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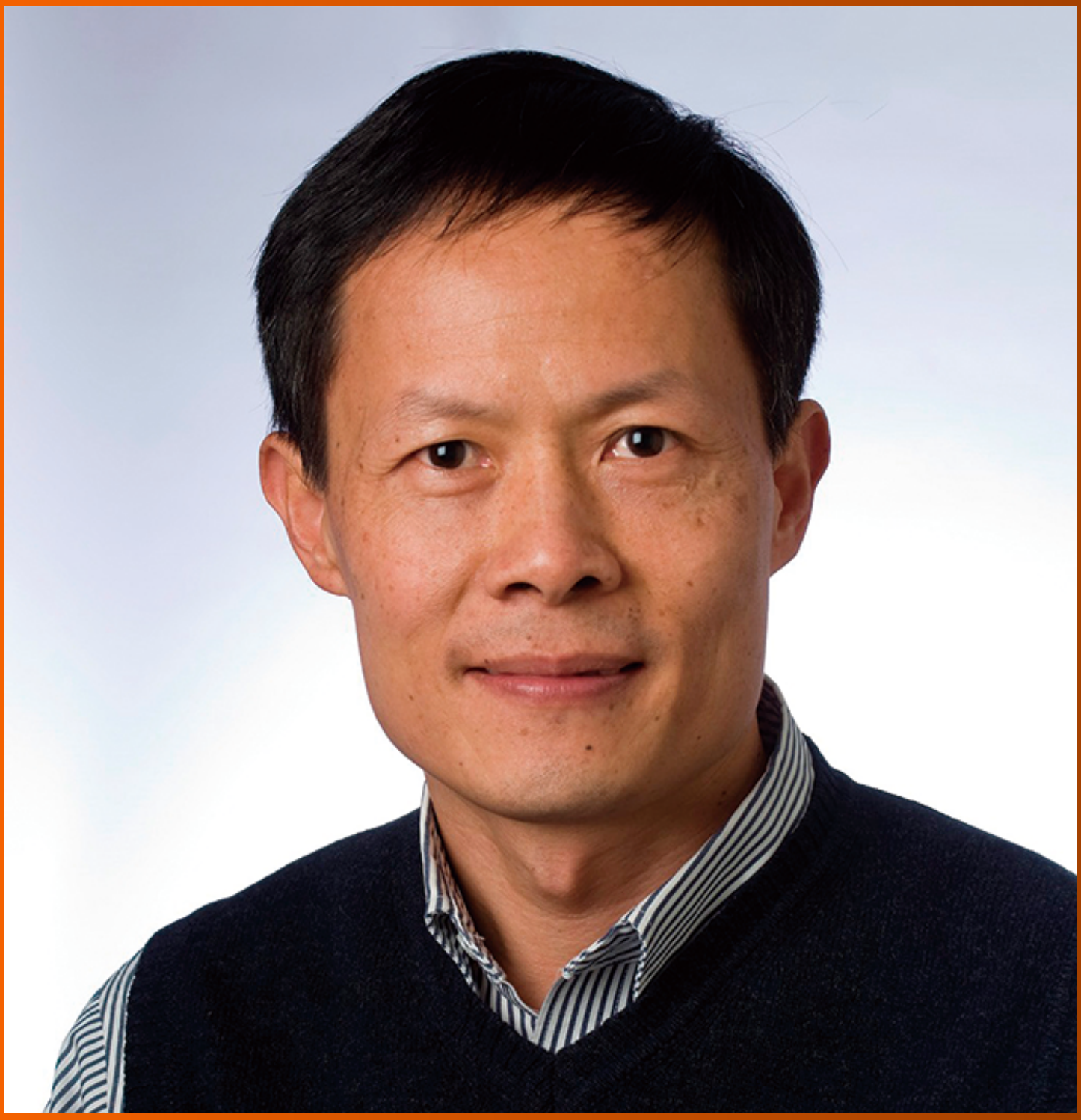

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ABOUT COVER

Peer Reviewer of *World Journal of Experimental Medicine*, Cory J Xian, PhD, Research Professor, UniSA Clinical and Health Sciences, University of South Australia, Adelaide, SA 5001, Australia. cory.xian@unisa.edu.au

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MINIREVIEWS

Bariatric surgery outcomes following organ transplantation: A review study

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Abstract

Weight gain is a frequent postoperative complication following a solid organ transplant which can be solved by bariatric surgery. The outcomes of bariatric surgery among patients with an organ transplant history are always a challengeable subject for surgeons and surgery candidates. In this review article, we aim to investigate the existence literature about the rates of morbidity and mortality, frequent complications in terms of graft function, remission in diabetes, hypertension, pulmonary and cardiovascular disorders, hepatic and renal functions, and immunosuppressive stability, as well as the safety of bariatric surgery among patients.

Key Words: Bariatric surgery; Organ transplantation; Complications

Core Tip: In this minireview article, we try to provide a broad introduction to the impacts of bariatric surgery on organ transplantation outcomes rather than as an exhaustive review. Moreover, this review will focus on major transplantations and type of bariatric surgery among morbidly obese patients. Within the broad categories of organ transplantation, we then conclude with remarks about the outcomes of bariatric surgery among patients with combined organ transplantation. Where possible, the readers are suggested to refer to the numerous comprehensive clinical studies reporting the predictors of adverse outcomes of organ transplantation following bariatric surgery.

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INTRODUCTION

Obesity is a frequent complication among patients who underwent solid organ transplantation, and may consequently affect the transplant population at multiple levels[1,2]. Graft function depends not only on the management 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[3]. Obesity in transplantation patients may also negatively impact preoperative and long-term outcomes after bariatric surgery[4,5]. Based on previous reports, obesity was linked to a higher odds of biopsy-proven acute rejection, mortality, allograft loss, and the development of diabetes[6]. Therefore, this study aims to compare the clinical outcomes of bariatric surgery among patients with prior organ transplantation. In this mini-review article, we tried to provide a broad introduction to the impacts of bariatric surgery on organ transplantation outcomes rather than as an exhaustive review. Moreover, this review will focus on major transplantations and type of bariatric surgery among morbidly obese patients including kidney transplantation, liver transplantation, heart transplantation, and sleeve gastrectomy (SG); pancreas transplantation and gastric banding surgery; lung transplantation and robotic Roux-en-Y gastric bypass (RYGB). Within the broad categories of organ transplantation, we then conclude with remarks about the outcomes of bariatric surgery among patients with combined organ transplantation. Where possible, the readers are suggested to refer to the numerous comprehensive clinical studies reporting the predictors of adverse outcomes of organ transplantation following bariatric surgery.

KIDNEY TRANSPLANTATION AND BARIATRIC SURGERY

The problem of obesity in renal transplant recipients has been well documented. Based on previously published reports, kidney recipients with obesity demonstrated enhanced rate of comorbidities such as respiratory and cardiovascular diseases, diabetes mellitus or posttransplant diabetes mellitus, dyslipidemia, and even wound complications[7-9]. Elli *et al*[10] evaluated the outcomes of SG in six patients who had a kidney transplant. There were no significant differences in excess weight loss (EWL) or percent of weight loss (WL) between the renal recipient group and patients without a history of kidney transplant. In addition, no preoperative and serious postoperative complications were observed in the transplant group. In another study, four kidney transplant patients diagnosed with hypertension (all subjects) and type 2 diabetes (T2D) underwent SG and 45% of EWL was observed 12 to 24 mo after surgery[1]. The authors reported a significant reduction in antihypertensive medications and complete remission of T2D one year after SG[1]. Significant weight loss, improvement of obesity-related conditions, preservation of graft function, and the estimated glomerular filtration rate (eGFR) were enhanced significantly in the subjects[1]. Furthermore, five renal recipient patients underwent bariatric surgery[4] RYGB and one SG and experienced 50% of EWL at 2 years after procedure. Preoperative evaluation revealed five subjects with hypertension, two with T2D, and one with chronic heart failure among the patients. After surgery, no postoperative complications and no alteration to the dosage of the immunosuppressant drugs were recorded[11]. However, in another study among ten patients with a history of kidney transplants, just two cases needed higher doses of tacrolimus and one decreased based on serum level[7]. Gheith *et al*[12] in 2017 reported a study to shed light on the effects of bariatric surgery on the outcomes of renal transplant recipients among 22 bariatric patients with a history of kidney transplant and 44 nonbariatric control subjects with a kidney transplant history. The overweight nonbariatric control group received a more potent induction immunosuppression compared to bariatric patients. In addition, no differences in graft functions or new onset of T2D were recorded in 22 bariatric patients with a history of kidney transplant compared to the control group. In a well-designed study, the outcomes of bariatric surgery were evaluated among 26 patients with a history of kidney transplant. However, the patients experienced more than 50% of EWL improvement in comorbidities without serious graft rejection, and declined tacrolimus blood levels (but remained within the therapeutic range), but the surgical risk was higher than the regular bariatric surgery population[13]. Table 1 demonstrates more studies on the outcomes of bariatric surgery in patients with a history of organ transplantation. In the most recent study, among 38 patients with solid organ transplantation, eight had a kidney transplant. Comorbidity-related medications such as tacrolimus were declined in most patients, while two subjects experienced transplant organ rejection after bariatric surgery[14].

Table 1 Outcomes of bariatric surgery in patients with a history of organ transplants

Organ	Type of bariatric surgery	Patients (*n*)	Potential risks	Mean BMI or weight changes after BS	Comorbidities/improvements	Ref.
Liver	RYGB	7	Gastric staple line leakage, EWL	From 44.34 ± 6.08 kg/m^2 to 26.47 ± 5.53 kg/m^2	DM, HTN, GERD, vascular disease, and OSA	Al-Nowaylati *et al*[17]
	LSG	12	Infections and leaks	Mean BMI decrease 12.9 kg/m^2	Nine out of 12 patients had DM and metabolic syndrome; four out of 12 patients showed a complete improvement after LSG	Tsamalaidze *et al*[27]
	Open SG	1	-	From 47 kg/m^2 to 29.8 kg/m^2	DM and arterial HTN	Butte *et al*[28]
	RYGB, LSG, jejunoileal bypass SG	11	Organ insufficiency	Mean BMI 28.3 ± 5.8 kg/m^2	Early surgical site infection, and bleeding	Safwan *et al* [29]
Kidney	Gastric bypass	5	-	Mean WL of 33 kg	DM, HTN, and hyperlipidemia	Arias *et al*[11]
	RYGB, LSG	5	-	50% EWL at 2 yr	DM, HTN, hyperlipidemia, polycystic ovarian syndrome, peripheral vascular disease, and CHF	Szomstein *et al*[7]
	LSG	10	Acute renal failure and sleeve stricture	57% EWL at 6 mo, and 75% EWL at 12 mo	Not mentioned	Golomb *et al* [30]
		6	-	44.1% EWL at 3 mo, and 75.9% EWL at 12 mo	Morbid obesity	Gazzetta *et al* [31]
Liver and kidney	LSG	9	Mesh dehiscence after a synchronous incisional hernia repair, bile leakage, and dysphagia that required reoperation	61% EWL	Mesh dehiscence after synchronous incisional hernia repair, bile leak, post-operative dysphagia	Lin *et al*[18]
Heart	RYGB and LSG	2	-	From 37.5 kg/m^2 to 27.5 kg/m^2 at 12 mo	HTN, hiperlipidemia, anemia, and hipomagnesemia	Tsamalaidze *et al*[32]
Heart and kidney	Vertical banded gastroplasty	2	Inadvertent laceration of the pancreas resulting in pseudocyst which may need percutaneous and then surgical drainage	Mean WL of 54 and 56 kg	Not mentioned	Rex *et al*[33]

BMI: Body mass index; BS: Bariatric surgery; RYGB: Roux-en-Y gastric bypass; EWL: Excess weight loss; LSG: Laparoscopic sleeve gastrectomy; SG: Sleeve gastrectomy; WL: Weight loss; DM: Diabetes mellitus; HTN: Hypertension; GERD: Gastroesophageal reflux disease; OSA: Obstructive sleep apnea; CHF: Congestive heart failure.

LIVER TRANSPLANTATION AND GASTRIC BYPASS

There is a positive correlation between body mass index (BMI) and nonalcoholic fatty liver disease (NAFLD), and individuals with obesity undergoing liver transplantation may be at enhanced risk for NAFLD recurrence[15,16]. Whereas some experts prefer to do the liver transplantation first, some others have suggested gastric bypass before liver transplant. In a study on seven patients with a history of orthotopic liver transplantation who underwent RYGB, two deaths in subjects with hepatitis C were reported 6 and 9 mo following bariatric surgery[17]. Gastric bypass may have contributed to the death of one case owing to multiple organ dysfunction syndrome. The other patients experienced improved gylcemic control, therapeutic weight loss, and balanced high-density lipoprotein levels with continued dyslipidemia in a long-time follow-up[17]. In another report, among five liver-recipient patients undergoing SG, five and four in preoperative assessment were diagnosed with hypertension and T2D, respectively. In postoperative screening, the patients illustrated a significant reduction in antihypertensive medications including mycophenolate 720 mg and tacrolimus 2 mg, and completed remission of T2D, and graft function remained preserved in subjects one year after SG[1]. Lin *et al*[18] reported the outcomes of SG in nine patients with prior liver transplant. In the first month after SG, three subjects

were diagnosed with postoperative complications including dysphagia that required reoperation, bile leak from the liver surface requiring laparoscopic drainage, and mesh dehiscence after synchronous incisional hernia repair. Hepatic and renal functions remained stable and no graft rejection was reported after surgery. In a case report study on a 51-year-old male liver recipient, he was diagnosed with steatohepatitis of the graft, gained 30 kg after organ transplant, and was on an oral hypoglycemic agent with HbA1c of 8%. After laparoscopic SG, completed remission in diabetes, reduction in BMI from 42 to 34, and stable graft functions were reported[19]. In one of the most recent studies on 19 cases with prior liver transplant undergoing SG or robotic RYGB, one patient was readmitted for abdominal pain owing to gastric ulcer[14] and related comorbidities were decreased in most of patients[10,14]. There were no organ rejections in this study at the 12-mo follow-up[14]. The tacrolimus blood levels declined to 4-6 ng/mL 6 mo after operation[13].

HEART TRANSPLANTATION AND SLEEVE GASTRECTOMY

In a previously mentioned study by Khoraki *et al*[1], one patient with a history of heart transplant was diagnosed with hypertension. The preferred surgery was SG and after the procedure, the subject experienced 45% of EWL and reduction in antihypertensive medications. Moreover, the left ventricular ejection fraction enhanced by 10% in the patient was reported after surgery. Significant weight loss, improvement of obesity-related conditions, and preservation of graft function were observed after SG [1]. In another study on six cases with heart transplant, three subjects underwent SG and three patients underwent robotic RYGB. One patient died 20 mo after robotic RYGB owing to the adverse effects of the tricuspid valve replacement, not directly related to bariatric surgery. One subject required early readmission due to abdominal pain and shortness of breath. No leaks were documented in either group [14]. The comorbidity-related medications were decreased in other cases[1,19].

PANCREAS TRANSPLANTATION AND GASTRIC BANDING SURGERY

Regarding pancreas recipients, there are no technical modifications to be considered. RYGB is not performed in these patients because of bowel drainage[10]. In a report, two patients with pancreas transplant maintained normal glycemic serum levels with HbA1c levels of 5.8% and 5.3%, respectively, at the one-year follow-up[20]. Weight gain in these patients may induce insulin resistance and return to insulin therapy despite proper graft function. Furthermore, calcineurin inhibitors for maintenance immune suppression can cause insulin resistance, and they are also responsible for weight gain post-transplantation[10]. However, laparoscopic gastric banding surgery to treat insulin resistance in a pancreas transplant recipient yielded good short-term outcomes[20].

LUNG TRANSPLANTATION AND ROBOTIC RYGB

For patients with lung transplant, robotic RYGB seems a preferable method compared to other types of weight loss surgery due the high reported rate of postoperative reflux[21,22]. In a study on two patients with lung transplant, no organ rejection was reported and comorbidity conditions declined significantly after surgery[14].

OUTCOMES OF BARIATRIC SURGERY AMONG PATIENTS WITH COMBINED ORGAN TRANSPLANTATION

The outcomes of bariatric surgery in patients with combined transplantation are one of the principal studies that have been performed by some researchers, but more studies with a long-term follow-up period are required to conclude the efficiency of weight loss surgery in this population. For instance, combined kidney-pancreas transplantation is a treatment option for end-stage diabetic nephropathy. Post-transplant weight gain enhances the risk for posttransplant comorbidities and death caused by pulmonary and cardiovascular disorders. Gastric banding is an established treatment for moderate morbid obesity for this population[20]. Based on reports on kidney pancreas recipients, although no organ rejection, declined HbA1c levels and significant weight loss were reported[14,20,23], but no reduction in medication doses was reported postoperatively[23]. In another study on a 65-year-old patient with combined kidney-liver transplant, 30 kg weight gain with the risk of graft impairment was reported 4 years after transplant. It has been reported that, after weight loss surgery, although the surgical risk was higher than the regular bariatric patients[13], BMI declined significantly with stable graft functions[19] and no development of diabetes[14,19] in patients with a history of kidney-liver

Table 2 Dose adjustment of immunosuppressive drugs following bariatric surgery in patients with a history of organ transplants

Organ	Type of bariatric surgery	Patients (*n*)	Immunosuppressant adjustment compared to patients without organ transplants	Ref.
Liver	LSG	12	No changes	Tsamalaidze *et al*[27]
		9		Lin *et al*[18]
	Bariatric surgery	56		Lazzati *et al*[34]
Kidney	Gastric bypass	2	Increased doses of sirolimus, tacrolimus, and mycophenolate mofetil	Rogers *et al*[35]
	Laparoscopic gastric bypass	5	No changes	Arias *et al*[11]
	LSG	10	Two patients with increased doses of tacrolimus and one decreased	Golomb *et al*[30]
		6	No changes	Gazzetta *et al*[31]
		5	Decreased dose of cyclosporine	Szomstein *et al*[7]
	Biliopancreatic diversion	1	No changes	López Deogracias *et al*[36]
Heart	Laparoscopic gastric banding, laparoscopic robotic-assisted RYGB, and LSG	3	No changes	Tsamalaidze *et al*[32], Ablassmaier *et al*[37]
Heart and kidney	Vertical banded gastroplasty	1	Changes based on serum level	Rex *et al*[33]

LSG: Laparoscopic sleeve gastrectomy; RYGB: Roux-en-Y gastric bypass.

transplantation. Immunosuppressive stability was enhanced from 39% to 47% after bariatric surgery in this population[13]. Table 2 presents more details of studies related to the immunosuppressant changes following bariatric surgery in patients with a history of organ transplants.

PREDICTORS OF ADVERSE OUTCOMES OF ORGAN TRANSPLANTATION FOLLOWING BARIATRIC SURGERY

Ethnicity and its impact on the outcomes of bariatric surgery among patients with a transplant history, are a remarkable issue that has been addressed by Edwards *et al*[24] in a recent report. In this survey on 335 patients from white and black races, preoperatively, black subjects were more likely to have hypertension and dialysis dependent chronic disease and be on chronic steroids. Nonetheless, mortality and morbidity rates were similar in both groups. Postoperatively, the black population were prone to have higher rates of renal failure, pulmonary disorders, and emergency readmissions, higher overall bariatric-related morbidity, and higher rates of pneumonia and progressive renal insufficiency compared to the white group. Nevertheless, race was not found to be an independent predictor of adverse outcomes following SG or RYGB in subjects with prior solid organ transplantation[24]. The same results can be seen in another cohort study with 610 patients with organ transplant and 320000 cases without organ transplant. While previous transplant subjects experienced a higher incidence of readmissions, surgical complications, and medical issues than the other group, but no difference in the incidence of death was observed[25]. On the other side, among patients with prior organ transplant, longer operative time and increased rates of morbidity, surgical site infection, acute and progressive renal failure, myocardial infarction, bleeding, and venous thromboembolism are undeniable after bariatric surgery[26]. Considering the potential for poorer outcomes in overweight people with prior solid organ transplant, there is significant interest in identifying optimal modalities to achieve significant and durable weight loss, including metabolic and bariatric surgery.

CONCLUSION

Cumulatively, reports suggested that bariatric surgery, regardless of the type of procedure (sleeve *vs* gastric bypass) and surgical approach (robotic assisted *vs* conventional laparoscopic), ensures significant weight loss and improvement of related conditions, together with good immunosuppressive maintenance, along with the absence of serious graft rejection or dysfunction and with a trivial mortality rate in this high surgical risk population. Due to the lack of a large size survey, we are unable to expand our analyses by bariatric procedure type and surgical approach. These are potential confounders that

may have influenced results. Further studies to assess bariatric surgery outcomes by organ transplant subtype and risks of organ rejection are necessary to advance our knowledge on this issue. Obesity medicine experts may choose to use this review article to educate patients with organ transplant about bariatric surgery and the options for them to promote weight loss postoperatively.

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FOOTNOTES

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