

Expand the Pool of Living Donors for Kidney Transplantation

Jayme E. Locke

Clin J Am Soc Nephrol 13: 1142–1143, 2018. doi: <https://doi.org/10.2215/CJN.07310618>

In this issue of the *Clinical Journal of the American Society of Nephrology*, de Weerd *et al.* (1) report findings from their meta-analysis examining outcomes after blood group–incompatible (ABO-incompatible) living donor kidney transplantation. Their analysis included single-center cohort studies that compared intracenter outcomes between ABO-incompatible and blood group–compatible (ABO-compatible) living donor kidney transplantation. Results from their meta-analysis showed that ABO-incompatible living donor kidney transplant recipients were at increased risk for graft loss, severe infection, and antibody-mediated rejection in the first post-transplant year compared with center-matched ABO-compatible living donor kidney transplant recipients. Although all 26 studies included in the meta-analysis reported inferior graft survival among ABO-incompatible recipients compared with their ABO-compatible counterparts (table 1 in the work by de Weerd *et al.* [1]), none of the reported differences were statistically significant, and as such, data from these single-center studies have provided the evidence to date that similar graft and patient survival can be achieved with ABO-incompatible living donor kidney transplantation compared with ABO-compatible living donor kidney transplantation. However, all 26 single-center cohorts were limited by small sample sizes, and as such, they were hampered by type 2 errors (*e.g.*, failure to reject a false null hypothesis or a “false negative conclusion”), highlighting the major strength and importance of the meta-analysis performed by de Weerd *et al.* (1). Specifically, death and graft loss remain relatively rare events post-transplant, making detection of statistically significant differences nearly impossible in the setting of small sample sizes. The meta-analysis by de Weerd *et al.* (1) overcomes this limitation by inclusion of large numbers of patients across multiple single-center cohorts, and it supports recent registry studies by Montgomery *et al.* (2) and Mustian *et al.* (3) as well as provides the first granular evidence that ABO-incompatible living donor kidney transplantation may not be as straightforward as once thought with outcomes that are, in fact, inferior to ABO-compatible living donor kidney transplantation.

Importantly, the reported 1-year post-transplant uncensored graft loss in this study was only 4.2% among ABO-incompatible living donor kidney trans-

plant recipients, suggesting that ABO-incompatible living donor kidney transplantation likely offers significant survival benefit over remaining on dialysis or waiting for a deceased donor kidney transplant to become available. Although reassuring, is this outcome acceptable? In the post-Norwood Act era, should we not instead look to optimize the number of ABO-compatible living donor kidney transplants through kidney paired donation? Kidney paired donation aims to facilitate living donor kidney transplantation by identifying two or more incompatible donor-recipient pairs and then generating two or more compatible transplants through swapping or exchanging of donor kidneys. Modeling simulations have projected that nearly 50% of incompatible donor-recipient pairs would find a compatible match in an optimized national kidney paired donation program, and with the inclusion of compatible pairs (who stand to benefit from better age or size match), larger gains are anticipated (4–6).

The idea of a national kidney paired donation program was first considered in 2000 when the first kidney paired donation transplants were performed at individual centers; however, given concerns that kidney paired donation might violate the “valuable consideration” provision of the National Organ Transplant Act (NOTA; 1984/88), the United Network for Organ Sharing (UNOS) did not launch its national kidney paired donation program until 2010 (7). The Norwood Act (2007) amended the NOTA such that, for paired kidney exchange, “kidneys” are not a valuable consideration, effectively legalizing the “exchange” of kidneys for the purposes of transplantation in the United States (8). Although the first living donor kidney transplant resulting from the UNOS-based kidney paired donation national program occurred in 2010, only 217 transplants have been performed between 2010 and 2017 (9). For perspective, the Methodist San Antonio produced 134 ABO-compatible living donor kidney transplants in just 3 years (10); similarly, our single-center kidney paired donation registry at the University of Alabama at Birmingham (UAB) generated 181 ABO-compatible living donor kidney transplants in just 3 years (J.E. Locke, unpublished data). Inefficiencies in automation and systems implementation have resulted in limited center participation and therefore, suboptimal performance of the UNOS-based

Department of Surgery, Division of Transplantation, Comprehensive Transplant Institute, University of Alabama at Birmingham, Birmingham, Alabama

Correspondence:

Dr. Jayme E. Locke, University of Alabama at Birmingham, 701 19th Street South, LHRB 748, Birmingham, AL 35294. Email: jlocke@uabmc.edu

national kidney paired donation program. Moreover, these inefficiencies have led to the development and growth of other “national registries” (e.g., the National Kidney Registry and the Alliance for Paired Donation) and single-center registries (e.g., Methodist San Antonio and UAB), fragmenting the kidney paired donation pool. This is problematic, because modeling consistently shows that match rates increase exponentially with increasing pool size (5,10).

What if we engaged colleagues with successful kidney paired donation programs, national kidney paired donation programs (like National Kidney Registry) with expertise in logistics and travel, and mathematicians with expertise in applied mathematics who could further enhance matching algorithms? What if, through this combined expertise, we created a single national living donor registry—a registry that would include all living donor-recipient pairs and more specifically, create the largest possible pool size? What would happen? Modeling simulations suggest that we could double the number of living donor kidney transplants (5). Moreover, the need for ABO-incompatible living donor kidney transplantation would decrease, and given the superior outcomes observed with ABO-compatible living donor kidney transplants, outcomes after living donor kidney transplantation would improve. This is not to say that therapeutic options, like ABO-incompatible living donor kidney transplantation, would no longer be necessary, but rather, the broader implementation of ABO-incompatible living donor kidney transplantation would no longer be required, allowing for these types of living donor kidney transplants to be performed exclusively at centers of excellence.

Although the concept of a single national living donor registry may be a bit grandiose, de Weerd *et al.* (1) provide the first granular data suggesting that we may need to think bigger. A single national living donor registry may just be an “idea worth spreading” (11).

Disclosures

None.

References

1. de Weerd, et al.: ABO-incompatible kidney transplant outcomes. *Clin J Am Soc Nephrol* 13: 1234–1243, 2018
2. Montgomery JR, Berger JC, Warren DS, James NT, Montgomery RA, Segev DL: Outcomes of ABO-incompatible kidney transplantation in the United States. *Transplantation* 93: 603–609, 2012
3. Mustian MN, Cannon RM, MacLennan PA, Reed RD, Shelton BA, McWilliams DM, Deierhoi MH, Locke JE: Landscape of ABO-incompatible live donor kidney transplantation in the US. *J Am Coll Surg* 226: 615–621, 2018
4. Segev DL, Gentry SE, Warren DS, Reeb B, Montgomery RA: Kidney paired donation and optimizing the use of live donor organs. *JAMA* 293: 1883–1890, 2005
5. Gentry SE, Segev DL, Simmerling M, Montgomery RA: Expanding kidney paired donation through participation by compatible pairs. *Am J Transplant* 7: 2361–2370, 2007
6. Montgomery RA, Zachary AA, Ratner LE, Segev DL, Hiller JM, Houp J, Cooper M, Kavoussi L, Jarrett T, Burdick J, Maley WR, Melancon JK, Kozlowski T, Simpkins CE, Phillips M, Desai A, Collins V, Reeb B, Kraus E, Rabb H, Lefell MS, Warren DS: Clinical results from transplanting incompatible live kidney donor/recipient pairs using kidney paired donation. *JAMA* 294: 1655–1663, 2005
7. UNOS: Kidney Paired Donation, 2017. Available at: <https://unos.org/donation/kidney-paired-donation/>. Accessed June 10, 2018
8. American Society of Transplant Surgeons Winter Symposium: The OPTN/UNOS KPD program: An idea whose time has come. Presented at the Winter Meeting, Miami, FL, January 24, 2014
9. OPTN/UNOS Kidney Transplantation Committee: Allowing Deceased Donor-Initiated Kidney Paired Donation (KPD) Chains; https://optn.transplant.hrsa.gov/media/2219/kidney_pccconcepts_201707.pdf. Accessed June 10, 2018
10. Bingaman AW, Wright FH Jr, Kapturczak M, Shen L, Vick S, Murphey CL: Single-center kidney paired donation: The Methodist San Antonio experience. *Am J Transplant* 12: 2125–2132, 2012
11. TEDx Birmingham: “Possibility”—Let’s Create a Single National Kidney Donor Exchange, 2017. Available at: https://urldefense.proofpoint.com/v2/url?u=https-3A__youtu.be_RZ-2DrQ8WBiNk&d=DwICAg&c=o3PTkfaYAd6-No7SurnLtwPssd47t-De9Do23lQNz7U&r=nucjvdENerjR9XDE3DFqCg&m=KAEXKE6NYJaxK9OyYtHehyrP6L0DIZc_s4lSMdQLoao&s=Gqf0OLDWKGRw53Zfk2nB5GxnBoU5CidgCP6k0-gae-ll&e=. Accessed June 10, 2018

Published online ahead of print. Publication date available at www.cjasn.org.

See related article, “ABO-Incompatible Kidney Transplant Outcomes: A Meta-Analysis,” on pages 1234–1243.