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Editorial

Overcoming the Body Mass Index as a Barrier in Kidney Transplantation

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Evidence suggests that obesity may contribute to the development of many acute and chronic disease states including chronic kidney disease (CKD). However, once these conditions have emerged, being obese appears to counterintuitively provide protective advantages and even survival benefits (1). Although the biologic plausibility of the so-called “obesity paradox” has remained unclear, the consistency of data is remarkable, leaving little doubt that these associations are beyond statistical discoveries. This is of particular importance in dialysis-dependent CKD patients in whom higher body mass index (BMI) is unfailingly associated with greater survival including during the time they await kidney transplantation, which may span over half a decade. The findings of the reverse epidemiology of BMI in dialysis patients challenge the very foundation of the conventional practice in transplant medicine, in that most kidney transplant centers mandate weight loss prior to kidney transplantation in obese dialysis patients, particularly those with a BMI >35 kg/m². In this context, several important questions have remained unanswered: (1) Can weight loss strategies be successfully implemented in obese transplant-waitlisted dialysis patients, and if so, can a reduction in body fat occur without loss of lean body mass? (2) Is there a difference in outcomes between intentional and unintentional weight loss, and would compulsory weight reduction approaches improve or deteriorate dialysis patient survival during the waiting period? (3) Would obesity prior to kidney transplantation have differential short- and long-term impacts on patient

and graft survival after transplantation? and (4) What are the implications of *de novo* weight gain after kidney transplantation, a frequently encountered scenario?

In this issue of the journal, Krishnan et al (2) present analyses of the associations between pretransplant BMI and posttransplant survival in a historical cohort from the UK over a 7-year period (1/2004–12/2010) and suggest that obese dialysis patients with a high BMI may be given a lower chance of kidney transplantation as shown in previous studies. An important finding is that the 1-year and 5-year patient survival was greater across all BMI groups for kidney transplantation as compared to continuing to be transplant-waitlisted. Obese dialysis patients with high BMI who underwent kidney transplantation achieved several-fold improvement in survival. Even though similar analyses were previously published from North American registries such as by Gill et al with data from 1995 (3) and Streja et al from 2001 (4), juxtapositioning findings from other countries with different demographics and clinical constellations and with more contemporary data is of major relevance here. Among newer findings by Krishnan et al is that the survival advantage of kidney transplantation becomes more obvious after several months postoperatively and continues to diverge upon longer follow-up periods. Krishnan et al (2) did not observe an increased graft loss in obese patients, although some recent studies including by Ahmadi et al (5) showed that obese patients achieve less survival benefits when compared to posttransplant patients of lower BMI ranges. The impact of larger muscle mass, however, may be in the opposite direction as shown in Figure 1, bringing up the frequently asked question as to how the utility of more appropriate body composition metrics to differentiate fat from lean body mass can be leveraged during both waitlisting period and after kidney transplantation.

Whereas we are not certain of any benefit of reinforcing a specific BMI or muscle mass threshold for kidney transplantation, many clinicians may have observed firsthand the complications that arise in morbid obesity, including prolonged kidney transplant surgery, wound dehiscence, longer hospitalization, higher rates of new onset diabetes and higher likelihood of delayed graft function (6). Data by Krishnan et al (2) and other similar data in recent years support the notion that dialysis patients with BMI >35 kg/m² benefit from kidney transplantation versus no transplantation at all; however, the number of morbidly obese patients

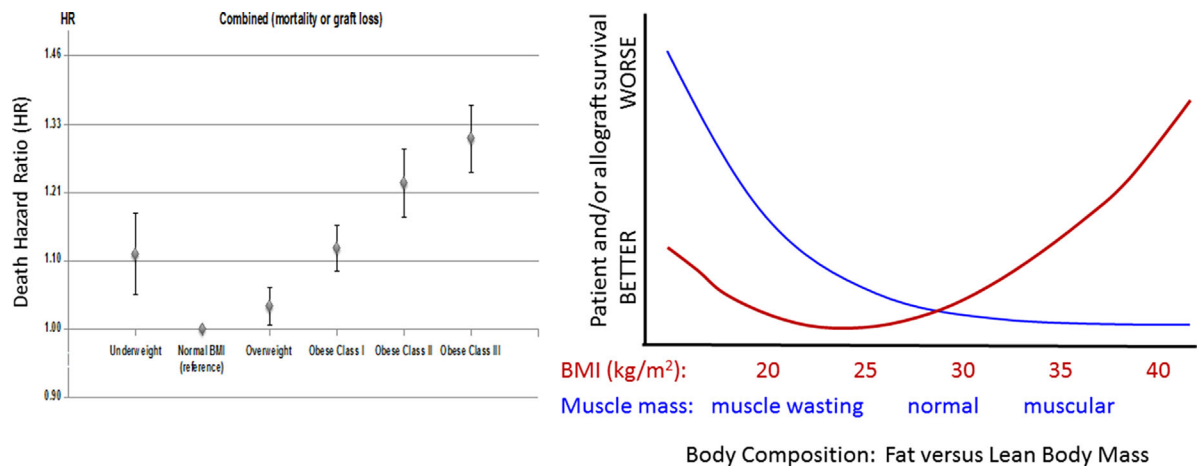


Figure 1: Left: Posttransplant death hazard ratio in 145 000 kidney transplant recipients from the SRTR 2001–2007 (5). Right: Schematic presentation of the impact of BMI versus muscle mass on kidney transplant outcomes.

in this and similar studies are quite small. Yet these studies disclose an apparent paradox, in that it is generally believed that the high-BMI patients are not offered kidney transplantation, which does not appear to be true. The very existence of these data imply that at least some morbidly obese dialysis patients do undergo transplantation. Nevertheless, in the study by Krishnan et al (2), this proportion was very small, in that out of 13 526 patients only 38 patients with a BMI >40 kg/m² received a kidney transplant and a further 28 patients of the same BMI range remained on the waiting list. Moreover, very few, if any, patients with a BMI >40 kg/m² made it beyond 2 years of follow-up in this cohort. Studies by Steja et al (4) and Ahmadi et al (5) suggest a quasi-U-shaped association in that both low and very high BMI ranges are associated with relatively fewer patients and lower graft survival compared to the BMI between 20 and 25 kg/m² although the overall survival gain is remarkable across all ranges of BMI. Whereas low BMI and unintentional weight loss may be markers of certain comorbid conditions that are associated with poor outcomes, there are no clear data about the benefits or harm of intentional weight loss in waitlisted dialysis patients.

In conclusion, the inferences from this and other recent BMI studies in kidney transplantation can be summarized as following: (1) During the years of transplant-waitlisting dialysis patients with higher BMI and in particular higher muscle mass appear to live longer and are more likely to make it alive to kidney transplantation as compared to those with lower BMI or those who lose weight unintentionally. (2) Upon kidney transplantation, obesity, and in particular morbid obesity, in kidney transplant recipients are associated with certain short-term challenges including delayed graft function. (3) In the long term and across all BMI ranges, there appear to be benefits of kidney transplantation as opposed to staying on dialysis therapy. (4) The highest long-term benefit of kidney transplantation belongs

to those with more reasonable BMI ranges as opposed to very low or very high BMI, whereas some data suggest the differential benefit of larger muscle mass in certain high BMI patients. The observed favorable outcomes of transplanted patients with higher BMI may be the result of nonrandom selection of healthier obese patients that remain unaccounted in these studies. Nevertheless, given these important data, we suggest that strict BMI threshold levels to withhold transplantation such as >35 kg/m² be revisited while other body composition metrics such as waist circumference and muscle mass assessments be added to current criteria. In-between patients across different BMI categories deserve equal chance of kidney transplantation.

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Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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