Interpreting Body Composition in Kidney Transplantation: Weighing Candidate Selection, Prognostication, and Interventional Strategies to Optimize Health

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Because obesity has reached epidemic proportions in the general US population, our national health promotion agenda articulated in Healthy People 2020 includes objectives for the achievement and maintenance of healthy body weight (1). The obesity epidemic has not spared the ESRD population. In the United States, the prevalence of obesity among kidney transplant recipients increased from 23 to 33% in the past decade (2). Body mass index (BMI), the most widely used anthropometric measure of overall body size, is recommended as part of the assessment of nutritional status for patients with ESRD by current clinical practice guidelines (3). However, the outcome implications of obesity in patients with ESRD are complex. High BMI has an established association with better survival among dialysis patients, but this association is confounded in part by underlying comorbidities and malnutrition that both reduce BMI and increase the risk for death. In contrast, transplant recipients with elevated BMI have been shown in many (but not all) studies to experience more commonly an array of adverse outcomes compared with transplant recipients with normal BMI (4,5).

It is increasingly recognized that BMI is an imperfect measure of adiposity. Measures of fat distribution such as waist circumference and waist-to-hip ratio have been directly associated with risks for cardiovascular death and mortality in dialysis-dependent and transplant patients for whom BMI was an inverse predictor of these outcomes (6, 16). Measures of sarcopenia and protein-energy malnutrition are also prognostic in ESRD and may help discriminate risk within BMI categories. In this issue of CJASN, Streja et al. (7) advance understanding of associations of body composition with transplant outcomes by linking pretransplantation DaVita hemodialysis organization and Scientific Registry of Transplant Recipients data for 10,090 renal allograft recipients in 2001 through 2007. The integrated data allowed study of BMI (as a marker of body size) and serum creatinine (as a marker of muscle mass) with posttransplantation graft and patient survival. Among the findings, the authors did not detect statistically significant differences in the adjusted risk for graft loss or posttransplantation mortality among patients with BMI values higher than the reference of 22 to <25 kg/m². However, serum creatinine level did seem to influence the outcomes. Compared with a reference serum creatinine level of 8 to <10 mg/dl, lower serum creatinine showed trends toward increased risk for death-censored graft failure and mortality in some models, and higher serum creatinine showed protective trends. The main significant findings in fully adjusted models were associations of serum creatinine ≥12 mg/dl with reduced risk for death and serum creatinine <4.0 mg/dl with increased risk for graft failure. The authors concluded that “pretransplant obesity does not appear associated with poor post-transplant outcomes” but that larger muscle mass, as reflected by higher serum creatinine, is associated with graft and patient survival advantages. Pending further studies, the authors “caution against categorical recommendation of weight loss to apparently obese dialysis patients as a requirement for transplant wait-listing.”

Streja et al. (7) should be applauded for advancing on previous registry and single-center studies by linking dialysis records to Scientific Registry of Transplant Recipients data to determine postdialysis BMI, considering serum creatinine to help distinguish muscle mass from weight, and including laboratory values not captured in the transplant registry as covariates. Beddu et al. (8) previously demonstrated that the protective association of high BMI with survival on hemodialysis is limited to patients with normal or high urinary creatinine excretion (a marker of muscle mass), whereas patients with high BMI, low muscle mass, and inferred high body fat have increased mortality. The new data of Streja et al. (7) extend the importance of combined assessment of body size and muscle mass measures to outcomes after kidney transplantation. Consistent with these findings, radiographic measures of central sarcopenia were recently correlated with mortality after liver transplantation (9).

These observational data should not lead to the conclusion that obesity is benign, and transplant pro-
fessionals should exercise caution when interpreting these findings and translating them into practice. With respect to data limitations, the study by Streja et al. (7) includes only patients who were evaluated for, listed for, and received transplants. Because many centers consider BMI in the evaluation for transplant candidacy, patients who have high BMI and receive a transplant likely are selected for better than average health or undergo transplantation at centers with specific expertise. There is also a risk for type II errors. In the model of death-censored graft failure, the point estimates suggest increased risk with BMI >35; however, the confidence intervals are wide because of the small number of patients who had high BMI and actually received a transplant (n = 820). In fact, the pattern of the point estimates closely resembles the U-shaped association of BMI with the risk for death-censored graft failure previously described by Meier-Kriesche in a larger sample of >51,000 kidney transplant recipients in the US Renal Data System (4). The study by Streja et al. (7) also has a relatively short median follow-up period of 832 days. It is possible that graft loss risk changes over time.

Even if BMI is considered a marker of adverse posttransplantation outcomes, we agree with the authors that excluding patients from transplant candidacy on the basis of BMI alone may not be appropriate. Patient-centered and societal perspectives should extend beyond relative differences among higher risk compared with ideal candidates and consider outcomes with transplantation compared with experience on long-term dialysis. Registry studies suggest that patients with high BMI receive a benefit from transplantation on mortality (10) and cardiovascular complications (11,12) compared with continued waiting, although this benefit may be lower than enjoyed by normal-weight patients. By current allocation policies, patients who benefit from transplantation should be considered candidates unless there are prohibitive risks. However, in an era of constrained organ supply, alterations in lifestyle that improve outcomes should be encouraged. Just as we require patients with alcoholic liver disease to stop drinking before transplantation, it may be reasonable to ask kidney transplant candidates to lose excess body fat and attempt to increase lean muscle mass by becoming more physically active and modifying their diet.

Posttransplantation risk adjustment also remains important to encourage centers to supply transplantation to all patients who can benefit. Because centers are graded for graft and patient survival, adjustment for the impact of adverse risk markers could be considered in center-specific outcomes metrics. Furthermore, patients with high adiposity and sarcopenia are likely to incur higher costs per case from increased risks for wound complications, pulmonary complications, and delayed graft recovery, resulting in reduced transplant center financial margins. Costs of long-term posttransplantation care also likely are increased. Without adjustment for the complexity and resource consumption associated with the care of patients with suboptimal body composition, there are significant disincentives to offer transplant access to higher risk groups.

From the individual patient management perspective, association studies offer little guidance on the potential benefits of planned weight reduction. The study by Streja et al. (7) compares patients of different BMI categories but does not study weight change within the individual or the impact on associated health problems. The article by Schold et al. (13) that is widely cited regarding outcomes associations of weight loss on the list cannot distinguish intentional weight loss from unintentional weight loss as a result of illness and other factors. Weight gain after transplantation is common. Pretransplantation obesity may exacerbate posttransplantation weight gain and contribute to development of the metabolic syndrome, which has been identified in >50% of prevalent renal transplant recipients in some samples and has been associated with impaired long-term allograft function (14). A new study from the Netherlands reported that 1-year posttransplantation BMI and BMI change were more strongly associated with death and graft failure than pretransplantation BMI (5). Thus, the transplant community should not retreat from the assertion that a healthy body weight is highly desirable and reduces long-term morbidity and mortality.

Although managing obesity is important, the authors make a strong case that the impact of sarcopenia in transplant recipients is even greater. Patients who are sedentary, protein malnourished, and debilitated have been shown to experience increased mortality after many procedures, including vascular, oncologic, and transplant surgeries. Multimodality interventions to promote gradual and consistent change in lifestyle, including structured exercise programs, dietary management, and smoking cessation, warrant evaluation for improving outcomes and possibly controlling costs by reducing the complications of obesity and frailty. Bariatric surgery also warrants further evaluation among truly morbidly obese transplant candidates because it may offer a more durable weight loss strategy (15).

Applying available data on the importance of body composition to the kidney transplant population may be facilitated by separating implications for candidate selection, risk stratification among selected candidates, and interventions to optimize health of the individual. Although current data have not defined limits of body composition that preclude clinical benefit from transplantation in patients who have passed a transplant evaluation, work such as the study by Streja et al. (7) should be pursued to help define accurate, practical measures of body composition that predict clinical outcomes. Prospective evaluations of the impact of targeted risk modification efforts including dietary changes, monitored exercise programs, and bariatric surgery are also urgently needed. Pending more evidence, we believe that as in nontransplant populations, achieving and maintaining healthy body composition on the basis of guidelines for nutrition in renal failure are important priorities for kidney transplant candidates and recipients.

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Disclosures

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References


See related article, “Associations of Pre-transplant Weight and Muscle Mass with Mortality in Renal Transplant Recipients,” on pages 1463–1473.