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Utilization of Deceased Donor Kidneys to Initiate Living Donor Chains

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Abstract

We propose that some deceased donor kidneys be allocated to initiate non-simultaneous extended altruistic donor chains of living donor kidney transplants to address in part the huge disparity between patients on the deceased donor kidney waitlist and available donors. The use of deceased donor kidneys for this purpose would benefit waitlisted candidates in that most patients enrolled in kidney paired donation systems are also waitlisted for a deceased donor kidney transplant and receiving a kidney through the mechanism of kidney paired donation will decrease pressure on the deceased donor pool. In addition, a living donor kidney usually provides survival potential equal or superior to that of deceased donor kidneys. If kidney paired donation chains that are initiated by a deceased donor can end in a donation of a living donor kidney to a candidate on the deceased donor waitlist, the quality of the kidney allocated to waitlisted patient is likely to be improved. We hypothesize that a pilot program would show a positive impact on patients of all ethnicities and blood types.

Introduction

Kidney paired donation (KPD) has been an important step in improving access to LD transplantation. In KPD, pairs of potential live kidney donors and their intended original recipients are matched with other pairs in similar circumstances to find combinations of transplants that allow the donors to fulfill their intention to donate, and their original intended recipients to receive transplants from a different compatible living donor (1). Non-

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simultaneous extended altruistic donor (NEAD) chains of kidney transplants, initiated by a non-directed living donor (NDLD), enabled further expansion of this practice, because the availability of the NDLD's kidney without a designated recipient increases the number of potential matches (2, 3). Donor and recipient chains, assembled by computer algorithms lead to a remarkable number of kidney transplants and improve opportunities for difficult to match candidates and ethnic minorities (2, 4). Patients on the deceased donor (DD) kidney waiting list (waitlist) also benefit since the chains are typically terminated by the last LD's kidney being transplanted into a candidate on the DD waitlist who does not have a LD (4, 5). Further, as most candidates participating in KPD are also listed on the DD waitlist, each LD kidney transplant that is performed through the mechanism of kidney paired donation (KPD) reduces the competition for kidneys among the remaining waitlisted candidates (4). In large KPD registries, the mean number of transplantations achieved per chain is between 4 and 5 (3, 6).

Proposal

Currently, the number of KPD chains is limited by the number of chain initiating kidneys (CIKs) from NDLDs. To increase the number of chains and thus the number of kidney transplants performed, we propose that CIKs also be obtained from the pool of DD kidneys, recognizing that almost every DD kidney, like NDLD kidneys, is non-directed. These chains could be ended by giving a LD kidney to someone on the deceased donor waiting list who does not have a potential LD and resides within the same OPO as the DD CIK once no additional KPD transplants are possible. This strategy has been proposed before; however, it has never been implemented (7).

This proposal is significantly different than list exchange because in list exchange the incompatible living donor first donates a kidney to the top patient on a deceased donor match run and subsequently a deceased donor kidney is allocated to that living donor's intended recipient who is given priority for subsequent deceased donor match runs. No trust is required, because the deceased donor pool is guaranteed to return a kidney so long as the intended, incompatible recipient remains healthy enough to receive a transplant and sensitization status does not preclude donor availability. In contrast, in our proposal, a deceased donor kidney would be allocated first to a patient in a KPD pool with a willing, but incompatible living donor who will be trusted subsequently, as in a NEAD chain, to donate a kidney to either another patient in a KPD pool or to a patient on the deceased donor waiting list.

While each DD kidney conventionally results in the transplantation of a single patient from the DD waitlist, we postulate that DD CIK-initiated chains would result in the transplantation of a minimum of two candidates for each DD CIK—assuming no reneging—and benefit those on the deceased donor kidney transplant wait list in several ways: 1) Candidates receive live donor kidney transplants reducing competition for deceased donor kidneys, 2) candidates are transplanted sooner, and 3) since the final living donor in a domino chain donates back to a patient on the DD waitlist and kidneys from LD, in general, have longer survival potential than do kidneys from DD, the quality of the organs available to waitlisted candidates may be improved (8, 9).

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The current kidney allocation system offers transplants in this order: highly sensitized, zero HLA mismatch, prior living donor, local pediatric candidates, and local adult candidates. The priority for DD-CIK could be assigned between any of these levels, but, if assigned between local pediatric candidates and local adults, it would not disrupt previously recognized priorities. Decisions would need to be made regarding whether or not to impose restrictions on the quality or number of DD kidneys that might be used as CIKs. It is important to recognize, that should DD CIK be given allocation priority in the same manner that is currently accepted for other priorities ahead of the local adult candidate level, then the kidney is allocated to someone from a KPD pool and there is no allocation of that organ to a mismatched adult on the deceased donor wait list at the local level. This means that while the deceased donor kidney does not go to the pool of waitlisted candidates of that particular blood type, it has not been "taken" from a specific candidate. In addition, decisions would need to be made regarding whether or not to impose restrictions on the quality or number of DD kidneys that might be used as CIKs.

Perhaps the biggest ethical concern about using DD kidneys as CIKs is that despite increasing the overall number of transplants, the strategy might appear unfair to candidates, especially blood type O candidates, who don't have a potential LD. This concern is exacerbated by the prediction and observation that KPD registries tend to have a greater number of ABO-incompatible pairs with blood type O-candidates than with candidates of the other blood types (1, 3). As "universal donors," blood type O-donors generally can be matched to a greater number of candidates and have greater matching potential than other blood type donors. Therefore, blood type O-patients with a long waiting time on the DD waitlist are most vulnerable to being disadvantaged since they generally can only be transplanted utilizing blood type O-donors who are most in demand (10). Fortunately, blood type O NDDs have been shown to release twice as many other O-donors partnered with sensitized recipients, thus reducing the competition for blood type O-grafts among waitlisted patients (4).

There is a perceived conflict between the individual benefit for the patient without a living donor versus the collective benefit of multiple transplants being performed through a chain. However, the current DD kidney allocation system (KAS) prioritizes patients on match runs based on a set of rules including those about zero HLA mismatches (0-MM) kidneys, highly sensitized patients, and multivisceral transplants (11). For example, a blood type O-DD kidney can be allocated to a non-blood type O-patient with zero HLA mismatches (0-MM) because the years of graft survival gained by a 0-MM transplantation are considered to outweigh the disadvantage of not transplanting a blood type O-patient at the top of the DD waitlist. In point of fact, the current system, sometimes prioritizes the use of a blood type O, 0-MM organ into a non-blood type O, highly sensitized recipient above all other kidney alone candidates (11).

Even though the DD waitlist candidates without potential living donors may not be transplanted within a chain, a chain results in the transplantation of recipients who otherwise would have remained on the DD waitlist. Further, most chains end with the transplantation of a waitlisted candidate who may not have an incompatible potential living donor (4, 5). Transplantation of these recipients thus benefits those remaining on the DD waitlist whose

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relative waiting time is reduced. In addition, the return of a chain-ending LD kidney to a candidate on the DD waitlist, benefits all those DD waitlist candidates of the same blood type. In sum, initiating a chain with the DD kidney results in large benefit associated with more transplantations that remove more candidates from the DD waitlist, thus reducing competition for other kidneys.

Rules for the use of DD CIK could be formulated to promote balance between the blood types of kidneys used for DD CIK and the blood types of kidneys returned to the DD pool. For example, a blood type O CIK could be given to a blood type O KPD candidate whose blood type A donor LD's kidney could be used for a highly sensitized blood type A candidate, whose blood type O HLA incompatible LD could then terminate the KPD chain by donating to the blood type O DD waitlist instead of to another possible KPD candidate with a non-blood type O donor. Rules for when a chain would be terminated to allow a living donor kidney to be given to the list could be modeled using the Scientific Registry of Transplant Recipients' Kidney-Pancreas Simulated Allocation Model(KPSAM) to estimate the benefit of ending chains with donors of specific blood types (12).

A comparison of the expected outcomes of DD and LD kidneys to establish relative value would be straightforward to calculate, and as LD kidneys are generally accepted to have longer survival potential than most DD kidneys, all other factors being similar (8), we suggest that, if multiple DD waitlist candidates receive LD's kidneys rather than waiting for a DD kidney, there would be more post-transplant benefit to candidates on the DD waitlist. The newly implemented OPTN DD KAS uses a scoring system, the Kidney Donor Profile Index (KDPI), based on donor characteristics to estimate the expected longevity of DD kidneys. A similar profile for assessing the relative quality of LD and DD kidneys has already been proposed.(9) A KDPI that includes both DD and LD kidneys could be incorporated into the existing Kidney Allocation Score without additional changes to the allocation system. This would enable patients and transplant centers to weigh the benefit of accepting a specific living donor versus continuing to wait for a different living or deceased donor offer.

If DD were to be used as CIK, consideration would need to be given to competing prioritizations such as transplanting a DD waitlist recipient with a long expected post-transplant survival, transplanting a very highly sensitized DD candidate who may wait years before their next offer, or using the DD kidney to initiate a chain providing multiple LD transplants with overall greater cumulative EPTS. Allocation policy would need to weigh the life years provided by multiple transplants arising from chains with the benefit to candidates on the DD waitlist and the probability of DD waitlist candidates receiving a similar quality kidney in the future.

There are several logistical complexities of this proposal (Table 1). Prospective chains frequently unravel because later transplants in a chain are dependent on the initial transplants going forward. Robust methods would need to be developed to insure that donors and recipients are prepared for transplant and that disruptions in the chains can be rapidly repaired. Patients would need to be thoroughly informed about the risks of KPD (13) and those specific to this modification. For example, the first pair within a chain will received a

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DD kidney while donating a LD kidney to the next pair. The logistics of organ transport are less of an issue as it has been demonstrated that LD and 0-MM DD kidneys, shared nationally with longer cold times, function well (14, 15).

Using DD kidneys to initiate donor chains may help to maximize KPD, but ultimately the potential for growth will be limited by the number of individuals who are willing to be live kidney donors and by living donor pairs listed in the registries. Therefore, the benefit of this proposed policy is limited by the greater need to increase living organ donation in a safe and ethical manner. Therefore, work done by participants of the 2014 Living Donor Conference to share best practices, develop educational materials, and reduce barriers to donation remains extremely important.(16)

Allocation of DD kidneys as CIKs should be managed through consistent policies. Clearly, defined protocols are needed to insure that potential living donors and their intended recipients are informed about the complexities of chain donations. Nationalization of KPD may facilitate full implementation of this proposal; however, providing variances for one or more of the current registries to implement this proposal may enable an informative trial period from which we could better understand its impact.

Conclusions

The allocation of DD kidneys to initiate NEAD chains has the potential to increase the number of candidates removed from the DD waitlist by producing additional kidney transplants utilizing living kidney donors who are incompatible with their intended recipient. This would reduce the DD kidney waiting list and improve the quality of the pool of kidneys available. The development of a DD CIK allocation system will require the development of additional tools to assess the relative benefits of deceased and living kidney donation. The use of DD as CIKs can be evaluated through modeling and potentially through the use of pilot studies.

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Abbreviations

CIK	Chain Initiating Kidney
DD	Deceased Donor
KAS	Kidney allocation System
KPD	Kidney Paired Donation
NEAD	Non-simultaneous Extended Altruistic Donor
NDLD	Non-directed Living Donor
OPTN	Organ Procurement and Transplantation Network

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Table 1

Challenges Prior to and after Implementation

Anticipated Challenges	**Potential Solutions**
To develop appropriate DD-CIK allocation strategies	Priority for DD-CIK could be assigned between local pediatric candidates and local mismatched adults
To develop appropriate living donor allocation strategies	Living donor kidneys resulting from DD CIK chains should be allocated to the waiting list according to the existing deceased donor allocation protocol.
To resolve logistical barriers to allocation given the existence of multiple KPD Registries	Provides variances for one or more of the current registries to implement this strategy.
To prepare strategies to handle chains that unravel	Could be modeled after strategies developed by existing registries such as using CIKs to repair ongoing chains (3), or a KPD registry could be asked to end the next chain to the DD list.
To allocate and use living donor kidneys in a timely manner	Participating patients and donors must be completely prepared for surgery and fully informed of the additional risks associated with chains such as the potential for them to unravel.
To assess added benefit to the entire waiting list of using a kidney as DD CIK	One year after implementation of a trial the number and characteristics of the patients transplanted and their donors should be reviewed. The quality of the grafts could be compared using a living donor risk index analogous to the current deceased donor kidney risk index.
The limited number of participants in KPD registries and limited number of willing and healthy living donors.	Push forward adoption of best practices for both KPD and living donation as advocated by national consensus conferences in 2012 (13) and 2014 respectively. (16)