Editorial Perspective

Donor Kidney Function – Are We Focusing on the Trees or the Forest?

Bryan N. Becker

University of Illinois-Chicago, Chicago, Ill., USA

The idea that a healthy individual would take a surgical risk, become a patient, and donate an organ to another individual is now commonplace in today's transplant environment. Given overarching trends in the US population such as obesity and aging, it is likely that donor risk assessment is transforming too at transplant centers across the country. At the core of any living kidney donor assessment is the evaluation of kidney function. These two contrasting articles, one by Tan et al. [1] and the other by Rao et al. [2], focus on assessing kidney function in potential donors.

Tan et al. [1], advocate for measuring true glomerular filtration rate (GFR) along with imaging kidneys to determine renocortical volume as a surrogate for identifying glomerulopenia. They also offer an alternative, approximating creatinine clearance after cimetidine blockade of creatinine secretion for 3–4 days.

Rao et al. [2] present a different perspective, emphasizing three aspects of 'gold standard' GFR techniques that they view as concerning. These are variability in technique and measurement using ^{125}I -iothalamate GFR, radiation risk, and cost. These authors base part of their argument on general population data and suggest that a precise estimate of kidney function 'when the GFR is between 75 and 105 ml/min/1.73 m² may not be critical' [2]. Thus, they conclude that the routine use of a 'gold standard' GFR test with iothalamate is not necessary.

Both articles define a defensible and steadfast stance on the issue of living kidney donor GFR assessment. How do we reconcile these opposing views for the benefit of the donors and the recipients of those kidneys? The precision of GFR measurement, while important, has to be considered in light of the fact that living kidney donation as we have practiced it in the USA for the last decade appears to be safe. Perioperative and long-term mortality rates have not significantly changed and are similar to those of age- and comorbidity-matched Third National Health and Nutrition Examination Survey (NHANES III) participants [3].

That noted, rates of living donor kidney transplantation finally trended up in 2009 after several consecutive years of a decrease [4]. Some of this increase in living donors might be attributable to a willingness of transplant centers to examine non-traditional potential donors as an important new source of living donors. Such potential donors may be older individuals, individuals with mild hypertension or modest levels of obesity [5]. As Tan et al. [1] note, application of estimating equations to a population of healthy individuals has the risk of mislabeling individuals with chronic kidney disease. Yet, meta-analysis from more than 4.7 million person-years of observation suggests that these same estimating equations are predictive of outcomes in the general population [6]. To dismiss the use of estimating equations would be to eschew this

important observation and the inherent cost-effectiveness of these equations.

Using such estimating equations leaves a gap in assessing kidney function that is clinically significant for the candidacy of a potential donor. This gap lies between individuals with excellent kidney function and those with GFR levels clearly <60 ml/min/1.73 m². Individuals who fall into this gap, if otherwise healthy, probably do mandate a 'gold standard' GFR test. Not only is precise measurement of GFR for such individuals important for the potential donor, but data suggest that recipient outcomes are better for those who receive donor kidneys from individuals with higher levels of GFR [7].

Interestingly, Tan et al. [1] and Rao et al. [2] raise two other important issues in the contrasting articles. First, multiple imaging procedures can raise the risk of cumu-

lative radiation exposure over time. The argument that the one-time assessment of kidney size or a nuclear GFR study is dangerous may seem hyperbolic but the test deserves consideration in the context of the imaging burden that any potential donor may have experienced up to that point in life. Second, both articles point to the need to develop better science around understanding the intersection between functional, histological, and imaging-related data as they relate to kidney work over time.

What we know at present is that transplant centers have been choosing donors with relative success. Can we do a better job? Certainly. Is it necessary to expand our testing to a 'gold standard' GFR test in every potential donor? Probably not at present, based on existing evidence and outcomes and weighing the other features that inform our healthcare delivery such as cost and safety.

References

- 1 Tan JC, Busque S, Ho B, Myers BD: Formal assessment of donor kidney function: pro. *Am J Nephrol* 2011;33:198–200.
- 2 Rao PS, Jindal RM, Elster EA, Salifu MO: Iothalamate scan does not have role in the routine measurement of kidney function in donors of living kidney transplantation. *Am J Nephrol* 2011;33:201–203.
- 3 Segev DL, Muzaale AD, Caffo BS, Mehta SH, Singer AL, Taranto SE, McBride MA, Montgomery RA: Perioperative mortality and long-term survival following live kidney donation. *JAMA* 2010;303:959–966.
- 4 Axelrod DA, McCullough K, Brewer E, Becker BN, Segev DL, Rao P: Kidney and pancreas transplantation in the United States 1999–2008: the changing face of living donation. *Am J Transplant* 2010;10:987–1002.
- 5 Iordanous Y, Seymour N, Young A, Johnson J, Iansavichus AV, Cuerden MS, Gill JS, Poggio E, Garg AX: Donor Nephrectomy Outcomes Research (DONOR) Network: Recipient outcomes for expanded criteria living kidney donors: the disconnect between current evidence and practice. *Am J Transplant* 2009;7:1558–1573.
- 6 Matsushita K, van der Velde M, Astor BC, Woodward M, Levey AS, de Jong PE, Coresh J, Gansevoort RT, Chronic Kidney Disease Prognosis Consortium: Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts. *Lancet* 2010;375:2073–2081.
- 7 Issa N, Stephany B, Fatica R, Nurko S, Krishnamurthi V, Goldfarb DA, Braun WE, Dennis VW, Heeger PS, Poggio ED: Donor factors influencing graft outcomes in live donor kidney transplantation. *Transplantation* 2007;83:593–599.