Transplant International

INVITED COMMENTARY

Organ donors – does size really matter?

Wai H. Lim[1,2] & Germaine Wong[3,4,5]

1 Department of Renal Medicine, Sir Charles Gairdner Hospital, Perth, WA, Australia
2 School of Medicine, University of Western Australia, Perth, WA, Australia
3 Centre for Kidney Research, Children's Hospital at Westmead, Sydney, NSW, Australia
4 School of Public Health, Sydney Medical School, The University of Sydney, Sydney, NSW, Australia
5 Department of Renal Medicine and Transplantation Service, Westmead Hospital, Sydney, NSW, Australia

Correspondence
Wai H. Lim MBBS PhD FRACP, Department of Renal Medicine, Sir Charles Gairdner Hospital, Perth, WA, Australia.
Tel.: +61864572799;
Fax: +61864573942;
e-mail: wai.lim@health.wa.gov.au

Transplant International 2018; 31: 1086–1088

Received: 7 May 2018; Accepted: 22 May 2018

Obesity is highly prevalent in the community, with over 35% of the world's adult population considered overweight or obese. Paralleling the obesity epidemic, the prevalence of obese deceased donors with body mass index (BMI) of ≥30 kg/m^2 in the United States [1], the United Kingdom [2] and Australia [3] are 25%, 25% and 22%, respectively. With the greater acceptance and utilization of obese donors for kidney transplantation, studies examining the association between obese donors and kidney allograft outcomes are important to inform clinicians and patients regarding recipients' outcomes following acceptance of kidneys from obese donors.

Few studies have examined the influence of donor BMI and short-term events in both donation after brain death (DBD) and donation after circulatory death (DCD) kidney transplants, and found that the rate delayed graft function (DGF) was substantially higher in recipients of kidneys from obese donors with BMI of >30 kg/m^2 compared to recipients of kidneys from donors with BMI of between 18.5 and 24.9 kg/m^2 (51% vs. 31%) [4]. However, these early adverse events did not translate to a reduction in long-term allograft function or outcome [5]. This is not unexpected because the presence of DGF and evolution of adverse longer term allograft and patient outcomes has not yet been clearly established, with conflicting data showing inconsistencies between DGF and poorer allograft outcome in DBD and DCD kidney transplants. These observations may reflect a marked variation in the definition of DGF, the presence of competing events and that the

doi:10.1111/tri.13283

duration of DGF may be of greater importance in determining longer term allograft outcome compared to the simple metric of presence or absence of DGF [6]. Thus, any causal relationship between early events such as DGF and long-term allograft survival could not be reliably assumed [7,8]. Notwithstanding these uncertainties, donor height and weight are explicitly considered in the calculation of the kidney donor risk index (KDRI), a prognostic score that quantifies the risk of kidney allograft failure derived from a number of donor factors known to be associated with allograft and patient outcomes [9], with the goal of assisting clinicians in promoting a more efficient method of allocating donor kidneys to potential kidney transplant candidates.

In this issue, Arshad *et al.* [10] used data from the United Kingdom (UK) registry comprising of 17 590 adult patients with end-stage kidney disease who have received a deceased donor kidney transplant between 2003 and 2015 and found that incremental BMI categories beyond the "normal" BMI category of 18.5–25 kg/m^2 was associated with a greater risk of DGF, such that recipients of kidneys from obese donors have over a 20% greater risk of DGF compared to recipients of kidneys from normal BMI donors. The observed association between donor BMI above 25 kg/m^2 and warm ischemic time may have contributed to the greater risk of DGF, but given the missing warm ischemic time data in DBD donors and 40% of DCD donors, it is difficult to draw definitive conclusion from this observation. In addition, there was no association between donor BMI and early allograft survival at 90 days, perhaps allaying the concern that obese donors may pose a technical challenge for the transplant surgeon. Given that donors with higher BMI were significantly older and have more prevalent comorbid conditions such as diabetes, these donor characteristics are likely to have mitigated the effect of donor BMI in predicting longer term allograft outcome.

Similar to other observational studies, observational data are prone to biases including the presence of selection and reporting bias, as well as the effect of residual and unmeasured confounders (e.g. utilization of left versus right donor kidneys, variations in the type and intensity of induction and maintenance immunosuppression, differences in donor KDRI or severity of donor comorbid conditions) that may have influenced the association between donor BMI and outcomes. In addition, observations within individual transplant centres (or clusters) may be correlated and cannot be understated. A random effect model that considers the dependent "treatment effects" within centres would have reduced the biases and adjusted the effects for dependency between correlated data.

Clinicians should also be aware of the limitations when interpreting the findings of the studies examining the influence of donor BMI on kidney transplant outcomes. First, consideration of donor–recipient body size mismatch (rather than considering donor and recipient size as separate variables) may provide better assessment of the impact of donor size since the body sizes of the recipients are likely to directly modify the influence of donor size on kidney allograft outcomes [11]. Second, even though BMI is an accepted surrogate metric of body size, body surface area (BSA) may be a more reliable indicator of nephron mass [12], particularly for paediatric recipients [13]. Third, the relationship between donor BMI (and BMI categories) may not be linear and researchers should contemplate of using BMI as a continuous variable or in finer divisions to determine the most appropriate BMI thresholds (rather than using the World Health Organization predefined thresholds) associated with allograft outcomes.

Findings from this study suggest that recipients of obese donor kidneys are more likely to experience DGF, but long-term allograft survival does not appear to be affected by donor size. Nevertheless, the central question as to whether BMI or BSA is a better metric of body size or nephron mass remains unanswered. To further clarify the association between donor size and kidney transplant outcome, future studies should consider the relative or absolute mismatches in donor and recipient size (including the utility of different metrics to calculate body sizes) and whether this association is modified by other donor and recipient characteristics such as age and gender.

Funding

The authors have declared no funding.

Conflicts of interest

The authors have declared no conflicts of interest.

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