

INVITED COMMENTARY

Should donor body mass index influence kidney utilization by transplant centers?

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Last year the United Kingdom reported a record number of deceased organ donors but this did not translate into actual solid organ transplants performed [1]. Two explanations cited for this discrepancy are older age and increased rates of obesity among potential donors [2]. Empirical analysis of deceased donors from the United States has linked donor obesity with kidney discard rates, especially if additional donor characteristics combine to create a perception of unfavorable cumulative risk [3]. This is important because obesity is on the increase and constitutes one of the biggest public health burdens across the globe. In the United Kingdom, obesity [classified as a body mass index (BMI) of 30 kg/m² and greater] has doubled in prevalence from 15% in 1993 to 29% in 2016 [4] and is projected to increase further by 2035 [5]. However, no reciprocal increase has been observed in the proportion of obese deceased donors. This under-utilization may relate to subjective bias from transplant clinicians with regards to perceived short- or long-term risk associated with obese donor organs.

Previous studies exploring post-transplant outcomes using obese donor kidneys have shown mixed results.

Data from the United Kingdom suggest donor BMI is associated with delayed graft function (DGF) after kidney transplantation but has no impact on long-term allograft survival [6]. Reciprocally, data from the United States suggest sub-optimal long-term kidney allograft survival in the context of adjunct risks such as the combination of donation after cardiac death with extreme donor BMI (45 kg/m² or greater) [7]. Both of these studies did not specifically account for the interaction between donor and recipient BMI, which may have confounded the results. It is therefore with interest to read the analysis from Naik *et al.* [8] in this edition of *Transplant International*. Using data from the Scientific Registry of Transplant Recipients (SRTR), they analyzed 118 734 deceased donor and 84 377 living donor adult kidney transplant recipients between 2000 and 2014, with obese deceased and living donors comprising 27.2% and 21.9% of cohorts, respectively. Their primary conclusion is donor obesity (after both living and deceased donation) is an independent risk factor for long-term kidney allograft loss.

An important methodological difference in the analysis from Naik *et al.* compared to previous work was

statistical adjustment for the interaction between donor and recipient size match. However, this alone is unlikely to explain their findings. Recent extension work from Arshad *et al.* [6], using the same cohort as their previous study, observed no association between donor-to-recipient size mismatching and risk for kidney allograft loss in the United Kingdom [9]. While previous studies both identified an association between donor BMI and DGF [6,7], the analysis from Naik *et al.* suggests any effect of donor BMI on graft outcome is independent of DGF. The likeliest explanation is surreptitious pathophysiological changes are present in obese donors at the time of organ procurement. For example, obesity is associated with hyperfiltration-mediated glomerular injury through cellular and biological mechanisms that are not fully elucidated. It can be postulated that the pathophysiological effects of obesity within the donated kidney, exacerbated by ischemia-reperfusion injury in the milieu of transplantation, subsequently leads to clinical manifestations of renal injury [10].

So how should these results be interpreted by transplant clinicians? The authors are clear that their results should not dissuade utilization of obese donor kidneys as transplantation remains the optimal modality of renal replacement therapy for wait-listed candidates with end-stage kidney disease (ESKD). Mortality rates for recipients who receive obese donor kidneys (with potentially shorter graft survival) are likely to be superior compared with remaining on dialysis. Deceased donor organs traditionally considered sub-optimal and/or unfit for use can also be assessed, preserved and/or reconditioned to aid decision-making with regards to utilization [11]. Therefore, donor obesity should be no different from other unfavorable donor characteristics (e.g., age, diabetes, smoking, high-risk behavior) that kidney transplant candidates are appropriately counseled for during informed consent prior to surgery.

More dispiriting is the observation that long-term graft survival is worse for kidney transplants procured from obese living donors, raising anxiety for the long-term safety of living donors themselves. A systematic review and meta-analysis of short-term outcomes for living donors did identify a significantly higher creatinine rise (not significantly for estimated GFR) in obese donors with a BMI of 30 kg/m² and greater [12]. From a mid- and long-term perspective, living donors are observed to

have increased relative risk for ESKD (although absolute risk increase is low [13]) but this meta-analysis did not differentiate according to donor BMI. A subsequent report from Locke *et al.* [14], analyzing SRTR data for 119 769 living kidney donors linked to other datasets, described an 86% increased risk for ESKD from obese donors (adjusted hazard ratio 1.86; 95% confidence interval 1.05–3.30); for each unit increase in BMI above 27 kg/m² there was an associated 7% increase in ESKD risk. This increased risk may arise from hyperfiltration-mediated injury in the remaining kidney after donation [15]. Adaptive changes related to physiological change postdonation may be amplified for obese donors because of pathological changes related to underlying structural abnormalities. Further mechanistic work, and continued investigation of long-term registry data, is important to investigate this further. Of greater importance is the issue of counseling and mitigating risk. For example, obese living donors have increased risk for type 2 diabetes and hypertension postdonation that could aggravate any underlying obesity-related glomerulopathy [16]. Importantly, we must also not overlook those who lose weight to donate, as 73% will regain that weight within a year post-transplant (51% weighing more than predonation) [17]. Therefore, encouraging healthy lifestyle modifications before and after living kidney donation is critical and should be integrated into follow-up protocols.

Appropriate utilization of organs remains an important issue in kidney transplantation. It is widely acknowledged that increased supply of donors has come at the expense of quality such as age, co-morbidity, and obesity. By identifying a graded risk for graft loss using obese deceased and living donor kidneys, Naik *et al.* highlight the clinical impact of this observation. Should donor BMI influence organ utilization? With adequate counseling the simple answer is no but long-term surveillance and counseling of obese living donors is essential to attenuate their personal risk.

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