Living Donors—An Expanding Spectrum of Quality

By David Foley

Kidney transplantation remains the standard of care for patients with end stage renal disease (ESRD). Owing to the significant shortage of donor organs, transplant centers continue to expand the criteria for suitable kidney donors. As a result, there has been a progressive change in the spectrum of quality of kidney donors.

The increased use of transplanted kidneys recovered from expanded criteria deceased donors (ECD) and donation after cardiac death (DCD) both contribute to the change in the quality of kidney donors. Between 1997 and 2006, the number of standard criteria donors (SCD), ECD, and DCD kidney transplants increased by 22 percent, 59 percent, and 684 percent, respectively. In addition, between 2005 and 2006, there was a 7.4 percent increase in deceased donor kidney transplants and a 2 percent decrease in living donor (LD) kidney transplants, according to a 2007 OPTN/SRTR (Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients) Annual Report.

Despite the recent decreases in kidney transplants involving living donors, such donors continue to play a significant role in kidney transplantation. Contributing to the demand for LD kidney transplants are the minimal long-term risk to the donor and superior outcomes in the recipient compared with deceased donor kidney transplants.

Expanding the donor base
Transplant centers are expanding the acceptance criteria for living kidney donors. Recent data show an increased use of older living kidney donors. According to the 2007 OPTN/SRTR Annual Report, from 1997 to 2006, there was a 5.9 percent decrease in living donor (LD) transplants 18–34 years old and a concomitant 5.4 percent increase in living donors 50–64 years old. The percentage of living donors 55–64 and those over age 65 has remained essentially unchanged.

This trend is also illustrated in studies looking at practice patterns at transplant centers in the United States. Mandelbrot et al. performed a survey of U.S. transplant centers that looked at the medical evaluation of living kidney donors. When they compared their 2007 survey to a survey published in 1995, they found that most programs no longer have an upper age limit to be eligible for kidney donation (1). The percentage of programs in 2007 with no upper age limit (59 percent) nearly doubled from that identified in the 1995 survey (27 percent) (2).

To assess the influence of using more “marginal” or “high-risk” living kidney donors, one must look at the impact on both donors and recipients after donation. Ibrahim et al. recently studied long-term risk to the kidney donor in an analysis of 3698 kidney donors who had previously donated kidneys between 1963 and 2007. The authors ascertained the vital status and lifetime risk of ESRD in these donors and assessed glomerular filtration rate (GFR), urinary albumin excretion, prevalence of hypertension, GFR either before or after nephrectomy. In a single center study, Heimbach et al. retrospectively evaluated 553 consecutive living kidney donors and studied the effects of body mass index (BMI) on postnephrectomy renal function. At six to 12 months after donation, renal function and microalbuminuria did not differ across BMI (3).

In contrast, Rook et al. studied the impact of donor age and BMI on the renal functional reserve capacity of kidney donors before and after donor nephrectomy. Reserve capacity was assessed by GFR increase to dopamine infusion. The dopamine-induced increase in GFR was not different across BMI (4).

Risk factors that contribute to the classification of a marginal or high-risk kidney donor include obesity, age, presence of hypertension, and low GFR at the time of donation. Recent data show that more individuals with these pre-existing conditions are being accepted as kidney donors. Reese et al. defined living donors with hypertension, obesity, or low GFR as “medically complex donors.” Among the 9319 kidney donors he analyzed between July 2004 and December 2005, 2254 (24.2 percent) were complex: 1194 (12.8 percent) were obese, 956 (10.3 percent) were hypertensive, and 392 (4.2 percent) had low GFR (4).

Short-term outcomes for living kidney donors
Despite the increased use of medically complex kidney donors, the literature on outcomes for these select donors remains limited. Some data exist on the follow-up of kidney donors with obesity at the time of donation and renal function after nephrectomy. In a single center study, Heimbach et al. retrospectively evaluated 553 consecutive living kidney donors and studied the effects of body mass index (BMI) on postnephrectomy renal function. At six to 12 months after donation, renal function and microalbuminuria did not differ across BMI (5).

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Recipient outcomes
As use of older kidney donors for transplants expands, questions arise regarding recipient outcomes. In a recent analysis of data from the OPTN and United Network for Organ Sharing (UNOS), Gill et al. studied all first-kidney-only transplants from 1995 and 2003 and assessed outcomes of living donor transplantation as a function of donor age. GFR one year after transplantation decreased with increasing donor age. In multivariate analysis, the relative risk of graft loss of living donors 55–65 years was significantly greater than that with younger living donors (YLD), those ≤ 55 years. In comparison to transplants with deceased donors ≤ 55 years, the risk of graft loss with living donors 55–64 years was similar, while recipients from living donors 65 years and older had a higher relative risk of graft loss (9).

In a separate prospective cohort study of 739 first-time LD transplantations, Oien et al. studied the effects of donor age on short- and long-term recipient outcomes. Graft survival was unaffected by donor age ≥ 50 years as long as the recipients did not experience an early acute rejection episode. In the absence of acute rejection episodes, there was
In summary, over the past several years there has been a steady increase in the use of "medically complex" or "high-risk" living kidney donors, including those who are older, obese, have hypertension, or have low GFR. Despite the limited long-term data evaluating the outcomes in these patients, up to one-quarter of transplant centers are approving these donors (4). Recipients clearly benefit from receiving a living donor kidney from an older or medically complex donor compared with dialysis. The data also suggest that outcomes are significantly better than receiving an ECD kidney. Whether there is a true benefit over waiting for an SCD donor remains to be determined.

In these instances, short- and long-term safety to the donor should take precedence over recipient needs for a kidney transplant. Although informed consent remains a critical component to the LD evaluation process, one may argue that true informed consent is limited in this group of donors owing to the lack of long-term follow-up. These donors need to be made aware that the long-term consequences of kidney donation for patients defined as medically complex or older are unknown, and the transplant community needs to proceed cautiously when approving these kidney donors.

It is essential that future studies include close follow-up of both medically complex and older living donors. It is also critical to study the long-term benefits to recipients of receiving one of these kidneys compared with SCD deceased donor transplantation. This will allow for true risk-benefit analyses when considering the use of these donors in the future.

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References