

Letter to the Editor

Counseling Potential Donors to the Risk of ESRD After Kidney Donation: Glass Half-Full or Half-Empty?

To the Editor:

Living kidney donation accounts for about 6000 kidney transplants in the United States annually (1). While it is important to quantify risks to potential donors, studies examining donor outcomes are limited and the appropriate control group is debatable. In 2009, Ibrahim et al (2) reported, in a single center study, 11 cases of end-stage renal disease (ESRD) out of 3698 donors between 1963 and 2007 (rate of 0.3%). Though not matched directly to a healthy cohort, they reported similar rates of ESRD compared to the general population. Nephrologists have long craved a large-scale comparison study to help counsel potential donors about the risk of ESRD.

A recent publication by Muzaale et al (3) tried to fill this gap by identifying 96 217 donors from 1994 to 2011 via the Organ Procurement and Transplantation Network (OPTN) and comparing them to healthy participants from the National Health and Nutrition Examination Survey (NHANES) study. The authors identified 9364 controls from NHANES that were considered healthy enough to donate using strict inclusion criteria. Using iterative radius matching and bootstrapping (4), they extrapolated additional data points to come up with an *n* of 96 217 healthy, nondonor controls. However, there are some concerns with this technique. First, while technically valid, the article did not clearly state the value (or potential pitfalls) of generating control data points using bootstrapping. The actual ratio of donors to available control patients was 10:1 prior to bootstrapping. This same author group published a similar study in 2010 from the same OPTN cohort to examine peri-operative mortality for donors, however only used 9364 NHANES controls (5). Second, there were considerable missing data points in the donor group, which could lead to errors when matching. Third, over a 15-year follow-up, the event rate of ESRD was low in the healthy nondonor population, and there may have not been sufficient follow-up to appreciate their risk of ESRD. For example, there were no cases of ESRD in the white nondonor control subgroup. These limitations should be taken into consideration when assessing the risk of ESRD of donors in comparison to the control group of this study. Other outcomes, such as cardiovascular events, hypertension, albuminuria and decreases in GFR may be equally relevant to disclose to potential donors. The study also does not report the cause of ESRD

among donors, which is of interest, since the vast majority of donors were related to their recipients and had double the incidence of ESRD compared to unrelated donors (34.1 vs. 15.1 per 10 000), implying a potential genetic predisposition to developing ESRD. Nevertheless, the study concludes that rates of ESRD are higher in live donors compared to similar individuals that did not donate, but still much lower than in the general population.

In sum, this is the first large scale, national database analysis to show a small increased risk of ESRD in kidney donors. By reporting absolute risk, rather than relative risk (8× higher risk), one may minimize the difference between donors and controls. This may be most appropriate, as the risk does indeed appear to be small. Given concerns with matching, the most valuable data from this study may be the ESRD event rate in donors — 1 out of 133 Black donors, 1 out of 300 Hispanic donors and 1 out of 440 White donors. Is this type of risk acceptable for a parent donating to their child? What about a child donating to a parent? What about for an altruistic donor? Should recommendations change for Black or Hispanic donors? Can we identify genetic predispositions to chronic kidney disease/ESRD (i.e. APOL1 gene mutations) that should preclude donation? Overall, there are many questions that remain unanswered but this study identifies a potential, albeit small, increased risk of ESRD after donation and highlights the need for further research.

Regarding article entitled: "Risk of End-Stage Renal Disease Following Live Kidney Donation" published on JAMA 2014; 311(6):579–586. doi:10.1001/jama.2013.285141.

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Disclosure

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