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Management of obesity in kidney transplant candidates and recipients: A clinical practice guideline by the DESCARTES Working Group of ERA

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ABSTRACT

The clinical practice guideline Management of Obesity in Kidney Transplant Candidates and Recipients was developed to guide decision-making in caring for people with end-stage kidney disease (ESKD) living with obesity. The document considers the challenges in defining obesity, weighs interventions for treating obesity in kidney transplant candidates as well as recipients and reflects on the impact of obesity on the likelihood of wait-listing as well as its effect on transplant outcomes. It was designed to inform management decisions related to this topic and provide the backdrop for shared decision-making. This guideline was developed by the European Renal Association's Developing Education Science and Care for Renal Transplantation in European States working group. The group was supplemented with selected methodologists to supervise the project and provide methodological expertise in guideline development throughout the process. The guideline targets any healthcare professional treating or caring for people with ESKD being considered for kidney transplantation or having received a donor kidney. This includes nephrologists, transplant physicians, transplant surgeons, general practitioners, dialysis and transplant nurses. Development of this guideline followed an explicit process of evidence review. Treatment approaches and guideline recommendations are based on systematic reviews of relevant studies and appraisal of the quality of the evidence and the strength of recommendations followed the Grading of Recommendations Assessment, Development and Evaluation approach. Limitations of the evidence are discussed and areas of future research are presented.

Keywords: body mass index, guideline, kidney transplantation, obesity, practice guideline

INTRODUCTION

Obesity has emerged as one of the greatest global health threats in modern times. In the setting of end-stage kidney disease (ESKD), obesity poses additional challenges, particularly for people being considered for kidney transplantation and those having received a donor kidney in the past.

Patients with ESKD living with obesity benefit from transplantation as do kidney transplant candidates with normal weight, but obesity increases the risk of cardiovascular, metabolic and surgical complications. There is disagreement about how to validly assess obesity. Optimal management strategies and treatment goals are not well defined and thresholds for accepting people for transplantation remain a source of controversy.

This clinical practice guideline (CPG) aims to help decision-making related to obesity in patients with ESKD being considered for kidney transplantation or having received a donor kidney in the past. The document considers the challenges in defining obesity, weighs interventions for treating obesity in kidney transplant candidates as well as recipients and reflects on the impact of obesity on the likelihood of wait-listing as well as its effect on transplant outcomes. This guideline is intended to assist the professional community in making decisions about pathways and care and the interplay between obesity and kidney transplantation, help patients and caregivers gain insight and facilitate joint decision-making in this field.

METHODS FOR GUIDELINE DEVELOPMENT

This guideline was developed by the Developing Education Science and Care for Renal Transplantation in European States (DESCARTES) scientific working group of the European Renal Association (ERA). A detailed description of the guideline development methods is available in the supplementary material (Supplement 1. Detailed methods for guideline development).

In brief, ERA's DESCARTES working group delegated a small group of content experts to the guideline development group. These content experts were chosen based on their previous involvement with a European Renal Best Practice (ERBP) position statement on pre-emptive transplantation and their expertise in assessment and management of transplant candidates and transplant recipients [1]. The group was supplemented with methodologists to supervise the project and provide methodological expertise in guideline development throughout the process [2]. The group first convened in July 2017 and ultimately consisted of 11 participants, including 8 nephrologists, 2 surgeons and 4 methodologists (categories not mutually exclusive). It included seven men and four women. Patients or their caregivers were not actively involved in the development process.

According to the rules of the ERA, the members of the guideline development group completed a centralized Declaration of Interest form that is available online at https://www.era-online.org/en/about-era/governance/disclosure-of-interest-doi/.

We allowed members of the guideline development group to have past financial or intellectual conflicts of interest but insisted on transparency.

The group identified five clinical questions, for which systematic reviews were conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses principles [3]. Outcomes reflected both benefits and harms and were rated according to their relative importance in the decision-making process. Statements were formulated and rated for strength and certainty according to Grading of Recommendations Assessment, Development and Evaluation and accompanied by a detailed rationale linking the evidence to the recommendations [4].

When areas of uncertainty were identified, the guideline development group considered making suggestions for future research based on the importance to patients or the public and on ethical and technical feasibility.

Finally, each chapter provides an overview of recommendations made by other guideline bodies. The list was not meant to be exhaustive, but rather was intended to provide a concise overview of other recommendations made.

We will aim to facilitate implementation of this guideline by dissemination through the promotional channels used by both the publishing journal and the ERA, including e-mail updates to members and subscribers, e-seminars, presence on social media and presentations during national and international conferences. Although this will hopefully serve to increase awareness, we acknowledge barriers to widespread implementation related to attitudes and behaviour may remain.

CHAPTER 1. WHAT MEASURE BEST REFLECTS OBESITY AS A RISK FACTOR FOR KIDNEY TRANSPLANTATION IN PATIENTS WITH ESKD?

Recommendations

We suggest measuring waist circumference or waist:hip ratio in addition to body mass index (BMI) in patients with ESKD living with obesity who are being assessed for kidney transplantation. (2C)

Advice for clinical practice

- BMI is defined as weight in kilograms squared divided by the height in meters. Obesity is defined as a BMI $\geq$30 kg/m^2 and can be subdivided into classes 1 (BMI 30–34 kg/m^2), 2 (BMI 35–39 kg/m^2) and 3 ($\geq$40 kg/m^2).
- Waist circumference is measured under the midline of the participant's armpit, at the midpoint between the lower part of the last rib and the top of the hip [5]. Abdominal adiposity is usually defined as a waist circumference >102 cm in men and >88 cm in women [5].
- Hip circumference is measured at the maximum circumference over the buttocks. Waist:hip ratio is defined as the ratio of the circumference of the waist to that of the hips. Abdominal adiposity is usually defined as a waist:hip ratio >0.9 in men and >0.85 in women [5].

- The conicity index is defined as the waist circumference (m)/[0.109 × square root of (weight [kg]/height [m])].

Rationale

Background

BMI is strongly correlated with body fat in the general population and is used worldwide to define the whole range of alterations in nutritional status, from malnutrition to extreme obesity [6]. Various guideline development bodies have recommended the metric for assessing and monitoring nutritional status also people with ESKD, and various kidney transplant programmes restrict transplantation to people with BMIs less than certain cut-off values [7, 8]. However, BMI may not be the best or even a good tool for defining risk related to body composition, as it is poor at discriminating the ratio of fat to lean tissue within body weight. Abdominal adiposity represents an accumulation of fat around the viscera and is more strongly associated with insulin resistance, diabetes and dyslipidaemia than peripheral or subcutaneous fat. Surrogate measures of abdominal adiposity and segmental fat distribution, such as waist circumference, waist:hip ratio and the conicity index are better correlated with all-cause and cardiovascular death in the general population than BMI [9]. Whether that is true also for people with ESKD awaiting a donor kidney is uncertain. Hence we aimed to identify the measure of obesity that correlates best with adverse outcomes in patients with ESKD or advanced chronic kidney disease (CKD) waiting for a kidney transplant.

Summary of the evidence

(Supplement 2| Study selection flow diagrams—Chapter 1)
(Supplement 3| Summary evidence tables—Chapter 1)

Studies in people treated with dialysis. We identified two observational studies conducted in prevalent or incident dialysis patients that aimed to assess the risk of death associated with BMI, waist circumference, waist:hip ratio or the conicity index [10, 11].

The first prospective cohort study included 537 people treated with chronic dialysis [10]. The investigators found increasing BMI to be associated with a decreasing risk of all-cause and cardiovascular mortality in univariable analysis. Point estimates for waist circumference, however, indicated increasing girth may have been associated with higher risks of overall and cardiovascular death. On the one hand, such findings suggest BMI may be an imperfect measure of adiposity rather than other mechanisms of confounding or collider stratification being at play [12]. On the other hand, analyses seemed to have incorrectly assumed a linear relation between BMI and outcome, which may invalidate findings altogether. In addition, interpretation of the study results and the multivariable models is hampered by incomplete reporting of confounding structures and detailed model parameters.

The second prospective cohort study included 173 people treated with chronic dialysis [11]. In univariable and multivariable analyses, both increasing tertiles of the conicity index and waist circumference seemed to be associated with an increased risk of death. The effect estimates for the conicity index exceeded those of waist circumference, and individual confidence intervals lost statistical significance in the lower tertiles after adjustment. BMI was measured but not tested for its association with outcome.

Studies in transplant recipients. We identified one prospective observational study conducted in prevalent or incident kidney transplant recipients that aimed to assess the risk of death associated with BMI or waist circumference [13]. It included 993 prevalent kidney transplant recipients, followed for ∼3 years. In the unadjusted analysis there was no clear association between BMI and risk of death. When adjusted for waist circumference as a potential confounder, it appeared that people with lower BMI had a higher risk of death, but the models provided no statistically significant correlation. Conversely, in a model adjusted for BMI and the same covariates, the hazard of death increased with waist circumference.

In a prospective cohort, including 572 kidney transplant recipients, neither pre-transplant BMI nor waist:hip ratio were associated with the development of new-onset cardiovascular disease [14]. A retrospective study, including 248 kidney transplant recipients, assessed the value of other morphometric measures in addition to BMI, but found none convincingly predicted surgical complications [15].

We found no studies assessing measures of obesity as a risk factor for kidney transplantation in patients with advanced CKD being evaluated for pre-emptive transplantation.

Translation of the evidence into recommendations

The major difficulty in identifying which measure best identifies obesity in chronic disease lies in the definition of what is 'best'. If we are looking for a modifiable risk factor, then it needs to differentiate between good and bad outcomes. For decades, BMI has been used as a surrogate for body fat, with obesity correlating well with adverse outcomes in the general population. However, in subpopulations of people with chronic disease—ESKD being no exception—numerous studies have reported that obesity confers a survival advantage. Rather than being a true causal association, this so-called obesity paradox is often the consequence of the data structures and analyses leading to selection bias. Of the five studies identified in our review of the evidence, only two directly compared BMI with other measures of body fat, making it difficult to evaluate whether reverse causation or collider stratification bias could have played a role in the findings. Also, even in studies that compare BMI with other measures of obesity, often analyses assume a linear relation between BMI and outcome, which is unlikely correct and invalidates model parameters.

Critics of BMI state that although it has been the most widely used metric to assess obesity and body fat, it cannot differentiate between muscle mass and adipose tissue or between peripheral and visceral fat. The comparative data we do have seem to support that misclassification may be an important limitation, as measures that do focus on visceral fat better identify those at risk for premature death after kidney transplantation. However, as analysis methods often fall short, it is difficult to judge whether this reflects a true characteristic of the measurement or rather results from analytical artefacts. With this in mind, we carefully suggest measuring indicators of central obesity such as waist circumference and waist:hip ratio in kidney transplant candidates in addition to BMI. Caution is needed when using these metrics for patients with polycystic kidney disease, as their enlarged kidneys may lead to falsely elevated indices.

Other guidelines on this topic

The Kidney Disease: Improving Global Outcomes (KDIGO) 2020 guidelines recommend kidney transplant candidates have their body habitus examined by a transplant surgeon at the time of evaluation and while on the waiting list (1B), but make no explicit reference as to how [16].

The ERBP 2015, Kidney Health Australia–Caring for Australasians with Renal Insufficiency (KHA-CARI) 2013 and British Transplantation Society (BTS) 2011 guidelines evaluate obesity and post-transplant outcomes with BMI, however, they do not make any comments on the role of waist circumference or waist:hip ratio [17–19]. The ERBP implicitly recommends using BMI as a measure of obesity in a statement recommending patients with a BMI $\geq$30 kg/m^2 reduce weight before transplantation.

Suggestions for future research

Prospective longitudinal studies that correctly correlate BMI, waist circumference, waist:hip ratio and conicity index with post-transplant outcomes are needed in order to define optimal measures for quantifying obesity in kidney transplant candidates. Exhaustive measurement of confounding variables and changes in obesity measures, transplantation as a time-varying variable and non-linear analytical methods that correctly reflect the relation between the obesity measure and outcome are necessary to correctly model causal associations.

CHAPTER 2. WHAT DEGREE OF OBESITY (BY LEVEL OF BMI) INFLUENCES THE OUTCOMES IN KIDNEY TRANSPLANT RECIPIENTS?

Recommendations

We suggest accepting people with ESKD and a BMI of 30–34 kg/m^2 for kidney transplantation if they are otherwise considered suitable (2C).

There are insufficient data to make a recommendation in the higher BMI categories (–D).

We recommend counselling patients living with obesity about possible increased risk of perioperative complications such as delayed graft function, wound-related morbidity, acute rejection and diabetes after transplantation (1C).

Advice for clinical practice

- Weigh BMI in the context of other risk factors when discussing transplantation.

Rationale

Background

Obesity is one of the greatest public health challenges of the 21st century. Its prevalence has tripled in many countries of the World Health Organization European Region since the 1980s, and the numbers of those affected continue to increase at an alarming rate [20]. In kidney transplant recipients, the prevalence of obesity has paralleled that of the general population [21]. Obesity can increase the risk of surgical complications after kidney transplantation and recipients living with obesity may have worse short- and long-term outcomes when compared with normal-weight recipients. However, when compared with remaining on dialysis, kidney transplantation may still provide survival benefits in the people living with obesity who are transplanted [22]. Currently there is no consensus on the degree of obesity above which the risk of perioperative complications becomes unacceptable or long-term outcomes worsen. It is a conundrum fuelled by the so-called obesity paradox, whereby, despite the known association between obesity and mortality in the general population, numerous studies have reported obesity as conferring a survival advantage among patients with chronic disease. Using BMI as a proxy for obesity (leading to misclassification as explained in Chapter 1), imperfect analyses failing to adjust for illness-related weight loss or collider stratification bias and incorrectly assuming a linear relation may explain these paradoxical results.

Yet despite the known limitations of BMI and the uncertain consequences of proceeding with transplantation in patients living with obesity, most transplant units will define an upper limit above which kidney transplantation is not offered unless weight loss is achieved [8]. The aim of this chapter is to explore the risks of kidney transplantation according to the degree of obesity at transplant to inform shared decision-making in this regard.

■ Summary of the evidence

(Supplement 2| Study selection flow diagrams—Chapter 2)
(Supplement 3| Summary evidence tables—Chapter 2)

We identified 34 studies: 8 systematic reviews with meta-analyses [23–30] and 26 observational studies not previously included in any of the systematic reviews or assessing different outcomes [31–56].

Systematic reviews

A first systematic review, including 17 studies, found that after adjustment, kidney transplantation in recipients with a BMI $\geq$30 kg/m^2 was associated with a slightly increased risk of death-censored graft loss and significantly increased the risk of delayed graft function, but it found little evidence for a difference in overall mortality in comparison to recipients with normal BMI [23].

A second systematic review, including 56 studies, found that compared with kidney transplantation in recipients with a BMI <30 kg/m^2, a BMI >30 kg/m^2 was associated with increased mortality; decreased 1-, 2-, and 3-year graft survival and decreased 1-, 2-, and 3-year patient survival in univariable analysis [24]. However, analysis of five studies that included BMI in regression analyses did not indicate that a BMI >30 kg/m^2 was associated with a difference in mortality while other studies suggested a higher 3-year patient survival in this group. There was also no significant difference in graft survival if only studies with adjusted estimates from multivariable analyses were included.

In a meta-analysis, the researchers found BMI >30 kg/m^2 to be associated with an estimated 50% increased risk of delayed graft function, a 17% increased risk of acute rejection, 45-min lengthening of the operating time, a 2.3-day longer hospital stay, a 3-fold increase in the risk of wound infection and incisional hernia, an almost five times higher risk of wound dehiscence and a 2-fold higher risk of post-transplant diabetes. All the analyses were unadjusted for confounding factors [24].

A third systematic review reported that in a meta-analysis including four studies, compared with a normal BMI, a BMI ≥30 kg/m^2 was associated with a 20% higher proportional hazard of death and graft failure [25]. However, this study included results from the author's own reanalysis of the Scientific Registry of Transplant Recipients data set that was previously published in a separate study [57]. This reanalysis contributed heavily (96% for the mortality analysis) to the meta-analysis. On sensitivity analysis that assigned equal weight to the meta-analysed studies, there was no longer a significant increase in mortality or graft failure in the group living with obesity.

A fourth systematic review, including 21 retrospective observational studies, found that compared with kidney transplantation in recipients with a normal BMI, a BMI >30 kg/m^2 was associated with twice the hazard of biopsy-proven acute rejection and graft loss, an estimated 20% higher hazard of death and 80% higher odds of delayed graft function [26]. However, unlike some of the other meta-analyses, there was no separate analysis of estimates that had been adjusted for confounding.

A fifth systematic review was identified that excluded large database studies and compared outcomes between kidney transplant recipients living with and without obesity [27]. This study reported that a pre-transplantation BMI ≥30 kg/m^2 was associated with an estimated 40% increased risk of delayed graft function but was not associated with acute rejection. Those living with obesity had about a 30% higher risk of losing their graft in the first year and about a 20% higher risk of losing it within 5 years. Obesity may also have increased the risk of death both at 1 and 5 years after transplantation. It is unclear whether individual estimates were corrected for confounding.

In a sixth systematic review, the effect of obesity on the risk of cardiovascular and all-cause mortality in all stages of CKD was assessed [28]. In 10 studies conducted in transplant recipients, there was a statistically significant association between obesity and all-cause mortality when BMI was assessed either as a continuous variable or in categories. Twenty-six studies used varying binary thresholds or categories that did not allow further analysis. Relationship correlations between BMI and cardiovascular mortality were inconsistent. Two studies reported no significant association between BMI and cardiovascular mortality when BMI was analysed continuously. The other study demonstrated a U-shaped relationship between cardiovascular mortality and BMI. Compared with the reference category of 24–26 kg/m^2, the risk was increased in those with a BMI >34 kg/m^2.

A seventh systematic review evaluated post-transplant outcomes in overweight recipients with a BMI of 25–30 kg/m^2 versus normal-weight recipients [29]. Overall, there was no clear evidence for an association between being overweight at the time of transplantation and acute rejection, death, graft loss or delayed graft function.

Finally, an eighth systematic review identified increasing BMI as a predictor of post-transplant diabetes mellitus [30].

Observational studies

In addition to the systematic reviews discussed above, we identified 26 observational studies not previously included in any of the reviews [31–56]. Thirteen provided estimates adjusted for potential confounding in western populations [31–43] while 11 only conducted univariable analyses. Two provided data for Asian populations [55, 56].

Where BMI was analysed as a continuous or nominal variable and adjustments were made for important confounding structures, it appeared that as BMI increased above the normal value, so did the risk for death [31–33], graft loss [31–34] and heart failure [35], unless numbers in the high BMI ranges were small [36, 37].

However, most studies analysed the effect of BMI on outcome as a binary variable, comparing BMI groups above versus below a certain value. Those that used a cut-off of 30 usually found little or no influence of BMI on outcome, whether that was death, graft loss, delayed graft function or hospital stay [38, 39].

That picture changed with increasing BMI. When higher cut-offs were used (≥35 [40], ≥40 [41] or ≥50 [42]), an increased risk of short- and long-term death [42], delayed graft function [42], length of hospital stay [40, 42] and cost [43] was noted, with higher risks seen as the cut-offs went up. An exception to that rule was Kim *et al.* [43], where hospital stay or readmission rate was not increased with BMI ≥40 kg/m^2.

Eleven other studies only provided unadjusted data [44–54].

In terms of Asian populations, an abstract publication that assessed only living donor transplants in Tokyo found no significant difference in unadjusted patient or graft survival but a higher incidence of acute rejection and subcutaneous abscesses in people with a BMI of 25–30 kg/m^2 and ≥30 kg/m^2 [55].

A prospective study from Korea found on multivariate analysis that a BMI ≥23 kg/m^2 was associated with increased cardiovascular disease post-transplant compared with kidney transplant recipients with a BMI <23 kg/m^2, which persisted after adjustments, but that there was no difference in acute rejection rates [56].

■ Translation of the evidence into recommendations

When BMI is assessed as a categorical factor and estimates are adjusted for potential confounding, it appears that, compared with having a normal BMI, a BMI between 30 and 34 kg/m^2 may not increase the risk of death or graft loss in the short or longer term but may be associated with an increase in the risk of delayed graft function, acute rejection, post-transplant diabetes mellitus and wound-related complications. Given these data, most clinicians would not want to withhold kidney transplantation for candidates with a BMI of 30—34 kg/m^2 who are otherwise considered suitable. Likewise, most transplant candidates would want the transplant despite a possibly higher risk of perioperative problems and diabetes after transplant. Ensuring patients living with obesity understand these risks, however, seems crucial for informed decision-making.

Data for higher BMI categories are sparse numerically and not separately meta-analysed as such in systematic reviews. This makes formulating recommendations based on these data alone problematic.

■ Other guidelines on this topic

The KDIGO 2020 guideline [16] suggested that kidney transplant candidates should not be excluded from transplantation because of obesity (as defined by BMI or waist:hip ratio) (2B). However, transplantation in patients with a BMI >40 kg/m^2 'should be approached with caution and patient counselling related to the increased risk of post-operative complications is recommended.'

The UK Renal Association 2011 guideline [19] stated that a BMI >30 kg/m^2 presented technical difficulties and increased the risk of perioperative complications and that individuals with a BMI >40 kg/m^2 were less likely to benefit from kidney transplant (2B).

The ERBP 2015 guideline [17] stated that the association between BMI and patient survival after kidney transplantation is controversial based on current literature. The guideline included a recommendation that kidney transplant candidates with a BMI >30 kg/m^2 should lose weight prior to kidney transplant (ungraded statement).

The KHA-CARI 2013 guideline [18] recommended that obesity alone should not preclude a patient from being considered for kidney transplant (1B). For pre-transplant BMI >40 kg/m^2, it suggested that the suitability for transplant be carefully assessed on an individual basis (2C). As patient and graft survival of transplant recipients living with obesity may be mediated by comorbid factors, particularly cardiovascular, it also recommended that transplant candidates living with obesity were screened for cardiovascular disease (1C).

Suggestions for future research

Given the lack of data in higher BMI categories, an adequately powered prospective observational study assessing the causal effect of class 2 (BMI 35–39 kg/m^2) and 3 obesity (BMI ≥40 kg/m^2) on post-transplant core outcomes would be welcomed. For studies to provide an unbiased estimate of the causal effect of obesity—as assessed by BMI—investigators would ideally start follow-up at a common time point well before transplantation and even dialysis initiation and measure weight repeatedly over time to allow adjustment for illness-related weight loss and collider stratification bias. In all obesity classes, longer-term comparisons and assessment of other measures of increased fat mass would be helpful.

CHAPTER 3. DOES OBESITY INFLUENCE THE BENEFIT–HARM BALANCE OF KIDNEY TRANSPLANTATION VERSUS DIALYSIS IN PEOPLE OTHERWISE CONSIDERED SUITABLE FOR TRANSPLANTATION?

Recommendations

We suggest that kidney transplantation, either from a deceased or living donor, is the optimal treatment for people with a BMI of 30–39 kg/m^2 and ESKD who are otherwise considered suitable for kidney transplantation (2C).

We suggest not delaying wait-listing or transplantation solely on the basis of increased BMI in people with a BMI of 30–39 kg/m^2 and ESKD who are otherwise considered suitable for kidney transplantation (2C).

Advice for clinical practice

- Weigh BMI in the context of other risk factors when discussing transplantation.

Rationale

Background

Obesity is one of the main reasons for denying individuals access to kidney transplantation. The available data currently do not suggest people with class 1 obesity (BMI 30–34 kg/m^2) have worse patient or graft survival, but data for higher BMI categories are sparse [23–29]. While the previous chapter addresses the impact of obesity on transplant outcomes, when discussing risks with patients it is important to compare the risks and benefits of kidney transplantation versus remaining on dialysis. Currently there is no consensus on the degree of obesity above which the risk of perioperative complications becomes unacceptable or patient outcomes are worsened by being transplanted. As such, pinpointing a threshold would be necessary for determining when the benefit–harm balance would no longer favour kidney transplantation over remaining on dialysis.

■ Summary of the evidence

(Supplement 2| Study selection flow diagrams—Chapter 3)
(Supplement 3| Summary evidence tables—Chapter 3)

National registry data from the USA and UK indicate that up to a BMI of 40 kg/m^2, people who have received a kidney transplant may have a survival advantage compared with those who remain on the waiting list [22, 58]. In an observational study conducted in the USA, the 1- and 5-year survival benefit with transplantation for patients living with obesity and with a BMI up to 40 kg/m^2 was similar to the survival benefit of those with a normal weight [58]. In all BMI bands, from a normal weight up to a BMI of 35–39 kg/m^2, transplantation with a standard criteria donor kidney was associated with a 66–68% reduction in the risk of death compared with remaining on dialysis. In case of transplantation with an extended criteria donor kidney, patients with a normal BMI and patients with a BMI of 35–39 kg/m^2 had a mortality risk reduction of 63% and 61%, respectively, compared with remaining on dialysis. In case of transplantation with a living donor, patients with a normal BMI and patients with a BMI of 35–39 kg/m^2 had a mortality risk reduction of 80% and 72%, respectively, compared with remaining on dialysis. There are some questions around the representativeness of the data for a European context. Baseline mortality risk on the waiting list is much higher than that in Europe. Also, including time spent inactively on the waiting list may have increased the difference between the two groups disproportionately for those living with obesity.

An observational study from the UK found a survival advantage with transplantation in all BMI bands, with a mortality difference increasing to >20% at 5 years compared with those remaining on the waiting list, and very little difference between BMI bands [22]. On analyses of patient survival with BMI as a continuous variable or using 5-kg weight bands, there was no cut-off observed in the higher BMI patients where there would be no benefit from transplantation. However, immortality bias may have played a role in these findings and few people had a BMI ≥35 kg/m^2.

There is some excess mortality early after transplant surgery in patients living with obesity compared with recipients without obesity. This risk is highest after extended criteria donor transplantation, and least after living donor transplantation. For example, the number of days needed to reach equal survival between transplant recipients and wait-listed patients when using a standard criteria donor kidney was 100 days for patients with a normal BMI, 179 days for those with a BMI of 35–39 kg/m^2 and 245 days for those with a BMI ≥40 kg/m^2.

Data from patients with a BMI ≥40 kg/m^2 are limited. Based on information from the USA, even those with a BMI ≥40 kg/m^2 may still have a substantial survival benefit with transplantation, although somewhat lower than those with lower BMI [58]. For example, standard criteria donor transplantation in patients with a BMI ≥40 kg/m^2 was associated with a mortality risk reduction of 48% compared with those remaining on dialysis, as opposed to a >66% reduction for patients with a BMI <40 kg/m^2. Here again, outcomes are best when the patient is transplanted with a living donor. Data from the UK also support the survival benefit with transplantation in the very obese, although patient numbers are small [22].

Finally, another large registry study from the USA [38] found a significant decrease in the long-term risk of heart failure with kidney transplantation compared with remaining on dialysis, even for those with a BMI ≥35 kg/m^2 [35].

■ Translation of the evidence into recommendations

The working group believes that although the studies used the reference standard statistical approach for comparing mortality between transplantation and dialysis patients, a moderate risk of bias still exists in the aforementioned studies. The limited number of patients with high-grade obesity (BMI ≥40 kg/m^2) and the extrapolation of dialysis survival from the USA contribute to this bias.

The best current evidence comes from large national registry studies. These suggest that patients living with obesity derive a significant benefit from transplantation as compared with remaining on the waiting list. Furthermore, the survival benefit appears to be sustained for all BMI grades, albeit at a different level. Therefore we suggest that transplantation be considered as the optimal treatment choice for patients living with obesity, explicitly discussing with the potential recipients the limitations of evidence in the higher BMI groups.

Although the recommendation for class 2 obesity (BMI 35–39 kg/m^2) seems incongruent with the recommendations made in the previous chapter, one must keep in mind that these are based on different data sets. From a utilitarian perspective alone, recommendations in higher BMI categories are problematic. From a dual perspective that includes that of the patient, we believe the suggestion to not delay wait-listing solely on the basis of increased BMI still holds, also for the category with a BMI of 35–39 kg/m^2. There is some evidence that transplantation also decreases the risk of long-term cardiovascular events in these patients and therefore we suggest timely listing and transplantation.

■ Other guidelines on this topic

The KDIGO 2020 guideline [16] suggests that kidney transplant candidates should not be excluded from transplantation because of obesity per se (2B). The 2015 ERBP guideline [17] recommends that patients with a BMI >30 kg/m^2 reduce weight before transplantation (ungraded statement). The KHA-CARI 2011 guideline [18] recommends that obesity should not on its own preclude a patient from being considered for kidney transplantation (1B). However, these recommendations also suggest that as a pre-transplant BMI >40 kg/m^2 may not be associated with a survival advantage compared with remaining on dialysis and suitability for transplant should be carefully assessed on an individual basis (2C). Finally, the BTS 2011 guideline [19] suggests that patients living with obesity (BMI >30 kg/m^2) present technical difficulties and are at increased risk of perioperative complications. Therefore they should be screened rigorously for cardiovascular disease and each case considered individually. Although obesity is not an absolute contraindication to transplantation, individuals with a BMI >40 kg/m^2 are less likely to benefit (2B).

Suggestions for future research

A prospective study recording obesity indices, including BMI and waist and hip circumference, at the time of assessment for transplantation eligibility and long-term important health outcomes would be helpful in understanding the benefit–harm balance in the subgroup of those living with obesity. Adequate recording of confounding and effect-modifying structures, i.e. the characteristics that influence BMI, chances of transplantation and outcome, as well as longitudinal follow-up of obesity measures to allow for adjustment for illness-related weight loss would be desirable. Teaming up with methodological experts in causal research will be imperative for ensuring adequate study design.

CHAPTER 4. WHAT ARE THE BENEFITS AND HARMS OF INTERVENTIONS AIMED AT WEIGHT LOSS IN KIDNEY TRANSPLANT CANDIDATES WITH ESKD?

Recommendations

We recommend encouraging kidney transplant candidates living with obesity to lose weight and having their nutritional status supervised by a multidisciplinary weight-management team (1D).

We suggest considering bariatric surgery in kidney transplant candidates with a BMI $\geq$40 kg/m^2 (2C).

We suggest considering bariatric surgery in kidney transplant candidates with a BMI $\geq$35 kg/m^2 with at least one major obesity-related condition that can be improved by weight loss (2D).

We suggest laparoscopic sleeve gastrectomy over other forms of bariatric surgery in kidney transplant candidates (2D).

Advice for clinical practice

Indications for bariatric surgery for the general population are BMI $\geq$40 kg/m^2 or BMI 35–39 kg/m^2 with at least one obesity-related comorbidity, such as type 2 diabetes mellitus, sleep apnoea, non-alcoholic fatty liver disease or heart disease.

Rationale

Background

Even if otherwise considered suited for kidney transplantation, patients living with obesity are often asked to lose wait before being wait-listed. However, given transplant candidates on dialysis must limit their intake of fresh fruits and vegetables to prevent hyperkalaemia and restrict their protein intake to prevent hyperphosphatemia, it is hard to lose weight with dietary measures alone [59]. In fact, an American study conducted early in the new millennium showed that among patients living with obesity who were required to lose weight to reach a BMI <30 kg/m^2 before being wait-listed, only 10% actually lost any weight and only 5% reached the target weight for listing [60]. Moreover, there is no clear evidence for the benefit of the widespread practice of deferring wait-listing to allow transplant candidates living with obesity to achieve the desired weight loss before transplantation. Patients with ESKD living with obesity who remain on dialysis even tend to have worse survival compared with their transplanted counterparts, irrespective of BMI [23, 24, 61].

Nevertheless, the development of treatments such as orlistat and minimally invasive bariatric surgery techniques may offer new opportunities for transplant candidates to easily achieve the desired BMI while avoiding the complications of the traditional surgical techniques based on intestinal bypass.

Currently there are three types of bariatric surgery [62]. Traditional malabsorptive procedures bypass a segment of small intestine, reducing the number of calories and amount of nutrients absorbed by the body. This includes biliopancreatic diversion with and without duodenal pouch, but is now rarely performed because of high complication rates. Newer bariatric surgery procedures are largely restrictive, aiming to reduce the size of the stomach and thereby limiting the amount of food that can be eaten. These procedures include intra-gastric balloon placement, adjustable laparoscopic gastric banding and laparoscopic sleeve gastrectomy. A third approach encompasses procedures that combine restriction with malabsorption such as Roux-en-Y gastric bypass. In the general population, these approaches lead to variable weight loss 1 year after surgery. Which interventions incur the best risk–benefit balance remains unclear.

■ Summary of the evidence

(Supplement 2| Study selection flow diagrams—Chapter 4)
(Supplement 3| Summary evidence tables—Chapter 4)

We did not retrieve any randomized controlled trial in transplant candidates living with obesity comparing different pre-transplant weight-management interventions. We found eight non-randomized comparative studies. The first was a non-randomized prospective intervention study [63, 64] and the second was a retrospective study [65], both including participants from the UK with CKD stages 3–5. The third, also a retrospective but multicentric cohort study, included patients with ESKD [66]. In addition, there were one prospective and four retrospective comparative studies in kidney transplant candidates from the USA [56, 67–70]. Two studies covered a multidisciplinary weight-management program [63–65], two covered laparoscopic sleeve gastrectomy [56, 67], one covered Roux-en-Y gastric bypass [68] and two reported on different bariatric procedures [66, 69, 70]. All studies had a high risk of confounding bias and, with the exception of one study [70], the design was such that the treatment effect on major clinical endpoints such as patient and graft survival could not be assessed. One large study, which was based on Medicare registry data and was focussed on patients with ESKD, did not provide data on the time on the waiting list and on post-transplantation follow-up, but did report transplantation rates [66]. We additionally included one pilot study investigating the effect of panniculectomy on transplant candidacy and outcomes, despite the fact that we did not consider the procedure as an intervention to correct obesity but rather an intervention focused on the prevention of post-transplant wound complications only [71]. On top of that, we found 22 case series without control groups including 1471 patients [72–93]. Because these studies lacked control groups and did not report major clinical outcomes, we could not use them to make inferences about the effect of each intervention. Nevertheless, we used them to provide an ‘upper bound’ of the estimated efficacy of each intervention on BMI reduction and to provide a source of information about potential complications/adverse effects in the specific clinical setting of weight-management procedures carried out on transplant candidates living with obesity. Finally, we found two systematic reviews of case reports and series [94, 95] and one clinical decision analysis [96].

Medical weight-management programs

Two comparative studies assessed the effects of a multidisciplinary weight-management program that included a low-fat kidney-specific diet, exercise and orlistat 3 × 120 mg daily in 201 patients with CKD stages 3–5 and an average BMI of 35 kg/m^2 [63–65]. After 6 months, people who had been included in the program weighed an average 6 kg less than those who had received standard care. The weight loss was sustained in the 2 years following enrolment [64].

The weight loss was associated with improvements in exercise performance testing as a measure of functional ability and with a temporary reduction of systolic blood pressure at 6 months [58, 59]. Sadly, that effect was lost at 12 and 24 months and the weight loss was not associated with fewer deaths or fewer major cardiovascular events such as myocardial infarction, stroke, hospitalization for congestive heart failure [64]. It also did not increase the likelihood of being wait-listed for kidney transplantation 6 years later [65]. Note that orlistat, a locally acting gastrointestinal lipase inhibitor that reduces the absorption of dietary fat, may increase intestinal absorption of oxalate due to reduced binding with free calcium, which is chelated by unabsorbed fat. The resulting hyperoxaluria can lead to nephrocalcinosis, parenchymal inflammation, fibrosis and ESKD [97]. Also, orlistat can lead to important drug interactions after kidney transplantation, particularly lowering of cyclosporine concentrations [98]. Continuing orlistat after transplantation with the aim of maintaining body weight is therefore ill-advised. These adverse effects were not addressed in the aforementioned studies.

Bariatric surgery

Roux-en-Y gastric bypass. We identified one retrospective cohort study that compared 14 kidney transplant recipients who had previously undergone Roux-en-Y gastric bypass with a historical cohort of 19 patients who had a BMI ≥36 kg/m^2 at the time of kidney transplant. Following bariatric surgery, patients achieved an average 35% weight loss by the time of transplant compared with controls [68]. However, baseline patient characteristics were not reported. Despite the obvious efficacy in achieving weight loss, there was no clear benefit for post-transplant patient or graft outcomes. In addition, the procedure was associated with a 30% higher risk of biopsy-proven acute rejection after transplantation.

One recent study by Ku *et al.* [70], on a population with Medicare coverage, compared 194 patients with a history of Roux-en-Y gastric bypass at the time of transplantation with 12 250 controls with a median follow-up of 1 year. The study did not find any association between Roux-en-Y gastric bypass and the rate of patient survival, graft failure, 30-day post-transplant hospital readmission and acute rejection. In this study, time at risk started at the time of transplantation as opposed to the time of wait-listing, preventing comparison between the decision to undergo bariatric surgery first versus direct wait-listing or live-donor transplantation. Therefore the effect of delaying transplantation because of bariatric surgery and of possible bariatric surgery complications was not accounted for. This might have caused overestimation of bariatric surgery benefit. On the other hand, only patients living with obesity who were able to undergo transplantation were used as controls. This might have caused underestimation of bariatric surgery benefit. Overall, the direction of the bias in the estimate of the effect of bariatric surgery is unpredictable. Finally, the use of a US population with Medicare fee-for-service coverage may limit the generalizability of the findings.

In addition, we found 10 series reporting 305 Roux-en-Y gastric bypass procedures, either open or laparoscopic. The average reduction in BMI varied between 4 and 17 kg/m^2 [72–81]. The case series did not stratify death rate by surgical procedure, therefore we could not distinguish mortality following Roux-en-Y gastric bypass procedures from mortality following other types of bariatric surgery. Moreover, only four series that included Roux-en-Y gastric bypass procedures reported mortality following bariatric surgery. Of 1152 patients, there were 17 deaths (1.5%) following surgery; 16 of them occurred within 45 days after the procedure. The cause of death that was reported in four cases was related to sepsis. The eight case series that reported transplantation rates showed that 96/223 patients (43%) eventually underwent kidney transplantation. In one series, 2/37 patients (5.4%) developed oxalate nephropathy and 1 lost his graft because of it [75]. One group recorded postoperative complications in a third of the cases [73]. There were two patients who developed an anatomic leak or stricture in the first 30 days after surgery. Four patients had a late complication, including a marginal ulcer, a small bowel obstruction requiring laparoscopy a cholecystitis requiring cholecystectomy and an anastomotic stricture requiring endoscopic dilation [73]. Other groups either had no postoperative complications [80] or did not report any [72, 74–78, 81].

There were two reviews of case reports and series, both updated to June 2019, that included 790 and 288 cases, respectively, which concluded that bariatric surgery techniques (pooled) achieve a 30–73% reduction of excess weight in patients with ESKD [94, 95]. Fifty percent of patients lose sufficient weight to enable wait-listing for transplantation [94]. The overall transplantation rate was 30%, the reported mortality was 2% [94] and the proportion of patients with major complications was 7%, with statistically significant though relatively low heterogeneity between studies. Guggino *et al.* [94] reported outcomes following kidney transplantation from two studies indicating numerically but not statistically fewer cases of delayed graft function and early hospital readmission for renal dysfunction in the bariatric surgery group, but an increased risk of acute rejection with Roux-en-Y gastric bypass procedures.

Sleeve gastrectomy. We found one prospective before–after study including 52 kidney transplant candidates with class 2 (BMI 35–39 kg/m^2) or 3 obesity (BMI ≥40 kg/m^2) who underwent laparoscopic sleeve gastrectomy because they failed to lose weight with a medical regimen [67]. On average, patients lost ∼20 kg and 7 BMI points. At 6 months, sleeve gastrectomy achieved a 38% weight loss, as opposed to 4% achieved using specialized medical treatment during the

6months before surgery. Weight reduction was associated with 36% less hypertension and 25% less diabetes. Unfortunately the study design did not allow comparison of sleeve gastrectomy versus available alternatives on major clinical outcomes.

In a second, small retrospective cohort study, 20 kidney transplant candidates who underwent sleeve gastrectomy before transplantation had a 30% lower incidence of hypertension prior to transplant, a 15% lower incidence of delayed graft function and a 17% lower hospital readmission rate due to kidney dysfunction after transplantation compared with a cohort of 40 age- and sex-matched similar-BMI transplant recipients who did not undergo surgical procedures before transplantation [99]. The mean BMI decreased from 41 to 32 kg/m^2 before transplantation. No complications, readmissions or deaths occurred following the procedure. After transplantation, one patient experienced delayed graft failure, but none developed diabetes. The 1-year allograft and patient survival were 100%. There were 15% fewer episodes of delayed graft function and 17% fewer kidney dysfunction–related readmissions in the recipients who had undergone bariatric surgery. Perioperative complications, allograft survival and patient survival were similar between groups.

A recent study by Ku *et al.* [70] compared 190 patients with a history of sleeve gastrectomy at the time of transplantation with 12 250 controls. Sleeve gastrectomy was associated with a 60% reduction of graft failure, whereas it did not affect patient survival, post-transplant 30-day readmission rate and acute rejection rate. Because of the limitations outlined above, the findings from this study must be interpreted with caution.

There were seven case series that included sleeve gastrectomy among the bariatric procedures, with a total of 811 sleeve gastrectomy procedures [72–74, 76–79]. Unfortunately, as mentioned above, the death rate was not stratified by the type of bariatric procedure. Overall, there were 17 deaths in 1150 bariatric procedures (pooled). In the only series in which it was possible to distinguish between different bariatric procedures, there was 1 death in 17 patients undergoing sleeve gastrectomy (6%), which occurred 21 days after the procedure as a result of mediastinitis.

There were 10 series focussed on laparoscopic sleeve gastrectomy only, which included 567 procedures [82–91]. The overall death rate prior to transplantation was 19/567 (3%). However, 13 of the patients died >3 months after surgery. Causes included cardiopulmonary arrest, stroke, myocardial infarction and septic shock. In one series, complications occurred more frequently among earlier cases [82]. Also, increased surgical experience was associated with shorter operative times, lower estimated blood loss and shorter hospital stay. The average reduction in BMI varied between 6 and 17 kg/m^2. A total of 161 patients (28%) ultimately received a donor kidney. The average time from sleeve gastrectomy to kidney transplantation ranged from 3 to 24 months. Only six case series reported outcomes after transplantation: 8/291 (3%) developed delayed had graft function, and 7/352 (2%) had graft loss.

Gastric banding. We identified no comparative study assessing gastric banding procedures. In three small series, including nine patients overall, gastric banding was associated with a total weight loss of 23% [74, 92, 93]. A recent study by Ku *et al.* [70] compared 119 patients with a history of laparoscopic gastric banding with 12 250 controls. The study did not find any association between laparoscopic gastric banding and the rate of patient survival, graft failure, 30-day post-transplant hospital readmission and acute rejection.

Panniculectomy. Finally, panniculectomy was proposed in transplant candidates with the aim of reducing the incidence of wound infections after transplantation [71]. The authors performed panniculectomy in 36 transplant candidates who were withdrawn from the wait-list for at least 3 months post-panniculectomy until complete wound healing was achieved. They found a numerically reduced incidence (5% versus 13%) of wound infections in the 21 patients who subsequently underwent transplantation versus a historical matched control group of 89 patients. However, most of the infections in the control group were superficial. Moreover, panniculectomy complications did occur: 43% had minor skin separation or infection and 11% had serious complications (two hematomas and one abscess) requiring reintervention and in one case blood transfusions.

■ Translation of the evidence into recommendations

Transplant candidates living with obesity may develop post-operative wound infections and dehiscence more easily than leaner donor kidney recipients. They appear to have a higher risk of delayed graft function and greater chance of post-transplant diabetes. In class 2 (BMI 35–39 kg/m^2) and 3 obesity (BMI $\geq$40 kg/m^2), comparative data on patient and graft survival are sparse. Yet currently the same can be said about interventions for achieving weight loss.

Multimodal medical multidisciplinary weight-management programs have the ability to reduce weight before transplantation but have few other proven benefits. That being said, it seems difficult to reason against expected gains of programs that are based on healthy nutrition and increased exercise. Any program should include health and life style modifications and individually tailored dietary prescriptions. Given that people with ESKD are prone to malnutrition, any diet is best supervised by a multidisciplinary team.

Patients who qualify for bariatric procedures may be offered the possibility of undergoing surgery before wait-listing. Although no comparative outcome data before and after transplant between different approaches exist, the limited data available suggest effective weight loss can be achieved and fewer obesity-related complications emerge at the time of transplant. The benefits, which increase with larger baseline weight, need to be weighed against inevitable risks of perioperative complications, which are presently not well characterized and may include patient death. Systematic reviews in the general population have not uncovered significant differences between Roux-en-Y gastric bypass and sleeve gastrectomy in terms of mortality or surgical risks, although adverse events are usually poorly reported [100]. Fatal complications appear to be rare, but how these extrapolate to an inherently immunocompromised population is unclear. Hence decision-making is best done on a case-by-case basis after carefully assessing the risk-benefit of prolonging the time to wait-listing.

Despite the absence of directly comparative data for the different surgical procedures, a few reasons exist for preferring laparoscopic sleeve gastrectomy over other types of bariatric procedures. Besides the recent evidence for a benefit on graft survival [70], compared with Roux-en-Y gastric bypass, sleeve gastrectomy does not seem to impair immunosuppressive drug absorption [101, 102] and does not affect oxalate absorption since it does not modify intestinal absorption [103], although it might be inferior in terms of patient proportion achieving the target BMI that would enable wait-listing. In the general population, sleeve gastrectomy generally achieves greater weight loss than adjustable gastric banding, the latter procedure giving rise to more late reoperations for removal of the gastric band [100].

■ Other guidelines on this topic

Most guidelines make generic statements on the need for weight loss and weight management, including surgery in transplant candidates or recipients. Currently no guidelines explicitly address the comparative benefits and harms of different strategies.

The KDIGO 2020 guideline suggests that weight loss interventions prior to transplantation should be offered in patients with obesity [16]. This includes gastric sleeve bariatric surgery for morbid obesity (2D).

Neither the ERBP, KHA-CARI or BTS discuss the possibility of bariatric surgery in kidney transplant candidates living with obesity.

Suggestions for future research

Randomized controlled trials or large comparative observational studies assessing the benefits and harms of strategies based on deferring transplantation to allow weight loss would be welcomed.

In the future, new medications for the treatment of obesity in dialysis patients, such as liraglutide, a glucagon-like peptide-1 receptor agonist with an anti-hyperglycaemic effect that carries a low risk of hypoglycaemia, may become available [104]. Especially in patients with class 1 obesity (BMI 30–34 kg/m^2), they may greatly increase the chance of achieving the desired target body weight without the need to resort to surgical treatments or to delay wait-listing.

Approaches to nutrition, physical activity and monitoring weight gain after bariatric surgery were not studied within the scope of the current guideline, but may provide valuable adjunct information for informing future recommendations.

CHAPTER 5. WHAT ARE THE BENEFITS AND HARMS OF BARIATRIC SURGERY PERFORMED AFTER KIDNEY TRANSPLANTATION?

Recommendations

We suggest considering bariatric surgery in kidney transplant recipients with a BMI ≥40 kg/m^2 (2C).

We suggest considering bariatric surgery in kidney transplant recipients with a BMI ≥35 kg/m^2 with at least one major obesity-related condition that can be improved by weight loss (2D).

We suggest laparoscopic sleeve gastrectomy over other forms of bariatric surgery in kidney transplant recipients (2D).

Advice for clinical practice

- Consider bariatric surgery after appropriate non-surgical measures have been tried but failed to achieve or maintain adequate, clinically beneficial weight loss.
- Check the reimbursement policy for bariatric surgery, as large differences exist between healthcare systems.

Rationale

Background

Obesity is common after kidney transplantation and trends in prevalence mirror those in the general population. Kidney transplant recipients gain an average of 10 kg during the first year after transplantation, with corticosteroid treatment being partly implicated. Obesity may have adverse effects on cardiovascular disease and wound healing, and life expectancy is reduced in comparison with leaner transplant recipients [21].

Sadly, non-surgical attempts at weight loss seldom result in important and sustained weight loss. Bariatric surgery provides an effective means for shedding excess body weight and in people with type 2 diabetes it lowers the risk of developing kidney disease [105]. However, surgery also comes with an inherent risk of prolonged wound healing, infection and anastomotic leaks [106]. In the post-transplant setting, that risk may be even more pronounced as a result of immunosuppression [107]. Malabsorptive procedures may carry an additional risk of reduced adsorption of immunosuppressants [108] and development of hyperoxaluria, with the consequent risk of nephrolithiasis and oxalate nephropathy [62].

■ Summary of the evidence

(Supplement 2| Study selection flow diagrams—Chapter 6)
(Supplement 3| Summary evidence tables—Chapter 6)

We found one—retrospective—cohort study comparing bariatric surgery in 43 participants before transplantation versus 21 who had undergone the procedure after transplantation [77]. Weight loss was similar in both groups; other outcomes were not reported. Groups represented very different people, with those undergoing bariatric surgery having predominantly gained weight after the transplant and undergoing malabsorptive surgery less frequently. This would have made direct comparison difficult anyhow. In the same study, however, patients who received bariatric surgery after transplantation were also compared with weight-matched controls who had not received bariatric surgery. Both the risk of death and graft loss were lower with bariatric surgery, although one transplant recipient lost his graft within 6 months of the surgery.

All other published data come from 13 case series, covering 171 patients [72, 81, 102, 107–115]. Because these studies lacked a control group and mostly did not report long-term clinical outcomes, we could not use them to make inferences about the effect of each intervention. Nevertheless, we used them to provide an 'upper bound' of the estimated efficacy of interventions on BMI reduction and to provide information about potential complications and adverse effects in the specific clinical setting of weight-management procedures carried out on transplant candidates living with obesity.

Roux-en-Y gastric bypass. The largest series used Medicare billing claims within the United States Renal Data System registry data [72] and included 87 kidney transplant recipients who had undergone bariatric surgery. Open Roux-en-Y gastric bypass was the most common procedure. Seven patients died within 90 days after surgery. One transplant recipient lost his graft due to rejection within 30 days after surgery. On average, the BMI decreased from 47 kg/m^2 before to 40 kg/m^2 after surgery.

Four series included 24 kidney transplant recipients, most of whom saw a substantial decrease in BMI without major complications [81, 109–111]. One patient died 4 months after the procedure from septic shock after developing splenic abscesses [111]. Data on graft function were not or ill reported.

Sleeve gastrectomy. In a first retrospective series, 10 kidney transplant recipients underwent laparoscopic sleeve gastrectomy [102]. One-year after surgery the median BMI decreased from 42 to 29 kg/m^2; urinary protein excretion and serum creatinine decreased significantly. One patient failed to lose any weight and underwent a second-stage biliopancreatic diversion and duodenal switch 14 months later. One patient developed acute kidney injury after repeated vomiting due to sleeve stricture, which finally required conversion to a gastric bypass 6 weeks after the primary operation.

A second series included five kidney transplant recipients with a BMI ranging from 37 to 54 kg/m^2 and related comorbidities including hypertension, dyslipidaemia, diabetes and gout, who all underwent sleeve gastrectomy between 3 and 22 years after kidney transplantation [112]. The authors reported an average loss of 12 BMI points, a reduction in medications, improved blood pressure control and reduced insulin requirements with improvement in graft function and proteinuria in four patients. All experienced a significant improvement in their quality of life and there were no complications or reported deaths [112, 111].

A third case series included six kidney transplant or combined kidney–pancreas transplant recipients who underwent laparoscopic sleeve gastrectomy between 31 and 131 months after transplant [108]. Their preoperative BMI ranged from 35 to 51 kg/m^2. The authors reported a mean weight loss of 28% at 1 month, 44% at 3 months, 74% at 6 months and 76% at 12 months. No significant regain in weight, change in glomerular filtration rate or change in dosage of immunosuppressive medications was observed during an average 15 months of follow-up. Complications included two patients being readmitted in the first 30 days after discharge for impairment of kidney function secondary to dehydration.

A fourth series reported on 10 solid organ transplant recipients living with obesity, 4 of whom were kidney transplant patients, and identified significant improvement in estimated glomerular filtration rate following laparoscopic sleeve gastrectomy in the kidney transplant patients [113]. One of the kidney transplant patients in the study underwent reoperation for bleeding from a short gastric vessel.

In an additional 10 patients who underwent sleeve gastrectomy after solid organ transplantation, 6 of whom had a previous kidney transplant, there were no significant differences in weight loss compared with 490 non-transplant patients [107]. No perioperative or postoperative complications were reported among the transplant patients.

Finally, in a sixth series, one of the four patients who had received bariatric surgery after transplantation experienced an initial, partly transient decline in kidney function and had excessive weight loss, decreasing to a BMI of 20 at 24 months [94]. One developed acute pancreatitis, which required long-term antibiotics and surgical drainage. Obesity-related complications improved in all patients.

Gastric banding. We found two cases who had undergone gastric banding after transplant, but outcome data were not separately reported [114].

■ Translation of the evidence into recommendations

There is limited low-level evidence suggesting bariatric surgery is feasible after kidney transplantation and does not come with an unacceptable risk of postoperative complications. In a limited number of case series with short follow-up, bariatric surgery resulted in weight loss and improvement in obesity-related comorbidities. However, the long-term impact of bariatric surgery on graft function and survival is presently unknown.

Despite the absence of directly comparative data for the different surgical procedures, a few reasons exist for preferring laparoscopic sleeve gastrectomy over other types of bariatric procedures.

Compared with Roux-en-Y gastric bypass, sleeve gastrectomy does not seem to impair immunosuppressive drug absorption [101, 102]. When the pharmacokinetics of sirolimus, tacrolimus, mycophenolic acid and mycophenolic acid glucuronide in two transplant recipients who had undergone gastric bypass were compared with published data in people without gastric bypass, significant differences were observed [101]. The area under the plasma concentration: dose ratios curve was lower for those having undergone a gastric bypass procedure. Hence transplant recipients most likely need higher doses of tacrolimus, sirolimus and mycophenolic acid derivatives after gastric bypass surgery to provide similar exposure as compared with regular kidney transplant recipients.

Also, sleeve gastrectomy does not affect oxalate absorption since it does not modify intestinal absorption [103]. However, there are suggestions of altered pharmacokinetics through decreased drug clearance due to increased drug exposure or decreased liver metabolism [116].

In the general population, sleeve gastrectomy generally achieves greater weight loss than adjustable gastric banding, the latter procedure giving rise to more late reoperations for removal of the gastric band [100].

■ Other guidelines on this topic

The KDIGO guideline 2020 suggests weight loss interventions prior to transplantation but make no reference to the post-transplant intervention [16].

Suggestions for future research

Further studies are required to determine long-term outcomes as well as the optimum timing and surgical approach for undertaking bariatric surgery in the kidney transplant population and the impact on pharmacokinetics of immunosuppressive medication.

The impact of bariatric surgery on graft function, graft survival and complication rates should be compared with cohorts of transplantation patients with similar initial BMIs who have not had bariatric surgery.

There is also a clear need for further research on the timing of surgery in relation to transplantation. One key question is whether the additional time spent on dialysis, preparing for, undertaking and recovering from bariatric surgery has a detrimental impact on the outcome of subsequent transplantation.

SUPPLEMENTARY DATA

Supplementary data are available at *ndt* online.

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CONFLICT OF INTEREST STATEMENT

None declared.

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