

PEER-REVIEW REPORT

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SPECIFIC COMMENTS TO AUTHORS

This is a narrative review exploring the role of obesity and bariatric surgery in relation to kidney transplantation. The topic is interesting and increasingly relevant, and the review is in general terms well written. The level of English is appropriate, but there is a number of phrasing issues. Few linguistic and typographic improvements are also advised. Appropriate research methods have been utilised. The title reflects the content adequately. The content of the abstract is sound, but is far less than 200 words, as opposed to the requirements of the journal. The key words correlate well with the content but are in excess of the given limit. Furthermore, I have numerous mainly minor revisions to recommend, as follows: In the Abstract: Preferably rephrase to "...and may potentially improve the immediate and later posttransplant outcomes". Preferably rephrase to "...and in potential living kidney donors". This is further applicable in the main text. Core tip: Many (instead of many). In the main text, on a number of occasions, terms that have been previously abbreviated are repeatedly written in full. The authors should consistently specify the type of studies they are discussing and the number of patients included, throughout the whole manuscript. In the second paragraph of the INTRODUCTION, the part "Most transplant centers..... by immunosuppression" lacks references. In the DEFINITION AND MEASUREMENT OF OBESITY section, it would be prudent to provide all BMI categories (including underweight, ideal and overweight) and underline that the provided definition and classification of obesity is the one of WHO. - In the part concerning the waist-to-hip ratio, "...are considered obese..." should be rephrased. In the section OBESITY AND ESRD, use consistently the WHO terminology (underweight, overweight, Class I, II) without repeating the relevant ranges in brackets. - In the same section, the part "in their analysis, Segev et al. [25] found..... than nonobese patients;" should be rephrased. - US and U.S. have been used interchangeably - be consistent. - In the sentence "However,

compared with patients with minimal weight change (< 1 kg).....” do the authors mean loss rather than change? - The authors state “Death on the waiting list was more common among those who lost weight (15%) or gained weight (15%) than among those who maintained stable weight (13%).” Was this a significant difference? - “Overall, blacks were more likely to lose weight and less likely to gain weight than whites.” should be rephrased to “black people” or “black race was associated with....” // white people/white race. - At the end of the first part of this section, the last two sentences are confusing. It appears the authors mean: “...weight loss was not associated with better access to transplantation (HR 0.96) on the whole, although this correlation was different...”. In the section Bariatric surgery in ESRD patients: - Preferably remove “in ESRD patients” and “in kidney transplant candidates” from the sentence “However, medical management.....and mortality rates [34,35].” - Rephrase the relevant sentence to “Bariatric surgery in ESRD patients is associated with weight loss ranging from 29.8% to 72.8% excess weight loss (%EWL)[36],...” - The sentence “Complications associated with..... hospitals (0.17%) [38].” ends up in a confusing way and should be rephrased as appropriate. Also, “approximately 11 times” seems to be the right phrasing. - “However, many studies have consistently shown that bariatric surgery is associated with slower eGFR decline and lower risk of kidney failure [39,40].” Do they authors mean pretransplant, posttransplant or both? - “....Kassam et al. [39] evaluated the modification of renal function..... stages 1 through 4 undergoing bariatric surgery” should change to: “the change in renal function”, and “stages 1-4” or “stages 1 to 4”. - “significant reduction in the BMI index in all patients” - remove “index”. - The authors state: “Kidney function and eGFR significantly improved in patients with CKD stages 2, 3a, and 3b, while a similar result was not observed among patients with CKD stages 1 and 4 [39], suggesting that the improvements in renal function are limited only to those patients with a mild reduction in kidney function.” Firstly, “Kidney function and eGFR”

should be rephrased, as eGFR is a marker of kidney function. Secondly, what was the measure of this significant improvement? Have the authors reviewed any studies reporting quantitative improvement of renal function metrics? Thirdly, the last part of the sentence does not seem to be an adequate interpretation of the referred outcomes. - “Open surgery may be associated with an increased mortality rate compared with the general population”. Do the authors mean in ESRD patients? - “Modanlou et al. [34] evaluated the results of 186 patients...”. I suspect this is 186 ESRD patients. - “The 30-day mortality in wait-listed and posttransplant patients was 3.5%,....” The authors should provide percentages for wait-listed and posttransplant patients, respectively, if these have been examined separately. - “...while the median EWL ranged between 31% and 66% [34].” The same applies here. - “Both LSG and RYGB achieve significant excess body weight loss (up to 80% within 24 months) and may increase the likelihood of being listed for kidney transplantation in up to 50.3% of patients,...”. Do the authors mean these procedures may increase the likelihood of being listed for kidney transplantation in up to 50.3% of patients, or that these procedures may convert 50.3% of ineligible patients into eligible for listing? - “....although a recent meta-analysis reported that only 25% of patients had access to transplant at a median follow-up of 48 months [36].” Were these patients in whom bariatric surgery was considered a prerequisite for listing? - “The correct timing of bariatric surgery is still an issue.” - A controversial issue? - “...of reoperation and readmission [500]...” The right reference is 50. - “LSG reduced hypertension and the need for antihypertensive medications and reduced the incidence of diabetes (59.6%).” What does the percentage 59.6% indicate? - “There was no, suggesting that LSG is safe and has the potential to reduce obesity-related comorbidities, possibly improving long-term outcomes.” The second part of the sentence does not seem to be an adequate interpretation of the first. Furthermore, how do the authors comment on the lack of survival benefit following LSG and renal transplant? - “Cohen et al. [51]

compared the outcome of bariatric surgery before and after transplantation: compared to BMI-matched controls, pretransplant bariatric surgery was associated with a 1-year increased risk of acute rejection and a decreased risk of delayed graft function.” It is preferable to say “pretransplant and posttransplant bariatric surgery”, if this is what the authors mean. This will be clearer to the reader. Also, it should be defined better what the two compared groups consisted of. - It would be useful for the authors to also include the following study in their review: Sheetz KH, Gerhardinger L, Dimick JB, Waits SA. Bariatric Surgery and Long-term Survival in Patients With Obesity and End-stage Kidney Disease. JAMA Surg. 2020;155(7):581-588. doi:10.1001/jamasurg.2020.0829 - “LSG results in sustained weight loss and is associated with an improvement in obesity-related comorbidities” This is mentioned for the first time here and without reference. - “Although pretransplant bariatric surgery is associated with acceptable outcomes for patients undergoing kidney transplantation, the correct timing has yet to be determined.” What do the authors mean when referring to the correct timing? They seem to refer to pretransplant bariatric surgery in this sentence - do they refer to the correct timing before listing/transplant? In any case, they do not seem to have strongly highlighted a controversy as such, regarding timings, in their discussion. In the OBESITY AND KIDNEY TRANSPLANTATION section: - “In a recent analysis, Glanton et al. [55] compared... waiting for a kidney”. Firstly, how many patients were included? Secondly, use appropriate punctuation, otherwise it appears as if only those on dialysis were obese. Thirdly, this is not meaningful without the actual percentages (and the statistical comparison, if one is available). - “Interestingly, the beneficial effect of transplantation was lost in the subgroup analysis of patients with class III obesity [56].” This should be further explained. - “The beneficial effect of kidney transplantation among obese patients was recently confirmed by Gill et al. [20],....”. The authors should highlight that this is a large cohort obtained from the US renal registry.



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- "Therefore, some authorsan unacceptable mortality risk [20,21]." What is considered an unacceptable mortality risk in this setting? - "Considering that some studies is mandatory [33,70]." This is not a robust statement as it implies that complications in this setting do not depend at all on the transplant procedure itself. In the section Bariatric surgery after kidney transplantation: - "....the availability of immunosuppressive drugs [36]." Do the authors mean bioavailability? - "The optimal timing of bariatric surgery limited impact on graft function." requires reference(s). - "In their innovative approach, Spaggiari et al.....and graft failure rates." What were the changes in BMI and other metrics? The outcomes imply that patients who had a bariatric procedure did not benefit from it in terms of improved transplant outcomes. How do the authors comment on that? In the section Bariatric surgery in living kidney donors - "living kidney transplantation" should change to "living-donor kidney transplantation" where applicable. - "RYGB is the most commonly used technique.....". The sentence that follows implies that rather than "RYGB is" it should be "RYGB has historically been".