Curr Transpl Rep (2014) 1:10–17
DOI 10.1007/s40472-013-0002-5

State of the Art Practices and Policies in Kidney Paired Donation

Shafi Malik · Edward Cole

Published online: 10 December 2013

Abstract Approximately one-third of kidney transplant candidates have medically acceptable living donors, but are unable to receive transplants due to donor–recipient incompatibilities. Kidney paired donation (KPD) is a strategy that matches incompatible pairs in order to find compatible matches, thus increasing living donor transplantation. The concept was first conceived in 1986. Since then, significant strides have been made. However, the technique remains underutilized. This article describes the current advances, types of paired donation programmes, registries, worldwide experience, outcomes, barriers, and limitations.

Keywords Renal transplant · Living donor · Paired exchange · Non-directed donation · Waiting list · Non-simultaneous extended altruistic donor · Bridge donor · List exchange · Domino paired donation · Blood group incompatibility · HLA matching · Tissue donor · Organ donation

Introduction

The field of transplantation has made major advances. However, the number of patients on the waiting list continues to grow and demand for organs is ever increasing [1]. As a consequence of the long waiting time, wait-listed patients continue to die or are taken off the wait list as they become too sick before receiving an organ offer.

S. Malik
Clinical Fellow Renal Transplantation Programme, Toronto General Hospital, 200 Elizabeth Street, Toronto, ON M5G 2C4, Canada
e-mail: dr_shafi@hotmail.com

E. Cole (✉)
University of Toronto, 190 Elizabeth St, RFE 1S-409, Toronto, ON M5G 2C4, Canada
e-mail: edward.cole@uhn.ca

Living donor renal transplantation is the preferred transplant option, providing a survival benefit compared to deceased donation [1]. However, in order to receive a living donor transplant, an acceptable donor is required. It is estimated that one-third of patients who have healthy, willing living donors are unable to receive a transplant due to blood type incompatibility or the presence of a donor-specific antibody (DSA) [2]. Blood group incompatible (ABOi) transplants have comparable long-term patient survival when compared to ABO compatible live donor transplants, but short-term graft loss has been found to be higher in the ABOi group [3••]. Only 6.5 % of highly sensitized patients in the United States receive a transplant each year. These sensitized recipients have to wait longer or undergo desensitization strategies in order to be transplanted. Various expensive desensitization strategies have been described in the literature; although patient outcomes from such strategies may be better when compared to the waiting list, they are certainly lower than with a compatible live donor transplant with increasing graft loss from antibody mediated rejection after 2 years [4•, 5]. In both cases, the increased immunosuppression required also adds to the risk. Thus, the opportunity to find a blood group and HLA compatible living donor offers substantial benefit. For many patients, this can be achieved using living donor exchange.

Kidney Exchange Programmes

Kidney paired exchange was first proposed in 1986 by Rapaport [6], and gained popularity in 1997 when such transplants were found to be ethically acceptable [7]. See Table 1 for the kidney paired donation (KPD) time line. The types of KPD programmes that exist today are described below (Fig. 1).

Multi Way Exchanges

This is a classic type of exchange where incompatible pairs D1, R1 & D2, R2, exchange kidneys in order for each to

Table 1 KPD time line

Year	Event
1986	KPD conceptualized by Felix Rapaport [6]
1991	First exchange performed in Korea [8, 9]
1995	3 way exchanges in Korea [9]
1999	First KPD transplant in Europe–Switzerland [10]
2000	First exchanges performed in US [11]
2000	New England paired kidney exchange program established [12]
2001	John Hopkins KPD program established [12]
2004	Dutch national living donor exchange program established [13]
2007	First non-simultaneous extended altruistic donor (NEAD) chain reported in US [14]
2009	Canada national KPD program established
2010	OPTN announces plan to establish a national KPD pilot program in US [15]
2010	First paired donation transplant from OPTN pilot program [15]

receive a compatible transplant, i.e. D1 donates to R2 and D2 donates to R1 (see Fig. 1). Exchanges are not limited to two pairs; three-way and four-way exchanges are also possible. In a two-way exchange, not only does D1 have to be compatible to R2, but D2 also needs to be compatible with R1. If D2 is not compatible to R1, then increasing the pairs in the exchange, i.e. three-way and four-way, will increase the probability of finding a suitable pair [16].

Domino Exchanges

Domino paired exchange can be open or closed. Typically, a non-directed donor (NDD), also known as an altruistic or good samaritan donor, starts by donating a kidney to a recipient in an incompatible pair, which then sets off a domino of exchanges. Domino exchanges are a powerful tool for increasing transplant numbers. This is because in a true paired exchange, both donor and recipient must match with another pair. In domino transplants, only one match at a time is required (see Fig. 1).

It is called a closed exchange when the last donor in the chain donates to a patient at the top of a deceased donor wait list (DDWL) and ends the chain. Open domino exchanges are also called NEAD chains. In this type of exchange, a NDD starts off the chain, but the last donor does not donate to a patient on a deceased donor wait list. Instead, he/she becomes a bridge donor waiting to start off another domino transplant chain. Bridge donors will usually be non blood type O, and may be harder to match [2]. The potential benefit of this type of chain is the ability to start additional chains with significant numbers of transplants. The concerns are the fact that the donor must put

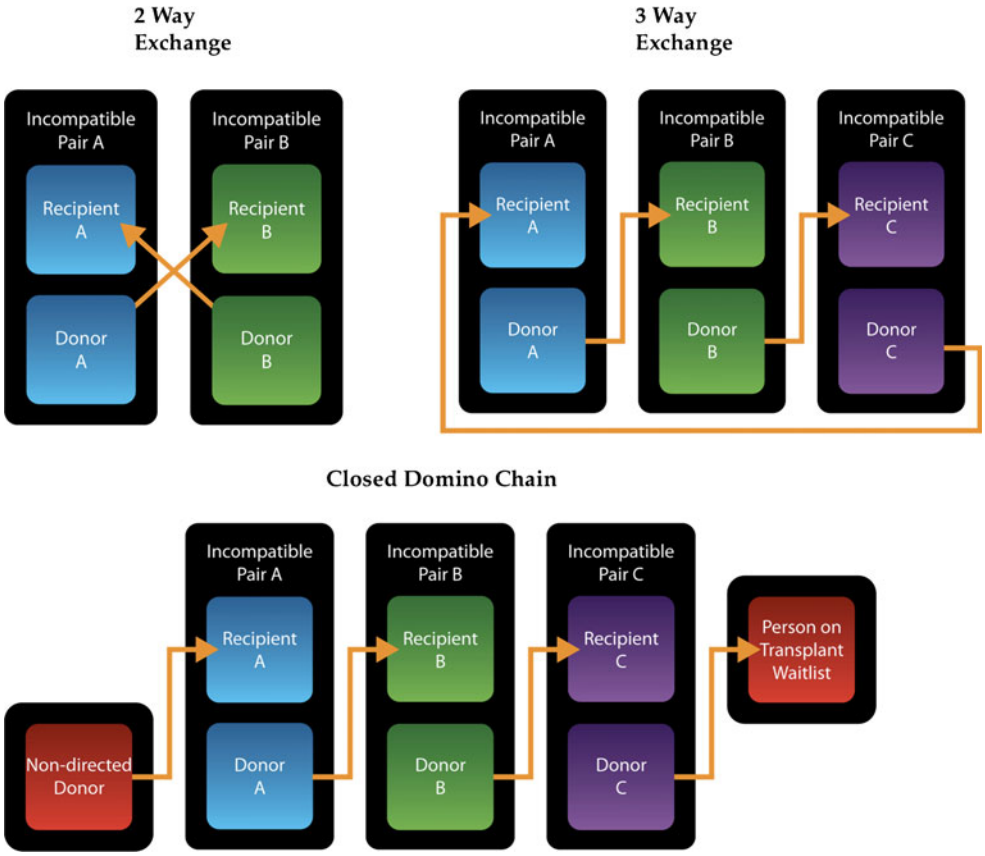

Fig. 1 Types of living donor exchange

his/her life on hold for an undetermined period of time, and the risk of the donor reneging, as his/her recipient has already benefitted. Nonetheless, this strategy has worked very well in some jurisdictions [14]. One disadvantage is that patients on the DDWL will not benefit, as a kidney is diverted away from the DDWL. A recent analysis of NDD-triggered NEAD exchanges from the National Kidney Registry reported that 77 NDD-initiated chains led to 373 transplantations for a mean chain length of 4.8 (median, 3; range, 1–30). Seven bridge donors were lost in the process due to donor reneging [17•].

List Exchange

Living donor exchange can also involve exchange with the deceased donor list. List exchange (LE) occurs when a donor of an incompatible pair donates to a compatible patient on a deceased donor wait list, and in return, the recipient of the incompatible pair gets prioritized for a deceased donor transplant. This type of exchange can avoid the risk of ABO or crossmatch incompatibility, and can yield an additional donor source for patients awaiting a deceased donor kidney [18]. List exchange is non-simultaneous, because the living donor donates first before the recipient is prioritized. In general, only unsensitized candidates, or those with few antibodies, have been accepted, with the justification that a sensitized candidate might wait for an extended period after the living donor's gift before a compatible deceased donor organ becomes available [2]. While the recipient will get a kidney sooner, he/she will not derive the additional benefit of receiving a living donor kidney. Concern has been expressed that O recipients on the deceased donor list would be disadvantaged, because most deceased donor kidneys in this type of exchange would go to O recipients, diverting them away from those already on the list. The contrary view is that without this exchange, such patients would be added to the list, so the list is actually shorter.

Altruistic Unbalanced Paired Kidney Exchange (AUPKE)

The SRTR 2011 report shows that 52.2 % of adult wait-listed candidates for a kidney transplant are blood group O. Blood group O recipients are disadvantaged by the fact that they can receive kidneys only from a blood group O donor, whereas a blood group O donor can donate to any blood group recipient.

Thus, there is an imbalance in the blood group representation in a typical KPD pool. In a simulated model using United Network for Organ Sharing (UNOS) data, Gentry et al. estimated that 60 % of KPD candidates are blood group O, whereas only 30 % of donors in such pools are blood group O [19]. Others have reported similar results; for example, in the Dutch KPD programme, around 67 % of ABOi pairs were found to have type O recipients, whereas only about 30 % of pairs have type O donors [20]. In traditional KPD pools of incompatible pairs, match rates for type O recipients with non–type O donors are around 15 %, whereas rates for other pairs with donors of other blood group types are close to 50 % [21]. Some consider this a drawback of KPD programmes.

To overcome this imbalance, it has been suggested that compatible pairs with a blood group O donor be encouraged to participate in a KPD. There are potential medical advantages for such pairs to participate in a KPD, as the recipient in this compatible pair has the opportunity to receive a kidney from a younger donor, better size-matched donor, or a more immunologically compatible donor (avoiding child-to-mother or husband-to-wife donation), thus resulting in longer graft half-life. Others may be motivated to participate for altruistic reasons. Ratner and colleagues published a proof of concept paper in 2010 where they explored the reasons why a compatible pair may want to participate in a KPD. Perceived benefit to the recipient was a factor that motivated such pairs to take part [22•]. Simulations show that if compatible pairs participate in KPD, even if only when they gain a tangible medical benefit, the 15 % match rate for type O recipients with non–type O donors would climb to 78 %, and up to 90 % if all compatible pairs participated whether they derived a benefit in doing so or not [19].

Paired Donation with Desensitization

Some patients are so highly sensitized that it may not be possible to find a donor to whom they do not have antibodies. In these circumstances, living donor exchange still may provide an important benefit, i.e. finding a donor to whom they have fewer and lower titre antibodies. In that case, desensitization therapy may be used to reduce the titre of antibodies further so that transplantation may proceed. Thus, for highly sensitized patients who have a cross match positive donor, a combined approach can be considered, e.g., if there is another donor who may be cross-match negative with only a weak DSA [23].

Registries

There are many national registries for KPD worldwide, including The Netherlands, Canada, France, United Kingdom, Australia and South Korea. In the United States, a government-organized registry is run by the UNOS. There are also a number of single and multi centre registries in the United States, such as the Alliance for Paired Donation, the National Kidney Registry, the New England Paired Kidney Exchange, and the Johns Hopkins Hospital consortium. The Methodist Hospital in San Antonio runs a very successful single centre registry [14].

Simulation

Simulation has played a key role in research in this area. Before registries were set up and prospective cohort data were available, centres used simulation models from existing transplant databases to study the potential impact of KPD. Interactive

software-based decision support systems to model, monitor, and visualize a conceptual KPD programme have been developed, which aim to assist clinicians in the evaluation of different allocation strategies [24, 25]. The work of Gentry and Segev was especially useful in this regard, as it pointed out the impact of the number of pairs entered on the number of matches and the importance of optimization as a matching strategy in order to include harder-to-match patients [26]. These models also give registries the ability to test matching algorithms, perform assessments of efficiency and feasibility, and to simulate the impact of different point allocations. Ultimately, they help patients in decision making [27].

Matching

Computer-based matching programmes are generally used. Match runs are typically run every 3 months in most programmes, although some programmes match much more frequently. In the Netherlands, the software is set up so that the potential recipient with the lowest match probability, in other words, the recipient with the smallest chance of finding a compatible donor in the pool, is ranked first [28]. As noted above, an optimization strategy has been shown to maximize the number of potential transplants while minimizing HLA disparity in simulated models [26]. They can also guarantee that no better set of matches could have been found [2].

Other Registries have chosen to match more frequently; in some cases, as soon as a match is identified. While the promise of an early match is attractive to patients and their physicians, these strategies are more likely to exclude those that are harder to match.

One other matching strategy is called Dynamic Optimization [29, 30]. It permits some hard to match patients to match right away, but others, even if there is someone they could match to immediately, wait to match until after more people arrive. It would allow people to still get the benefits of optimization without making every single patient wait for an accumulation of pairs. While this technology has promise, an implementable plan has not been provided, nor has it been tested it on real or realistic simulated patient data.

Cost Effectiveness

KPD is less expensive than dialysis or desensitization. It has been estimated that the United States health care system could save as much as $750 million if only 7 % of patients awaiting kidney transplantation in the United States participated in an optimized national KPD programme [26].

Outcomes

Patient and graft outcomes for pairs participating in KPD programmes have been found to be comparable to other living donor transplants. Data from UNOS show that at 5 years, both patient and graft survival are similar for KPD and matched directed live donor transplants [31]. Similarly, the Dutch national programme reported equitable 5-year graft survival for KPD recipients and directed living donation [32••]. Below is a description of published activity from individual programmes.

South Korea

In South Korea, a KPD programme has been in existence as early as 1991. The outcomes of a multi-centre closed domino paired exchange were reported in 2009. 16 centres participated and between 2001 and 2007; 179 transplants were performed with 70 domino chains initiated by NDD. The mean age of NDD was 43.7±8.8 (range, 37–50 years), with many (28 %) in a religious profession [33]. In addition, there were 45 two-pair chains, 15 three-pair chains, 7 four-pair chains, 2 five-pair chains and 1 six-pair chain. The median wait time between enrollment and transplantation was 13 months. One-year and 5-year graft survival rates were 98.3 % and 87.7 %, respectively, with a median follow-up of 46 months [33].

Dutch National Programme

The Dutch national paired donation programme was established in 2004, and recently reported its 5-year outcome data. The Dutch Transplant Foundation is responsible for allocation, while cross-matching is centrally performed at the National Reference Laboratory for Histocompatibility. Patients' sera are screened for HLA alloantibodies against HLA -A, -B, -C, -DR, and -DQ, but not against -DP [28]. The 472 enrolled pairs consisted of 269 ABO blood type incompatible pairs (83 transplanted) and 203 positive cross-match pairs (104 transplanted).

Most of the transplanted recipients (119/187, 64 %) had an age difference of less than 5 years with their original incompatible donors. The age differences with their actual donors varied widely, but the number of recipients with a donor> 5 years older was comparable to the number of recipients with a donor>5 years younger. The 5-year patient survival was 85 % and graft survival censored for death was 89 %. No differences were found between the original donor-recipient ABO incompatible and positive cross-match groups [32••].

UK National Programme

The KPD programme in the UK has been operating since 2006. The National Health Service Blood and Transplant (NHSBT) organization, responsible for managing and coordinating transplant activity in the UK, published their early results in 2008. Their matching algorithm used a points-based system based on geographical proximity between pairs,

calculated human leukocyte antigen antibody reaction frequency (cRF), HLA mismatch of potential transplant, and donor–donor age difference. All blood group compatible exchanges in the programme were considered, with the exception that blood group O donor kidneys were only used in group O recipients. Initially, all potential two-way exchanges were identified, with three way exchanges considered after the first year [34]. The KPD programme in the UK has yet to perform its first domino transplant.

120 patients were registered in the KPD scheme. Matching runs were done every 3 months. Of these, only eight transplants were performed between April 2007 and July 2008. The reasons for the lower than expected transplant rate were the ABO blood group disparity (there were more blood group A donors and not many group A or AB recipients, and the degree of cRF among HLA incompatible pairs was high), the high degree of sensitization (46 %of the patients had a calculated panel reactive antibody of>85 %), and sensitized patients even among the ABOi pairs. They also found that individual centres were pursing desensitization therapy separate from the KPD programme for enrolled patients from their respective centres [34]. This is in contrast to the Dutch and South Korean models, where blood group identical exchanges are prioritized in order to maximize transplant rates for patients with blood group O [20, 35]; an exception to this rule was in place for highly sensitized non O recipients, who may otherwise not find a cross-match negative donor.

United States

Most countries have opted to establish national registries that optimize the number of pairs and matches. In the United States, there are a number of independent registries plus a national one administered by UNOS. Those in favour of multiple registries believe the potential advantage is the benefit of competition leading to innovation. Recent data from the United States has suggested that KPD has been underutilized [2]. Factors contributing to underutilization include insurance costs, travel (less relevant now when most kidneys are shipped), reimbursement to donor when there are different insurance providers, and fragmented registries. However, it is likely true that KPD is not optimally utilized in most countries.

Segev et al. analysed data submitted to UNOS by transplant centres between 1 January 2000 and 27 August 2007. Two hundred and nine patients underwent transplantation through KPD and 89 patients were transplanted through list exchange. Of these, details of 186 KPD and 70 LE recipients were available for analysis. No differences in survival (patient and death censored graft survival) were found when compared to matched controls in live directed donations performed during the same time period [31].

The KPD programme at Methodist Specialty and Transplant Hospital, San Antonio, is an example of a successful single centre programme. The programme was initiated in 2008. In a recent report, a total of 134 KPD transplants had been performed, including 117 incompatible pairs and 17 compatible pairs. Of the KPD transplants, 36 % were two-way exchanges, 36 % were three-way exchanges and 28 % were domino transplants. NDD initiated three transplant chains; two resulted in bridge donors and one ended in a closed domino chain where a highly sensitized patient at the top of the DDWL received a transplant. Among the incompatible pairs, five highly sensitized recipients underwent desensitization prior to transplantation. The median time from listing in the KPD database to transplantation was 4.5 months (range, 1–18). Of the transplanted patients, 63 % had cross-match incompatibility with their original donors while 37 % had blood-type incompatibility [36].

Canada

A living donor exchange programme was launched by Canadian Blood Services in 2009. As of September 2013, there were 468 pairs registered and 218 transplants completed. The allocation points system has achieved steady state in terms of the distribution of the registered donor pool with “O” donors making up 61 %. Sensitized patients with cPRA<97 % have had a 50 % chance of a match within the programme. Sixty percent of registered recipients with a cPRA between 80 and 96 % have been transplanted. Key elements of the programme are: 1) Standardization of HLA laboratory practice across all participating programmes; 2) Standardized work-up and acceptance criteria for living donors; 3) Allocation optimization using a centralized software system with modelling capabilities to support evolution of the programme; 4) An advisory committee of transplant professionals from participating programmes to address in real-time logistical and medical issues; 5) Dedicated central support staff to rapidly implement change and coordinate exchanges between programmes; and 6) Annual review of the allocation system to ensure equitable access to transplantation.

Barriers and Limitations

Legal Barriers

Legal barriers could potentially prevent some countries from starting a KPD programme because of concerns about exchange of valuable commodities. However, in consultation with lawmakers, changes to enable living donor exchange have been made. For example, previously, in the UK, donors had to be genetically or emotionally related to be able to donate. However, these concerns were overcome, allowing both paired and NDD donation as of 2006 [34]. In the United States, the National Organ Transplantation Act (NOTA) of 1984 states that it is illegal to transfer a human organ for “valuable consideration.” It is questionable whether a KPD

would amount to valuable consideration. For this reason, a national registry was not established until Congress passed legislation in 2007 exempting KPD from NOTA [2].

Donor Reneging

Donor reneging was one of the first potential concerns in KPD. As a consequence, most programmes started by doing surgeries simultaneously. However, with time, and because of the complexities of surgeries at multiple sites and time zones, most groups no longer insist on this. One way of overcoming this problem in closed chains initiated by a NDD is to get each donor to donate before their recipient receives a kidney. Others feel that this could lead to a recipient losing their donor should the subsequent transplant fall through, e.g., because of a donor problem. These groups feel that the recipient of a pair should receive a kidney before their donor gives one. Regardless of what plan is chosen, the issues need to be addressed and donors and recipients need informed consent regarding the procedure in the event transplants do not proceed as planned. Donor reneging is of greatest concern in NEAD chains because the donor is waiting for an uncertain, possibly prolonged period. Reneging could also be due to a change in the medical condition of the donor, personal circumstances, change in employment or relocation [17•, 37]. Another strategy is to have the donor wait a maximum period of time to initiate the next chain and if no match occurs, to have him/her donate to the deceased donor list.

Transporting Kidneys

In smaller countries such as The Netherlands and South Korea, it may be easier to operate a national matching scheme. In countries like the US, geographic barriers have to be overcome for such a programme to be successful. Travel may lead to financial and personal burden on the pair and the donor or recipient may be separated from their support during and after the exchange. Donor follow-up by the surgeon doing the procedure also becomes difficult if the donor has travelled. Recent experience suggests that living donor kidneys can withstand longer cold ischemia, and hence donor kidneys may be shipped. In the United States, currently participating centres are generally responsible for packaging and transporting donor kidneys to recipient centres, unlike for deceased donor transplants, where organ procurement organizations (OPO) are responsible for this. Whether OPOs should also take up the responsibility of coordinating the shipping of organs involved in KPD is a matter of debate [38].

Recent studies have shown that it is possible to transport donor kidneys by air without any difference in short-term graft outcomes [39]. A proof of concept was demonstrated by Montgomery et al. in 2007, in a three-way KPD between Johns Hopkins Hospital (JHH) in Baltimore, MD, and California Pacific Medical Center (CPMC) in San Francisco, CA. All kidneys were functioning well at 1 year [40]. Segev and colleagues have now reported the outcome of 56 transplants where kidneys were transported among 30 transplant centres as part of KPD programmes in the United States and Canada. Distance travelled ranged from less than 1 mile to 2,570 miles, cold ischemia ranged from 2.5 to 14.5 h. No patient experienced delayed graft function (defined by the requirement for dialysis within 1 week of transplant). Creatinine nadir was<2.0 mg/dL in all but one patient [41••]. The potential risk of transportation by commercial jetliners would be delay or loss in transit, though there have been no reports of loss [42]. Thus, transportation should form a part of the informed consent prior to transplant and strategies for packaging and tracking should be in place.

Financial Barriers

In the United States, where donor and recipient pairs may have different insurance providers, reimbursement of transplant-related expenses can be a hurdle. Financial barriers need to be addressed for KPD to reach its potential. For deceased donor transplantation, a standard acquisition charge (SAC) exists, which is calculated on the previous year's total cost to the OPO in recovering deceased donor kidneys divided by the total number of deceased donor kidneys that are transplanted. A proposal has been suggested for such a SAC to cover KPD related expenses. Currently, transplant centres, Medicare and insurance companies are reluctant to pay some of the costs associated with KPD, such as donor travel costs, shipment of living donor kidneys to the recipient centre, costs related to incompatible living donor or NDD workup when a guarantee does not exist that the donor will donate to one of their covered beneficiaries [43].

Representatives from three major commercial payers have similarly made calls for standardization of costs related to evaluation and management of potential donors in KPD. They suggest this can best be done by a SAC model. Further, these commercial payers have also proposed that all costs between donor and recipient centres be channelled thorough OPSs [44].

Conclusion

In conclusion, KPD is an important strategy for increasing access to transplantation. Many countries have yet to establish KPD programmes, and in countries where they exist, they may be underutilized. As expected, outcomes from KPD are comparable to directed living donation. Legal issues have been resolved and shipping kidneys has addressed some of the practical difficulties. National and international collaboration is encouraged for sharing best practice and innovative strategies in order to increase the number of patients who benefit.

Acknowledgments The authors thank Canadian Blood Services for use of their image as Fig. 1.

Compliance with Ethics Guidelines

Conflict of Interest Shafi Malik declares that he has no conflict of interest.

Edward Cole is the chair of the Canadian Blood Services National Kidney Registry Steering Committee; this is a volunteer position.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Scientific OPaTNOa, 2011 RoTRSOS, Annual Data Report. Rockville MDoHaH, Services HRaSA, Healthcare, Systems Bureau DoT. 201.
2. Gentry SE, Montgomery RA, Segev DL. Kidney paired donation: fundamentals, limitations, and expansions. Am J Kidney Dis. 2011;57(1):144–51.
3.•• Montgomery JR, Berger JC, Warren DS, James NT, Montgomery RA, Segev DL. Outcomes of ABO-incompatible kidney transplantation in the United States. Transplantation. 2012;93(6):603–9. *Comprehensive study using SRTR data set*; *738 ABOi patients were included in the analysis and results indicated that long-term patient survival was similar to matched ABO compatible transplants*.
4.• Montgomery RA, Lonze BE, King KE, Kraus ES, Kucirka LM, Locke JE, et al. Desensitization in HLA-incompatible kidney recipients and survival. N Engl J Med. 2011;365(4):318–26. *Single center study reporting outcomes of desensitization using plasmapharesis and low dose intravenous immune globulin*.
5. Gloor J, Stegall MD. Sensitized renal transplant recipients: current protocols and future directions. Nat Rev Nephrol. 2010;6(5):297–306.
6. Rapaport FT. The case for a living emotionally related international kidney donor exchange registry. Transplant Proc. 1986;18(3 Suppl 2):5–9.
7. Ross LF, Rubin DT, Siegler M, Josephson MA, Thistlethwaite Jr JR, Woodle ES. Ethics of a paired-kidney-exchange program. N Engl J Med. 1997;336(24):1752–5.
8. Park K. Emotionally related donation and donor swapping. Transplant Proc. 1998;30(7):3117.
9. Kwak JY, Kwon OJ, Lee KS, Kang CM, Park HY, Kim JH. Exchange-donor program in renal transplantation: a single-center experience. Transplant Proc. 1999;31(1–2):344–5.
10. Thiel G, Vogelbach P, Gurke L, Gasser T, Lehmann K, Voegele T, et al. Crossover renal transplantation: hurdles to be cleared! Transplant Proc. 2001;33(1–2):811–6.
11. Zarsadias PMA, Morrissey PE. A pioneering paired kidney exchange. Student BMJ 2010(c):1562.
12. Kidney Link : Paired Donation Networks. Available from: http://www.kidneylink.org/PairedDonationPrograms.aspx.
13. de Klerk M, Keizer KM, Claas FH, Witvliet M, Haase-Kromwijk BJ, Weimar W. The Dutch national living donor kidney exchange program. Am J Transplant. 2005;5(9):2302–5.
14. Rees MA, Kopke JE, Pelletier RP, Segev DL, Rutter ME, Fabrega AJ, et al. A nonsimultaneous, extended, altruistic-donor chain. N Engl J Med. 2009;360(11):1096–101.
15. Transplant Pro : Kidney Paired Donation. Available from: http://transplantpro.org/kidney-paired-donation/page/2/.
16. McLellan F. US surgeons do first "triple-swap" kidney transplantation. Lancet. 2003;362(9382):456.
17.• Melcher ML, Veale JL, Javaid B, Leeser DB, Davis CL, Hil G, et al. Kidney transplant chains amplify benefit of nondirected donors. JAMA Surg. 2013;148(2):165–9. *Demonstrated that NDD can amplify transplant chains. On average*, *NDDs triggered five transplants*, *blood type O NDD triggered a mean chain length of 6.0s*.
18. Delmonico FL, Morrissey PE, Lipkowitz GS, Stoff JS, Himmelfarb J, Harmon W, et al. Donor kidney exchanges. Am J Transplant. 2004;4(10):1628–34.
19. Gentry SE, Segev DL, Simmerling M, Montgomery RA. Expanding kidney paired donation through participation by compatible pairs. Am J Transplant. 2007;7(10):2361–70.
20. de Klerk M, Witvliet MD, Haase-Kromwijk BJ, Claas FH, Weimar W. Hurdles, barriers, and successes of a national living donor kidney exchange program. Transplantation. 2008;86(12):1749–53.
21. Segev DL, Gentry SE, Melancon JK, Montgomery RA. Characterization of waiting times in a simulation of kidney paired donation. Am J Transplant. 2005;5(10):2448–55.
22.• Ratner LE, Rana A, Ratner ER, Ernst V, Kelly J, Kornfeld D, et al. The altruistic unbalanced paired kidney exchange: proof of concept and survey of potential donor and recipient attitudes. Transplantation. 2010;89(1):15–22. *This was a proof of concept survey studying the underlying attitudes of compatible donor recipient pairs that may take part in KPD*.
23. Montgomery RA. Renal Transplantation Across HLA and ABO Antibody Barriers: Integrating Paired Donation into Desensitization Protocols. Am J Transplant. 2010;10(3):449–57.
24. Chen Y, Li Y, Kalbfleisch JD, Zhou Y, Leichtman A, Song PX. Graph-based optimization algorithm and software on kidney exchanges. IEEE Trans Biomed Eng. 2012;59(7):1985–91.
25. Devi SP, Kumar SS, Rao KS. Evaluation of kidney transplantation programmes using system simulation. J Med Syst. 2012;36(3):1117–31.
26. Segev DL, Gentry SE, Warren DS, Reeb B, Montgomery RA. Kidney paired donation and optimizing the use of live donor organs. JAMA. 2005;293(15):1883–90.
27. Ferrari P, Fidler S, Wright J, Woodroffe C, Slater P, Van Althuis-Jones A, et al. Virtual crossmatch approach to maximize matching in paired kidney donation. Am J Transplant. 2011;11(2):272–8.
28. Keizer KM, de Klerk M, Haase-Kromwijk BJJM, Weimar W. The Dutch algorithm for allocation in living donor kidney exchange. Transplant Proc. 2005;37(2):589–91.
29. Dickerson JPA, Sandholm T. Dynamic Matching via Weighted Myopia with Application to Kidney Exchange. North America: AAAI Conference on Artificial Intelligence; 2012.
30. John P. Dickerson ADP, Tuomas Sandholm editor Optimizing kidney exchange with transplant chains: theory and reality. Proceedings of the 11th International Conference on Autonomous Agents and Multiagent Systems; AAMAS '12.
31. Segev DL, Kucirka LM, Gentry SE, Montgomery RA. Utilization and outcomes of kidney paired donation in the United States. Transplantation. 2008;86(4):502–10.
32.•• de Klerk M, Kal-van Gestel JA, Haase-Kromwijk BJ, Claas FH, Weimar W. Eight years of outcomes of the Dutch Living Donor Kidney Exchange Program. Clin Transpl. 2011:287–90. *Dutch KPD programme is a succesful model; in this paper, they present 5 year outcome data.*
33. Lee YJ, Lee SU, Chung SY, Cho BH, Kwak JY, Kang CM, et al. Clinical outcomes of multicenter domino kidney paired donation. Am J Transplant. 2009;9(10):2424–8.

34. Johnson RJ, Allen JE, Fuggle SV, Bradley JA, Rudge C. Early experience of paired living kidney donation in the United kingdom. Transplantation. 2008;86(12):1672–7.
35. Kim BS, Kim YS, Kim SI, Kim MS, Lee HY, Kim YL, et al. Outcome of multipair donor kidney exchange by a web-based algorithm. J Am Soc Nephrol. 2007;18(3):1000–6.
36. Bingaman AW, Wright Jr FH, Kapturczak M, Shen L, Vick S, Murphey CL. Single-center kidney paired donation: the Methodist San Antonio experience. Am J Transplant. 2012;12(8):2125–32.
37. Melcher ML, Leeser DB, Gritsch HA, Milner J, Kapur S, Busque S, et al. Chain Transplantation: Initial Experience of a Large Multicenter Program. Am J Transplant. 2012;12(9):2429–36.
38. Mast DA, Vaughan W, Busque S, Veale JL, Roberts JP, Straube BM, et al. Managing finances of shipping living donor kidneys for donor exchanges. Am J Transplant. 2011;11(9):1810–4.
39. Simpkins CE, Montgomery RA, Hawxby AM, Locke JE, Gentry SE, Warren DS, et al. Cold ischemia time and allograft outcomes in live donor renal transplantation: is live donor organ transport feasible? Am J Transplant. 2007;7(1):99–107.
40. Montgomery RA, Katznelson S, Bry WI, Zachary AA, Houp J, Hiller JM, et al. Successful three-way kidney paired donation with cross-country live donor allograft transport. Am J Transplant. 2008;8(10):2163–8.
41.•• Segev DL, Veale JL, Berger JC, Hiller JM, Hanto RL, Leeser DB, et al. Transporting live donor kidneys for kidney paired donation: initial national results. Am J Transplant. 2011;11(2):356–60. *First study reporting national results of transporting live donor kidneys for KPD. No patients experienced delayed graft function*.
42. Blumberg JM, Gritsch H, Veale JL. Kidney paired donation: advancements and future directions. Curr Opin Organ Transplant. 2011;16(4):380–4.
43. Rees MA, Schnitzler MA, Zavala EY, Cutler JA, Roth AE, Irwin FD, et al. Call to develop a standard acquisition charge model for kidney paired donation. Am J Transplant. 2012;12(6):1392–7.
44. Irwin FD, Bonagura AF, Crawford SW, Foote M. Kidney paired donation: a payer perspective. Am J Transplant. 2012;12(6):1388–91.