

Opinion

## The Conundrum of High Body Mass Index in Kidney Transplant Patients

Maria Irene Bellini <sup>1,\*</sup>, Joseph Ayathamattam <sup>2</sup>, Paul Elliot Herbert <sup>1,2</sup>

1. Renal and Transplant Directorate, Hammersmith Hospital, Imperial College NHS Trust, London, United Kingdom; E-Mails: [mariairene.bellini@nhs.net](mailto:mariairene.bellini@nhs.net); [paul.herbert@nhs.net](mailto:paul.herbert@nhs.net)
2. Imperial College, London, United Kingdom; E-Mail: [joseph.ayathamattam13@imperial.ac.uk](mailto:joseph.ayathamattam13@imperial.ac.uk)

\* **Correspondence:** Maria Irene Bellini; E-Mail: [mariairene.bellini@nhs.net](mailto:mariairene.bellini@nhs.net)

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### Abstract

Obesity is on the rise and the number of end stage renal disease patients who are obese parallel this trend. There is no universally accepted guideline for wait-listing end stage renal disease obese patients in order to reduce surgical complications and improve survival of the kidney graft. Criteria for acceptance are variable among transplant centres, as do post-transplant policies. Careful risk assessment to maximise the benefits of the limited organ donor resource must be undertaken prior to waitlist an obese kidney transplant candidate. Likewise, close post transplantation follow-up for this higher risk group should be implemented as per the general population, but the body mass index per se should not be a barrier to get access to transplantation.

### Keywords

Obesity; kidney transplant; bariatric surgery



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Kidney transplantation is the best approved renal replacement therapy [1], but the optimal management of the obese transplant candidates remains unclear. Kidney graft function depends in fact not only on proper regulation of immune processes, but also on the optimal control of underlying chronic diseases, such as obesity. The epidemic of obesity has paralleled that of chronic kidney disease (CKD) [2], with approximately 30% of the adult population worldwide being affected [3].

Obesity is often associated with systemic inflammatory conditions, hypertension and diabetes. These are established risk factors to increase the cardiovascular disease (CVD) as well as the CKD [4] of the high Body Mass Index (BMI) population. In addition, there is evidence of a direct causal connection between obesity and CKD, with a faster progression of CKD to end-stage renal disease (ESRD), due to the underlying renal hyperfiltration driven by the weight excess [5]. However, literature has shown that ESRD obese patients benefit from transplantation as do non-obese patients [6-8], and even in the paediatric population, no difference in graft or patient survival are reported among different BMI categories [9].

Why some centres are reluctant in wait-listing obese candidates? Surgery is indeed more challenging and encumbers an increased risk of peri-operative complications, along with a prolonged peri-operative time. Complications could not only jeopardise patient's safety, but also diminishing the already limited organ pool, indirectly damaging the non-obese candidates. Kidney transplant in the high BMI recipient is often associated with wound infection and dehiscence, lymphocele, hematoma, renal artery stenosis, renal vein thrombosis, acute rejection and delayed graft function [10, 11]. This higher surgical risk could translate into an overall longer hospital stay, although not always significant in high volume centres [12].

In recognition of an increased cost and economic resource utilization, some centres have therefore advocated for appropriate risk-adjustment reimbursement [13]. Other options have instead posed a cut-off to waitlist potential kidney transplant candidates. The most common BMI limit is 40 kg/m<sup>2</sup> (62%), followed by 35 kg/m<sup>2</sup> (36%) according to a Canadian survey in 2016 [14].

Given the limited organ donor pool, the ideal allocation policy would aim to transplant those candidates who would benefit most in the long-term with the lowest associated risks [15]. Since obesity is a modifiable condition associated with shorter life expectancy, the conundrum of whether high BMI recipients should be wait-listed prior or after weight loss has been a matter of debate for long time. Not surprisingly, obesity is therefore often representing a barrier to access kidney transplantation with dilemmas on the shoulders of professionals involved with the healthcare of high BMI dialysis population.

Which therapeutic intervention could improve access to transplantation for the obese population? Bariatric surgery (BS), the most efficient method of achieving durable weight loss, could represent a possible weight-loss strategy and bridge against wait-listing discrimination. There is support for the efficacy of transplant facilitation through effective pre-transplant weight reduction in some bariatric programmes [16]. However, the weight loss results usually take months before becoming clinically significant from a surgical risk perspective, therefore we sustain BS in a pre-emptive scenario, but do not strictly consider to waitlist recipients, particularly if already on dialysis. In addition to this, although promising [17], data regarding the renal impact and safety of BS in the dialysis population are insufficient [18]. BS seems to have a direct therapeutic effect on obesity-related nephropathy, reversing the glomerular hyperfiltration and

albuminuria. The weight loss also acts at a systemic level, improving the inflammatory status of the obese condition and often solving diabetes and hypertension, the most common leading causes of ESRD [19]. There are yet concerns about BS in terms of renal risk secondary to some procedures, such as gastric bypass. This in fact involves a higher degree of drug malabsorption with potential increased risk of acute rejection. On the other side, laparoscopic sleeve gastrectomy, a restrictive only procedure, is recommended as a feasible and first-choice procedure in the high BMI population [20].

Although BS may improve long-term kidney outcomes, there is no universal agreement in terms of benefit and timing in the ESRD population. The potential adverse events described for this particular surgery have also to be carefully evaluated in the short and mid-term: acute kidney injury, nephrolithiasis, and oxalate nephropathy [21, 22].

To conclude, BS aiming to increase transplant eligibility by reducing BMI in kidney transplant candidates is an interesting option, but the effect of surgical weight loss on post transplantation outcomes is still unknown [23].

Another important aspect to consider when wait-listing obese ESRD patients is the reverse epidemiology exhibited whilst in haemodialysis, a phenomenon described as the “obesity paradox”: higher BMI is associated with improved outcomes and lower BMI with reduced survival. The pathophysiology is complex, but a possible explanation is that obese persons are better nourished and are thought to be better immune responders against devastating chronic infectious and other diseases, which are often a cause of death in the lower BMI dialysis population [24]. More in details, the historical unintended weight loss is an independent predictor of death, with a J-shaped association with BMI and death and the nadir of the curve for normal BMI patients [25].

The obesity paradox seen for the ESRD transplant candidates does not yet extend to the post-transplant setting, with obesity and weight gain are associated with reduced survival and CVD, as per in the general population [26]. In our view, interventions like BS could therefore have a stronger indication in the post-transplant scenario, but in order to achieve a durable weight loss, a more generalised strategy with lifestyle interventions and physical rehabilitation are paramount. Weight gain post-transplant should be actively discouraged and kidney transplant recipients should be referred to a dietitian as soon as practicable after transplantation, with regular follow up to monitor the weight of individual transplant recipients. Dietary advice should be individualized including meal plans, exercise plans and specific goals. A possible initial strategy of weight loss therapy should be to reduce body weight by approximately 10% from baseline, with weight loss of 1-2 kg per month. With success, further weight loss can be attempted if indicated through further assessment [27].

The immunosuppressive therapy plays a major role in the post-transplant obese population to prevent the rejection/graft loss and to avoid the detrimental metabolic side effects. As obesity is associated with an increased risk of steroid induced diabetes and CVD risk factors [28], our centre policy is to withdraw them early, within the first week post-transplant [12]. Alternative new drugs as belatacept with better metabolic risk profile look promising in order to reduce drug-induced toxicities, such as hypertension and diabetes [29], with the potential of improving long-term renal function. Studies in de novo belatacept recipients have shown higher mean non-HDL cholesterol and lower mean triglycerides blood levels when compared to Calcineurin Inhibitor (CNI) treated patients [30]. Although this interesting preliminary evidence in favour of belatacept, we do not encourage a complete CNI withdrawal, since it is associated with a higher rate of rejection in

comparison to tacrolimus, the most commonly used CNI [31]. In our centre, we aim to a CNI minimisation, with a tacrolimus through level of 5-8 ng/ml; our policy is also to use alemtuzumab induction for all the kidney transplant recipients in order to provide an effective immunosuppressive steroid-sparing cover [32].

In conclusion, while obesity can increase the risk of surgical complications or impact in the community costs, selected obese patients can achieve good outcomes after kidney transplantation. Obesity is a chronic metabolic condition that in a pre-transplant setting does not intrinsically differ from other chronic disease, such as diabetes [33, 34]. Since outcomes of being on dialysis are worse than those transplanted [7], there should be no a priori reason or BMI cut-off for treating obese ESRD patients differently from those with other comorbidities. Individual assessment of the potential candidate prior to wait-listing should focus on the accompanying comorbidities with an overall consideration of the life expectancy and frailty [35]. High BMI is not an absolute contraindication to access transplantation [36], rather it should be considered as one part of an individualized risk stratification with a shifting view in the post-transplant scenario. If techniques as robotic surgery [37] could decrease the peri-operative risks for this population without increasing the overall procedure costs, they could be explored as an option for more equity in access to the common organ donor resource.

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MIB wrote the article and searched the literature; JA searched the literature; PH reviewed the article.

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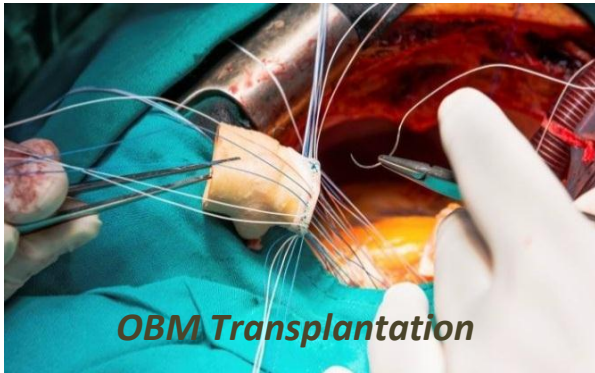
The authors have declared that no competing interests exist.

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