INVITED COMMENTARY

Complex kidney donors: should we stretch our limits?

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Live donor kidney transplantation is the preferred treatment for many patients with kidney failure. In countries with low rates of deceased organ donation, live donors are often the only opportunity for these patients to receive a kidney transplant. In Japan and many others Asian countries such as India and Philippines, live donor source accounts for over 80% of all kidney transplants. This compared to less than 50% in United Kingdom, United States, and Australia [1,2]. Consequently, marginal live kidney donors are being considered for transplantation but there are growing concerns that such practices may inadvertently expose these live donors to unacceptable risks of adverse outcomes postdonation compared to the average live donor. The current Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines suggest a cautious approach in the selection of nonstandard live kidney donor candidates because every effort should be made to safeguard our living donors against unnecessary harms [3]. Post-transplant outcomes also differ between live donor types, with recipients of older live donor kidneys being associated with a higher risk of allograft failure and poorer allograft function compared to recipients of younger live donor kidneys [4,5], paralleling the differences in allograft outcome between expanded versus standard criteria deceased donor kidney transplants [6].

Prior work, conducted in Western countries, indicated the estimated postdonation lifetime risks of kidney failure, cardiovascular disease, and all-cause mortality are up to 11 times higher compared to

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healthy nondonors [7,8]. In the United States, the lifetime risk of kidney failure varied by age and race, with donors 60 years or older and black donors having the highest cumulative incidence of kidney failure at 15 years [7]. Similar findings were observed in another Norwegian study and showed that kidney donors were 30–40% more likely to experience cardiovascular disease and all-cause mortality compared to healthy nondonors [8]. In this analysis, the marginal live donors (29% with hypertension, 24% aged >70 years, and 34% with body mass index >30 kg/m^2) were excluded so granular postdonation details of these high-risk donors, particularly in the long-term are unknown.

In this issue, Kinoshita *et al.* [9] retrospectively reviewed data from a single center in Tokyo, Japan, to examine the postdonation kidney function of marginal live kidney donors and also the allograft outcome of recipients of these donor kidneys compared to standard live donor kidneys, the former being the critical aspect of this research work. Of these donors, 99 (34%) were considered as medical complex live donors (MCLD), defined by the Japanese Transplantation Committee as donors aged 71–80 years, body mass index of 30–32 kg/m^2, blood pressure of ≤130/80 mmHg with antihypertensive agents (and albuminuria of <30 mg/g creatinine), diabetes mellitus with glycated hemoglobin of ≤6.5% maintained on oral hypoglycemic agents (and albuminuria of <30 mg/g creatinine), or glomerular filtration rates of 70–80 ml/min/1.73 m^2 (measured using inulin, radioisotopes, or creatinine clearance methods) [10]. In the cohort of MCLD, 30% of donors were aged 71–80 years, 66% had hypertension, and 22% had diabetes and 24% with more than 1 risk factor. Over a median follow-up period of 4.5 years for live donors, they found a lower pre- and postdonation eGFR in MCLD compared to standard live donors (mean difference of 2–3 ml/min/1.73 m^2) but the average annual change in eGFR was almost identical between MCLD [+0.27 (95% confidence interval −0.54 to 1.09)] and standard live donors [+0.26 (95% confidence interval −0.03 to 0.56)]. These findings are somewhat encouraging, suggesting the presence of medical abnormalities may not have a deleterious impact on the short- to medium-term change in eGFR. However, data pertaining to the longer-term expected renal and patient survivals or quality of life data of these donors were not available. Other pressing concerns, including the perioperative risk and events, related hospital morbidity and readmission rates for older patients and those with prevalent vascular risk factors such as diabetes were also not considered. Similar to other retrospective studies, observational data are prone to selection and reporting bias, as well as the influence of residual and unmeasured confounders (e.g., duration and severity of hypertension, change in donor vascular risk factor profile, and body mass index postdonation) on the association between exposure and outcome.

Individual transplant program and clinicians have key responsibilities to adhere to the "do no harm" dictum when selecting potential live donors for transplantation. While we recognize the immense survival advantages for the recipients receiving the donor kidneys and the need to respect donor autonomy, the short- and long-term postdonation risk of peri-operative complications, hypertension, kidney failure, and mortality risk among our life donors are not negligible compared to healthy nondonors. The likelihood of these adverse events occurring among our complex medical donors will probably be much higher than our standard live donors. Therefore, there is an absolute obligation to ensure our donors understand the risks and are as informed as they can be.

Protection of the health risk and outcome of potential live donors is paramount to all transplant programs, and donor clinicians should ensure a multidisciplinary team-based approach and integrate the service of an independent live donor advocate and psycho-social counseling in the clinical decision-making and informed consent processes when considering a MCLD for kidney donation. Each transplant program must have certain predetermine acceptable risk thresholds when considering MCLD for kidney donation. A standardized country-specific approach should also be implemented to facilitate quality assurance process and ensure each transplant program has in place a rigorous follow-up process to capture the long-term safety data of each MCLD.

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