Selected Summaries

The live kidney donor: Do we now understand the risks better?

Grams ME, Sang Y, Levey AS, Matsushita K, Ballew S, Chang AR, Chow EK, Kasiske BL, Kovesdy CP, Nadkarni GN, Shalev V, Segev DL, Coresh J, Lentine KL, Garg AX; Chronic Kidney Disease Prognosis Consortium. (Division of Nephrology, Johns Hopkins University School of Medicine, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, and the Departments of Surgery and Epidemiology, Johns Hopkins University, Baltimore; Division of Nephrology, Tufts Medical Center, Boston; Division of Nephrology, Geisinger Medical Center, Danville, Pennsylvania; Department of Medicine, Hennepin County Medical Center, University of Minnesota, Minneapolis; Memphis Veterans Affairs Medical Center and University of Tennessee Health Science Center, Memphis; Division of Nephrology, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, USA; Medical Division, Maccabi Healthcare Services and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; Centers for Abdominal Transplantation and Outcomes Research, Saint Louis University, St Louis; Departments of Medicine and Epidemiology and Biostatistics, Western University, and the Institute for Clinical Evaluative Sciences, London, Ontario, Canada). Kidney-failure risk projection for the living kidney-donor candidate. *N Engl J Med* 2016;**374:**411–21.

SUMMARY

Over 25 000 living donor kidney transplants are done every year around the world; about 6000 in India. It is a challenge to communicate risks associated with kidney donation to donors in view of the limited understanding of the long-term risk of development of kidney disease in a healthy population and whether the risk is different in kidney donors.

Grams and colleagues took advantage of the data collected by the Chronic Kidney Disease Prognosis Consortium to quantify the risk of developing kidney failure in a population similar to the one that would be composed of typical kidney donors. Close to 5 million people from seven general population cohorts—six from North America and one from Israel—composed mostly of white men, were followed up for 4–16 (mean 6.4) years. Those with a eGFR <45 ml/1.73 m^2, insulin-dependent diabetes, those on four or more antihypertensive drugs or with uncontrolled hypertension, albumin creatinine ratio (ACR) >300 mg/g, known cardiovascular disease, stroke or peripheral vascular disease were excluded from analysis since they would not be kidney donors. There were a total of 3900 events of end-stage renal disease (ESRD). The authors computed association between 13 health characteristics and development of ESRD: age, race, sex, eGFR, ACR, systolic blood pressure, presence of non-insulin-dependent diabetes mellitus (NIDDM), use of antihypertensive drugs, smoking status, body mass index, low-density lipoprotein (LDL)–cholesterol and history of kidney stones. This led to generation of coefficients that were used to calculate the risk of developing ESRD over 15 years or over lifetime. Their base case was a donor with the age of 45 years, systolic BP of 120 mmHg, urine ACR of 4 mg/g, BMI of 26 kg/m^2, non-smoker, and without diabetes or hypertension. They found a graded association of development of ESRD with eGFR, blood pressure, ACR and smoking. Diabetes conferred the single highest risk.

The highest 15-year risk of ESRD was in middle-aged African–American men. As expected, the risks of short-term ESRD increased progressively for donor-candidates from the age of 20 to 60 years, but fell in older donor-candidates. An important finding from the study is that the reluctance to use older donors may be misplaced provided they are healthy at the time of donation, since they have a lower lifetime risk of developing ESRD compared to younger donors.

The authors applied the same equation to 57 508 donors from the US Organ Procurement and Training Network over a 10-year period starting 2005. The 15-year risk of developing end-stage kidney failure among those who actually donated a kidney was 3.5–5.3 times higher than those who did not donate but were eligible to do so, but varied according to race and sex. Overall, in the absence of donation, the projected 15-year risk (in the absence of donation) for the average black men donor candidates was 0.21% and the observed risk (after donation) was 0.96%. The corresponding projected and observed 15-year risks among black women were 0.12% and 0.59%; the risks among white men were 0.07% and 0.34%, respectively, and the risks among white women were 0.04% and 0.15%, respectively.

The editorial that accompanies the paper describes a few of the study limitations, especially related to the use of short-term data to make long-term estimates.[1] For example, NIDDM would not cause ESRD during this relatively short observation period, leading to underestimation of risk. The methodology used in this study favours diseases that progress and cause ESRD relatively quickly. This study could not have factored in any disease that has an eGFR decline <12.5 ml/minute/year in a 20-year individual with a starting eGFR of 100 ml/minute. The editorial suggests that the association observed with hypertension and proteinuria could have been confounded by pre-existing kidney disease.

Older studies that followed up donors for up to 12 years showed that their long-term kidney risks were similar to the general population.[2] However, recent realization has led to studies that compared development of complications in donors with that in selected controls who matched the donors, who are typically healthier than the general population. An American study[3] showed 8-times increased risk over a 7.6-year follow-up, and a Norwegian study[4] showed an 11-fold increase in risk over a 15.2-year follow-up.

COMMENT

It is a challenge to communicate long-term risks to patients, particularly for low-frequency events, in situations where decisions are based on emotions. An individual, who is faced with certain death as dialysis may not be available, cannot be expected to think rationally. This happens when the welfare of the donor depends upon the health of the recipient, such as between spouses or when the loss of a breadwinner adversely affects children.

What are the implications of this study for Indian donors and transplant surgeons? These results undoubtedly represent an advance in terms of refining risk calculation, but we should be cautious in applying the same data to other populations around the world. In particular, using North American data for people with different body type and composition, dietary habits, baseline eGFR and age at which people donate is fraught with risks.

Finally, it must be pointed out that for most donors, the rate of ESRD is low: <1% over 15 years.

Besides the fact that we need to develop an appropriate tool for conveying risk to our donors in a way they can understand, it is shameful that we do not have our own data on long-term outcome of living kidney donors despite having the largest population of such people.

It is worth mentioning a report from the Sind Institute of Urology and Transplantation, Karachi, Pakistan.[5] They followed up 2696 donors for up to 25 years, and found that these donors had done well. However, they could not follow up over 500 additional donors, and the outcomes in those could have a crucial bearing on the overall data.

Finally, we must develop the art of having nuanced conversation with our donors—convey risk as far as possible factoring in their background. Developing tools that aid in decision-making, such as the online risk calculator at *www.transplantmodels.com/esrdrisk* will be helpful. We can best serve our population by generating our own data. Since these studies take time, it is a pity that we have not made better use of the time that has already gone by.

REFERENCES

1 Steiner RW. The risks of living kidney donation. *N Engl J Med* 2016;**374:**479–80.
2 Ibrahim HN, Foley R, Tan LP, Rogers T, Bailey RF, Guo H, *et al*. Long-term consequences of kidney donation. *N Engl J Med* 2009;**360:**459–69.
3 Muzaale AD, Massie AB, Wang MC, Montgomery RA, McBride MA, Wainright JL, *et al*. Risk of end-stage renal disease following live kidney donation. *JAMA* 2014;**311:**579–86.
4 Mjøen G, Hallan S, Hartmann A, Foss A, Midtvedt K, Øyen O, *et al*. Long-term risks for kidney donors. *Kidney Int* 2014;**86:**162–7.
5 Rizvi SAH, Zafar MN, Jawad F, Aziz T, Hussain Z, Hashmi A, *et al*. Long-term safety of living kidney donation in an emerging economy. *Transplantation* 2016;**100:** 1284–93.

VIVEKANAND JHA
The George Institute for Global Health, India
219-221, Splendor Forum
Plot No. 3, Jasola District Centre
New Delhi
vjha@pginephro.org