

Living Donor Exchange Program in Kidney Transplantation: An Underexploited Organ Resource

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Living Donor Exchange Programs (LDEPs) in kidney transplantation—also known as kidney paired donation or crossover transplantation—emerged in the early 1990s as a way to overcome immunological barriers in sensitized patients against their living donor. Indeed, ABO blood group incompatibility or pre-existing donor-specific antibodies to HLA lead to the exclusion of at least one-third of healthy donors.¹

In addition to recovering valuable organs in a context of ongoing organ shortage, LDEPs have the advantage of providing excellent graft survival associated with living donor transplantation and eliminating the burden of increased immunosuppression used in ABO-incompatible transplantation. They can also offer advantages for ABO- or HLA-compatible pairs with a high degree of HLA mismatch, or an older donor.² Simulations using the Australian matching algorithm were able to improve HLA matching for recipients of compatible pairs with high eplet mismatch to their own donor while increasing the match rates in incompatible pairs.³

Single centers around the world reported the results of their individual programs. What soon became very clear was the strong correlation between the number of transplants achieved and the addition of new pairs to the list, leading some authors to advocate the replication of single-center programs on a national level.⁴ Very small pools of fewer than 15 pairs often result in no matches at all, whereas simulations of a national pool, carried out by increasing the number of pairs willing to travel outside their region in the United States, predicted a match rate of around 47%.¹

The first national exchange program was initiated in The Netherlands in 2004, with the aim of achieving a

high number of possible matches by enlarging the pool of participants. The Netherlands is part of EuroTransplant (an organ-donor allocation organization in Europe that includes The Netherlands, Belgium, Germany, Luxembourg, Austria, Hungary, Croatia, and Slovenia), but its LDEP program operates under the auspices of the Dutch Transplantation Foundation. It works on a common protocol for living donor evaluation throughout the country. Donor/recipient matching is done 4 times a year, and surgical transplantation is carried simultaneously, with donor traveling to the recipient center.⁵ Since then, national programs have been established in other countries such as the United Kingdom, Canada, and Australia with some differences such as organ transport instead of donor travel in the United Kingdom and Australian programs. In these programs, 30%–45% of the listed patients were transplanted with a living donor.⁶ Prolonged ischemia times associated with transporting kidneys long distances do not reduce the benefit of LDEP. Based on data from the United Network for Organ Sharing/Organ Procurement and Transplantation Network, a retrospective cohort study found that cold ischemia time (CIT) up to 8 h was associated with a slight increase in the rate of delayed graft function but did not impact on renal function or allograft survival.⁷ Comparing LDEP shipped versus nonshipped kidneys in the United States from 2008 to 2015, Treat et al⁸ showed that each hour of CIT was associated with a 5% increase in the risk of delayed graft function. However, CIT was not associated with graft failure or mortality.

Moving from a national to an international program was the logical next step that some countries took to increase the size of the donor pool, improve the chances of a kidney match, and reduce the number of hypersensitized patients on the waiting list. In Europe, the first international program was established in 2016 between 1 center in Austria, 1 in the Czech Republic, and 1 in Israel. Another program was initiated in 2018 between some, but not all, centers in Spain, Italy, and Portugal. In 2019, an international program of LDEP was initiated within the ScandiTransplant allocation organization, which brings together Sweden, Denmark, Finland, Norway, and Iceland. The recently published results showed a 40% transplantation rate of the enrolled pairs, an excellent 1-y graft survival of 96%, and 4% delayed graft function in the 47% of those with a CIT >6 h.⁹

Other strategies to increase the donor pool are also considered. These include listing >1 potential donor and

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integrating altruistic donors—also known as nondirected anonymous donors—who can initiate domino chains ending with the last donor donating to a recipient from the waitlist or initiating a future nondirected chain.⁶ The inclusion of compatible pairs who might benefit from better donor quality or HLA match increases the number of donors.³ Furthermore, as recently shown by de Klerk et al,¹⁰ increasing options within the same pool for difficult-to-match highly immunized or long waiting candidates by modifying the algorithm of the allocation program and allowing ABO- and HLA-incompatible allocation resulted in higher transplant rates.

In Belgium, the national protocol for LDEP was developed in 2006 in accordance with the Belgian law, in collaboration with EuroTransplant and the Dutch LDEP program. Despite its approval by the 7 Belgian transplant centers in 2009, the first run for matching was not performed until 2013. Since 2014, only 13 pairs have been transplanted within this program, of which 9 pairs came from a single center. In addition to the relatively low number of pairs listed, the barriers were related to the program being considered a low priority, which led to the discontinuation of pair matching in 2019 because of a lack of funding to address increased operational costs.

What lessons can we learn from the ineffectiveness of our national program?

First, for such a program to work, physician and center motivation is critical to increasing the number of couples on the list and, consequently, the number of matches that lead to transplantation. Not surprisingly, the most motivated center with the longest patient list achieved the highest number of transplants. Second, funding is essential to run the program including list management, pair matching, database, and periodic evaluation. For this, the relevant national authorities must be convinced of the need and priority to support such a program by allocating the necessary funds to cover the costs. In the absence of such support, our program was suspended for 5 y.

A revival of our national LDEP is under consideration. Improving the effectiveness of the program will require reflection on (1) establishing clinical leadership to convince nephrologists, surgeons, politics, and the public on

the relevance of LDEP and its enormous underexploited potential, (2) increasing the numbers of pairs on the list by including altruistic donors and the compatible pairs that might benefit from the program, (3) considering ABO-incompatible transplantation for highly sensitized patients, (4) maximizing the chances of matching through efficient optimization of algorithms, and (5) dedicating a coordination team and ensuring periodic evaluation. Finally, moving from a national to an international program would broaden the horizon and open up a wider range of opportunities. Belgium is part of EuroTransplant and, like the other participating countries, would benefit from the establishment of an international program at EuroTransplant. Until now, legislation and practical administration seemed to be insurmountable obstacles. However, as the ScandiTransplant exchange program has recently shown, barriers to international exchange can be overcome with strong motivation and will power.

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