient characteristics	Bariatric surgery pretransplant (n=4)	Bariatric surgery posttransplant (n=3)
Mean age at kidney transplant (yr)	45.7	50.3
Male sex	3	2
DM before transplantation	3	2
Cause of ESKF		
DM	3	2
GN	1	1
Type of transplant		
LDKT	2	0
DDKT	2	3
Mean BMI at time of renal transplant (kg/m <sup>2</sup> )	29.6	33.4
Bariatric surgery characteristics		
Mean age at bariatric surgery (yr)	42.7	53.6
Mean BMI at time of bariatric surgery (kg/m <sup>2</sup> )	35.6	39.0
Mean HbA1c at the time of bariatric surgery (%)	8.2	7.8
Type of bariatric surgery		
LSG	2	2
RYGB	2	1
On dialysis at time of bariatric surgery	2	0
Time from bariatric surgery to transplant (yr)	2.3	-
Time from transplant to bariatric surgery (yr)	-	4.3
Maintenance immunosuppression		
Prednisolone+cyclosporine A+mycophenolate	3	2
Prednisolone+tacrolimus+mycophenolate	1	1

DM, diabetes mellitus; ESKF, end-stage kidney failure; GN, glomerulonephritis; LDKT, living-donor kidney transplantation; DDKT, deceased-donor kidney transplantation; BMI, body mass index; HbA1c, glycosylated hemoglobin; LSG, laparoscopic sleeve gastrectomy; RYGB, Roux-en-Y gastric bypass.

derwent both bariatric surgery and KT, including four who underwent bariatric surgery before KT and three who underwent bariatric surgery after KT. Their baseline characteristics are shown in Table 1. Five of the seven patients were men, and the average age of all patients at the time of bariatric surgery was  $47.4 \pm 9.6$  years. The average weight and BMI at the time of bariatric surgery were  $103.8 \pm 8.4$  kg and  $37.1 \pm 3.2$  kg/m<sup>2</sup>, respectively. Five of the seven patients had end-stage kidney failure (ESKF) due to DM, while the remaining two had ESKF from glomerulonephritis without concomitant DM. Four patients underwent LSG, and three underwent RYGB. An overview of the seven cases is presented in Table 2.

### Metabolic outcomes

The cohort achieved mean percentage of total weight loss (%TWL) of 23.8% (range, 14.2%–33.3%) at 1 year and 18.6% (range, 10.1%–

26.9%) at 5 years after bariatric surgery. The patients who underwent bariatric surgery after KT had higher preoperative BMI (mean, 39 kg/m<sup>2</sup>) compared to those who underwent bariatric surgery before KT (mean, 35.6 kg/m<sup>2</sup>); however, they also experienced a greater %TWL and less weight regain. The patients who had bariatric surgery after KT had a 1-year mean %TWL of 29.6%, whereas those who had bariatric surgery before KT had a 1-year mean %TWL of 19.5% ( $P=0.040$ ). At 5 years after bariatric surgery, the mean %TWL was 24.8% in those who underwent bariatric surgery after KT but 15.5% in those who had bariatric surgery before KT ( $P=0.049$ ). The mean BMI was comparable across both groups at 5 years after bariatric surgery (28.6 kg/m<sup>2</sup> in those who had bariatric surgery before KT vs. 29.8 kg/m<sup>2</sup> in those who had bariatric surgery after KT ( $P=0.692$ )).

Weight loss outcomes (%TWL) after bariatric surgery are depicted in Fig. 1. The most profound weight loss was seen in the first year following bariatric surgery in all cases. Among the patients who underwent KT after bariatric surgery, only one (case 3) experienced weight gain within the first 2 years following KT.

Among patients with DM, glycemic control improved after bariatric surgery. The mean HbA1c concentration before bariatric surgery fell from 8% to 6.5% at 5 years after bariatric surgery. Two patients without pre-existing DM did not develop diabetes after KT. However, the patients who underwent KT after bariatric surgery experienced a smaller improvement in HbA1c at 5 years after bariatric surgery than did patients who underwent KT before bariatric surgery (mean decrease in HbA1c, 0.67% vs. 3%). Despite the initial improvements in glycemic control following bariatric surgery, these three patients required intensification of their glycemic regimen to basal bolus insulin therapy immediately post-KT. An example (case 4) is depicted in Fig. 2, where the patient had worsening glycemic control post-KT despite good weight maintenance. One patient (case 7) had pre-existing non-alcoholic steatohepatitis cirrhosis that did not improve after bariatric surgery; they eventually died from liver cirrhosis at 4 years after bariatric surgery.

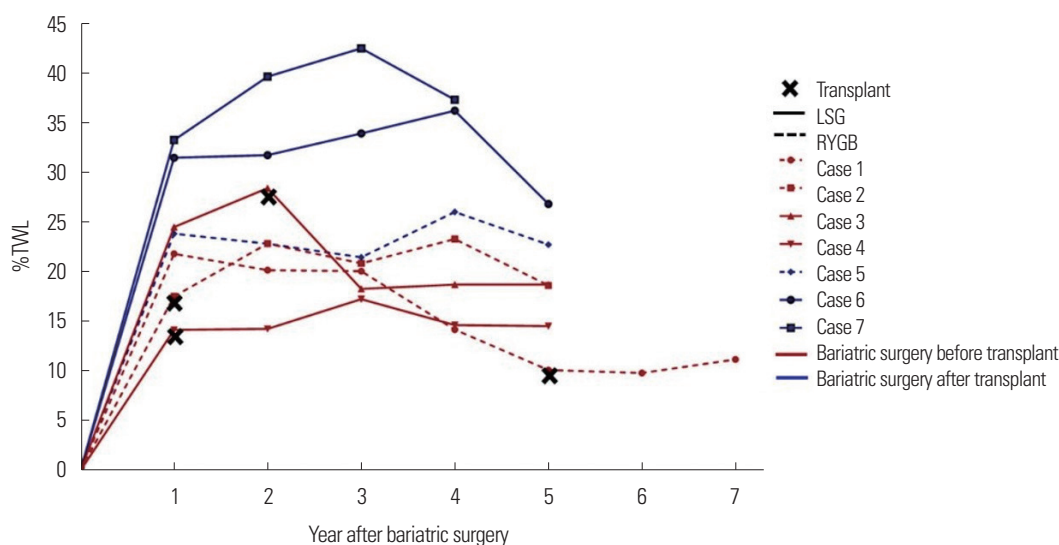
### Kidney outcomes

There was no graft loss in the first year after KT and bariatric surgery among the seven patients, nor was there any graft loss attributed to obesity during the duration of follow-up. Among the

**Table 2.** Case details

No.	Sex	Age (yr)	Ethnicity	Year of transplant	Year of bariatric surgery	Type of surgery	Weight before bariatric surgery (kg)	BMI before bariatric surgery (kg/m <sup>2</sup> )	Weight before transplant (kg)	BMI before transplant (kg/m <sup>2</sup> )	DM	HbA1c before bariatric surgery (%)	5-Year HbA1c (%)	1-Year %TWL	5-Year %TWL	Graft and mortality outcome
Bariatric surgery before transplant																
1	Male	64	Chinese	2017	2012	RYGB	100.3	34.3	90.1	30.8	Yes	9.0	8.4	21.8	10.1	-
2	Female	50	Chinese	2015	2014	RYGB	90.0	36.1	74.2	29.7	Yes	8.2	6.5	17.6	18.7	-
3	Male	39	Chinese	2016	2015	LSG	112.0	40.2	84.5	30.3	No	-	-	24.6	18.8	Graft rejection (2016)
4	Male	43	Chinese	2017	2015	LSG	103.0	31.8	88.3	27.9	Yes	7.5	7.8	14.2	14.6	-
Bariatric surgery after transplant																
5	Male	67	Chinese	2010	2014	RYGB	109.3	40.6	89.8	33.5	Yes	6.4	4.9	23.9	22.8	Graft rejection (2018)
6	Male	55	Malay	2012	2014	LSG	113.7	38.0	101.2	32.9	Yes	9.2	5.0	31.5	26.9	Death (myelodysplastic syndrome and pneumonia) (2020)
7	Female	56	Chinese	2008	2015	LSG	98.4	38.4	84.2	33.8	No	-	-	33.3	-	Graft failure (2019) Death (non-alcoholic steatohepatitis cirrhosis) (2020)

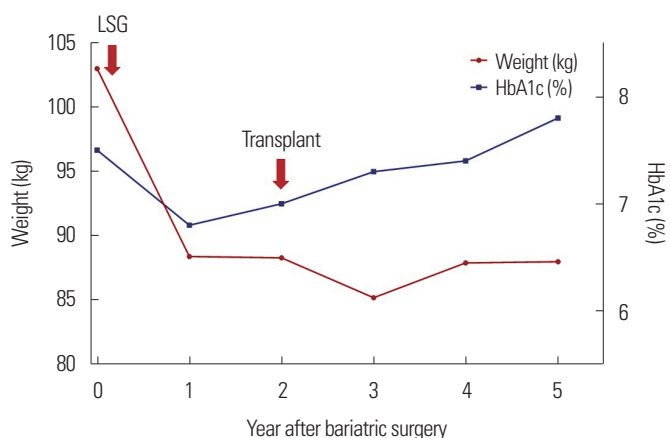
BMI, body mass index; DM, diabetes mellitus; HbA1c, glycosylated hemoglobin; %TWL, percentage of total weight loss; RYGB, Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy.



**Figure 1.** Individual weight loss outcomes after bariatric surgery. %TWL, percentage of total weight loss; LSG, laparoscopic sleeve gastrectomy; RYGB, Roux-en-Y gastric bypass.

patients who underwent bariatric surgery before KT, one (case 3) developed acute antibody-mediated rejection post-KT requiring treatment with plasma exchange, intravenous immunoglobulins, and thymoglobulin. However, this was attributed to the greater im-

munological risks inherent in an ABO-incompatible KT procedure rather than to the bariatric surgery performed in the preceding year. Among those who underwent bariatric surgery after KT, one developed graft rejection 8 years posttransplant and another developed



**Figure 2.** Case 4 trends in weight and glycosylated hemoglobin (HbA1c) after bariatric surgery. LSG, laparoscopic sleeve gastrectomy.

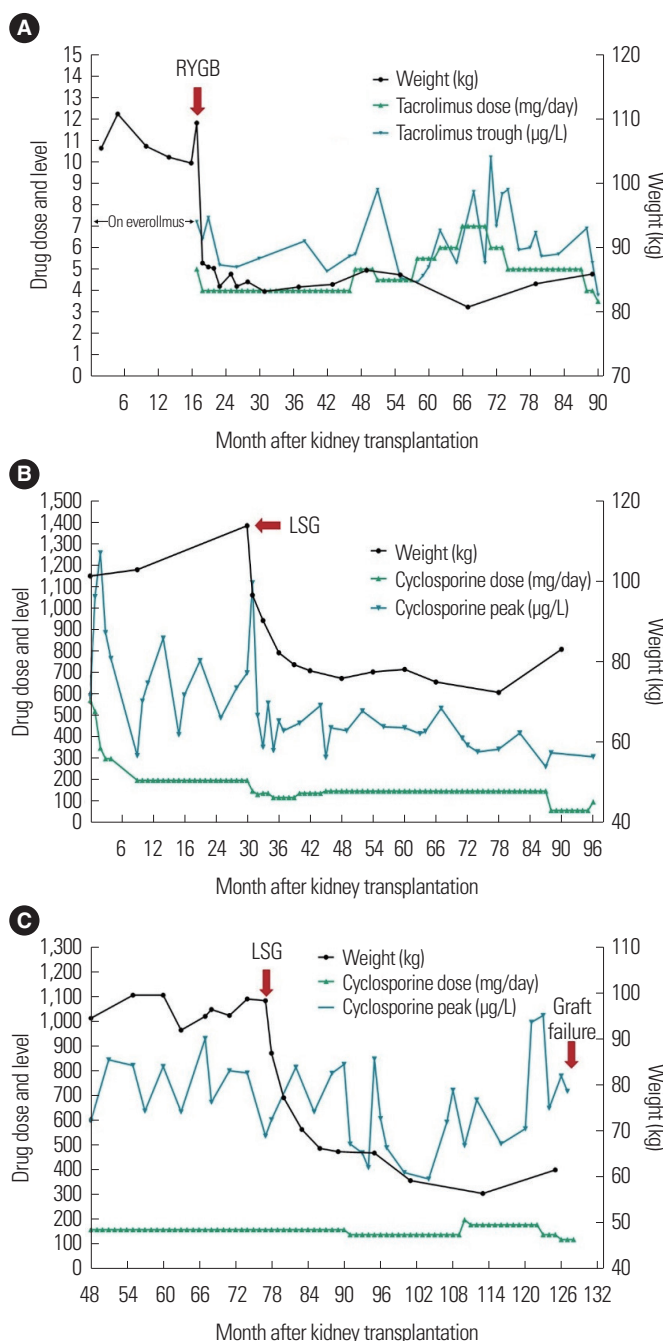
graft failure 11 years posttransplant, with both cases occurring 4 years after bariatric surgery. The immunosuppression levels following bariatric surgery were stable over these 4 years, so the graft failure was not attributed to malabsorption from bariatric surgery (Fig. 3C). None of the included patients developed new kidney stones after bariatric surgery.

### Impact on immunosuppression

Patients who underwent bariatric surgery after KT had no significant changes in immunosuppression doses or drug levels in the immediate postoperative period. One patient (case 5) was converted from mTOR inhibitor therapy to CNI maintenance immunosuppression before bariatric surgery to reduce the risk of poor wound healing. Despite weight loss in the year following bariatric surgery, this patient’s immunosuppression levels and doses remained stable with no need for major changes in dosing. Fig. 3 depict the individual immunosuppression levels and doses in relation to weight before and after bariatric surgery.

### Surgical complications

There were no deaths in the first 90 days after bariatric surgery or KT. None of the patients developed any major postoperative complications, such as cardiovascular events, AKI, delayed wound healing, or infection. Patients who were on haemodialysis prior to bariatric surgery required pre-emptive adjustments of dry weight to prevent readmissions for fluid overload during weight loss.



**Figure 3.** Trends in weight loss and immunosuppression doses and levels after kidney transplantation: (A) case 5, (B) case 6, and (C) case 7. RYGB, Roux-en-Y gastric bypass; LSG, laparoscopic sleeve gastrectomy.

## DISCUSSION

This case series describes the role of bariatric surgery in KT recipients and candidates in a uniquely Asian setting. Regardless of whether bariatric surgery was performed before or after KT, satis-



factory weight loss outcomes were achieved at 1 year and 5 years after bariatric surgery. Individuals who underwent KT after bariatric surgery had a smaller %TWL than those who underwent KT before bariatric surgery. Cohen et al.<sup>12</sup> also reported that patients who underwent bariatric surgery after KT had a lower median BMI at 5 years after surgery compared to those who underwent bariatric surgery before KT. This could have been influenced by the addition of glucocorticoids and immunosuppression post-KT. In this study, it could also be explained by the fact that patients who underwent KT after bariatric surgery had lower preoperative BMI compared to those who underwent KT before bariatric surgery. Individuals with higher preoperative BMI have been shown to achieve greater %TWL compared to those with lower preoperative BMI.<sup>18</sup> It could also be reflective of the lead-time bias towards patients who underwent KT before bariatric surgery, as they may have already experienced immunosuppression-related weight gain prior to undergoing bariatric surgery. Importantly, the mean BMI at 5 years after bariatric surgery (29 kg/m<sup>2</sup>) was comparable across groups, with all patients achieving a BMI < 32.5 kg/m<sup>2</sup>.

There was a significant variation in weight loss outcomes among the seven participants, with the 1-year %TWL ranging from 14.2% to 33.3% and the 5-year %TWL ranging from 10.1% to 26.9%. Of note, the two patients (cases 6 and 7) who eventually died experienced the largest %TWL in both the short- and long-term periods following bariatric surgery. This represents the complexity of weight management in KT patients, where a multitude of other factors may also contribute to weight, such as nutrition, sarcopenia, immunosuppression, chronic infections, fluid overload states, and organ failure. This association between low BMI and higher mortality has been described previously in KT cohorts. Streja et al.<sup>19</sup> analyzed 10,090 KT recipients for 6 years post-KT and observed that a lower BMI (< 22 kg/m<sup>2</sup>) correlated with higher post-KT mortality. Similarly, Chang and McDonald<sup>20</sup> reported that posttransplant weight loss > 5% after KT was associated with increased mortality compared to individuals with either stable weight or moderate weight gain. Thus, this illustrates the importance of conducting holistic management in the follow-up of KT patients after bariatric surgery rather than focusing on absolute weight loss alone. If the degree of weight loss is greater than expected, the above factors should be taken into consideration.

Improvements in glycemic control following bariatric surgery were seen in the five patients with underlying DM. In a meta-analysis of KT candidates and recipients who underwent bariatric surgery, improvement or remission of type 2 DM was observed in 64% and 72% of patients, respectively.<sup>21</sup> However, in this series, patients who underwent KT after bariatric surgery later developed worsening glycemic control posttransplant, requiring intensification of diabetes treatment. This emphasizes that, while bariatric surgery does result in improvement of comorbidities among KT patients, they remain at risk of worsening metabolic complications posttransplant, due to glucocorticoid and immunosuppression use. Although none of the patients in this small series developed new diabetes after transplantation, previous local studies have reported a high incidence of diabetes (24.2%) at 5 years post-KT, which was associated with poorer graft and patient survival rates.<sup>22</sup> Thus, managing physicians should remain alert to the potential need to intensify diabetes treatment after transplant, even if patients experience improvements or normalization of blood glucose after bariatric surgery.

Not all metabolic comorbidities may improve following bariatric surgery and KT. One patient (case 7) had pre-existing non-alcoholic steatohepatitis cirrhosis diagnosed 6 years prior to bariatric surgery, and their demise occurred 4 years later despite appropriate weight loss. On the whole, several studies have described improvement and resolution of non-alcoholic steatohepatitis and fibrosis following metabolic surgery.<sup>23</sup> However, reports of worsening hepatic outcomes have been published, predominantly in patients with underlying severe liver disease.<sup>24</sup> This emphasizes the importance of timely intervention for obesity before the development of irreversible end-organ damage. Clinicians need to be vigilant in managing metabolic complications and timing the surgery, particularly in this complex cohort of patients who may have multi-organ impairment.

In this series, none of the patients developed any major postoperative complications following either KT or bariatric surgery. There were also no differences in long-term allograft outcomes or kidney function between the groups. While some studies have reported an increased risk of acute graft rejection among KT patients with a history of bariatric surgery, most found no significant difference in infection rates, kidney function or mortality.<sup>10,12</sup> A recent large meta-analysis by Lee et al.<sup>21</sup> reported no difference in 30-day mortality (0.5%) following bariatric surgery among patients status post-KT

versus ESKF patients on the KT waitlist. Cohen et al.<sup>12</sup> even suggested that patients who underwent bariatric surgery had a reduced risk of long-term allograft failure and lower mortality. The reported safety of bariatric surgery can encourage both physicians and patients to turn towards this treatment option when conventional methods of weight loss fail and to prevent metabolic complications after transplant, which adversely impact graft and patient survival.

Following bariatric surgery, multiple factors may affect immunosuppression doses and levels, making this a significant point of concern across previous studies. Malabsorptive procedures such as RYGB may theoretically result in poorer absorption of medications, leading to a risk of graft rejection. An earlier study by Marterre et al.<sup>25</sup> reported that an increase in cyclosporine dose was required post-RYGB. In a pilot study, Rogers et al.<sup>8</sup> described significant differences in the pharmacokinetics of sirolimus, tacrolimus, and mycophenolate mofetil in patients who had undergone gastric bypass, in that these individuals required higher medication doses. On the other hand, significant weight loss following bariatric surgery may also lead to reductions in dose requirements.<sup>26</sup> Reassuringly, despite these theoretical concerns, most case reports document stable immunosuppression doses after bariatric surgery, as was observed in our present study.<sup>10,27,28</sup> Nonetheless, close monitoring is imperative to prevent allograft dysfunction from drastic changes in drug exposure until further large-scale studies are available.

To our knowledge, this is the first case series analyzing the effects of bariatric surgery on KT patients and candidates conducted in an Asian setting. While larger transplant registry studies provide a good representation of White and Black populations, hardly any Asian patients were included in these studies, limiting their applicability in Asian countries, which are facing an obesity epidemic.<sup>11,12</sup> Asians have a propensity to develop cardiometabolic disease from excess adiposity, so lower BMI cut-offs for obesity and bariatric surgery are used in these populations.<sup>29</sup> Ethnicity has also been shown to influence weight loss outcomes after bariatric surgery, with non-White patients losing less weight compared to their Caucasian counterparts.<sup>30</sup>

Another strength of this study is the long-term follow-up over 5 years after bariatric surgery to better appreciate the sustainability of weight loss and the extent of weight regain. Lastly, comprehensive chart reviews were performed for each patient, facilitating de-

tailed graphical representation with granular resolution of weight, glycemic control, immunosuppression doses, and drug levels—particularly in the perioperative period—which prior, larger registry studies were not able to achieve.<sup>11</sup>

Still, our study has several limitations. First, it is a retrospective study of a small number of patients within a single center and was unable to provide evidence to support long-term graft survival or patient survival. However, as it is the largest and most established center for bariatric surgery and KT in Singapore, this case series could be considered reflective of practice patterns toward bariatric surgery in this study population. Second, it lacks a control cohort of KT patients with obesity who did not undergo bariatric surgery. Third, this study is unable to ascertain the true burden of obesity among KT recipients and candidates as well as refusal rates for bariatric surgery in suitable patients.

Future multicenter prospective studies of bariatric surgery among Asian patients would help to confirm the findings of this series, including long-term treatment outcomes on weight, graft function, and survival. Physician and patient factors influencing referrals for bariatric surgery among ESKF or KT individuals, including barriers to referral or proceeding with bariatric surgery, should be further studied. The health literacy of KT patients regarding the impact of obesity on graft and patient survival and the role of bariatric surgery as a treatment option could also be explored. Last, it would also be interesting to examine the role of simultaneous KT and bariatric surgical procedures, which has been described to be safe and efficacious in a recent study.<sup>31</sup>

In conclusion, this study demonstrated that bariatric surgery can be safely performed in KT recipients and candidates. It results in sustainable weight loss and improvements in metabolic comorbidities. No major perioperative complications, graft injury, or changes in immunosuppression doses were observed. Nonetheless, these patients are a more complex cohort with possible multi-organ involvement, and close monitoring by a multidisciplinary team is imperative.

## CONFLICTS OF INTEREST

The authors declare no conflict of interest.

## AUTHOR CONTRIBUTIONS

Study concept and design: PCL and ST; acquisition of data: SYTT; analysis and interpretation of data: SYTT, PCL, and SG; drafting of the manuscript: SYTT, PCL, QYH, and ST; critical revision of the manuscript: PCL, SG, TK, and ST; statistical analysis: SYTT; administrative, technical, or material support: TK; and study supervision: PCL and ST.

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