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LETTER TO THE EDITORS

Pre-transplant bariatric surgery is not associated with an increased risk of infection after kidney transplant

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Dear Editors,

Obesity has become increasingly prevalent in those seeking transplants for the treatment of end-stage renal disease (ESRD). While those who are obese maintain the survival benefit of kidney transplant over dialysis, obesity is associated with negative outcomes after solid organ transplants [1]. Many transplant programs have a target weight or body mass index (BMI) requirements for listing, making weight a significant barrier to transplantation [2–5]. Behavioral modifications, while encouraged, generally have only a modest impact. Therefore, attention has turned to bariatric surgery (BS) as a strategy to improve access to transplants. According to the American Society of Transplant Surgeons Obesity in Transplantation Taskforce, the preferred timing of BS is before kidney transplantation [6]. However, BS may impair normal absorption of nutrients, alter stomach acidity and alter drug absorption [7,8]. The effect of pre-transplant BS on post-transplant infection is largely unknown. Changes to anatomy could alter the absorption of medications used for infection prevention after kidney transplant and the bypass of the host natural barrier defenses of the stomach could increase infectious risk in an immunosuppressed population [9]. A recent study at our institution suggested an increased risk of fungal infections in liver transplant recipients with pre-transplant BS [10]. No similar studies exist in kidney transplant recipients (KTR).

We report infectious complications of 69 KTRs transplanted between 1/1/1994–12/31/2016 with pre-transplant BS. Forty-one (59.5%) had an RYGB (Roux-en-Y gastric bypass), 19 (27.5%) had gastrectomy and 9 (13.0%) had BS of unknown methodology. These patients were matched to 1067 controls via frequency for BMI at time of transplant, age, cause of ESRD, and transplant year. KTRs at our center receive infection prophylaxis with topical nystatin/clotrimazole for oropharyngeal candidiasis prevention, valganciclovir, or acyclovir for 3–6 months based on donor–recipient risk stratification and trimethoprim-sulfamethoxazole double-strength daily for 12 months. Figure 1 demonstrates a summary of key baseline characteristics and outcomes.

The median time from BS to kidney transplant was 5.2 years (IQ range 2.6–10.4). Patients who underwent pre-transplant BS were more likely to be female (65% BS vs. 32% control, $P < 0.001$) and non-Hispanic Whites (91% BS vs. 80% control, P: 0.02). Baseline characteristics were otherwise similar, including induction immunosuppression, high-risk CMV (cytomegalovirus) serostatus, and delayed graft function. Mean tacrolimus trough levels were lower in the pre-transplant BS group at 3 months post-transplant (7.4 BS vs. 8.0 control, $P = 0.03$), but not at 6 months (7.0 BS vs. 7.0 control, $P = 0.95$) or 1 year (7 BS vs. 6.9 control, $P = 0.8$). Maintenance immunosuppression was otherwise similar between groups, including the use of steroids. The decision regarding steroid continuation versus steroid withdrawal at our center is not based on prior bariatric surgery status.

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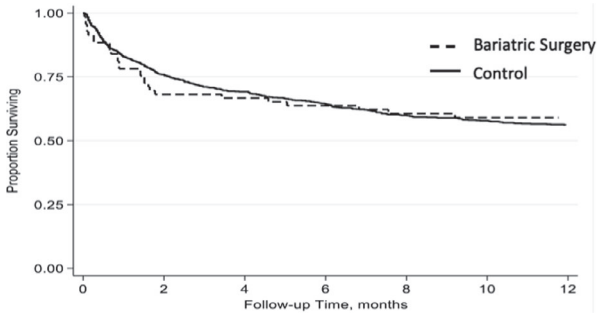
Baseline characteristics

	Bariatric Surgery (n=69)	Control (n=1067)	p
Age at transplant, mean (sd)	53.1 (11.3)	52.9 (12.2)	0.89
Recipient Female *% (n)*	65% (45)	32% (346)	**<0.001**
Diabetes as cause of ESRD	40 % (27)	37% (404)	0.78
Non-Hispanic White % (n)	91% (63)	80% (855)	**0.02**
BMI at transplant (sd)	29.7 (5.0)	28.8 (4.5)	0.10

Risk of infection in first year after transplant

Univariate	Hazard Ratio (HR)	95% CI	P value
Bacterial infection	1.08	0.66-1.77	0.76
Fungal infection	2.31	1.19-4.47	**0.01**
Viral infection	0.43	0.20-0.93	**0.03**
CMV infection	0.49	0.16-1.46	0.20
BK infection	0.13	0.02-0.84	**0.03**
Multivariate[a]	**Hazard Ratio (HR)**	**95% CI**	**P value**
Bacterial infection	0.89	0.56-1.42	0.62
Fungal infection	1.75	0.91-3.35	0.09
Viral infection	0.39	0.19-0.81	**0.01**
CMV infection	0.40	0.15-1.07	0.07
BK infection	0.13	0.02-0.81	**0.03**

[a]Adjusted for: age, sex, nonwhite race, donor type, BMI at transplant, delayed graft function, sensitization, CMV serostatus, donor race, donor sex, and induction



Kaplan-Meier curve for graft loss in bariatric surgery vs. control

Figure 1 Baseline characteristics and outcomes.

We examined the risk of confirmed bacterial, viral, and fungal infections in the first year after transplant. KTRs in the pre-transplant BS cohort did not have an increased risk of bacterial infection (HR 1.08, 0.66–1.77, $P = 0.76$). The most common type of bacterial infection was urinary tract infection (UTI), making up 60.6% of infection overall followed by intra-abdominal infection (13.1%) and pneumonia (3.5%). Skin and skin structure infection occurred in 8.2% of the total population (15.2% BS vs. 8.4% control). *E. coli* was the most frequently isolated bacteria in both groups.

The pre-transplant BS group demonstrated lower rates of viral infection (HR 0.43, 95% CI 0.20–0.93, $P = 0.01$), which persisted after adjustment for differences in baseline characteristics. This was driven primarily by a lower risk of BK virus infection (HR 0.13, 95% CI 0.02–0.81, $P = 0.03$), although the overall incidence was low, with only one patient in the BS group with BK virus infection.

Ten (14%) KTRs in the pre-transplant BS group had a fungal infection vs 66 (6%) in the control group. On univariate analysis, there was a significantly higher risk of fungal infection in the pre-transplant BS group (HR 2.31, 95% CI 1.19–4.47, $P = 0.01$). However, when adjusted for baseline characteristics the difference was not significant (HR 1.75, 95% CI 0.91–3.35, $P = 0.09$). Of those who developed a fungal infection, 73.2% would be considered noninvasive, including skin and skin structure infection, oropharyngeal candidiasis, and fungal UTI. Candida species were the most frequently isolated causative organisms.

Patients in the pre-transplant BS cohort did not exhibit a statistically increased risk of graft loss (HR 1.5 95% CI 0.98–2.28, $P = 0.06$), although there was a trend toward increased graft loss. However, the risk of biopsy-proven acute rejection (antibody-mediated or cellular) was not increased in the BS cohort (HR 1.21, 95% CI 0.69–2.16, $P = 0.51$). The risk of all-cause mortality was also not different among groups (HR 1.24, 95% CI 0.82–1.9, $P = 0.30$).

This is one of the largest studies in KTRs with pre-transplant BS from a single center to date and included a matched control of over 1000 patients. The results of our study suggest theoretical concerns regarding increased risk of infection in KTRs with pre-transplant bariatric surgery may not be clinically substantiated. Our results did show an increased risk of fungal infections in the BS cohort, but this association did not persist when adjusted for baseline variables, and furthermore, most fungal infections in our patients were

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noninvasive, which was reassuring. A recent study in liver transplant recipients with pre-transplant RYGB demonstrated an increased risk of fungal infections and a trend toward an increase in bacterial infections [10]. The authors concluded that pre-transplant RYGB should be considered a risk factor for invasive fungal infection after liver transplant, and fungal prophylaxis protocols should be updated to reflect the inclusion of this factor. However, this may be related to anatomical or surgical factors specific to liver transplants, as we did not find this in our population, although our study was not limited to RYGB.

In conclusion, our findings suggest augmentation of standard infection prophylaxis after kidney transplant for patients with BS is likely unnecessary at our center, as we did not find an increased risk of any types of infection after controlling for differences in baseline demographics. This study reinforces current literature suggesting BS before transplant is a safe and effective weight loss strategy in the setting of morbid obesity.

Conflict of interest

The authors have no conflicts of interest.

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