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 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 waitlisting 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 ERA’s Descartes working group on Transplantation. 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 health care professional treating or caring for people with end-stage kidney disease 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 (GRADE) 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 waitlisting 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 carers 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 from 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 an 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 eleven participants, including eight nephrologists, two surgeons, and four methodologists (categories not mutually exclusive). It included seven men, and four women. Patients or their carers were not actively involved in the development process. According to the rules of 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 PRISMA 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 GRADE 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 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 email 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 wide-spread implementation related to attitude and behaviour may remain.
Chapter 1. What measure best reflects obesity as a risk factor for kidney transplantation in patients with end-stage kidney disease?

Recommendations

We suggest measuring waist circumference or waist-to-hip ratio in addition to body mass index in patients with end-stage kidney disease living with obesity, being assessed for kidney transplantation. (2C)

Advice for clinical practice

- Body mass index (BMI) is defined as weight in kilograms squared divided by the height in meters. Obesity is defined as a BMI ≥ 30 kg/m² and can be subdivided into classes 1 (BMI 30-34 kg/m²), 2 (BMI 35-39 kg/m²) and 3 (≥ 40 kg/m²).
- 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-to-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-to-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 in people with ESKD, and various kidney transplant programmes restrict transplantation to people with BMIs below 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 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-to-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, which correlates best with adverse outcomes in patients with ESKD or advanced 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, aiming to assess the risk of death associated with BMI, waist circumference, waist-to-hip ratio, or the conicity index [10, 11].
A first, prospective cohort study, included 537 people treated with chronic dialysis [10]. The investigators found increasing BMI to be associated with 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.

A second, prospective cohort study, included 173 people treated with chronic dialysis [11]. In univariable and multivariable analysis both increasing tertiles of the conicity index and waist circumference seemed to be associated with 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, aiming to assess the risk of death associated with BMI or waist circumference [13]. It included 993 prevalent kidney transplant recipients, followed for about three years. In the unadjusted analysis, there was no clear association between BMI and risk of death. When adjusted for waist circumference as potential confounding, 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 as waist circumference did.

In a second, prospective cohort, including 572 kidney transplant recipients, neither pre-transplant BMI nor waist-to-hip ratio were associated with development of new onset cardiovascular disease [14]. A third, 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 obesity as a risk factor for kidney transplantation in patients with advanced CKD being evaluated for preemptive 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 do 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 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-to-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
KDIGO 2020 recommends kidney transplant candidates to 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].
ERBP 2015, Kidney Health Australia – Caring for Australasians with Renal Insufficiency (KHA-CARI) 2013 and British Transplantation Society (BTS) guidelines 2011 evaluate obesity and post-transplant outcomes with BMI, however do not make any comments on the role of waist circumference or waist-to-hip ratio [17-19]. ERBP implicitly recommends using BMI as a measure of obesity in a statement recommending patients with a BMI ≥30 kg/m² reduce weight before transplantation.

Suggestions for future research
Prospective longitudinal studies that correctly correlate BMI, waist circumference, waist-to-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 change in obesity measure, transplantation as 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 end-stage kidney disease and a BMI of 30 to 34 kg/m² 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 peri-operative 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 WHO European Region since the 1980s, and the numbers of those affected continue to rise 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 to normal weight recipients. However, when compared with remaining on dialysis, kidney transplantation may still incur 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 peri-operative 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 the 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 was 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; eight 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 ≥ 30 kg/m² was associated with a slightly increased risk of death censored graft loss and significantly increased the risk of delayed graft function, but 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 in comparison to kidney transplantation in recipients with a BMI <30 kg/m², a BMI >30 kg/m² was associated with increased mortality, decreased one-, two- and three-year graft survival and one-, two- and three-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/m² was associated with a difference in mortality whilst other studies suggested a higher three-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 meta-analysis, the researchers found BMI>30 kg/m² to be associated with an estimated 50% increased risk of delayed graft function, a 17% increased risk acute rejection, 45 min lengthening of the operating time, a 2.3 day longer hospital stay, a threefold increase in the risk of wound infection and incisional hernia, an almost five times higher risk of wound dehiscence, and a two-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 to a normal BMI, a BMI ≥ 30 kg/m² 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 dataset 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 in comparison to kidney transplantation in recipients with a normal BMI, a BMI >30 kg/m² was associated with twice the hazard of biopsy proven acute rejection and graft loss, an estimated 20% higher hazard of death, an 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 obesity and without obesity [27]. This study reported that a pre-transplantation BMI ≥30 kg/m² 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 five years. Obesity may also have increased the risk of death both at one and five years after transplantation. It is unclear whether or not 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 chronic kidney disease was assessed [28]. In ten 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/m², the risk was increased in those with a BMI >34 kg/m².

A seventh systematic review evaluated post-transplant outcomes in overweight recipients with a BMI of 25-30 kg/m² 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] whilst 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] or heart failure [35]; unless numbers in high BMI ranges were small [36, 37].

Most studies, however, 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 2016, where hospital stay or readmission rate was not increased with BMI ≥40 kg/m² [43].

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 higher incidence of acute rejection and subcutaneous abscesses in people with a BMI of 25-30 kg/m² and ≥ 30 kg/m² [55].

A prospective study from Korea found on multivariate analysis that a BMI ≥23 kg/m² was associated with increased CVD post-transplant compared to kidney transplant recipients with BMI <23 kg/m², 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 to having a normal BMI, a BMI between 30 and 34 kg/m² may not increase the risk of death or graft loss in 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 to 34 kg/m², who are otherwise considered suitable. Likewise, most transplant candidates would want the transplant despite a possibly higher risk of peri-operative
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 is sparse, both 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**

  KDIGO 2020 [16] suggested that kidney transplant candidates should not be excluded from transplantation because of obesity, (as defined by body mass index or waist-to-hip ratio) (2B). However, transplantation in patients with a BMI >40 kg/m² “should be approached with caution and patient counselling related to the increased risk of post-operative complications is recommended.”

  The UK Renal Association 2011 [19] guideline stated that BMI >30 kg/m² presented technical difficulties and increased risk of peri-operative complications and that individuals with a BMI >40 kg/m² 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/m² 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/m² 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/m²) and 3 obesity (BMI ≥40 kg/m²) 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 timepoint 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 30-39.9 kg/m² and end-stage kidney disease 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/m² and end-stage kidney disease 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/m²) have worse patient or graft survival, but data for higher BMI categories are sparse [23-29]. Whilst 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 worsen 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 United States and the United Kingdom indicate that up to a BMI of 40 kg/m², people who have received a kidney transplant may have a survival advantage compared to those who remain on the waiting list [22, 58]. In a observational study conducted in the USA, the one- and five-year survival benefit with transplantation for patients living with obesity and with a BMI up to 40 kg/m² 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 between 35 and 39 kg/m², transplantation with a standard criteria donor kidney was associated with a 66% to 68% reduction in the risk of death compared to 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/m² had a mortality risk reduction of 63% and 61%, respectively, compared to 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/m² had a mortality risk reduction of 80% and 72%, respectively, compared to 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 over 20% at five years in comparison 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/m².

There is some excess mortality early after transplant surgery in patients living with obesity compared to 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 to 39 kg/m² and 245 days for those with a BMI ≥ 40 kg/m².

Data from patients with a BMI ≥ 40 kg/m² are limited. Based on information from the US even those with a BMI ≥40 kg/m² 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/m² was associated with a mortality risk reduction of 48% compared to those remaining on dialysis, as opposed to a greater than 66% reduction for patients with a BMI < 40 kg/m². Here again, outcomes are best when the patient is transplanted with a living donor. Data from the UK also supports the survival benefit with transplantation in the very obese, although patient numbers are small [22].

Finally, another large registry study from the United States (38) found a significant decrease in the long-term risk of heart failure with kidney transplantation compared to remaining on dialysis, even for those with a BMI ≥35 kg/m² [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/m²) and the extrapolation of dialysis survival from the US 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 to remaining on the waiting list. Furthermore, the survival benefit appears to be sustained for all BMI grades, albeit at a different level. Therefore, we recommend that transplantation should 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 II obesity (BMI 35-39 kg/m²) seem incongruent with the recommendations made in the previous chapter, one must keep in mind these are based on different data sets. From a utilitarian perspective alone recommendations in higher BMI categories are problematic. From a dual perspective which includes that of the patient, we believe the suggestion to not delay waiting solely on the basis of increased BMI still holds, also for the category with a BMI between 35-39 kg/m². There is some evidence that transplantation decreases the risk of long term cardiovascular events, also 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/m² reduce weight before transplantation (Ungraded Statement). The 2011 KHA-CARI guideline [18] recommend 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/m² may not be associated with a survival advantage compared to
remaining on dialysis, suitability for transplant should be carefully assessed on an individual basis (2C). Finally, the 2011 BTS guideline [19] suggests that patients living with obesity (BMI >30 kg/m²) present technical difficulties and are at increased risk of peri-operative complications. Therefore, they should be screened rigorously for cardiovascular disease and each case considered individually. Although obesity is not an absolute contra-indication to transplantation, individuals with a BMI >40 kg/m² are less likely to benefit (2B).

**Suggestions for future research**

A prospective study recording obesity indices, including BMI, 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 ≥40 kg/m². (2C)

We suggest considering bariatric surgery in kidney transplant candidates with a BMI ≥35 kg/m² 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 ≥40 kg/m² or BMI 35-39 kg/m² 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 weight before being waitlisted. 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/m² before being waitlisted, 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 to 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. These include biliopancreatic diversion with and without duodenal pouch but are now rarely performed because of high complication rates. Newer bariatric surgery procedures are largely restrictive, aiming to reduce the size of the stomach 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 one 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], the second a retrospective study [65], both including participants from the UK with CKD stages 3 to 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 US [56-67]. Two studies covered a multi-disciplinary weight management program [63-65], two laparoscopic sleeve gastrectomy [56, 67], one covered Roux-en-Y gastric bypass procedure [68], 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 also based on Medicare registry data and was focussed on patients with ESKD, did not provide data on time on 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 group, including 1471 patients [72-93]. Because these studies lacked a control group 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 weigh-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 x 120 mg daily in 201 patients with CKD stages 3 to 5 and an average BMI of 35 kg/m² [63-65]. After six 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 two 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 six 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 waitlisted for kidney transplantation six 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, which compared 14 kidney transplant recipients who had previously undergone Roux-en-Y gastric bypass with an historical cohort of 19 patients who had a BMI greater ≥ 36 kg/m² at the time of kidney transplant. Following bariatric surgery, patients achieved an average 35% weight loss by the time of transplant compared to 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 and co-workers, on a population with Medicare coverage, compared 194 patients with history of Roux-en-Y gastric bypass at time of transplantation with 12250 controls with a median follow-up of 1 year [70]. 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 time at transplantation as opposed to time of wait-listing, preventing the comparison between the decision to undergo bariatric surgery first vs 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 cause 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 US population with Medicare free-for service coverage may limit the generalizability of the findings.

In addition, we found ten series reporting 305 Roux-en-Y gastric bypass procedures, either open or laparoscopic. The average reduction in BMI varied between 4 and 17 kg/m² [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. Out of 1152 patients, there were 17 deaths (1.5%) following surgery. Sixteen of them occurred within 45 days after procedure. 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 in which, two in 37 patients (5.4%) developed oxalate nephropathy, and one lost his graft because of it [75]. One group recorded post-operative 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, and which included 790 and 288 cases respectively, which concluded that bariatric surgery techniques (pooled) achieve 30% to 73% of excess weight in patients with ESKD [94, 95]. 50% of patients lose sufficient weight to enable wait-listing for transplantation [94]. Overall transplantation rate was 30%; reported mortality was 2% [94], proportion of patients with major complications 7%, with statistically significant though relatively low heterogeneity between studies. Guggino and colleagues 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 [94].
**Sleeve gastrectomy**

We found one prospective before-after study including 52 kidney transplant candidates with class 2 (BMI 35-39 kg/m²) or 3 obesity (BMI ≥40 kg/m²), who underwent laparoscopic sleeve gastrectomy because they failed to lose weight with a medical regimen [67]. On average, patients lost about 20 kg, and 7 BMI points. At six months, sleeve gastrectomy achieved 38% excess weight loss, as opposed to 4% achieved using specialized medical treatment during the six months before surgery. Weight reduction was associated with 36% less hypertension and of 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 an 17% lower hospital readmission rate due to kidney dysfunction after transplantation, compared to 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/m² before transplantation. No complications, readmissions, or deaths occurred following the procedure. After transplantation, one patient experienced delayed graft failure, but none developed diabetes. One-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.

The recent study by Ku and co-workers compared 190 patients with history of sleeve gastrectomy at time of transplantation with 12250 controls [70]. Sleeve gastrectomy was associated with a sixty percent reduction of graft failure, whereas it did not affect patient survival, post-transplant 30-day re-admission 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, death rate was not stratified by type of bariatric procedures. Overall, there were 17 deaths out of 1150 bariatric procedures (pooled). In the only series in which it as possible to distinguish between different bariatric procedures, there was one death out of 17 patients undergoing sleeve gastrectomy (6%), which occurred 21 days after the procedure as a result of mediastinitis. There were ten series focussed on laparoscopic sleeve gastrectomy only, which included 567 procedures [82-91]. Overall death rate prior to transplantation was 19/567 (3%). However, 13 of them died beyond 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/m². 161 patients (28%) ultimately received a donor kidney. Average time from sleeve gastrectomy to kidney transplantation ranged between 3 and 24 months. Only six case series reported outcomes after transplantation: 8/291 (3%) developed delayed graft function, and 7/352 (2%) 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]. The recent study by Ku and co-workers compared 119 patients with history of laparoscopic gastric banding with 12250 controls [70]. 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 waitlist for at least three months post-panniculectomy until complete wound healing was achieved. They found a numerically reduced incidence (5% vs 13%) of wound infections in the 21 patients who subsequently underwent transplantation versus an historical matched control group of 89 patients. However, most of the infections in the control group were superficial. Moreover, panniculectomy complications did occur: 43% minor skin separation or infection, and 11% serious complications (2 hematomas and 1 abscess) requiring re-intervention 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/m²) and 3 obesity (BMI ≥40 kg/m²) 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 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 style modifications, and individually tailored dietary prescriptions. Given 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 waitlisting. 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 increases with larger baseline weight, need to be weighed against inevitable risks of perioperative complications, which are presently not well characterised, and that 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 also here 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 time to waitlisting.

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], in comparison 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 waitlisting. 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.

KDIGO 2020 suggest 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 ERBP, nor KHA-CARI, or the 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/m²), 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/m². (2C)

We suggest considering bariatric surgery in kidney transplant recipients with a BMI ≥35 kg/m² 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 10 kg during the first year after transplantation, 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 excess 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 resorption of immunosuppressants [108] and development of hyperoxaluria with 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 hadn’t received bariatric surgery. Both the risk of death and graft loss were lower with bariatric surgery, although one transplant recipient loss his graft within six 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 that 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 fell from 47 before to 40 kg/m² after surgery.

Four series included 24 kidney transplant recipients, most of whom saw a substantial drop in BMI without major complications [81, 109-111]. One patient died four 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 dropped from 42 to 29 kg/m²; urinary protein excretion and serum creatinine decreased significantly. One patient failed to lose any weight and underwent a second-stage bilipancreatic diversion and duodenal switch 14 months later. One patient developed acute kidney injury after repeated vomiting due to sleeve stricture, which was 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/m² and related comorbidities including hypertension, dyslipidaemia, diabetes or gout, who all underwent sleeve gastrectomy between three 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, 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][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/m². 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 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 ten solid organ transplant recipients living with obesity, four of whom were kidney transplant patients, and identified significant improvement in eGFR 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 ten patients who underwent sleeve gastrectomy after solid organ transplantation, six
of whom had a previous kidney transplant, there were no significant differences in weight loss in comparison to 490 non-transplant patients [107]. No peri-operative 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 dropping to a BMI of 20 at 24 months [94]. One developed acute pancreatitis, which require 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 post-operative complications. In a limited number of case-series with short follow up, bariatric surgery results in excess weight loss and improvement in obesity related comorbidity. 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. In comparison 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 to published data in people without gastric bypass, significant differences were observed [101]. The area under the plasma concentration curve to dose ratios 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 an 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 2020 KDIGO guideline 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 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 to 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.

FUNDING
Activities of Descartes are supervised by the Council of ERA, which approves and provides an annual budget based on a proposition made by the chair of Descartes. ERA is partly funded by industry, but its council was not involved with and does not interfere with topic choice, question development or any other part of the guideline development process. Neither the society nor the working group received any funds directly from industry to produce this guideline.

ACKNOWLEDGEMENTS
We wish to acknowledge European Renal Best Practice for their input in this manuscript. Some of the methodologists involved have in the past and continue to serve on the Advisory board of this committee of ERA, which served as its guideline development body.

CONFLICT OF INTEREST STATEMENT
None declared.
REFERENCES

1. Abramowicz D, Hazzan M, Maggiore U, et al. Does pre-emptive transplantation versus post start of dialysis transplantation with a kidney from a living donor improve outcomes after transplantation? A systematic literature review and position statement by the Descartes Working Group and ERBP. Nephrology Dialysis Transplantation 2016;31(5):691-697
2. Nagler EV, Webster AC, Bolignano D, et al. European Renal Best Practice (ERBP) Guideline development methodology: towards the best possible guidelines. Nephrology Dialysis Transplantation 2013;29(4):731-738
3. Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLOS Medicine 2009;6(7):e1000097
4. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336(7650):924-926
5. Durrer Schutz D, Busetto L, Dicker D, et al. European Practical and Patient-Centred Guidelines for Adult Obesity Management in Primary Care. Obesity Facts 2019;12(1):40-66
6. Bouchard C. BMI, fat mass, abdominal adiposity and visceral fat: where is the 'beef'? International journal of obesity (2005) 2007;31(10):1552-1553
7. Clinical practice guidelines for nutrition in chronic renal failure. K/DOQI, National Kidney Foundation. American journal of kidney diseases : the official journal of the National Kidney Foundation 2000;35(6 Suppl 2):S1-140
8. Stenvinkel P, Ikizler TA, Mallamaci F, et al. Obesity and nephropathy: results of a knowledge and practice pattern survey. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 2013;28 Suppl 4:iv99-104
9. Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet (London, England) 2004;364(9438):937-952
10. Postorino M, Marino C, Tripepi G, et al. Abdominal obesity and all-cause and cardiovascular mortality in end-stage renal disease. Journal of the American College of Cardiology 2009;53(15):1265-1272
11. Cordeiro AC, Qureshi AR, Stenvinkel P, et al. Abdominal fat deposition is associated with increased inflammation, protein-energy wasting and worse outcome in patients undergoing haemodialysis. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 2010;25(2):562-568
12. Banack HR, Stokes A. The 'obesity paradox' may not be a paradox at all. International journal of obesity (2005) 2017;41(8):1162-1163
13. Kovesdy CP, Czira ME, Rudas A, et al. Body mass index, waist circumference and mortality in kidney transplant recipients. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 2010;10(12):2644-2651
14. Gwon JG, Choi I, Jung CW, et al. Impact of changes in waist-to-hip ratio after kidney transplantation on cardiovascular outcomes. Scientific Reports 2021;11(1):783
15. Pinar O, Rod X, Mageau A, et al. Surgical complications risk in obese and overweight recipients for kidney transplantation: a predictive morphometric model based on sarcopenia and vessel-to-skin distance. World Journal of Urology 2020;12:12
16. Chadban SJ, Ahn C, Axelrod DA, et al. KDIGO Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation. Transplantation 2020;104(4S1 Suppl 1):S11-S103
17. Abramowicz D, Cochat P, Claas FH, et al. European Renal Best Practice Guideline on kidney donor and recipient evaluation and perioperative care. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association
2015;30(11):1790-1797
18. Campbell S, Pilmore H, Gracey D, et al. KHA-CARI guideline: recipient assessment for transplantation. Nephrology (Carlton, Vic.) 2013;18(6):455-462
19. Dudley C, Harden P. Renal Association Clinical Practice Guideline on the assessment of the potential kidney transplant recipient. Nephron. Clinical practice 2011;118 Suppl 1:c209-224
20. World Health Organisation. Health-topics - Noncommunicable-diseases - Obesity. https://www.euro.who.int/en/health-topics/noncommunicable-diseases/obesity.
21. Hoogeveen EK, Aalten J, Rothman KJ, et al. Effect of obesity on the outcome of kidney transplantation: A 20-year follow-up. Transplantation 2011(8):869-874
22. Krishnan N, Higgins R, Short A, et al. Kidney Transplantation Significantly Improves Patient and Graft Survival Irrespective of BMI: A Cohort Study. American Journal of Transplantation 2015(9):2378-2386
23. Hill CJ, Courtney AE, Cardwell CR, et al. Recipient obesity and outcomes after kidney transplantation: a systematic review and meta-analysis. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 2015;30(8):1403-1411
24. Lafranca JA, JN IJ, Betjes MG, et al. Body mass index and outcome in renal transplant recipients: a systematic review and meta-analysis. BMC medicine 2015;13:111
25. Ahmad SF, Zahmatkesh G, Streja E, et al. Body mass index and mortality in kidney transplant recipients: a systematic review and meta-analysis. American journal of nephrology 2014;40(4):315-324
26. Sood A, Hakim DN, Hakim NS. Consequences of Recipient Obesity on Postoperative Outcomes in a Renal Transplant: A Systematic Review and Meta-Analysis. Experimental and clinical transplantation : official journal of the Middle East Society for Organ Transplantation 2016;14(2):121-128
27. Nicoletto BB, Fonseca NK, Manfro RC, et al. Effects of obesity on kidney transplantation outcomes: a systematic review and meta-analysis. Transplantation 2014;98(2):167-176
28. Ladhani M, Craig JC, Irving M, et al. Obesity and the risk of cardiovascular and all-cause mortality in chronic kidney disease: a systematic review and meta-analysis. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 2017;32(3):439-449
29. Li C, Jin H, Xiao L, et al. Association Between Overweight and Renal Transplant Outcomes: A Meta-Analysis. Experimental and clinical transplantation : official journal of the Middle East Society for Organ Transplantation 2017;15(5):527-531
30. Chang S, Jiang J. Association of Body Mass Index and the Risk of New-Onset Diabetes After Kidney Transplantation: A Meta-analysis. Transplantation Proceedings 2018;50(5):1316-1325
31. Naik AS, Sankhu A, Cibrik DM, et al. The Impact of Obesity on Allograft Failure After Kidney Transplantation: A Competing Risks Analysis. Transplantation 2016;100(9):1963-1969
32. Kim SM, Choi JH, Son MJ, et al. Is Body Mass Index a Significant Independent Risk Factor for Graft Failure and Patient Death in the Modern Immunosuppressive Era? Transplantation Proceedings 2020;52(10):3058-3068
33. Schold JD, Augustine JJ, Huml AM, et al. Effects of body mass index on kidney transplant outcomes are significantly modified by patient characteristics. American Journal of Transplantation 2020
34. Kostakis ID, Kassimatis T, Bianchi V, et al. UK renal transplant outcomes in low and high BMI recipients: the need for a national policy. Journal of Nephrology 2020;33(2):371-381
35. Lentine KL, Xiao H, Brennan DC, et al. The impact of kidney transplantation on heart failure risk varies with candidate body mass index. American heart journal 2009;158(6):972-982
36. Krishnan N, Higgins R, Short A, et al. Kidney Transplantation Significantly Improves Patient and Graft Survival Irrespective of BMI: A Cohort Study. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 2015;15(9):2378-2386
37. Bellini MI, Koutroutsos K, Nananpragasam H, et al. Obesity affects graft function but not graft loss in kidney transplant recipients. Journal of International Medical Research 2020;48(1):300060519895139
38. Huang E, Bunnapradist S. Pre-Transplant Weight Loss and Survival after Kidney Transplantation. American journal of nephrology 2015;41(6):448-455
39. Heng AE, Aniort J, Pereira B, et al. Renal transplant in obese patients and impact of weight loss before surgery on surgical and medical outcomes: A single-center cohort study. Experimental and Clinical Transplantation 2019;17(5):604-612
40. Pieloch D, Mann R, Dombrovskiy V, et al. The impact of morbid obesity on hospital length of stay in kidney transplant recipients. Journal of renal nutrition: the official journal of the Council on Renal Nutrition of the National Kidney Foundation 2014;24(6):411-416
41. Aziz F, Ramadorai A, Parajuli S, et al. Obesity: An Independent Predictor of Morbidity and Graft Loss after Kidney Transplantation. American journal of nephrology 2020;51(8):615-623
42. Kanthawar P, Mei X, Daily MF, et al. Kidney Transplant Outcomes in the Super Obese: A National Study From the UNOS Dataset. World journal of surgery 2016;40(11):2808-2815
43. Kim Y, Chang AL, Wima K, et al. The impact of morbid obesity on resource utilization after renal transplantation. Surgery 2016;160(6):1544-1550
44. Bennett WM, McEvoy KM, Henell KR, et al. Morbid obesity does not preclude successful renal transplantation. Clinical transplantation 2004;18(1):89-93
45. Kirnap M, Ayvazoglu SE, Akdur A, et al. Outcome of renal transplantation in obese recipients. Transplantation 2016;S308
46. Alnimri M, Friedman GG. Effect of obesity on transplant outcome one year post kidney transplant. Journal of the American Society of Nephrology 2018;29:148
47. Liese J, Bottner N, Buttner S, et al. Influence of the recipient body mass index on the outcomes after kidney transplantation. Langenbecks Archives of Surgery 2018;403(1):73-82
48. Collini A, Piccioni SA, Miccoli S, et al. Body mass index and long-term outcome of renal transplant recipients: single center analysis of 1000 transplants. Transplant International 2019;32:420
49. Erturk T, Berber I, Cakir U. Effect of Obesity on Clinical Outcomes of Kidney Transplant Patients. Transplantation Proceedings 2019;51(4):1093-1095
50. Hui A, Suh N, Sypek M. Removing the BMI BIAS in kidney transplantation: Outcomes of kidney transplantation in patients with BMI >35. Transplantation 2020;104(SUPPL 3):S215-S216
51. Mor E, Yemini R, Eisner S, et al. Obesity and outcome following renal transplantation; comparison between living and deceased donor transplants. Transplant International 2019;32:75
52. Mehta A, Ghazanfar A, Marriott A, et al. Where to draw the line in surgical obesity for renal transplant recipients: An outcome analysis based on body mass index. Experimental and Clinical Transplantation 2019;17(1):37-41
53. Luke NA, Tantisattamo E. Obesity as a predictor of renal allograft function. Journal of the American Society of Nephrology 2018;29:147
54. Warzyszyńska K, Zawistowski M, Karpeta E, et al. Early Postoperative Complications and Outcomes of Kidney Transplantation in Moderately Obese Patients. Transplantation Proceedings 2020;52(8):2318-2323
55. Kihara Y, Iwamoto H, Yokoyama T, et al. Investigation of body mass index and cases of living renal transplantation performed in this department. Transplantation 2016;S662
56. Kim KY, Cho JH, Jung HY, et al. Effect of Changes in Body Mass Index on Cardiovascular Outcomes in Kidney Transplant Recipients. Transplantation proceedings 2017;49(5):1038-1042
57. Hataimizadeh P, Molnar MZ, Streja E, et al. Recipient-related predictors of kidney transplantation outcomes in the elderly. Clinical transplantation 2013;27(3):436-443
58. Gill JS, Lan J, Dong J, et al. The survival benefit of kidney transplantation in obese patients. American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 2013;13(8):2083-2090
59. Tariq N, Moore LW, Sherman V. Bariatric surgery and end-stage organ failure. The Surgical
Outcomes in Patients with Chronic Kidney Disease and End-Stage Renal Disease: A Systematic Review. Transplantation 2013;93(6):1359-1371

60. Howard RJ, Thai VB, Patton PR, et al. Obesity does not portend a bad outcome for kidney transplant recipients. Transplantation 2002;73(1):53-55

61. Harhay MN, Ranganna K, Boyle SM, et al. Association Between Weight Loss Before Deceased Donor Kidney Transplantation and Posttransplantation Outcomes. American journal of kidney diseases : the official journal of the National Kidney Foundation 2019;74(3):361-372

62. Camilleri B, Bridson JM, Sharma A, et al. From chronic kidney disease to kidney transplantation: The impact of obesity and its treatment modalities. Transplantation reviews (Orlando, Fla.) 2016;30(4):203-211

63. Cook SA, MacLaughlin H, Macdougall IC. A structured weight management programme can achieve improved functional ability and significant weight loss in obese patients with chronic kidney disease. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 2008;23(1):263-268

64. MacLaughlin HL, Cook SA, Kariyawasam D, et al. Nonrandomized trial of weight loss with orlistat, nutrition education, diet, and exercise in obese patients with CKD: 2-year follow-up. American journal of kidney diseases : the official journal of the National Kidney Foundation 2010;55(1):69-76

65. MacLaughlin HL, Hall WL, Condy J, et al. Participation in a Structured Weight Loss Program and All-Cause Mortality and Cardiovascular Morbidity in Obese Patients With Chronic Kidney Disease. Journal of renal nutrition : the official journal of the Council on Renal Nutrition of the National Kidney Foundation 2015;25(6):472-479

66. Sheetz KH, Gerhardinger L, Dimick JB, et al. Bariatric Surgery and Long-Term Survival in Patients With Obesity and End-stage Kidney Disease. JAMA Surgery 2020;155(7):581-588

67. Freeman CM, Woodle ES, Shi J, et al. Addressing morbid obesity as a barrier to renal transplantation with laparoscopic sleeve gastrectomy. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 2015;15(5):1360-1368

68. Thomas IA, Gaynor JJ, Joseph T, et al. Roux-en-Y gastric bypass is an effective bridge to kidney transplantation: Results from a single center. Clinical transplantation 2018;32(5):e13232

69. Outmani L, Kimenai H, Roodnat JJ, et al. Clinical outcome of kidney transplantation after bariatric surgery: A single-center, retrospective cohort study. Clinical Transplantation 2020:e14208

70. Ku E, McCulloch CE, Roll GR, et al. Bariatric surgery prior to transplantation and risk of early hospital re-admission, graft failure, or death following kidney transplantation. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 2021

71. Troppmann C, Santhanakrishnan C, Kuo JH, et al. Impact of panniculectomy on transplant candidacy of obese patients with chronic kidney disease declined for kidney transplantation because of a high-risk abdominal panniculus: A pilot study. Surgery 2016;159(6):1612-1622

72. Modanlou KA, Mutthyala U, Xiao H, et al. Bariatric surgery among kidney transplant candidates and recipients: analysis of the United States renal data system and literature review. Transplantation 2009;87(8):1167-1173

73. Jamal MH, Corcelles R, Daigle CR, et al. Safety and effectiveness of bariatric surgery in dialysis patients and kidney transplantation candidates. Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery 2015;11(2):419-423

74. Al-Bahri S, Fakhry TK, Gonzalvo JP, et al. Bariatric Surgery as a Bridge to Renal Transplantation in Patients with End-Stage Renal Disease. Obesity surgery 2017;27(11):2951-2955

75. Troxell ML, Houghton DC, Hawkey M, et al. Enteric oxalate nephropathy in the renal allograft: an underrecognized complication of bariatric surgery. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 2013;13(2):501-509

76. Cohen JB, Tewksbury CM, Torres Landa S, et al. National Postoperative Bariatric Surgery Outcomes in Patients with Chronic Kidney Disease and End-Stage Kidney Disease. 2019;1(3):975-982
77. Cohen JB, Lim MA, Tewksbury CM, et al. Bariatric surgery before and after kidney transplantation: long-term weight loss and allograft outcomes. 2019;1(6):935-941
78. Dobrzycka M, Proczko-Stepaniak M, Kaska L, et al. Weight Loss After Bariatric Surgery in Morbidly Obese End-Stage Kidney Disease Patients as Preparation for Kidney Transplantation. Matched Pair Analysis in a High-Volume Bariatric and Transplant Center. Obesity Surgery 2020;30(7):2708-2714
79. Yemini R, Nesher E, Carmeli I, et al. Bariatric Surgery Is Efficacious and Improves Access to Transplantation for Morbidly Obese Renal Transplant Candidates. 2019;1(8):2373-2380
80. Takata MC, Campos GM, Ciovica R, et al. Laparoscopic bariatric surgery improves candidacy in morbidly obese patients awaiting transplantation. Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery 2008;4(2):159-164; discussion 164-155
81. Alexander JW, Goodman H. Gastric bypass in chronic renal failure and renal transplant. Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition 2007;22(1):16-21
82. Kim Y, Shi J, Freeman CM, et al. Addressing the challenges of sleeve gastrectomy in end-stage renal disease: Analysis of 100 consecutive renal failure patients. Surgery 2017;162(2):358-365
83. Kim Y, Jung AD, Dhar VK, et al. Laparoscopic sleeve gastrectomy improves renal transplant candidacy and posttransplant outcomes in morbidly obese patients. American Journal of Transplantation 2018;18(2):410-416
84. Kim Y, Bailey AJ, Morris MC, et al. Kidney transplantation after sleeve gastrectomy in the morbidly obese candidate: results of a 2-year experience. Surgery for Obesity & Related Diseases 2020;16(1):10-14
85. Lin MY, Tavakol MM, Sarin A, et al. Laparoscopic sleeve gastrectomy is safe and efficacious for pretransplant candidates. Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery 2013;9(5):653-658
86. Kienzl-Wagner K, Weissenbacher A, Gehwolf P, et al. Laparoscopic sleeve gastrectomy: gateway to kidney transplantation. Surgery for obesity and related diseases : official journal of the American Society for Bariatric Surgery 2017;13(6):909-915
87. Carandina S, Genser L, Bossi M, et al. Laparoscopic Sleeve Gastrectomy in Kidney Transplant Candidates: a Case Series. Obesity surgery 2017;27(10):2613-2618
88. Hidalgo JE, Roy M, Ramirez A, et al. Laparoscopic sleeve gastrectomy: a first step for rapid weight loss in morbidly obese patients requiring a second non-bariatric procedure. Obesity surgery 2012;22(4):555-559
89. Bouchard P, Tchervenkov J, Demyttenaere S, et al. Safety and efficacy of the sleeve gastrectomy as a strategy towards kidney transplantation. Surgical Endoscopy 2020;34(6):2657-2664
90. Gaillard M, Tranchart H, Beaudreuil S, et al. Laparoscopic sleeve gastrectomy for morbid obesity in renal transplantation candidates: a matched case-control study. Transplant International 2020;33(9):1061-1070
91. Kassam AF, Mirza A, Kim Y, et al. Long-term outcomes in patients with obesity and renal disease after sleeve gastrectomy. American Journal of Transplantation 2020;20(2):422-429
92. Newcombe V, Blanch A, Slater GH, et al. Laparoscopic adjustable gastric banding prior to renal transplantation. Obesity surgery 2005;15(4):567-570
93. Koshy AN, Coombes JS, Wilkinson S, et al. Laparoscopic gastric banding surgery performed in obese dialysis patients prior to kidney transplantation. American journal of kidney diseases : the official journal of the National Kidney Foundation 2008;52(4):e15-17
94. Guggino J, Coumes S, Wion N, et al. Effectiveness and Safety of Bariatric Surgery in Patients with End-Stage Chronic Kidney Disease or Kidney Transplant. Obesity 2020;28(12):2290-2304
95. Orandi BJ, Purvis JW, Cannon RM, et al. Bariatric surgery to achieve transplant in end-stage organ disease patients: A systematic review and meta-analysis. American Journal of Surgery 2020;220(3):566-579
96. Choudhury RA, Hoeltzel G, Prins K, et al. Sleeve Gastrectomy Compared with Gastric Bypass for Morbidly Obese Patients with End Stage Renal Disease: a Decision Analysis. Journal of
Gastrointestinal Surgery 2020;24(4):756-763

97. Singh A, Sarkar SR, Gaber LW, et al. Acute oxalate nephropathy associated with orlistat, a gastrointestinal lipase inhibitor. American journal of kidney diseases: the official journal of the National Kidney Foundation 2007;49(1):153-157

98. Evans S, Michael R, Wells H, et al. Drug interaction in a renal transplant patient: cyclosporin-Neoral and orlistat. American journal of kidney diseases: the official journal of the National Kidney Foundation 2003;41(2):493-496

99. Kim Y, Jung AD, Dhar VK, et al. Laparoscopic sleeve gastrectomy improves renal transplant candidacy and posttransplant outcomes in morbidly obese patients. American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 2018;18(2):410-416

100. Colquitt JL, Pickett K, Loveman E, et al. Surgery for weight loss in adults. The Cochrane database of systematic reviews 2014(8):Cd003641

101. Rogers CC, Alloway RR, Alexander JW, et al. Pharmacokinetics of mycophenolic acid, tacrolimus and sirolimus after gastric bypass surgery in end-stage renal disease and transplant patients: a pilot study. Clinical transplantation 2008;22(3):281-291

102. Golomb I, Winkler J, Ben-Yakov A, et al. Laparoscopic sleeve gastrectomy as a weight reduction strategy in obese patients after kidney transplantation. American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 2014;14(10):2384-2390

103. Semins MJ, Asplin JR, Steele K, et al. The effect of restrictive bariatric surgery on urinary stone risk factors. Urology 2010;76(4):826-829

104. Mann JFE, Ørsted DD, Brown-Frandsen K, et al. Liraglutide and Renal Outcomes in Type 2 Diabetes. The New England journal of medicine 2017;377(9):839-848

105. O’Brien R, Johnson E, Haneuse S, et al. Microvascular Outcomes in Patients With Diabetes After Bariatric Surgery Versus Usual Care: A Matched Cohort Study. Annals of internal medicine 2018;169(5):300-310

106. Hadjievangelou N, Kulendran M, McGlone ER, et al. Is bariatric surgery in patients following renal transplantation safe and effective? A best evidence topic. Int J Surg 2016;28:191-195

107. Elli EF, Gonzalez-Heredia R, Sanchez-Johnsen L, et al. Sleeve gastrectomy surgery in obese patients post-organ transplantation. Surgery for obesity and related diseases: official journal of the American Society for Bariatric Surgery 2016;12(3):528-534

108. Gazzetta PG, Bissolati M, Saibene A, et al. Bariatric Surgery to Target Obesity in the Renal Transplant Population: Preliminary Experience in a Single Center. Transplantation proceedings 2017;49(4):646-649

109. Szomstein S, Rojas R, Rosenthal RJ. Outcomes of laparoscopic bariatric surgery after renal transplant. Obesity surgery 2010;20(3):383-385

110. Arias RH, Mesa L, Posada MC, et al. Kidney transplantation and gastric bypass: a better control of comorbidities. Obesity surgery 2010;20(7):851-854

111. Gullo-Neto S, Padoin AV, Queiroz de Carvalho JE, et al. Metabolic surgery for the treatment of type 2 diabetes in pancreas after kidney transplant candidates. Transplantation proceedings 2014;46(6):1741-1744

112. Viscido G, Gorodner V, Signorini FJ, et al. Sleeve Gastrectomy after Renal Transplantation. Obes Surg 2018;28(6):1587-1594

113. Khoraki J, Katz MG, Funk LM, et al. Feasibility and outcomes of laparoscopic sleeve gastrectomy after solid organ transplantation. Surgery for obesity and related diseases: official journal of the American Society for Bariatric Surgery 2016;12(1):75-83

114. Del Prado P, Papasavas PK, Tishler DS, et al. Laparoscopic placement of adjustable gastric band in patients with autoimmune disease or chronic steroid use. Obesity surgery 2014;24(4):584-587

115. Gheith O, Al-Otaibi T, Halim MA, et al. Bariatric Surgery in Renal Transplant Patients. Experimental and clinical transplantation: official journal of the Middle East Society for Organ
116. Chan G, Hajjar R, Boutin L, et al. Prospective study of the changes in pharmacokinetics of immunosuppressive medications after laparoscopic sleeve gastrectomy. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 2020;20(2):582-588
117. Zoccali C, Abramowicz D, Cannata-Andia JB, et al. European best practice quo vadis? From European Best Practice Guidelines (EBPG) to European Renal Best Practice (ERBP). Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association 2008;23(7):2162-2166
118. Cross NB, Craig JC, Webster AC. Asking the right question and finding the right answers. Nephrology (Carlton, Vic.) 2010;15(1):8-11
119. Tong A, Gill J, Budde K, et al. Toward Establishing Core Outcome Domains For Trials in Kidney Transplantation: Report of the Standardized Outcomes in Nephrology-Kidney Transplantation Consensus Workshops. Transplantation 2017;101(8):1887-1896
120. Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. Journal of clinical epidemiology 2011;64(4):401-406