Bariatric Surgery in Renal Transplant Patients

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Abstract

Objectives: The idea of transplanting organs is not new, nor is the disease of obesity. Obese transplant recipients have greater risk of early death than their cohorts, which is not due to increased rejection but due to obesity-related complications, including arterial hypertension, diabetes, and delayed graft function. Here, our aim was to evaluate the effects of bariatric surgery versus lifestyle changes on outcomes of moderate to severely obese renal transplant recipients.

Materials and Methods: Twenty-two morbidly obese patients with stable graft function who underwent bariatric surgery were compared with 44 obese patients on lifestyle management (control group). Both groups were evaluated regarding graft and patient outcomes.

Results: The studied groups were comparable demographically. In the bariatric study group versus control group, we observed that the mean body mass index was 38.49 ± 9.1 versus 44.24 ± 6 (P = .024) at transplant and 34.34 ± 7.6 versus 44.38 ± 6.7 (P = .002) at 6 months of bariatric surgery. Both groups received a more potent induction immunosuppression, but this was significantly higher in the obese nonbariatric control group (P < .05). There were more patients with slow and delayed graft functions in the same nonbariatric group. The 2 groups were comparable regarding new-onset diabetes after transplant, total patients with diabetes, and graft outcomes (P > .05).

Conclusions: Bariatric surgeries are feasible, safe procedures for selected obese renal transplant recipients.

Key words: Metabolic surgery, Obesity, Outcome, Renal transplant

Introduction

The idea of transplanting organs is not new, nor is the disease of obesity.1 Most scientific work in the transplant population has focused on acute and chronic rejection despite obesity being a serious complication.2 No optimal medical therapies have been described for patients with morbid obesity, especially in transplant patients. Patients may become obese and develop renal insufficiency or failure or become obese after transplant. Organ insufficiency can often be cured by transplant, but patients with morbid obesity are less likely to receive a transplant.3

Transplant is the best approved method for renal replacement therapy. Graft function depends not only on proper regulation of immune processes but also on the optimal control of chronic diseases, especially obesity and metabolic syndrome, which may lead to a number of disorders exerting adverse effects, including to the transplanted organ.4

Recent advances in bariatric surgery may offer new options for severely obese patients with type 2 diabetes mellitus and chronic kidney disease. Nevertheless, the existing data for these patients with advanced chronic kidney disease are scarce. In addition, bariatric surgery should not be considered as a cure for diabetic nephropathy but only as a bridge to renal transplant.5

Morbidly obese patients have 2 times the number of cardiac events, a higher incidence of delayed graft rejection, and reduced life expectancy.6-12 Moreover, they have more wound infections and require longer surgical time.8,13,14 In view of the last findings, the United Network for Organ Sharing has developed criteria for transplant that include body mass index (BMI) at 30 to 35 kg/m².
Obesity can be altered and must be altered to accelerate a patient’s ability to qualify for transplant surgery. There are several surgical options for the obese transplant patient, with the procedure of choice being under debate over the past few years. A laparoscopic adjustable gastric band before transplant surgery, despite its slower weight loss, is a consideration as it has lower perioperative risk compared with other weight loss surgeries.15,16 Roux-en-Y gastric bypass has also been considered to be the best method for pretransplant weight loss,17 with moderate perioperative risk that may include hazard of bowel anastomoses and malabsorption. Another long-term study18 of patients with chronic kidney disease concluded that gastric bypass surgery is safe and effective for achieving significant long-term weight loss and relief of comorbid conditions in dialysis patients who are preparing for transplant.

Weight gain after renal transplant is not uncommon and may reach 20% of lean patients within 2 years after transplant.19 This may in part be explained by a corticosteroid effect and the actions of leptin.20 Leptin is a hormone produced by adipose tissue and stimulated by steroids and plays a key role in regulating energy intake and loss, including appetite and metabolism.21 Increased leptin has been found in patients with end-stage renal disease, which prevents progression to morbid obesity and drops after renal transplant.20,22 Obese transplant recipients have greater risk of early death than their cohorts, which is not due to increased rejection but due to obesity-related complications,23 including arterial hypertension, diabetes, and delayed graft function.24 Currently, there are several case reports and series that bariatric surgery after transplant is safe, feasible, and effective.25,26

In this study, our aim was to evaluate the effects of bariatric surgery versus lifestyle changes on outcomes of moderate to severely obese renal transplant recipients.

Materials and Methods

Between 2000 and 2012, the Hamed Al-Essa Organ Transplant Centre of Kuwait performed 1019 kidney transplants. During this period, all renal transplant patients who had over 1 year of follow-up and who were still moderately to morbidly obesity were offered a surgical approach for weight loss. Those who were interested were referred by their treating nephrologist to the Bariatric Surgery Clinic for treatment of morbid obesity if conservative approaches had failed. Of these 1019 patients, 22 morbidly obese patients with stable graft function underwent bariatric surgery for their obesity. An additional 44 patients were selected and maintained on lifestyle management for their moderate to severe obesity, thus serving as control group. We excluded nonobese and mildly obese patients from this study. The study adhered to the Declaration of Helsinki and national regulations and was approved by the ethical committee of our transplant center. All patients gave written informed consent to share their data in this study.

Evaluation

Each patient was evaluated clinically with thorough history taking and physical examination monthly in the outpatient clinic. Laboratory tests included complete blood count, creatinine, creatinine clearance, liver function tests, calcium, phosphorus, blood oxalate (every 6 mo), and fasting blood sugar. Patients also were tested for urinary protein level (g/24 h), serum drug levels, virology profile (Cytomegalovirus, Epstein-Barr virus, and parvovirus), and abdominal ultrasonography.

Immunosuppression

Our immunosuppression protocol consisted of 5 doses of antithymocyte globulin (Sanofi US, Bridgewater, NJ, USA) for high-risk patients (as retransplants, prior pregnancy, blood transfusion, HLA-antibody positive, and/or more than 4 HLA mismatches) or 2 doses of IL-2 receptor blocker (basiliximab; Novartis, Inc., Basel, Switzerland) for low-risk patients. Maintenance therapy consisted of prednisolone, mycophenolic acid sodium, and a calcineurin inhibitor. The dose of calcineurin inhibitor was gradually decreased until the lowest dose by the end of the first year was guided by the 12-hour trough level. We kept the cyclosporine level between 200 and 250 ng/mL during month 1 and between 150 and 200 ng/mL for several months, between 125 and 150 ng/mL for 2 months, and then from 75 to 125 ng/mL until end of year 1. Similarly, we kept tacrolimus trough levels between 8 and 10 ng/mL during the first 3 months and then from 5 to 8 ng/mL thereafter. Maintenance immunosuppression with a sirolimus-based regimen was used for rejection-free patients with low immunologic risk after 3 months of transplant.
Statistical analyses
Descriptive and comparative statistics were performed using SPSS version 21 (SPSS, Inc., Chicago, IL, USA). Continuous variables were reported as mean and range unless otherwise specified and were compared using *t* test. Categorical variables were compared using chi-square test. *P* = .05 was considered significant in all cases.

Results
Sixty-six renal transplant recipients with BMI above 35 kg/m² were enrolled in this study. Of these patients, 22 underwent bariatric surgery to overcome moderate to severe obesity, and 44 continued with their lifestyle management for weight loss. In both groups, most renal transplant recipients were women (63.6% men vs 84.09% women with mean age of 40.6 ± 12.3 vs 42 ± 10.5 years), and most of the patients had received their grafts from female donors in their third decade of life (Table 1). Both groups were comparable demographically (*P* > .05).

Most of the patients in both groups received hemodialysis before transplant. Both groups were comparable regarding their original kidney disease (with glomerulonephritis and diabetes as the main identified causes of end-stage kidney disease), virology profile (hepatitis B virus, hepatitis C virus, and Cytomegalovirus); type of kidney donor and blood group, and pretransplant comorbidities (*P* > .05; Table 1). However, pretransplant bone disease was significantly higher in the bariatric group (*P* < .001). Both groups of patients received a potent induction immunosuppression, but this was significantly higher in the obese nonbariatric group (*P* = .014; Table 1).

We observed that the mean BMI was 38.49 ± 9.1 in the bariatric group versus 44.24 ± 6 kg/m² in the obese nonbariatric group at transplant (*P* = .024) and 34.34 ± 7.6 in the bariatric group versus 44.38 ± 6.7 kg/m² in the obese nonbariatric group at 6 months after bariatric surgery (*P* = .002).

As shown in Table 2, we could not observe any significant differences in the laboratory metabolic parameters (mean hemoglobin, albumin, serum creatinine, and serum cholesterol) for patients in both groups (*P* > .05). Despite the achieved therapeutic trough levels of calcineurin inhibitors, we found that the mean tacrolimus dose at last follow-up among patients maintained on this agent was significantly lower in the nonbariatric group with significantly lower targeted level (*P* = .02). However, we did not observe significant differences in the dose or targeted cyclosporine levels (*P* > .05).

<table>
<thead>
<tr>
<th>Table 1. Demographic Data of the Study Groups</th>
<th>Bariatric Group (n = 22)</th>
<th>Nonbariatric Group (n = 44)</th>
<th><em>P</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient mean age, y</td>
<td>40.6 ± 12.3</td>
<td>42 ± 10.5</td>
<td>.63</td>
</tr>
<tr>
<td>Donor mean age, y</td>
<td>35.5 ± 11.4</td>
<td>34.8 ± 7.9</td>
<td>.80</td>
</tr>
<tr>
<td>Nationality (K/non-K)</td>
<td>21/1</td>
<td>31/13</td>
<td>.01</td>
</tr>
<tr>
<td>Donor sex (male/female)</td>
<td>14/8</td>
<td>12/32</td>
<td>.68</td>
</tr>
<tr>
<td>Patient sex (male/female)</td>
<td>5/17</td>
<td>12/53</td>
<td>.06</td>
</tr>
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<td>5/17</td>
<td>12/52</td>
<td>.68</td>
</tr>
</tbody>
</table>

Abbreviations: CMV, Cytomegalovirus; IgM, immunoglobulin M; IL-2, interleukin 2; K, Kuwaiti

<table>
<thead>
<tr>
<th>Table 2. Laboratory Parameters in Both Groups</th>
<th>Bariatric Group (n = 22)</th>
<th>Nonbariatric Group (n = 44)</th>
<th><em>P</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin, g/L</td>
<td>102 ± 2.9</td>
<td>82 ± 4.4</td>
<td>10</td>
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<tr>
<td>Serum albumin, g/L</td>
<td>32.6 ± 3.6</td>
<td>34.8 ± 3.9</td>
<td>.06</td>
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<tr>
<td>Serum creatinine, μmol/L</td>
<td>Basal 1274 ± 47</td>
<td>1613 ± 104</td>
<td>.18</td>
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<tr>
<td>6 month 1129 ± 30</td>
<td>131 ± 40</td>
<td>10</td>
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<tr>
<td>1 year 1077 ± 27</td>
<td>132 ± 50.5</td>
<td>.085</td>
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<tr>
<td>3 years 943 ± 35</td>
<td>126 ± 44</td>
<td>.09</td>
<td></td>
</tr>
<tr>
<td>5 years 1276 ± 105</td>
<td>177 ± 119</td>
<td>.12</td>
<td></td>
</tr>
<tr>
<td>Creatinine at last follow-up, µmol/L</td>
<td>Basal (2 wk after transplant) 4.6 ± 0.78</td>
<td>4.6 ± 0.89</td>
<td>.97</td>
</tr>
<tr>
<td>Last follow-up 4.3 ± 0.63</td>
<td>4.4 ± 1.1</td>
<td>.65</td>
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<tr>
<td>Tacrolimus basal dose, (mg/day) 8.9 ± 2.9</td>
<td>6.43 ± 4</td>
<td>.08</td>
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<tr>
<td>Tacrolimus basal level, (μg/mL) 9.38 ± 1.7</td>
<td>3.06 ± 2</td>
<td>.08</td>
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<tr>
<td>Tacrolimus last dose, (mg/day) 3.83 ± 1.7</td>
<td>2.47 ± 1.45</td>
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<td>Tacrolimus last level, (μg/mL) 6.79 ± 1.7</td>
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<tr>
<td>Neoral basal dose, (mg/day) 377 ± 133</td>
<td>236 ± 22</td>
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<tr>
<td>Neoral basal level, (μg/mL) 396 ± 144</td>
<td>216 ± 48</td>
<td>.56</td>
<td></td>
</tr>
<tr>
<td>Neoral last dose, (mg/day) 1458 ± 48</td>
<td>1426 ± 45</td>
<td>.88</td>
<td></td>
</tr>
<tr>
<td>Neoral last level, (μg/mL) 981 ± 31</td>
<td>80 ± 20</td>
<td>.88</td>
<td></td>
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</table>

Results are presented as means ± standard deviation.
As shown in Table 3, we observed that the number of patients with BK viruria, viremia, and nephropathy was significantly higher in the obese nonbariatric group ($P = .008, .034$, and $.01$). Moreover, there were more patients with slow and delayed graft functions were in the nonbariatric group ($P < .05$) with significantly worse patient outcome. However, the 2 groups were comparable regarding new-onset diabetes after transplant, total number of patients with diabetes, and graft outcomes ($P > .05$).

### Discussion

The prevalence of metabolic syndrome increases after transplant due to weight gain and the detrimental metabolic effects of immunosuppressive drugs. Corticosteroids cause insulin resistance, hyperlipidemia, abnormal glucose metabolism, and arterial hypertension. The calcineurin inhibitor tacrolimus is diabetogenic by inhibiting insulin secretion, whereas cyclosporine causes hypertension and increases cholesterol levels. Obese patients with BMI higher than $35 \text{ kg/m}^2$ will frequently fail traditional methods for weight loss, and surgical interventions should be considered after a trial of lifestyle changes.

There are scarce data on surgical treatment of obesity after renal transplant. In our study, we aimed to evaluate the effects of bariatric surgery compared with lifestyle changes on outcomes of moderately to severely obese renal transplant recipients. In this study, we observed that most patients in the bariatric group were females at middle age, and this observation was matched with that reported in a recent study by Salazar and associates$^{27}$ as most of their bariatric cases were female patients at middle age.

Both groups in our study were comparable regarding their original kidney disease (with glomerulonephritis and diabetes as the main identified causes of end-stage kidney disease), virology profile (hepatitis B virus, hepatitis C virus, and Cytomegalovirus), type of kidney donors and blood groups, and pretransplant comorbidities ($P > .05$; Table 1).

Interestingly, we observed significant reductions in mean BMI at 6 months after bariatric surgery among renal transplant recipients ($P = .002$), but this was lacking in the control group (without bariatric surgery). Also, there was a trend toward reduction in the number of patients maintained on statin therapy in the bariatric group. This finding was matched with the only prospective randomized study performed to date by O’Brien and associates,$^{28}$ who confirmed the effectiveness of surgical treatment and reported that $92.8\%$ of patients achieved recovery from metabolic syndrome. They added that bariatric surgery might also help renal function$^{4,29,30}$ and possibly help in reduction of proteinuria.$^{28}$

In a meta-analysis of 13 studies, Bolignano and Zoccali$^{29}$ reported that weight loss was achieved by bariatric surgery, with significant reduction in BMI in all analyzed studies. They reported glomerular filtration rate reduction in 6 studies on hyperfiltration patients, with increased rate in 1 study on patients with stages $3/4$ chronic kidney disease. However, albuminuria levels decreased in 6 studies and proteinuria levels decreased in 5 studies.$^{30}$

Moreover, Choudhury and associates$^{31}$ added that, in morbidly obese patients with end-stage kidney disease, Roux-en-Y gastric bypass may be more effective than optimistic weight loss results after lifestyle management (diet and exercise), thus improving access to renal transplant.

We could not observe any significant differences in the laboratory metabolic parameters (mean hemoglobin, albumin, serum creatinine, and serum cholesterol) of patients in both groups ($P > .05$). The number of diabetic patients before transplant was comparable in both groups ($P = .69$); however, there was a trend of higher numbers of patients with new-onset diabetes after transplant in the nonbariatric group, although this did not rank to significance ($P = .11$). Therefore, the 2 groups were comparable regarding the total number of patients with diabetes.
and graft outcomes ($P > 0.05$). This observation was not matched with the recovery from diabetes achieved and reported by Marterre and associates$^{32}$ and Buchwald and associates,$^{33}$ possibly because of the difference in the nature of patients and type of immunosuppression protocols used among our patients.

Unfortunately, we found that the number of patients with BK virus infection (viruria, viremia, and nephropathy) was significantly higher in the obese nonbariatric group ($P = .008, .034$, and $0.1$), possibly due to the use of more potent immunosuppressive agents. In addition, the number of patients with slow and delayed graft function was significantly higher in the same group ($P < .05$) with significantly worse patient outcomes. The worse immediate graft function was matched with that shown in a previous meta-analysis by Navaneethan and associates.$^{24}$

With achieved therapeutic trough levels of calcineurin inhibitors in both groups, the mean tacrolimus dose at last follow-up was significantly lower in the nonbariatric group with significantly lower targeted level ($P = .02$). This observation might be explained by lower tacrolimus absorption in the bariatric group. However, we did not observe significant differences in the dose or targeted cyclosporine levels ($P > 0.05$).

It was worth noting that our bariatric group passed their intervention without significant complications, except in 2 patients. One intervention was complicated by left femoral deep venous thrombosis, and the other intervention had delayed wound healing. The safety of this surgery in our group was matched with that reported in many other studies.$^{26,32-34}$ In a larger series from 2013 involving laparoscopic sleeve gastrectomy in patients awaiting solid-organ transplant, Lin and associates$^{35}$ reported that laparoscopic sleeve gastrectomy is well-tolerated, technically feasible, and improves candidacy for transplant.

Of course, the benefits of adding gastric bypass surgery to lifestyle and medical care strategies of renal transplant recipients must be weighed against the risk of adverse events. One of the reported adverse effects was the higher risk of renal stones and increased urine oxalate and calcium oxalate supersaturation,$^{35,36}$ which was not detected among our group of patients who showed only a slight nonsignificant rise of serum oxalate compared with the control group. This finding can be explained by the adherence of our patients to high fluid intake.

Conclusions

Bariatric surgeries are feasible, safe procedures for selected obese renal transplant recipients.

References


