The National Kidney Registry
Time to Buy In?

Bushra Syed and Joshua J. Augustine

In this issue of CJASN, Leeser et al. (1) describe patient and graft survival in patients who participated in the National Kidney Registry, a nonprofit, 501(c) organization founded in 2007 to facilitate living kidney donor exchange. Outcomes of recipients of paired kidneys in the National Kidney Registry (n=2363) were compared with outcomes in all living donor recipients from registry data (n=54,497), control unrelated living donor recipients (n=25,900), and control patients who received kidneys through non-National Kidney Registry paired donation (n=4535). Because of shipping of most kidneys, National Kidney Registry transplants had a notably greater cold ischemic time (9 hours versus 1 hour for the primary control group). This correlated with a higher risk of delayed graft function in National Kidney Registry recipients, with a 1.4 times risk (5% versus 3%; P<0.001) compared with other living donor recipients. However, at a median of 3.7 years of follow-up for National Kidney Registry recipients, death-censored graft survival and patient survival were similar compared with control living donor recipients as a whole.

In contrast to analysis of National Kidney Registry data, an Australian paired exchange cohort with a median follow-up of 6.6 years demonstrated that cold ischemic time was associated with outcomes in recipients of donors >50 years of age. Compared with cold ischemic time of 1–2 hours, cold ischemic time of 4–8 hours was associated with an increased odds of overall and death-censored graft failure with these older paired donors (hazard ratio, 1.93; 95% confidence interval, 1.21 to 3.09; P=0.006 and hazard ratio, 1.91; 95% confidence interval, 1.05 to 3.49; P=0.04, respectively (2). The follow-up in the current National Kidney Registry analysis is relatively short, and future studies with longer follow-up times are required to determine whether long-term survival is negatively affected by the greater cold ischemic time and delayed graft function in the National Kidney Registry cohort.

One surprising finding is that National Kidney Registry recipients appeared to have superior death-censored allograft survival compared with recipients of non-National Kidney Registry paired exchange kidneys. Compared with this control group, National Kidney Registry recipients were more likely to be black, with a higher percentage with prior transplantation, greater dialysis vintage, greater cold ischemic time, and a substantially higher rate of alloantibody sensitization as measured by panel reactive antibody (PRA). Despite these risk factors, the National Kidney Registry recipients displayed superior death-censored graft survival. It is unclear what may have led to improved outcomes in the National Kidney Registry recipients. Recipients who participated in the National Kidney Registry may have been carefully selected with favorable resources, education, and adherence. National Kidney Registry recipients may also have had lower rates of donor-specific antibodies or need for desensitization, although such data were not available for the non-National Kidney Registry cohort. Rates of desensitization in the National Kidney Registry have dropped to <5% since 2018 (3). This illustrates a strength of the program, allowing for matching of compatible donors despite an over one fifth of recipients being highly sensitized with a PRA>80%. Recipients with a PRA≥98% remained disadvantaged as expected in the National Kidney Registry (4). This risk can be mollified by matching with a paired donor with a lower titer cross-match compared with the intended pair.

Original concepts of paired donation envisioned single hospitals and simultaneous transplants between paired donors (5). However, the success of national exchange programs relies on the ability to separate transplants by geographic space and time, particularly when they involve longer transplant chains. One concern with delaying subsequent transplants is that chains may be broken, but a recent report from the National Kidney Registry found a low rate of broken chains of 5.8% (6). Primary reasons for chain breakage in that analysis included donor medical issues or donors backing out while serving as bridge donors (i.e., donors who donate at least 1 day after their intended recipient has received a kidney).

One trend has been a shift away from bridge donors, and to greater participation in an advanced donation program. Advanced donation occurs before transplantation of the intended recipient, sometimes by months, and before an alternative donor being selected for their intended recipient. Preliminary data showed that advanced donation facilitated chains of transplants in National Kidney Registry, with approximately five transplants averaged for each advanced donation-associated chain (7). One advantage of advanced donation is that a prospective caregiver for the recipient may donate, recover from donor surgery, and later
serve as a healthy support person for their intended recipient. Additionally, a donor who has a specific window of time for donation, related to work or travel, may donate at an earlier convenient time. A risk related to advanced donation is that the intended recipient may later encounter medical issues leading to deactivation from the transplant list, and this risk is emphasized in the consent of donor-recipient pairs for advanced donation in the National Kidney Registry (7).

Other innovation has led to the success of national registry programs, and such innovation has been spearheaded by the National Kidney Registry (3). As above, at the expense of longer cold ischemic time, shipping of kidneys has improved convenience and willingness of living donors to participate without the need to travel to recipient centers, which may be thousands of miles away (8). The National Kidney Registry utilizes global positioning system to track donor kidneys during transport, allowing for monitoring of displaced kidneys. The National Kidney Registry also implemented donor blood cryopreservation in 2015 allowing for cryopreserved donor cells to be shipped to recipient centers. This process improved the timeliness of crossmatches and eliminated the need for donors to provide repeat blood samples. Donor computerized tomography scans are shared on the National Kidney Registry website to avoid the need for donors to provide repeat blood samples.

Ideally there will be greater unification and national participation in large donor exchange programs in the United States over time. If the early success of the National Kidney Registry is sustained, it may be the program of choice for national participation. The National Kidney Registry has led the way in technology and innovation, and outcomes demonstrate success for those classically disadvantaged for living donor transplant, including black recipients and ABO favorable pairs (blood group O, as well as compatible donor-recipient pairs. Compatible pairs who could otherwise proceed locally without exchange may be particularly helpful in facilitating transplant chains in the National Kidney Registry, especially if the donor is O with a non-O recipient, or the recipient is AB with a non-AB donor (V. Chipman, B. Lee, M. Cooper, M.C. Cuffy, M. Ronin, G. Hil, S. Flechner, A. Thomas, D.A. Mandelbrot, A.D. Waterman, C.E. Freise, G.R. Roll, unpublished data).

References

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See related article, “Patient and Kidney Allograft Survival with National Kidney Paired Donation,” on pages XXX–XXX.