The application of BMI-based eligibility criteria may represent an unjustified barrier to renal transplantation in people with obesity.

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Abstract

The prevalence of both obesity and end-stage kidney disease are increasing. In many centers, obesity is considered a relative contraindication to kidney transplantation due to an association with short- and longer-term adverse outcomes. This leads to delayed transplant waitlisting and longer organ waiting times for people with obesity. This review evaluates whether intentional pre-transplant weight loss in people with obesity improves kidney transplant outcomes.

There are currently no data showing that non-surgical weight loss of 10% or more improves graft or patient survival over 4-5 years. Outcomes from bariatric surgery cohorts have been generally neutral or favourable after pre-transplant weight loss of ~25%.

Given the survival benefit of kidney transplantation compared to maintenance dialysis, and the difficulty of achieving and maintaining weight loss, the common practice of recommending weight loss to achieve arbitrary targets prior to waiting list activation needs to be carefully considered.
Introduction

The prevalence of both obesity and end stage kidney disease (ESKD) are increasing worldwide \(^1\),\(^2\). In line with the prevalence of excess weight in the general population, at least 60% of patients with ESKD are overweight or have obesity \(^3\). In addition to its established relationships with the traditional chronic kidney disease (CKD) risk factors of atherosclerosis, diabetes and hypertension, obesity is an independent risk factor for the development and progression of CKD \(^4\).

Obesity is involved in the pathogenesis of hypertension, atherosclerosis, insulin resistance and dyslipidemia through the secretion of pro-inflammatory and atherogenic adipokines from adipose tissue, contributing to vascular dysfunction and a pro-thrombotic state \(^5\). Additionally, obesity leads to physiologic changes in the kidney, including hyperfiltration and increased tubular reabsorption of sodium, promoting the development of glomerular hypertension and podocyte hypertrophy. Obesity-related glomerulopathy is characterized by glomerular hypertrophy, proteinuria, progressive glomerulosclerosis and loss of renal function \(^5\)–\(^7\). In isolation, the clinical course of obesity-related glomerulopathy is typically slowly progressive, but it may lead to renal failure and ESKD in up to one-third of affected patients \(^6\),\(^8\).

Following kidney transplantation, retrospective cohort studies have observed that obesity is associated with an increased risk of adverse outcomes when compared to graft recipients without obesity, particularly acute surgical and new-onset metabolic complications. A meta-analysis of 56 observational studies across several eras of transplantation (1993 – 2014) included over 209,000 renal transplant recipients and observed that those with BMI >30 kg/m\(^2\) had higher risk of wound complications, including infection (RR=3.13; [95% confidence interval (CI) 2.08-4.71]), dehiscence (RR=4.85; [95% CI 3.25-7.25]) and incisional hernia (RR=3.06; [95% CI 1.05-7.06]) \(^9\). The incidence of new-onset diabetes after transplant (NODAT) was also elevated (RR 2.24 [95% CI 1.45-3.45]). A modest effect was observed on the incidence
of acute rejection (RR=1.17 [95% CI 1.01-1.37]) and delayed graft function (RR=1.52 [95% CI 1.35-1.72]), although these findings should be interpreted cautiously in the absence of stratification for immunological factors, immunosuppression era and transplant pathway (i.e. live donor, cardiac or brain-dead deceased donation). No significant differences were observed in chronic rejection, graft loss or eGFR at 1, 3 and 5 years. Recipients without obesity had a subtle benefit in terms of 3-year graft survival and overall mortality, although these outcomes were not compared against people with obesity who continued maintenance dialysis. Sub-analyses among studies that included BMI in regression models found no relationship between BMI and graft survival and mortality, with higher BMI paradoxically associated with improved patient survival overall (HR 0.93; CI 0.89-0.97). Although several international guidelines note that there are insufficient data to preclude an otherwise eligible patient from kidney transplantation on the grounds of obesity alone (Table 1), obesity is often regarded as a relative barrier to kidney transplantation. Some guidelines recommend aiming for a body mass index (BMI) <30 kg/m² prior to transplantation, and even in regions without specific recommendations, such as Australia and New Zealand, people with obesity are less likely to be listed for deceased donor transplantation. Transplant centers commonly use BMI targets as a criterion for recipient eligibility, reducing access to renal transplantation for people with obesity until relatively arbitrary goals are achieved. This practice is based on the premise that the additional risks associated with obesity in the recipient might offset the benefits of kidney transplantation and be reversible with weight loss prior to transplantation.

While in the setting of CKD, there is evidence to suggest that weight loss in people with obesity can reduce hyperfiltration and albuminuria and slow the progression of GFR decline, the benefit of weight loss prior to kidney transplantation on post-transplant outcomes is less clear.

Furthermore, achieving and maintaining weight loss is not straightforward, especially in the setting of ESKD. Obesity is a chronic, relapsing disease process, and for most people with obesity, lifestyle interventions alone do not lead to sustained weight loss. The next tier of more intensive treatments,
such as very-low-energy diets and obesity pharmacotherapy, are a particular challenge in people with ESKD due to complex nutritional requirements and a lack of clinical trial data demonstrating their safety and efficacy in this population. Bariatric surgical procedures facilitate substantial weight loss and metabolic improvements, but the typical result (mean total weight loss of ~25-30%) will often fall short of achieving a BMI <30-35 kg/m² in people with severe obesity pre-operatively 19.

The survival benefit for renal transplantation, as compared to maintenance dialysis, extends to people with obesity 20,21 and increased wait time to transplantation is associated with moderately reduced overall survival 22. Therefore, it is necessary to consider whether the benefits of weight loss warrant delaying activation for transplantation until arbitrary targets are attained. The purpose of this review is to evaluate whether intentional pre-transplant weight loss in people with obesity improves kidney transplant outcomes.

Methods

A search for English-language articles was conducted in June 2021 using MEDLINE, EMBASE and Google Scholar databases. Search terms included “renal transplant”, “kidney transplant”, “obesity”, “overweight”, “weight loss”, “bariatric surgery”, “outcomes”, “graft survival” and “mortality” for studies published up until June 2021. Studies were included if they examined the association between weight loss prior to kidney transplantation and post-transplant outcomes in at least 5 patients. Articles that were not written in English, not conducted in humans, and conference abstracts were excluded.

Results
Of 224 articles retrieved in the initial search, 16 studies were identified that reported original data on post-transplant outcomes in at least 5 participants after pre-transplant weight loss. Four reported outcomes after unspecified methods of weight loss in retrospective observational cohorts traversing several historical eras of transplantation (Table 2) and 11 studies (9 retrospective single-centre cohorts, one prospective single-centre cohort, one prospective single-centre non-randomised trial) examined pre-transplant bariatric surgery (Table 3). Although one bariatric surgery study \(^23\) presented data on 20 participants also included in a subsequent larger \(n=41\) cohort \(^24\), both papers have been included here because only the earlier study included a matched control group.

**Post-transplant outcomes after unspecified methods of pre-transplant weight loss in people with obesity**

A contemporary report of 893 kidney transplant recipients found no difference in graft survival rates in patients with and without obesity \(^25\), but those with obesity who had lost >10% weight had lower graft and overall survival rates than those who did not lose weight pre-allograft. People with obesity who achieved a BMI <30 kg/m\(^2\) still had a residual excess risk of wound complications compared to those without obesity.

These observations were supported by a large analysis of adult deceased donor kidney transplant recipients in the U.S. between 2004-2014 \((n=94,465)\) which found those with weight loss ≥10% between listing and transplantation were at higher risk of longer hospitalization, all-cause graft loss and post-transplant mortality \(^26\). Recipient BMI category at listing did not modify the association between weight loss and graft loss or mortality but did strengthen the association with length of stay, meaning that even in recipients with obesity, weight loss was associated with poorer outcomes compared to maintenance of a stable weight.
A retrospective analysis of more than 160,000 waitlisted and transplanted patients in the United States between 1990 and 2003 found that weight loss during waitlisting was not associated with post-transplant mortality or graft loss in any baseline BMI category.

The only study attempting to distinguish between volitional and unintentional weight loss examined outcomes among 328 adult kidney transplant candidates initially designated inactive on the waiting list due to obesity (BMI ≥30 kg/m²) and later transplanted. Median BMI at time of registration and transplantation was 38 and 36 kg/m² (respectively), compared to 27 kg/m² in patients wait-listed directly. Median time to transplantation was 618 (interquartile range [IQR] 337, 1106) vs 298 (IQR 113, 680) days for non-activated vs control patients (p<0.001). No differences were found between groups in graft or patient survival. Further analyses stratified initially non-activated recipients into quartiles based on the percentage change in BMI recorded at first registration and at transplantation, finding no differences in patient or graft survival within 4 years of transplantation between quartiles (median BMI at registration and listing 40.1 and 32.6 kg/m² [Q1] and 36.6 and 37.6 kg/m² [Q4]). In a simulation of how initially non-activated candidates would have fared had they been transplanted at their first registration BMI, non-activated potential organ recipients were compared with controls matched for initial BMI (315 pairs). By the time of transplantation, median BMI was lower for initially non-activated recipients than matched controls (35.7 vs. 37.5 kg/m², p<0.001) and no differences between groups were found in patient or graft survival over 4 years.

**Post-transplant outcomes after bariatric surgery prior to transplantation**

Small retrospective cohort studies involving participants with BMI of 39-44 kg/m² prior to surgery and 27-33 kg/m² at time of transplantation, have generally shown favorable outcomes up to 5 years after bariatric surgery (Table 3). Overall, there were high rates of graft survival (66% to 100%) and low mortality
(0% to 17%) in people who underwent bariatric surgery prior to kidney transplantation. No patients who underwent pre-transplantation bariatric surgery were reported to develop NODAT in 3 studies, while 1 study reported NODAT in 2/23 (8.7%) patients at one year follow-up in both bariatric surgery and matched control groups. Six studies reported on wound infections, which ranged from 0% to 71%. Where post-transplant outcomes were compared between patients who had undergone bariatric surgery and a non-surgical control group, no significant differences between groups were found in graft loss, patient survival, NODAT and wound infections following transplantation apart from one retrospective cohort study of 43 patients who underwent various bariatric procedures pre-transplantation that found a higher risk of acute rejection at 1 year (adjusted odds ratio [aOR] 1.19 [95% CI 1.07-1.33]) and lower risks of delayed graft function (aOR 0.53 [95% CI 0.42-0.68]), all-cause allograft failure (adjusted hazard ratio [aHR] 0.31 [95% CI 0.29-0.33]) and mortality (aHR 0.57 [95% CI 0.53-0.61]) up to 5 years compared with controls matched for pre-bariatric surgery BMI.

**Discussion**

Despite the association between obesity and adverse outcomes after kidney transplantation, the limited available data do not indicate a clear benefit of weight loss prior to transplantation in improving graft or patient survival over 5 years. In this patient population, bariatric surgery appears to be an efficacious and safe procedure to induce sustained weight loss, with lower-than-expected rates of NODAT and no adverse effects on graft and patient survival.

Like in other chronic disease states, an apparent “obesity paradox” has repeatedly been observed in dialysis-dependent people, with higher BMI associated with increased overall survival. In a meta-analysis of the risk of cardiovascular and all-cause mortality in 1,534,845 participants with CKD in 165 studies, each
1kg/m² increase in BMI was associated with a 3% and 4% lower all-cause and cardiovascular mortality respectively in patients on haemodialysis. While there is no clear explanation for this observation, several possibilities have been proposed, including residual confounding by unmeasured variables or selection biases involving the inclusion of particularly resilient people who developed ESKD after surviving other complications of obesity and CKD. Biologically-driven explanations include the availability of greater energy reserves in the form of adipose tissue and muscle, making people with obesity less likely to develop protein energy wastage in response to inflammation. Biologically-driven explanations include the availability of greater energy reserves in the form of adipose tissue and muscle, making people with obesity less likely to develop protein energy wastage in response to inflammation. Better short-term haemodynamic stability in people with obesity may enable them to tolerate larger intradialytic ultrafiltration volumes without cumulative recurrent hypotensive sequelae compared to people without obesity.

Kidney transplantation remains the preferred management of ESKD and the overall survival rate following engraftment is excellent. From the Australian and New Zealand Registry (ANZDATA), patient survival after deceased donor transplantation at 5 years from 2011-2012 (n=1044) and 2013-2014 (n=1135) approximates 90%. Observational data show a clear mortality benefit of transplantation compared with continued renal replacement therapy. Unadjusted long-term follow-up of 5020 patients from ESKD onset demonstrated a lower overall risk of death (RR 0.25) in those undergoing transplantation (n=799) compared to those who remained on dialysis. In a retrospective cohort of 6697 kidney transplant recipients with a median follow-up of 8.2 years, the rate of death was higher in patients on dialysis for >1.5 years pre-transplant compared to those with shorter duration on dialysis prior to transplantation (HR 1.62, 95% CI 1.43-1.83). Furthermore, pre-emptive transplantation was independently associated with a lower risk of graft loss (HR 0.76, 95% CI 0.59-0.98) and greater overall survival.

The mortality benefit of transplantation compared with continued dialysis extends to people with obesity. Although there are limited data for patients with severe obesity (BMI ≥40 kg/m²), there does not
appear to be a BMI cut-off at which transplantation is no longer associated with a survival benefit of around 50% or greater at one and five years, compared with remaining on the waiting list.\textsuperscript{21,46}

The mortality advantages conferred by renal transplantation are durable, with the extent being partially a function of the generally poor long-term prognosis associated with chronic dialysis. These outcomes may be subject to significant selection biases, particularly in people with obesity, and ideally, would be tested prospectively through large, high-quality prospective long-duration comparisons but, as preference swings toward transplantation as the preferred management of ESKD, such analyses are unlikely to be forthcoming.

Data on other post-transplantation outcomes in people with BMI $\geq 40$ kg/m$^2$ are also scarce. A comparison of 747 kidney transplant recipients with BMI $\geq 40$ kg/m$^2$ and 28,981 recipients with BMI 18-39 kg/m$^2$\textsuperscript{48} found that those with severe obesity had higher rates of comorbidities prior to transplantation (including diabetes) and higher 30-day readmission rates (34 vs 27%, $P<0.001$), although BMI $\geq 40$ kg/m$^2$ was not a predictor of readmission in a multivariate analysis. Length of stay was not different between groups and outcomes such as delayed graft function, post-operative complications, wound infections and NODAT were not reported. In a retrospective review of nearly 75,000 U.S. renal transplant recipients from 2004-2009, of whom 2.1% (n=1561) had BMI $>40$ kg/m$^2$, multivariable logistic regression indicated increasing risks of delayed graft function and non-death censored graft failure with increasing categories of obesity, compared to those without obesity.\textsuperscript{49} Nonetheless, these outcomes are outweighed by the significant benefit patients receive from timely transplantation.

It is notable that the two largest retrospective cohort analyses addressing this question\textsuperscript{26,27} came to different conclusions regarding the effect of pre-transplant weight loss on graft loss and mortality after
kidney transplantation. This discrepancy is likely due to the studies encompassing distinct transplantation periods, and differences in underlying patient characteristics. In the study by Harhay et al 26 which found an adverse effect of substantial weight loss, a more recent era of transplantation was represented (2004-2014 vs 1990-2003) and the overall cohort was older (median age 53 vs 59% under 50 years) and had a higher prevalence of obesity (35% vs 22%) compared with the study by Schold and colleagues 27. Neither study described the method used to achieve weight loss or whether it was intentional.

The findings from this review are consistent with a recent systematic review that examined outcomes of bariatric surgery before or after kidney transplantation 50, which found graft survival of 98% at 1 year (7 studies) and 100% beyond 1 year (3 studies) 50. The current review includes 7 of the 11 studies included in the systematic review (4 were excluded due to reporting on fewer than 5 patients who underwent kidney transplantation after bariatric surgery) along with an additional 4 studies, and extends the previous findings by examining wound complications and NODAT, (outcomes particularly associated with obesity in renal transplant recipients), as well as post-transplant outcomes after non-surgical weight loss.

**Obesity as a risk factor for CKD and post-transplant outcomes**

Obesity is involved in the pathogenesis of hypertension, atherosclerosis, insulin resistance and dyslipidemia through the secretion of pro-inflammatory and atherogenic adipokines from adipose tissue, contributing to vascular dysfunction and a pro-thrombotic state 5. Additionally, obesity leads to physiologic changes in the kidney, including hyperfiltration and increased tubular reabsorption of sodium, promoting the development of glomerular hypertension and podocyte hypertrophy, resulting in obesity-related glomerulopathy, characterized by glomerular hypertrophy, proteinuria, progressive glomerulosclerosis and loss of renal function [16-18]. In isolation, the clinical course of obesity-related glomerulopathy is usually stable or slowly progressive, but it may lead to renal failure and ESKD in up to one-third of affected patients 6,8. Measures to reduce proteinuria, such as renin-angiotensin-aldosterone
system blockade and weight loss (particularly via bariatric surgery), have renoprotective effects, although long-term prospective data are lacking.\textsuperscript{6,7}

There is some indication, mainly from retrospective cohort studies, that after kidney transplantation, obesity is associated with an increased risk of adverse outcomes when compared to recipients without obesity, particularly acute surgical and new-onset metabolic complications. A meta-analysis of 56 observational studies across several eras of transplantation (1993 – 2014) included over 209,000 renal transplant recipients and observed that those with BMI >30 kg/m$^2$ had higher risk of wound complication including infection (RR=3.13; [95% confidence interval (CI) 2.08-4.71]), dehiscence (RR=4.85; [95% CI 3.25-7.25]) and incisional hernia (RR=3.06; [95% CI 1.05-7.06]) \textsuperscript{9}. The incidence of new-onset diabetes after transplant was also elevated (RR 2.24 [95% CI 1.45-3.45]). A modest effect was observed on the incidence of acute rejection (RR=1.17 [95% CI 1.01-1.37]) and delayed graft function (RR=1.52 [95% CI 1.35-1.72]), although these findings should be interpreted cautiously in the absence of stratification for immunological factors, immunosuppression era and transplant pathway (i.e. live donor, cardiac or brain-dead deceased donation). Recipients without obesity had a subtle benefit in terms of 3-year graft survival (RR=0.95-0.97), which has been interpreted as clinically non-inferior and of doubtful significance in real terms, where the question of survival benefit has not been compared against outcomes for patients with obesity who continue maintenance dialysis. No significant differences were observed in chronic rejection, graft loss or eGFR at 1, 3 and 5 years. Overall mortality (RR=1.52, [95% CI 1.14-2.03]) favored lower BMI recipients, but did not compare recipients with obesity to those who remained un-transplanted. Sub-analyses among studies that included BMI in regression models found no relationship between BMI and graft survival and mortality, with higher BMI paradoxically associated with improved patient survival overall (HR 0.93; CI 0.89-0.97) \textsuperscript{9}. 
A range of potential methodological and organic factors may explain the lack of observed benefit associated with weight loss, particularly that achieved without bariatric surgery, on transplant outcomes. Retrospective registry and cohort analyses have difficulty capturing the nuance of clinical decision-making factors around the time of both wait-list activation and potential organ allocation. Transplanting units generally attempt to favourably influence outcomes through individualized organ acceptance based on donor-recipient size mismatching and other anatomical considerations beyond conventional immunological matching, therefore inclusion for analysis on the basis of the transplantation event introduces substantial selection biases. Nonetheless, overall these observations appear to indicate that, in appropriately optimized circumstances, obesity alone is not a reasonable barrier to engraftment in otherwise suitable candidates.

At a physiological level, pre-optimized stratification and care of obesity-related complications, such as hypertension and impaired glucose tolerance/type 2 diabetes, in this population through rigorous transplant work-up and post-transplant care may mean there is less scope for further risk reduction with weight loss.

While obesity is clearly associated with cardiovascular disease in the general population, there is no corresponding cardiovascular mortality signal after kidney transplantation. It has been speculated that this may be a function of retrospective observations subject to both selection bias in favor of patients who are otherwise fitter (despite obesity) and to center effects driven by local wait-list activation and organ-acceptance practices. Alternatively, given that ESKD itself is an independent cardiovascular risk factor, the contribution of BMI may be less relevant to the overall risk of cardiovascular mortality in those otherwise fit enough to undergo transplantation. Furthermore, although BMI is correlated with health and metabolic outcomes on a population level, it does not indicate an individual's cardiometabolic risk, adiposity, visceral fat or muscle mass.
Additionally, with the exception of bariatric surgery cohorts, most studies to date have not been able to distinguish between intentional and unintentional weight loss. Outcomes in people with unintentional weight loss are likely to be adversely affected by the underlying cause of weight loss (such as concurrent illness, inflammation or malignancy) and its consequent impact on nutritional status, sarcopenia and frailty. Sarcopenia, with or without obesity, is associated with higher mortality \(^{37}\). Even intentional weight loss may compromise nutritional status and exacerbate sarcopenia, particularly in the at-risk population with ESKD, compounding the operative challenges posed by persistent excess abdominal adipose tissue. While Heng et al \(^{25}\) found a lower graft survival amongst patients with obesity who had lost >10% of their body weight, they postulated that weight loss catabolism may create a state of protein malnutrition and heightened systemic inflammation as contributing mechanisms. Among those who achieved a BMI <30 kg/m\(^2\), they still had residual excess risk of wound complications, possibly due to a persistent panniculus which may complicate surgical access and increase the risk of wound infections, although the mechanism is unclear.

Treatment of obesity is particularly challenging in people with ESKD. Renal dietary requirements, comorbidities that may limit exercise tolerance, and fatigue from kidney failure and dialysis complicate the implementation of effective lifestyle interventions \(^{58}\), and there is very little data to guide the use of obesity pharmacotherapy in this population \(^{59}\). A prospective, open-label, non-randomised study \(^{60}\) of 44 adults with mean BMI 35.7 kg/m\(^2\) and CKD stage 3-5, including 20 on dialysis, found that a low-fat 600 kcal deficit diet and exercise intervention plus orlistat 120 mg three times daily resulted in weight loss of 8 kg (8%) at 24 months, compared to less than 1 kg (1%) in a control group of 20 patients who declined to participate in the intervention. This indicates that people with ESKD can achieve clinically beneficial weight loss without bariatric surgery, but the magnitude of weight loss expected from non-surgical interventions is unlikely to allow a person with severe obesity to meet BMI-based transplant eligibility criteria. This is
highlighted by a retrospective observation of a lifestyle intervention-based weight management program in 80 patients of a kidney transplant clinic (mean BMI 39.2 kg/m²)⁶¹. Of the 21 patients (26%) who sustained weight loss to a BMI <35 kg/m² for the duration of follow-up, none had an initial BMI ≥40 kg/m².

Moreover, the likelihood of weight regain after diet-induced weight loss ²⁷ is particularly high after transplantation, due to the resolution of uremia (and associated suppression of appetite), and corticosteroid-based maintenance immunosuppressive regimens that may exacerbate weight gain and metabolic risks. Schold et al ²⁷ found that recipients with the largest weight loss (>12%) pre-transplantation had the largest weight gain in the first 6 months post-transplantation and 40% returned to a BMI at or above their waitlisted BMI by 12 months post-transplantation. In contrast, patients who underwent sleeve gastrectomy prior to transplantation achieved sustained weight loss at most recent follow up (mean 617 ± 464 days), with a BMI of 33.7 ± 4.7 compared to 32.3 ± 2.9 kg/m² at time of kidney transplantation ³¹. Therefore, it is imperative that weight loss interventions in people with ESKD ensure optimal pre-transplant nutrition and do not terminate at wait-list activation or transplantation, but include a long-term focus on weight management.

Limitations and future directions

The primary limitation of this review is the lack of controlled, comparative data on how intentional weight loss in people with obesity affects kidney transplant outcomes. Additionally, given the survival advantages offered by renal transplantation, the key reference group for comparison is not those who were transplanted at higher levels of obesity, but those in whom transplantation was forsaken in favor of maintenance dialysis. Prospective controlled studies examining the effect of intentional weight loss on short- and longer-term transplant outcomes, and their optimal timing (i.e. before or after transplantation) will be of value. In the general population, many complications of obesity (including hypertension,
hypertriglyceridemia, glycemic control in T2D) begin to improve with as little as 3-5% weight loss \textsuperscript{62,63} with progressive improvement toward resolution with larger weight loss. In this context, examination of whether the amount and/or method of weight loss (e.g. medical intervention vs bariatric surgery) influences transplant outcomes will be of value. Observational studies of small patient cohorts indicate conventional immunosuppressive regimens seem to be well-tolerated and safely adjusted within standard therapeutic monitoring protocols following sleeve gastrectomy and RYGB \textsuperscript{64,65}, though studies focused on the pharmacology of immunosuppressive drugs after bariatric surgery are lacking.

**Conclusions**

Although there is an association between obesity and some adverse outcomes in those who receive a renal allograft, particularly wound complications and new-onset diabetes, there is currently very little published data to support the premise that pre-transplant weight loss to achieve an arbitrary BMI cut-off improves post-engraftment outcomes. In particular, studies to date do not indicate that pre-transplant non-surgical weight loss of 10% or more, even in people with obesity, improves graft or patient survival over 4-5 years. Outcomes from small retrospective bariatric surgery cohorts have been generally neutral or favourable after pre-transplant weight loss of \(~25\%\), with few post-bariatric surgery patients experiencing graft failure or mortality in a short follow-up period. Given the survival benefit of kidney transplantation compared to maintenance dialysis, and the difficulty of achieving and maintaining weight loss in people with ESKD, the common practice of recommending weight loss to achieve arbitrary targets prior to waiting list activation needs to be carefully considered. Prospective trials are required to examine the impact of different methods of intentional weight loss on transplant outcomes in people with obesity and evaluate whether any potential benefits outweigh the morbidity associated with increased time to engraftment or perpetual transplant ineligibility.
### Table 1: BMI recommendations for kidney transplantation eligibility in international guidelines

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>BMI requirements (kg/m²)</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Society of Transplantation&lt;sup&gt;66&lt;/sup&gt;</td>
<td>&lt; 30</td>
<td></td>
</tr>
<tr>
<td>Canadian Transplant Society&lt;sup&gt;11&lt;/sup&gt;</td>
<td>Target &lt;30</td>
<td>Few data suggest that patients with obesity should be denied transplantation (Grade C)</td>
</tr>
<tr>
<td>European Renal Best Practice Transplantation Guideline Development group&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Target &lt;30</td>
<td>Recommend that patients with a BMI &gt;30 kg/m² reduce weight (ungraded)</td>
</tr>
<tr>
<td>Transplantation Society of Australia and New Zealand&lt;sup&gt;13&lt;/sup&gt;</td>
<td>None</td>
<td>Likelihood of deriving significant benefit from transplantation must outweigh risks (Aust.), and ≥80% likelihood of surviving ≥5 years after transplantation (NZ).</td>
</tr>
<tr>
<td>U.K. Renal Association&lt;sup&gt;67&lt;/sup&gt;</td>
<td>None</td>
<td>Patients with obesity (BMI &gt;30 kg/m²) should be screened rigorously and each case considered individually. Those with BMI &gt;40 are less likely to benefit.</td>
</tr>
<tr>
<td>Kidney Disease Improving Global Outcomes&lt;sup&gt;68&lt;/sup&gt;</td>
<td>Relative contraindication</td>
<td>Recommend dietary counselling or bariatric surgery particularly for class II or III obesity (BMI ≥ 35 kg/m²)</td>
</tr>
<tr>
<td>Author</td>
<td>Study type</td>
<td>N, Population</td>
</tr>
<tr>
<td>------------</td>
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</tr>
<tr>
<td>Schold 2007&lt;sup&gt;27&lt;/sup&gt;</td>
<td>Retrospective observational cohort, 1990-2003 Follow-up ≤14y</td>
<td>124,713 recipients (20,669 [17%] of recipients had BMI ≥30 kg/m&lt;sup&gt;2&lt;/sup&gt;); 6010 of obese [29%] lost ≥4% weight pre-transplant</td>
</tr>
<tr>
<td>Huang 2015&lt;sup&gt;28&lt;/sup&gt;</td>
<td>Retrospective observational cohort, 2006-2012 Follow-up 4y</td>
<td>328 recipients initially designated inactive due to BMI ≥30 (median 38 kg/m&lt;sup&gt;2&lt;/sup&gt;) vs 74,066 controls (median 27 kg/m&lt;sup&gt;2&lt;/sup&gt;)</td>
</tr>
<tr>
<td>Heng 2019&lt;sup&gt;25&lt;/sup&gt;</td>
<td>Retrospective observational cohort, 2007-2011 Follow-up ≤5y</td>
<td>893 recipients (380 [43%] with BMI ≥30); 78 of obese [21%] lost &gt;10% weight pre-transplant</td>
</tr>
<tr>
<td>Harhay 2019&lt;sup&gt;26&lt;/sup&gt;</td>
<td>Retrospective observational cohort, 2004-2014. Follow-up 5y.</td>
<td>94,465 recipients (32,808 [35%] with BMI ≥30), 10,614 of total [11%] lost ≥10% weight pre-transplant.</td>
</tr>
</tbody>
</table>

Table 2: Studies investigating the association between pre-transplant weight loss in people with obesity and post-transplant outcomes.

BMI, body mass index; LSG, laparoscopic sleeve gastrectomy; NODAT, new onset diabetes after transplant, aHR, adjusted hazard ratio; NR, not reported
<table>
<thead>
<tr>
<th>Author</th>
<th>Study type</th>
<th>n, surgery type</th>
<th>Follow-up time (years)</th>
<th>BMI pre-bariatric surgery; at transplant (kg/m²)</th>
<th>Graft survival</th>
<th>Mortality</th>
<th>Other outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim 2018</td>
<td>Retrospective single-centre cohort</td>
<td>20 LSG; 20 BMI-matched control recipients</td>
<td>Mean 1.7 (LSG) vs 4.6 (control)</td>
<td>41.5; 32.3</td>
<td>LSG vs control: reduced DGF (5 vs 20%, P=0.046); ns difference in graft loss (10 vs 15%)</td>
<td>LSG vs control: ns difference (0 vs 2.5%)</td>
<td>LSG vs control: ns difference in postoperative infections (10 vs 18%), surgical complications (0 vs 5% vs 0%) and NODAT (0 vs 16%)</td>
</tr>
<tr>
<td>Yemini 2019</td>
<td>Retrospective single-centre cohort</td>
<td>16; LSG (13) or RYGB (3)</td>
<td>Mean 3.9</td>
<td>41.5; 29.0</td>
<td>DGF 13%, graft loss NR</td>
<td>NR</td>
<td>Postoperative infections, surgical complications, NODAT NR</td>
</tr>
<tr>
<td>Cohen 2019</td>
<td>Retrospective single-centre cohort</td>
<td>43; gastric bypass (27), SG (9), AGB (6), unspecified (1)</td>
<td>Mean 3.6</td>
<td>43.0; 32.0</td>
<td>Bariatric surgery vs control: HR 0.31; (95% CI 0.29-0.33)</td>
<td>Reduced risk of mortality (HR 0.58, 95% CI 0.53-0.61)</td>
<td>3 deaths (1 each of malignancy, cardiovascular disease and infection).</td>
</tr>
<tr>
<td>Kim 2020</td>
<td>Retrospective single-centre cohort</td>
<td>41 LSG*</td>
<td>Mean 1.8</td>
<td>41.4; 32.4</td>
<td>DGF 2.4%, (institutional rate 13.3%), graft loss NR.</td>
<td>0</td>
<td>Postoperative infections 8 (20%), surgical complications 3 (7%), NODAT 0.</td>
</tr>
<tr>
<td>Gaillard 2020</td>
<td>Retrospective single-centre cohort</td>
<td>12 LSG</td>
<td>Median 1.4</td>
<td>39.3; 30.1</td>
<td>DGF NR, graft loss 8.3%</td>
<td>2</td>
<td>Postoperative infections 2, surgical complications, NODAT NR.</td>
</tr>
<tr>
<td>Thomas 2018</td>
<td>Retrospective single-centre cohort</td>
<td>14 RYGB</td>
<td>Median (amongst those with a)</td>
<td>42.5; 28.9</td>
<td>RYGB vs control: graft loss 29 vs 26% (ns.)</td>
<td>RYGB vs control: 0 vs 16% (P=0.13)</td>
<td>RYGB vs control: ns differences in postoperative infections 71 vs 74%, Surgical</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Cohort</td>
<td>BMI (BMI)</td>
<td>DGF (%)</td>
<td>Graft loss (%)</td>
<td>Complications</td>
<td>Postoperative infections</td>
</tr>
<tr>
<td>-------</td>
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<td>-------------------------</td>
</tr>
<tr>
<td>Kassam</td>
<td>Prospective single-centre cohort</td>
<td>45 LSG</td>
<td>Mean 2.3</td>
<td>44.0; 33.4</td>
<td>DGF NR, graft loss NR</td>
<td>0</td>
<td>Postoperative infections, surgical complications, NODAT NR</td>
</tr>
<tr>
<td>Bouchard</td>
<td>Retrospective single-centre cohort</td>
<td>14 LSG</td>
<td>Median 0.8</td>
<td>42.3; 31.0</td>
<td>DGF NR, graft loss 0</td>
<td>0</td>
<td>Postoperative infections 0, Surgical complications, NODAT NR</td>
</tr>
<tr>
<td>Hajjar</td>
<td>Retrospective single-centre cohort</td>
<td>31 LSG</td>
<td>Median 2.0</td>
<td>43.7; 31.9</td>
<td>DGF 32.1%, graft loss 0</td>
<td>1</td>
<td>Postoperative infections, surgical complications, NODAT NR</td>
</tr>
<tr>
<td>Kienzl-Weigner</td>
<td>Prospective single-centre non-randomized trial</td>
<td>7 LSG</td>
<td>Mean 3.2</td>
<td>38.8; 31.3</td>
<td>DGF 57.1%, graft loss 0</td>
<td>0</td>
<td>Postoperative infections, surgical complications, NODAT NR</td>
</tr>
<tr>
<td>Outmani</td>
<td>Retrospective single-centre cohort</td>
<td>23; LSG (11), RYGB (9), AGB (3)</td>
<td>Median 5.1</td>
<td>42.3; 33.8</td>
<td>Bariatric surgery vs controls: ns difference in DGF 35 vs 39% or graft loss 36 vs 34%</td>
<td>Bariatric surgery vs control: 1 vs 0 (ns)</td>
<td>Bariatric surgery vs control: ns difference in post-operative infections 13 vs 4%, NODAT 9 vs 9%</td>
</tr>
</tbody>
</table>

**Table 3: Studies investigating pre-transplant bariatric surgery and the association with graft survival and post-transplant mortality**

*n=41 includes n=20 reported in Kim et al which is shown separately here due to comparison with a control cohort.

BMI, body mass index; LSG, laparoscopic sleeve gastrectomy; RYGB, Roux-en-Y gastric bypass; AGB, adjustable gastric banding; NODAT, new-onset diabetes after transplant; DGF, delayed graft function; ns, not significant; NR, not reported.
References


Author/s:
Tan, A; Wilson, S; Sumithran, P

Title:
The application of body mass index-based eligibility criteria may represent an unjustified barrier to renal transplantation in people with obesity

Date:
2021-12-28

Citation:

Persistent Link:
http://hdl.handle.net/11343/299323