

Kidney transplantation in obese patients

Minh-Ha Tran, Clarence E Foster, Kamyar Kalantar-Zadeh, Hirohito Ichii

Minh-Ha Tran, Division of Transfusion Medicine and Apheresis, Department of Pathology and Laboratory Medicine, University of California, Irvine, School of Medicine, Irvine, CA 92697, United States

Clarence E Foster, Hirohito Ichii, Division of Transplantation, Department of Surgery, University of California, Irvine, School of Medicine, Irvine, CA 92697, United States

Kamyar Kalantar-Zadeh, Division of Nephrology, Department of Medicine, University of California, Irvine, School of Medicine, Irvine, CA 92697, United States

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Correspondence to: Hirohito Ichii, MD, PhD, Division of Transplantation, Department of Surgery, University of California, Irvine, School of Medicine, 333 City Boulevard West Suite 1205, Orange, Irvine, CA 92697, United States. hichii@uci.edu
 Telephone: +1-714-4568698
 Fax: +1-714-4568796

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Abstract

The World Health Organization estimated that in 2014, over 600 million people met criteria for obesity. In 2011, over 30% of individuals undergoing kidney transplant had a body mass index (BMI) 35 kg/m² or greater. A number of recent studies have confirmed the relationship between overweight/obesity and important comorbidities in kidney transplant patients. As with non-transplant surgeries, the rate of wound and soft tissue complications are increased following transplant as is the incidence of delayed graft function. These two issues appear to contribute to longer length of stay compared to normal BMI. New onset diabetes after transplant and cardiac outcomes also appear to be increased in the obese population. The impact of obesity on patient survival after kidney transplantation remains controversial, but appears to mirror the impact of extremes of BMI in non-transplant populations. Early experience with (open and laparoscopic) Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy support excellent weight loss (in the range of 50%-60% excess weight lost at 1 year), but experts have recommended the need for further studies. Long term nutrient deficiencies remain a concern but in general, these procedures do not appear to adversely impact absorption of immunosuppressive medications. In this study, we review the literature to arrive at a better understanding of the risks related to renal transplantation among individuals with obesity.

Key words: Body mass index; Overweight; Obese; Kidney transplant; Transplant complications; Transplant outcomes; Patient survival; Graft survival

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Core tip: Extremes of body mass index (BMI) appear to impact survival in kidney transplant recipients, but this effect appears to parallel that seen in the general population. Skin and soft-tissue complications, particularly wound infections and lymphocele formation, are higher among obese patients. In addition, the

rate of delayed graft function is also higher, and contributes to longer length of stay following transplant in this population. New onset diabetes after transplant also appears to be influenced both by BMI at time of transplant as well as increasing BMI following transplant. Measures of central adiposity, such as waist-to-hip ratio, may enhance risk assessment. Bariatric surgery appears promising to aid in reducing excess weight both pre- and post-transplant, but further studies are needed. Obesity should not constitute an absolute contraindication to transplantation but individualized risk assessment is necessary.

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INTRODUCTION

The World Health Organization defines overweight and obesity as having a body mass index (BMI = weight in kg/m² height) of ≥ 25 m/kg² and ≥ 30 m/kg², respectively. Using these definitions, WHO has estimated that in 2014, more than 1.9 billion adults were overweight of whom, over 600 million met criteria for obesity^[1].

A number of recent studies have confirmed the relationship between overweight/obesity and a number of important comorbidities - including risk for diabetes, cardiovascular disease (CVD), many cancers, gallbladder disease, and osteoarthritis^[2-5]. Extremes of BMI are strong predictors of increased mortality^[6] and rising BMI increases both direct healthcare costs and indirect costs related to reduced productivity and premature mortality^[7].

In 2011, 23% of United States kidney transplant recipients met criteria for obesity (BMI 30-34.9), 9.4% for morbid obesity (BMI 35-39.9), and 2.1% for very-morbid obesity (BMI ≥ 40)^[8]. Given the rising prevalence of obesity among kidney transplant candidates, we sought to review the literature to arrive at a better understanding of the risks related to renal transplantation among individuals with obesity.

LITERATURE SEARCH

A literature search was conducted on PubMed using search terms "obesity" AND "renal transplantation", "obesity" AND "kidney transplantation". In addition, the bibliographies of selected articles were reviewed for additional references. Cohort studies comparing outcomes between BMI categories, case series, systematic reviews, meta-analyses, and studies using data from established registries (*i.e.*, SRTR, UNOS) were preferentially selected. Authors reviewed

the available literature and synthesized findings in collaboration to produce the following review of obesity-related complications following renal transplantation. Where feasible, complication rates were categorized as described below and reported rates across series summarized as mean, median and range.

RECIPIENT RISKS ASSOCIATED WITH OBESITY

Recipient risks can be categorized as skin and soft tissue complications (such as wound infections and wound dehiscence), anastomotic and perinephric complications (such as lymphocele, hematoma, vascular), complications related to intrinsic allograft function [such as delayed graft function (DGF), immunologic rejection, graft survival], and systemic complications [such as sepsis, hospital readmissions, new onset diabetes after transplantation (NODAT), and patient survival]. Data of interest were derived from cohort studies comparing outcomes between BMI groups, case series, case control studies, meta-analyses, analyses of large transplant registries, and authoritative reviews. Outcomes of particular interest were those reiterated as significant between multiple studies.

Data for specific complications was gleaned mostly from cohort studies^[9-20], most^[9,11,13,15,17-19] used a BMI cutoff of ≥ 30 . Some studies used more varied BMI cutoffs for their analyses^[10,12,14,16,20]. One study^[20] was not amenable to table summarization and therefore was excluded from Table 1. Of interest, the obese groups tended to be older than the nonobese groups.

Skin and soft tissue complications

Wound dehiscence and wound infection were especially common themes in studies analyzing complications by BMI category. Between studies, however, the prevalence of individual complications was variable.

Wound dehiscence occurred at a median rate of 23.8% with a mean rate of 16.2% and range of 3% to 14.3%^[15-17,19]. The highest reported rate of wound dehiscence, 36%, was noted in a study^[16] using BMI > 35 as a cutoff for their high-BMI analytic group. This may depict a gradient risk for this complication associated with rising BMI. Likewise, the lowest risks for this complication, in the 3% range, were noted in two studies^[18,19] whose obese comparator group represented a lower overall BMI distribution than other studies. Furthermore, Behzadi *et al.*^[18], did not report specific BMI ranges, but had no patients with a BMI > 35 . This issue again supports the graded impact of BMI upon certain outcomes.

Two studies^[9,19] using a cutoff BMI of 30, reported wound infection at rates of 15% to 18.2% among their obese recipients. A third study^[14], which utilized a cutoff BMI of ≥ 35 , reported far higher wound

Table 1 Post-transplant complications among obese vs nonobese patients

Ref.	Groups		Complication	Outcome differences	
	Obese	Nonobese		Obese	Nonobese
Singh <i>et al</i> ^[9] 1999-2002	BMI > 30 (34.1 ± 3.68) n = 33 Age 48 ± 11.1	BMI ≤ 30 (23.6 ± 3.18) n = 35 Age 43.5 ± 13.5	OR time (min)	155 ± 59	119 ± 44
			LOS (d)	13.7 ± 10	9.48 ± 4.8 (P = 0.029)
			DGF	33.3%	17.1% (P = 0.12)
			Wound infection	18.2%	0 (P = 0.01)
			Lymphocele	18.2%	2.94% (P = 0.02)
			Perinephric HTMA	12.1%	0 (P = 0.05)
			Incisional hernia	6%	3.7% (P = 0.68)
			NODAT	9%	3.7% (P = 0.41)
			1/5 yr graft surv	75%/63%	98.9/94.5 (P = NS)
			1/5 yr pt surv	87.5/79.2	98.9/95.6 (P = NS)
Cacciola <i>et al</i> ^[10] 1993-2003	BMI ≥ 35 n = 24 (Group B) Age 45 (20-61)	BMI 30-34.9 n = 90 (Group A) Age 45 (25-70)	DGF	16.5%	22% (P = NS)
			1 yr graft surv	94%	97% (P = 0.51)
			1 yr patient surv	100%	100%
Mehta <i>et al</i> ^[11] 1999-2002 Living donor	BMI ≥ 30 n = 16 Age 50 ± 16	BMI < 30 n = 37 Age 43 ± 16	Acute rejection	19%	8% (P = 0.35)
			Wound Cxn	19%	13.5% (P = 0.68)
			Other Cxns	25%	11% (P = 0.22)
			DGF	19%	2.7% (P = 0.077)
			LOS (d)	8.4 ± 7	6.4 ± 5 (P = 0.68)
			1/3 yr graft surv	LD 100/100 DD 92/75	LD 95/91 DD 94/90
			1/3 yr pt surv	LD 100/100 DD 92/83	LD 97/95 DD 96/94
Marks <i>et al</i> ^[12] 1995-2000	BMI ≥ 35 (35-56) n = 23 Age DD: 44 ± 14 Age LD: 46 ± 1	BMI ≤ 25 (17-28) (n = 224) Age DD: 48.5 ± 13 Age LD: 43 ± 13	LOS (d)	LD 10.2 ± 8.0 DD 12.9 ± 9.0	LD 6.0 ± 4.1 DD 7.8 ± 3.0
			Readmission 6 mo	LD 82% DD 92%	LD 20% DD 49%
			Mult admits 1 st 6 mo	LD 44% DD 50%	LD 21% DD 18%
			Major wound infxn	LD 44% DD 33%	LD 2% DD 4%
			Graft loss 1 yr/3 yr	6.4/42.9	5.3/7.7
			Pt death 1 yr/3 yr	7.6/46.2	3.5/11.8
			DGF	31.3%	20.5% (P = 0.253)
Grosso <i>et al</i> ^[13] 2000-2010	BMI > 30 n = 64 Age 49.1 ± 12.9	BMI ≤ 30 n = 312 Age 49.8 ± 11.1 (BMI 25-30) Age 44.9 ± 13.7 (BMI < 25)			
Schwarznaeu <i>et al</i> ^[14] 2000-2004 Living donor	BMI > 25 (28.1 ± 2.6) n = 25 Age 49.2 ± 10.9	BMI < 25 (21.4 ± 2.0) n = 56 Age 42.8 ± 13.6	1 yr graft survival	94.6%	76% (P < 0.001)
Bardonnaud <i>et al</i> ^[15] 2004-2008	BMI ≥ 30 (35.1 ± 4.35) n = 21 Age 53.3 ± 11.19	BMI < 30 (22.9 ± 3.17) n = 179 Age 46.7 ± 15.05	DGF	38% ± 0.5%	14% ± 0.34% (P = 0.004)
			Lymphocele	14.3%	4.5 (P = 0.062)
			Wound dehiscence	4.8% ± 0.22%	2.2% ± 0.15% (P = 0.485)
			(pretransplant DM)	29%	6% (P < 0.0001)
			LOS (d)	24.9	15.6 (P = 0.008)
Gusukuma <i>et al</i> ^[16] 1998-2008	BMI ≥ 35 (36.8 ± 1.7) n = 47 Age 46.5 ± 10.9	BMI < 30 (22.6 ± 3.3) n = 2822 Age 40.7 ± 12.1	1 yr graft/pt surv	93.6%/95.6%	97.7%/98.1% (P = NS)
			5 yr graft/pt surv	84.0%/89.1%	88.8%/90.5% (P = NS)
			DGF	16.7% ± 19.3%	13.5% ± 16.2% (P = NS)
			Wound dehiscence	19.1%	1.9% (P < 0.001)
			Lymphocele	6.4%	2.6% (P = 0.054)
			NODAT	36%	16.2% (P < 0.001)
Furriel <i>et al</i> ^[17] 1984-2008	BMI ≥ 30 (32.44 ± 1.86) n = 26 Age 46.08 ± 12.75	BMI < 25 (22.03 ± 1.79) n = 295 Age 41.51 ± 13.23	LOS (d)	15.9 ± 16.7	11.3 ± 11.4 (P < 0.001)
			DGF	26.9%	16.9%
			Lymphocele	7.7%	1.4%
Behzadi <i>et al</i> ^[18] 2006-2008 Age 39.8	BMI ≥ 30 (none > 35) n = 34	BMI < 30 n = 146	Wound dehiscence	11.5%	0.7%
			RAS	17.6%	2.8% (P < 0.001)
			Hematoma	47.9%	17.6% (P = 0.009)
			Wound Cxn	64.7%	9.6% (P < 0.001)
			Renal vein thromb	2%	0% (P < 0.05)
			DGF	8.8%	6.80%
Johnson <i>et al</i> ^[19] 1994-2000	BMI ≥ 30 (32.0 ± 0.3) n = 59	BMI < 30 (23.4 ± 0.2) n = 434	Lymphocele	2.9%	1.40%
			Wound breakdown	14%	4% (P < 0.01)
			Wound dehiscence	3%	0% (P < 0.01)
			Wound Infection	15%	8% (P = 0.11)

BMI: Body mass index; Cxn(s): Complication(s); DD: Deceased donor; DGF: Delayed graft function; DM: Diabetes mellitus; HTMA: Hematoma; LOS: Length of stay; LD: Living donor; NODAT: New onset diabetes after transplant; OR time: Operating time; pt: Patient; RR: Relative Risk; Surv: Survival; NS: Not significant.

infection rates of 33%-44%. Other studies^[11,18] used a more general descriptor of "wound complication", thus preventing estimates of specific outcomes among their patient populations. A smaller study noted a rate of surgical site infections following renal transplant in 108 patients of 5%; age > 60 and BMI > 30 were found to be risk factors^[21].

Anastomotic and perinephric complications: For studies reporting it, lymphocele occurred at a median rate of 7.7% among obese recipients with a mean of 9.9% and range of 2.9% to 18.2%^[9,15,17-18]. Two studies reported a higher rate of hematoma among obese recipients^[9,18]. One study^[18] reported a rate of renal artery stenosis as high as 17.6% among obese patients, accompanied by a 2% rate of renal vein thrombosis. This study group as a whole was younger than most (mean age 39.8) so it is unclear as to why these specific complications should predominate simply due to obesity. In another study, both age > 60 and BMI > 30 were found to be risk factors for lymphocele (rate of occurrence 11%)^[21].

Complications related to intrinsic allograft function

DGF was higher among obese patients with a median rate of 16.7% and a mean of 22.8% with a range of 8.8% to 38.1%^[9-11,15-18]. In a separate study, Ditunno *et al.*^[20] reported the occurrence of DGF amongst 145/521 (27.8%) recipients with a BMI < 30 compared to 20/42 (47.6%) recipients with a BMI ≥ 30. A retrospective review of all renal transplant recipients in the United Network for Organ Sharing database (2004-2009) demonstrated significant risk increase for DGF among obese patients with odds ratios (compared to BMI < 30) rising in parallel with degree of obesity - BMI 30 to 34.9: 1.34 (95%CI: 1.27, 1.42); BMI 35-39.9: 1.68 (95%CI: 1.56, 1.82); BMI ≥ 40: 2.68 (95%CI: 2.34, 3.07)^[22].

Another study determined risk of DGF as higher in obese patients, but higher still in those with BMI ≥ 35; furthermore, the rate of biopsy proven acute rejection was found to be higher in this latter group as well^[23]. Using patients with a BMI 20-24.9 as a reference group, the OR for DGF rose in parallel with degree of obesity - BMI 25-29.9: 1.08 (95%CI: 0.71, 1.65); BMI 30-34.9: 1.95 (1.16, 3.19); BMI ≥ 35: 4.49 (2.24, 9.00). A similar trend was noted for biopsy proven acute rejection - BMI 25-29.9: 0.96 (0.67, 1.38); BMI 30-34.9: 1.28 (0.83, 1.98); BMI ≥ 35: 2.43 (1.48, 3.99). The authors used BMI category at time of transplant for this analysis.

In an analysis of over 11836 transplant patients in the Scientific Registry of Transplant Recipients, and after adjusting for case mix and malnutrition-inflammation variables, Molnar *et al.*^[24] determined that pretransplant BMI remained an independent and significant predictor of DGF. Following adjustment, multivariate analysis demonstrated that for each Standard Deviation (1

SD = 6.0 kg/m²) increase from normal, the risk of DGF was increased by 35% (OR: 1.35, 95%CI: 1.27-1.45). Compared to normal (BMI 22-24.99), BMI 25-29.99, 30-34.99, and ≥ 35 had the following OR for development of DGF: 1.30, 1.42, and 2.18.

Systemic and cardiovascular complications

Two studies reported varied rates of new onset diabetes after transplant (NODAT) of 9% and 36%^[9,16]. The higher estimate comes from Gusukuma *et al.*^[16] using BMI of ≥ 35 as their cutoff. In a study of 167 renal transplant recipients^[25] NODAT developed during the 1st post-transplant year in 64 (38.2%). Using multivariate regression, the authors determined significant risk factors to be age > 50 at time of transplant (HR 2.50, 95%CI: 1.72, 3.65), waist circumference in men > 94 cm (HR 1.95, 95%CI: 1.17, 3.25) and in women > 80 cm (HR 4.50, 95%CI: 1.87, 10.86).

Of interest, a number of short-term studies have demonstrated improved glycemic control and diabetic parameters following conversion from tacrolimus (Tac) to cyclosporine (CsA) in patients with NODAT^[26-28]. However, one small study with long-term follow up suggests that the glycemic benefits associated with CsA conversion may only be short-lived^[29].

The absence in long-term incidence of NODAT between CsA and Tac based immunosuppression was further supported by a single-center study of 704 patients, nondiabetic at time of transplant (1999-2005)^[30]. BMI was, however, identified as an important risk factor. In this study, the emergence of NODAT was determined between cyclosporine based immunosuppression (*n* = 533) and then following conversion to tacrolimus (in 171 patients at a mean post-transplant time of 17.3 ± 17.7 mo) based immunosuppression. Most common reasons for conversion include rejection events or for difficulty maintaining therapeutic CsA levels) based immunosuppression. Of note, target long-term prednisone dosing in this study was 10 mg/d. Multivariate time-dependent Cox regression analysis found no difference in the adjusted 5-year risk of NODAT-free survival following conversion from CsA to Tac (87.4%) compared to CsA only groups (91.0%, *P* = 0.90). Multivariate analysis confirmed that conversion from CsA to Tac did not increase the risk for NODAT; instead, significant associations included recipient age [per year: 1.04 (95%CI: 1.02, 1.06)]; BMI at transplant [per unit increment: 1.09 (95%CI: 1.05, 1.13)]; and previous fasting glucose level [1.06 (95%CI: 1.05, 1.08)]^[30].

Length of stay (LOS) is generally higher in obese patients, with a median of 13.7 d, mean of 14.9 d, and range of 8.4 to 24.9 d^[9,11,12,15,16]. This is in comparison to a median of 9.5 d, mean of 11.32 d, and range of 6.4 to 15.6 d for the lesser BMI comparators. Authors cited emergence of DGF as a likely cause of prolonged LOS.

Elevated BMI in the setting of kidney transplantation

has been associated with increased transplant-related complications and concerns for poorer rates of graft and patient survival. In a recent analysis of 51927 adult renal transplant recipients registered to the USRDS database (1988-1997), extremes of BMI (< 18 and > 36) were significantly associated with worse patient survival and poorer graft survival - the latter independent of patient survival^[31]. The risk for graft loss by cox proportional hazard model was similar for BMI < 18: 1.213 (95%CI: 1.110, 1.326) - as it was for BMI 34-36: 1.205 (95%CI: 1.084, 1.339); and highest for BMI > 36: 1.385 (95%CI: 1.300, 1.551). Similar U-shaped outcome patterns were noted for death censored graft loss, long-term graft loss beyond 6 mo, death with functioning graft, and infectious death.

A single-center study of 1102 renal allograft recipients with baseline pre-transplant cardiac disease among 19.2% demonstrated that the 5-year cumulative incidence of a composite cardiac outcome [comprised of congestive heart failure (CHF), Atrial fibrillation, and myocardial infarction] increased significantly between the lowest and highest BMI quartiles - BMI 14.2-22.9: 8.7% (SE 2.4%); BMI 29.8-46.9: 29.3% (SE 5.4%). This increase in the composite was driven primarily by increases between 1st and 4th quartiles in CHF (3.6% vs 18.4%) and atrial fibrillation (1.0% vs 10.7%); the cumulative incidence of myocardial infarction, however, did not increase by BMI quartile^[32].

Weight gain following transplant may represent a particularly concerning risk factor. In a 20-year follow up study of a cohort of 1810 patients, a cox proportional hazards model was used with adjustment for cardiovascular risk factors to determine relative risk of death and death-censored graft failure. After multivariable adjustment, the authors found that each 5 kg/m² increment in BMI during the first year after transplant contributed a 1.23 (95%CI: 1.01, 1.50) and 1.18 (95%CI: 1.01, 1.38) additional relative risk for death and death-censored graft failure, respectively. The relative risk for mortality and graft-failure in patients with BMI > 30 was 1.39 (95%CI: 1.05, 1.86)^[33]. In a study of 292 renal transplant recipients, multivariate analysis demonstrated that an increase in BMI of > 5% contributed to a death censored hazard ratio for 1-year graft loss of 2.82 (95%CI: 1.11, 7.44)^[34].

In conflict with this finding are results from a recent study by Nicoletto *et al*^[35]. Meta-analysis of 21 studies involving 9296 patients found an association between obesity and DGF (RR: 1.41, 95%CI: 1.26, 1.57) but not with acute graft rejection. Interestingly, the association between graft-loss, death by CVD, and all-cause mortality was dependent upon transplantation era. In studies assessing 5-year survival, for example, the authors determined using univariate meta-regression that year of publication became significant. Subgroup analysis stratified by year of publication

(before or after 2003) demonstrated a difference in the association of obesity on 5-year survival - those studies prior to 2003 (RR 1.96, 95%CI: 1.55, 2.48) vs studies post-2003 (RR 1.06, 95%CI: 0.85, 1.31). Similar findings were noted for 1-year survival and graft loss at 5 years. Death by CVD was increased, but all studies evaluated predated 2003. The authors speculate the change due to modern-era (post-2000) Tac-based immunosuppression and steroid-sparing or rapid tapering based protocols compared to previous era transplants.

Chang *et al*^[36] used data from the New Zealand Dialysis and Transplant (ANZDATA) Registry to examine relationships between BMI at transplant and subsequent outcomes. 5684 patients age ≥ 16 at time of transplant (1991-2004) were included and followed until death or through 2005. Obesity was a risk factor for graft and patient survival lost significance when entered into multivariate analysis. Underweight (BMI < 18.5) status, as opposed to normal BMI (18.5-24.9), was found to be a predictor of late (> 5 years) graft loss with HR 1.70 (95%CI: 1.10, 2.64). The adverse effect of underweight status on graft survival was attributed to the likelihood that due to lesser degrees of adiposity, higher graft-kidney concentrations at a given blood level could have led to higher rates of calcineurin inhibitor nephrotoxicity^[36-39]. When analyzed as a time-varying covariate using BMI at the start of periods 0-1 years, 1-5 years, and > 5 years post-transplant, BMI ≥ 30 was not associated with poorer graft or patient survival^[36].

In a combined systematic review (of 11 studies representing 305392 participants) and meta-analysis of 4 studies, Ahmadi *et al*^[40] determined that compared to normal BMI, extremes of weight were associated with increased post-transplantation mortality risk. The hazard ratios for mortality risk were 1.09 (95%CI: 1.02-1.20), 1.07 (95%CI: 1.04-1.12), and 1.20 (95%CI: 1.14-1.23) based upon underweight, overweight, and obese BMI, respectively. The authors concluded that the "obesity survival paradox is unlikely in kidney transplant recipients since both extremes of pre-transplantation BMI are linked to higher mortality in this population".

BARIATRIC SURGERY IN RENAL TRANSPLANT RECIPIENTS

Pre-transplant patients

Given the associated technical difficulties, surgical site complications, and outcomes-related concerns, transplant programs may impose a maximal BMI eligibility threshold for transplant. To this regard, data support the efficacy of transplant facilitation through effective pretransplant weight reduction using bariatric surgery^[41,42]. In the largest of these series, laparoscopic sleeve gastrectomy (LSG) in 27 pretransplant patients

with a mean age of 57 years and mean preoperative BMI of 48.3 (range 38-60.4) underwent LSG with subsequent mean percentage excess weight loss at 1, 3, and 12 mo of 17%, 26%, and 50%^[42].

LSG involves subtotal gastric resection of the fundus and body to create a smaller tubular gastric conduit without otherwise modifying gastrointestinal nutrient flow^[42]. Despite being a restrictive as opposed to a malabsorptive procedure (such as Roux-en-Y gastric bypass or biliopancreatic diversion) postoperative nutrient deficiencies remain a concern^[43,44].

Two studies in non-transplant patients compare outcomes between LSG and Roux en Y Gastric Bypass. While overall mortality was similar, LSG is less invasive with lower morbidity rates (20.5% RYGB vs 6.5% LSG) and comparable degrees of weight loss at 6, 12, and 18 mo, while RYGB appeared to be more efficacious in terms of achieving diabetes remission^[45,46]. Another study^[46] supports similar degrees of weight loss between procedures but comparable rates of diabetes resolution; rates of resolution for hypertension and gastroesophageal reflux disease (GERD) were superior with RYGB. Given the premise of LSG, it is not surprising that GERD may actually increase postoperatively^[47].

Post-transplant patients

Accumulating data also support the safety and efficacy of bariatric surgery in reducing obesity-related morbidity in renal transplant patients. Patient selection is critical and the involvement of an experienced bariatric surgery service is crucial in pairing the appropriate procedure with the individual patient's circumstances^[48].

Long term (median of 14 mo) follow up of 8/10 renal transplant recipients following LSG demonstrated significant reduction in BMI^[49]. Median preoperative BMI was 42 (37-49); following LSG the median BMI at 6 mo and one year were 31 and 29, respectively. The median percentage excess weight loss was 54% at 3 mo, 57% at 6 mo, and 75% at 1 year. It must be noted that in 2 patients, LSG was unsuccessful or complicated. In one subject, it failed to control weight gain and subsequent conversion to biliopancreatic diversion and duodenal switch became necessary; in another, a sleeve stricture developed accompanied by nausea, vomiting, and a transient rise in creatinine. Importantly, LSG did not interfere with maintenance of immunosuppression and the associated weight loss was accompanied by improvements in both serum creatinine and urinary protein excretion.

In another series, 5 female renal transplant recipients with a mean BMI of 52.2 (range: 48-69) underwent Roux-en-Y gastric bypass (in 4) and LSG (in 1). Percent of excess weight loss at 2 years was over 50% in all patients. No postoperative complications were noted nor were alterations to immunosuppressant dosing required^[50].

In perhaps the largest series to date, Våge *et al*^[51]

present long-term outcomes data on 117 patients undergoing LSG in the post-renal transplant setting. Patients in this series had the following baseline characteristics, presented as mean (\pm SD): Age 40.3 (10.7) years, BMI 46.6 (6.0) kg/m²; type 2 diabetes was present in 23 (19.7%), hypertension in 50 (42.7%), hyperlipidemia in 14 (12.0%), sleep apnea in 15 (12.8%). Of interest, the majority of benefit had been achieved by 12 mo and remained stable for most outcomes through 24 mo follow up. These benefits included reduction in BMI to 30.3 (5.9) and 30.6 (5.6) kg/m² by 12 and 24 mo. By 24 mo, remission of the aforementioned baseline comorbidities had occurred in 80.7%, 63.9%, 75.8%, and 93.0%, respectively. Not unexpectedly, rates of gastroesophageal reflux disease increased in a statistically significant manner from 12.8% at baseline to 27.4% at 24 mo. Complications included hemorrhage (requiring transfusion) in 6 (5.1%), anastomotic leak in 2 (1.7%), abscess without leak in 1 (0.9%), and wound infection in 3 (2.6%). Of interest, alanine aminotransferase (ALT) elevations noted in 42.7% of patients at baseline resolved to rates of 4.7% and 7.4% by 12 and 24 mo. The authors attributed to this to a potential impact on rates of non-alcoholic steatohepatitis.

In an analysis of United States Renal Data System data (1991-2004) by Modanlou *et al*^[52], 188 cases of bariatric surgery were undertaken in renal allograft candidates and recipients. Thirty-day mortality after bariatric surgery was found to be 3.5% in both listed and transplanted patients. An additional 3.5% died 31-90 d postoperatively. Median excess body weight loss was estimated at 31% to 61%. Importantly, the majority of cases involved open Roux-en-Y gastric bypass, and the authors found mortality risks among these patients similar to non-renal populations. Increasing experience with bariatric surgery in the renal population and emergence of less invasive options such as LSG were raised as promising factors bearing potential for future, prospective study.

It is important to note that nutrient deficiencies often emerge following bariatric surgery, whether LRYGB or LSG. In addition to iron, folic acid, vitamin B12, and zinc deficiencies, Vitamin D deficiencies may emerge and contribute to reduced calcium absorption with secondary hyperparathyroidism^[44]. The latter is an important consideration since renal-failure mediated secondary hyperparathyroidism and disturbances in bone and mineral disorders often persists following transplant^[53]. Recently, two cases of enteric oxalate nephropathy in the renal allograft were reported as a complication of fat malabsorption resulting from gastric bypass surgery^[54].

CONCLUSION

The risk of surgical site and soft-tissue complications are increased among obese individuals as compared

to overweight or nonobese (*i.e.*, BMI < 30) recipients, as is the risk of DGF; together, these issues contribute to increased LOS. Patient and graft survival are poorer in underweight BMI recipients (*i.e.*, < 18.5), but the U-shaped survival curves applicable to extremes of BMI may also be applicable to non-transplant populations. Therefore, current studies appear to support a neutral impact of obesity upon long-term graft and patient survival^[36,40]. Increased risk of NODAT appears to be associated with age, BMI, and waist circumference. Measures of central adiposity (waist-to-hip ratio and waist circumference) in non-transplant patients appear to be strong predictors of cardiovascular mortality^[55]. The use of these measures were found to be predictors of NODAT and therefore may be useful (in addition to age, BMI, fasting blood glucose) during pre-transplant evaluation as well as following transplant for risk stratification and intervention. Bariatric surgical procedures are an option but careful patient selection and procedural considerations are warranted. Furthermore, regardless of technique, ongoing assessment for development of nutrient deficiencies is warranted. Extremes of BMI should not constitute contraindications to kidney transplant per se, but individualized risk assessment is necessary. Future areas of research should focus on reducing recognized complications associated with renal transplantation in the setting of obesity – particularly reduction of surgical site complications (*i.e.*, wound infections and lymphocele) and DGF.

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