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LETTER TO THE EDITORS

Response to Kute: 'Facilitators to National Kidney Paired Donation Program'

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Sirs,

We read with interest the letter from Dr Kute, *et al.* [1], regarding our article 'Comparison of time on the cadaveric kidney donor waitlist versus time on the kidney paired donation registry in the Australian program' published in the October, 2012 edition of *Transplant International* [2]. The authors raise several important points with regard to kidney paired donation (KPD), which need to be interpreted in the context of the country or region where a KPD programme is operating, the individual centres' experiences in managing immunological complex patients and the available resources.

Since the concept of KPD was first introduced [3], improved outcomes of ABO incompatible transplantation associated with modern immunosuppression [4,5] and in many cases with standard immunosuppression [6] have removed an important source on unsensitized recipients from potential KPD pools [7,8]. Thus, in many developed countries with sufficient resources ABO incompatible transplantation has become standard of practice, and unsensitized ABO incompatible pairs tend to proceed to directed live donor transplantation, unless the high baseline anti-ABO antibody titre is not amenable by apheresis [5]. Removing unsensitized ABO-incompatible pairs from a KPD programme has the significant disadvantage of reducing the pool size and thus the chance of matching. However, Kute *et al.* point out that in developing countries like India, the costs of antibody removal protocols and risk of infections in ABO incompatible renal transplantation make a KPD programme more attractive [1]. As a consequence, a larger number of donors are available to be matched to recipients registered in a KPD programme. This observation is very important and useful to advice policy makers at a regional or national level.

The authors also advocate wider participation of compatible live donor pairs in a KPD programme [9], also known as unbalanced KPD [10–12], which occurs when a compatible pair (say O donor with A patient) participates in KPD helping an incompatible pair also receive a kidney. Patients are most amenable to participate in unbalanced KPD if they perceive a benefit from trading away a compatible donor. One benefit would be if matching allocation can guarantee a better HLA-matched KPD donor, which will allow less immunosuppression and lower infective risk, which is particularly important in developing countries as identified by Kute *et al.* [1]. To achieve this goal, the metrics of the matching software are critical and an algorithm that considers HLA matching [13], rather than a virtual cross-match approach [8] is preferred. Other benefits in unbalanced KPD can be considered, for instance, the patient of the compatible pair will, in exchange, receive priority in the cadaveric list in the event that the live kidney he receives through KPD fails in the future. So by participating in exchange, the patient of the compatible pair will receive a 'guarantee' in the future for cadaveric list. While in developed countries the willingness to register compatible pairs may be very limited, the experience from countries like India is likely to demonstrate that inclusion of a small number of ABO and HLA compatible pairs will result in a significant increase in the number of matched pairs. By demonstrating that a pair including a highly-sensitized recipient at one centre could be transplanted by including an ABO and HLA compatible pair at the same centre should encourage the transplant community to include these pairs in the KPD programme.

The probability to find a suitable pair for a KPD exchange is greatly influenced by the pool size. Because recipients with broad sensitization only have a limited number of rare donor HLA genotypes they can source [7,14], any attempt to reduce the number of potential donors with rare genotypes should be avoided. This includes considering national rather than regional or single centre programmes. The concern that transporting live donor organs rather than moving the donor to the recipient's centre may result in inferior outcomes because of prolonged cold ischaemia time (CIT) is unjustified in view of the US experience with median CIT of 7.2 h (range 2.5–14.5) [15] and our own with median CIT of

5.8 h (range 2.1–13.4) (unpublished) with no case of delayed graft function related to prolonged CIT. There are some important advantages of organ transport, including preservation of donor anonymity, undisrupted family care and support and donor suitability assessment in accordance with the practices of the centre performing the donor surgery. When transport is involved in multi-center KPD, it is critical to have a central coordination centre to organize the KPD (before the transplant) and to time the operations and organ transport (at the time of the transplant). We do agree with the authors that more experience is needed to determine the outcome of transplants from live donors aged $\geq$65 years to younger recipients. Some reassurance with regard to this concern comes from a recent report suggesting that recipients of live donor kidneys from older donors up to 70 years of age have similar patient and graft survival [16] than recipients of younger donors, albeit with inferior, but not progressive renal function at 3 years. In our KPD programme, donors older $\geq$70 years are not accepted; moreover, while our KPD allocation software ignores donor–donor or donor–recipient age differences in the allocation [8] based on the experience with directed live donors in Australia [17], it won't allow an age gap of >30 years between an older donor and a younger recipient. Our observation that even highly-sensitized patients, who usually have excessively long waiting time on a deceased donor programme can be matched and transplanted through a KPD programme within a relatively short period on the KPD registry [2] is an additional argument favouring establishment of KPD in countries where maintenance dialysis is not a viable option. In 2011, 9.6% of live donor kidney transplants in Australia were enabled by the national KPD programme even without including compatible pairs. We believe that if most unsensitized ABO incompatible pairs and even ABO and HLA compatible pairs are included in a live donor exchange programme the proportion of live donor kidney transplants through KPD could be substantially higher.

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Conflict of interest

None.

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References

1. Kute VB, Vanikar AV, Shah PR, *et al.* Facilitators to National Kidney Paired Donation Program. *Transplant Int* 2013; doi:10.1111/tri.12078.
2. Ferrari P, Fidler S, Woodroffe C, Tassone G, D'Orsogna L. Comparison of time on the deceased donor kidney waitlist versus time on the kidney paired donation registry in the Australian program. *Transplant Int* 2012; **25**: 1026.
3. Rapaport FT. The case for a living emotionally related international kidney donor exchange registry. *Transplant Proc* 1986; **18**: 5.
4. Tanabe K. Japanese experience of ABO-incompatible living kidney transplantation. *Transplantation* 2007; **84**: S4.
5. Tyden G, Kumlien G, Genberg H, Sandberg J, Lundgren T, Fehrman I. ABO incompatible kidney transplantations without splenectomy, using antigen-specific immunoadsorption and rituximab. *Am J Transplant* 2005; **5**: 145.
6. Flint SM, Walker RG, Hogan C, *et al.* Successful ABO-incompatible kidney transplantation with antibody removal and standard immunosuppression. *Am J Transplant* 2011; **11**: 1016.
7. Ferrari P, Fidler S, Holdsworth R, *et al.* High transplant rates of highly-sensitised recipients with virtual crossmatching in kidney paired donation. *Transplantation* 2012; **94**: 744.
8. Ferrari P, Fidler S, Wright J, *et al.* Virtual crossmatch approach to maximize matching in paired kidney donation. *Am J Transplant* 2011; **11**: 272.
9. Ferrari P, De Klerk M. Paired kidney donations to expand the living donor pool. *J Nephrol* 2009; **22**: 699.
10. Roth AE, Sonmez T, Unver MU. Kidney paired donation with compatible pairs. *Am J Transplant* 2008; **8**: 463.
11. Kranenburg LW, Zuidema W, Weimar W, *et al.* One donor, two transplants: willingness to participate in altruistically unbalanced exchange donation. *Transpl Int* 2006; **19**: 995.
12. Ratner LE, Ratner ER, Kelly J, *et al.* Altruistic unbalanced paired kidney exchange at Columbia University/New York-Presbyterian hospital: rationale and practical considerations. *Clin Transplant* 2008; 107.
13. Saidman SL, Roth AE, Sonmez T, Unver MU, Delmonico FL. Increasing the opportunity of live kidney donation by matching for two- and three-way exchanges. *Transplantation* 2006; **81**: 773.

14. Montgomery RA, Lonze BE, Jackson AM. Using donor exchange paradigms with desensitization to enhance transplant rates among highly sensitized patients. *Curr Opin Organ Transplant* 2011; **16**: 439.
15. Segev DL, Veale JL, Berger JC, *et al.* Transporting live donor kidneys for kidney paired donation: initial national results. *Am J Transplant* 2011; **11**: 356.
16. Balachandran VP, Aull MJ, Charlton M, *et al.* Kidneys from older living donors provide excellent intermediate-term outcomes after transplantation. *Transplantation* 2012; **94**: 499.
17. Ferrari P, Lim W, Dent H, McDonald SP. Effect of donor-recipient age difference on graft function and survival in live-donor kidney transplantation. *Nephrol Dial Transplant* 2011; **26**: 702.