

INVITED COMMENTARY

Insights from a ten-year, prospective study of live kidney donors

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Live organ donation poses a complicated set of ethical issues for transplant professionals who carry the dual responsibilities of promoting their patients' health and well-being [1]. With donor nephrectomy, we enable patients to assume health risks. On the other hand, many donors describe the gift of an organ as consistent with their sense of duty or moral well-being [2–4]. These individuals view organ donation as the right thing to do. It is our responsibility, then, as a transplant community, to reveal the long-term consequences of donation and thereby ensure that a potential donor can make an informed choice. Over the past ten years, the transplant community has benefitted from innovative research to characterize the medical risk to donors, including studies of survival, cardiovascular disease, end-stage renal disease, and outcomes in pregnancy. Most of these research advances have relied upon large retrospective cohorts of donors with appropriate comparator groups and linkage to administrative health databases that record important medical events such as initiation of dialysis [5–9]. However, assessing the long-term

well-being and quality of life of live kidney donors will require different approaches and ideally, prospective data. With this study of 100 live kidney donors followed over 10 years, Klop, Janki *et al.* have contributed valuable new information about health and quality of life for this unique group of individuals [10].

This article reports outcomes of kidney donors previously randomized for a trial of laparoscopic versus mini-laparotomy nephrectomy at two Dutch transplant centers. Participants underwent annual laboratory and blood pressure evaluations. They also completed the Medical Outcomes Study Short Form-36 (SF-36) and the Multidimensional Fatigue Inventory-20 (MFI-20) self-assessments. The investigator team should be congratulated for the prospective design of their study and the excellent follow-up rate: Annual data on kidney function and blood pressure were available in 90%, and 80% of donors responded to the SF-36 and MFI-20. Ninety-four percent of donors were alive at ten years. With respect to the development of hypertension, the authors found no difference

in the median systolic blood pressure following vs. prior to kidney donation (130 and 128 mmHg, respectively, $P = 0.622$). New-onset hypertension did occur in 23 patients (25.6%); these patients had a mean age of 57 compared to 45 years for those who remained normotensive ($P = 0.001$).

The results reported about renal function pose some challenges to interpretation. It appears that the authors used the Cockcroft–Gault formula to estimate creatinine clearance. They report that creatinine clearance remained fairly stable between one and 10 years of follow-up (average 76.1 ml/min compared to the 10-year value of 76.6 ml/min, $P = 0.858$). At 10 years, approximately 19% of the cohort had low creatinine clearance in the 30–60 ml/min range. Compared to other donors, those with low follow-up creatinine clearance had significantly lower “baseline” creatinine clearance (median 60 ml/min versus median 94 ml/min for the group with creatinine clearance > 60 at 10 years, $P < 0.001$) and were older at follow-up (median age 75 vs. 57 years, $P < 0.001$). A median baseline pre-nephrectomy creatinine clearance value of 60 ml/min begs the question of whether these were truly baseline values or instead early postdonation values. Many readers will probably desire additional information about this group, so that donor selection committees in the future can eliminate individuals at risk of deterioration in renal function. As the authors acknowledge, the interpretation of the blood pressure and renal function results are hindered by the absence of a comparison group of nondonors. Moreover, a sample size of 100 individuals may be insufficient to capture rare but important events such as progression to dialysis or death.

In the realm of self-reported quality of life, Klop, Janki *et al.* lend important insights into donor status 10 years of distant from donation. Across the domains of the SF-36 (which include physical health, mental health, emotional health and social functioning), the donors had self-assessments that were as good as or better than norms for the age-adjusted general population. These findings of good quality of life confirm the reassuring results from other high-quality donor studies, including the RELIVE cohort and a cohort assembled by the DONOR network [11,12]. Klop, Janki *et al.* also reported that, after undergoing nephrectomy, the donors had decreased SF-36 scores in the realms of physical function (-7.0 , $P < 0.001$), bodily pain (-7.0 $P = 0.001$) and general health (-7.1 $P < 0.001$). MFI-20 scores were higher (worse) in general fatigue ($P < 0.001$), physical fatigue ($P < 0.001$), activity level ($P = 0.019$), and motivation ($P = 0.030$). Some diminishment in quality of life is plausibly attributed to the aging process over ten years, but without an appropriate comparison group, it is not possible to parse the contribution of kidney donation.

At this point in transplantation, we can present prospective donors with compelling data regarding the anticipated medical consequences of living with one kidney. The majority of studies suggest that live kidney donors enjoy survival and cardiovascular health that is similar to healthy individuals and better than the general population [6,8,9,13]. The risk of end-stage renal disease is substantially increased by kidney donation, although the rate is $< 1\%$ by 15 years [5]. For donors who subsequently become pregnant, kidney donation is associated with higher risks of preeclampsia and gestational hypertension [7]. We can also counsel donors about the potential financial burden arising from lost wages, travel and healthcare costs, and potential difficulties obtaining insurance coverage [14]. With respect to quality of life, a number of previous studies have reported good quality of life for kidney donors [11,12]. However, these studies have generally been limited by short-term follow-up, retrospective design, or use of administrative databases, introducing the potential for selection bias [15].

Klop, Janki *et al.* have demonstrated the feasibility of a prospective cohort study in which close contact is maintained with live organ donors over a long period. This work is resource-intensive and unlikely to be successful through routine follow-up by transplant center staff; therefore, it will require investment, experienced investigators, and creative methods to keep the donor population committed to ongoing communication. Large prospective studies are particularly difficult to conduct in countries like the United States without centralized medical care. Moreover, as organ donation is a singular decision, prospective donor cohorts should be assessed with both generic quality of life instruments such as the SF-36 as well as specific, validated instruments designed to assess the donor experience. For example, Rodrigue *et al.* have developed questions that measure donor expectations about personal emotional growth and changes in relationship dynamics with the organ recipient [3].

Finally, our understanding of the consequences of kidney donors will be enriched if we ask donors to consider whether, 10 years later, they believe that organ donation was the right thing to do. When we have that information, transplant professionals and prospective donors may feel more comfortable that the trade-offs between medical risks and overall well-being were worth the decision to give up an organ.

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